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Almost 30 years since it was first reported in 1983, the HIV epidemic remains a serious public health issue globally, and particularly in countries of the WHO South-East Asia Region (SEAR). The overwhelming global efforts to combat HIV/AIDS over the past 10 years have led to fewer HIV epidemics. New infections have declined by over 25% in 29 countries worldwide, including four of the five high HIV burden countries in SEAR (India, Myanmar, Nepal and Thailand but not Indonesia) since the epidemic peaked in 2001.1

More importantly, the survival of people living with HIV (PLHIV) and their ability to enjoy productive lives have improved significantly over the past decade due to the scaled-up provision of life-saving antiretroviral therapy (ART). Moreover, ART is not only a priority life-saving intervention; but it can also reduce the incidence of tuberculosis (TB) by up to 90%.1

HIV is the strongest risk factor for developing active TB disease and PLHIV are 20 to 30 times more likely to develop active TB than HIV negative people.2 In some countries up to 82% of people with TB have HIV.1 TB is a major killer among PLHIV and accounts for more than 25% deaths among this group worldwide.2 In 2011, 430 000 out of 1.7 million AIDS-related deaths (25%) were caused by HIV-associated TB disease.3 The world had reached the Millennium Development Goal (MDG) targets of halting and reversing the TB epidemic in many high prevalent states,3 but HIV–TB coinfection is a challenge to reduce the global target of 50% deaths due to TB by 2015. The target is linked to MDG and endorsed by the stop TB partnership/UNAIDS in 2006 and recommitted by the Member States at the United Nations high level meeting on AIDS in 2011.1-3 While the HIV and TB epidemics are declining in almost all high-burden countries, HIV-related TB continues to remain a serious challenge for the health sector response by national governments and threatens the survival of PLHIV.1,3

Of the estimated 34 million people living with HIV globally, about one third are thought to have concomitant latent TB. In 2011, of the over 8.7 million incident TB cases worldwide, 1 million were among PLHIV. The WHO South-East Asia Region accounts for nearly 15% of the global burden of new HIV/TB infections. Five countries of the Region are among the 22 highest TB burden countries in the world (Bangladesh, India, Indonesia, Myanmar and Thailand). Among these, four countries (India, Indonesia, Myanmar and Thailand) have a high burden of TB and HIV. While Nepal is not among the countries with the highest TB

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burden, the number of PLHIV is high\textsuperscript{1,3} which poses a potential threat of HIV–TB coinfections in the country.

In 2011, nearly 5 million people were living with TB in SEAR, and approximately 140,000 of the estimated 3.5 million people who newly developed TB were HIV-positive.\textsuperscript{3}

Collaborative TB–HIV activities between national TB and HIV programmes are vital to prevent, diagnose and treat TB among PLHIV, and HIV among individuals with TB, to achieve the goal of reducing TB-related deaths. World Health Organization (WHO) has provided clear policy recommendations on interventions needed to achieve this collectively known as collaborative TB–HIV activities.\textsuperscript{4,5} These include: (i) establishing mechanisms for collaboration between HIV and TB programmes (joint planning, coordinating bodies, surveillance, and monitoring and evaluation); (ii) reducing the HIV burden among TB patients through HIV testing and counselling, provision of ART and co-trimoxazole preventive therapy (CPT) to TB patients living with HIV, and HIV prevention, care and support services for TB patients and (iii) reducing the burden of TB among PLHIV with the Three I’s for HIV/TB: – intensified TB case-finding; isoniazid preventive therapy; and infection control in health-care and congregate settings.\textsuperscript{3–5} The progress made towards achieving these goals in countries of the Region has been variable.\textsuperscript{1,3}

Highly active antiretroviral therapy (HAART) is recognized as a great achievement in public health as it has not only prevented deaths among PLHIV, but has also reduced common opportunistic infections, especially \textit{Mycobacterium tuberculosis}, in people living with HIV.\textsuperscript{6} For ART to have the maximum benefit, it is important to detect people living with TB–HIV co-infection early National TB programmes should provide HIV testing and counselling to anyone presenting with signs and symptoms of TB and people with confirmed TB. ART also must be made available for all PLHIV who have active TB irrespective of their immune status or CD4 cell count. Simultaneously, HIV programmes should refer PLHIV attending treatment and care facilities for early TB assessment, so that active TB can be detected early and treatment initiated without delay.

While the number of TB patients identified as HIV-positive and enrolled on ART has grown steadily in the Region as well as globally,\textsuperscript{3} necessary testing systems appear to be still inadequate In 2011 worldwide 40% of TB patients had a documented HIV test result while on average only 32% of TB patients knew their HIV status in SEAR.\textsuperscript{3} This means that two out of three TB patients were not aware of their HIV status in the Region. Lowest HIV testing rates were recorded in Myanmar and Indonesia while India and Thailand recorded high rates.\textsuperscript{3} Perhaps, stigma associated with HIV prevents people with TB from attending HIV care services for an HIV test, and clinicians in TB clinics appear to be still reluctant to offer HIV testing (known as provider-initiated counselling and testing) to patients under their care.\textsuperscript{1,3} About 59% of the TB patients diagnosed with TB–HIV co-infection were provided with lifesaving ART in SEAR compared with 48% globally though the proportion varied widely across the Region, Myanmar had the highest with 80% ART coverage and Indonesia lowest 42% among the high TB/HIV burden countries in SEAR.\textsuperscript{3} To reach the Global Plan’s target of providing ART to all TB patients known to be living with HIV by 2015 the coverage of ART for HIV-positive TB patients needs to be improved.

In 2011 about 400,000 PLHIV in the Region were assessed for TB during their last visit, of whom the largest number was in India compared to 2.3 million globally,\textsuperscript{3} India and
Myanmar have assessed and recorded the TB status of almost all HIV patients enrolled for HIV care at the last visit.\textsuperscript{1,3}

HIV-associated TB deaths can be further reduced by offering co-trimoxazole preventive therapy to TB patients living with HIV. Over 89% patients in this group in SEAR have benefitted from this measure, since many national programmes have offered CPT and intensified TB screening of PLHIV at HIV treatment and care service points.\textsuperscript{3} It is heartening to note that TB–HIV collaborative activities are progressing steadily in the Region. India and Thailand have fully integrated nationwide implementation of this collaboration, other high-burden countries like Indonesia and Myanmar, as well as low prevalence countries such as Bangladesh, Maldives and Sri Lanka have started scaling-up services. However, Nepal is yet to institute strong TB–HIV collaborative programmes.

The global target of halving TB–HIV deaths by 2015 can be realized only if services are scaled up through concerted and joint efforts of National AIDS and TB programme to detect HIV–TB coinfected people early and ensure them treatment.\textsuperscript{2}

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Janani Suraksha Yojana: the conditional cash transfer scheme to reduce maternal mortality in India – a need for reassessment

Rajesh Kumar Rai\(^a\), Prashant Kumar Singh\(^b\)

Alongside endorsing Millennium Development Goal 5 in 2000, India launched its National Population Policy in 2000 and the National Health Policy in 2002. However, these have failed thus far to reduce the maternal mortality ratio (MMR) by the targeted 5.5% per annum. Under the banner of the National Rural Health Mission, the Government of India launched a national conditional cash transfer (CCT) scheme in 2005 called Janani Suraksha Yojana (JSY), aimed to encourage women to give birth in health facilities which, in turn, should reduce maternal deaths. Poor prenatal care in general, and postnatal care in particular, could be considered the causes of the high number of maternal deaths in India (the highest in the world). Undoubtedly, institutional delivery in India has increased and MMR has reduced over time as a result of socioeconomic development coupled with advancement in health care including improved women’s education, awareness and availability of health services. However, in the light of its performance, we argue that the JSY scheme was not well enough designed to be considered as an effective pathway to reduce MMR. We propose that the service-based CCT is not the solution to avoid/reduce maternal deaths and that policy-makers and programme managers should reconsider the ‘package’ of continuum of care and maternal health services to ensure that they start from adolescence and the pre-pregnancy period, and extend to delivery, postnatal and continued maternal health care.

**Key words:** Maternal Mortality ratio, continuum of care, cash incentive.

Background

The high incidence of maternal deaths, especially in developing countries, has been of growing concern to programme managers and policy-makers. To reduce maternal deaths, global leaders promised to extend every possible effort in a series of protocols, starting from the Safe Motherhood Initiative in 1987, followed by the International Conference on Population and Development in 1994. The Millennium Development Goals (MDGs) in 2000, endorsed by leaders from 190 countries, re-emphasized the importance of improving maternal health in MDG5, and set a target of a 75% reduction in the maternal mortality ratio (MMR) from 1990 by 2015.\(^1\) India is a signatory to the MDGs and managed to reduce the MMR by 66%, that is, from an estimated 600 to 200 maternal deaths per 100 000 live births, which is an average annual decrease of 5.2% during the period 1990–2010.\(^2\) Despite this turning point, the MMR remains the highest in the world. It is evident that the JSY scheme was not well enough designed to be considered an effective pathway to reduce MMR. We propose that the service-based CCT is not the solution to avoid/reduce maternal deaths and that policy-makers and programme managers should reconsider the ‘package’ of continuum of care and maternal health services to ensure that they start from adolescence and the pre-pregnancy period, and extend to delivery, postnatal and continued maternal health care.

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point, the MMR is still incongruously high and fails to meet MDG5.

India launched its National Population Policy (NPP) in 2000 and the National Health Policy (NHP) in 2002. The NPP set ambitious goals to be achieved by 2010, including reducing the MMR to 100 per 100,000 live births. The NHP reiterated its commitment to achieving this goal and to increase institutional deliveries to 80%.³ The failure of the NPP and the NHP to reduce the MMR pointed to the need for health policies and programmes to be given a new direction, and this led to the establishment of the National Rural Health Mission (NRHM) in 2005. Under the broad ambit of NRHM, the Government of India launched a broad conditional cash transfer scheme called Janani Suraksha Yojana (JSY) in April 2005, to encourage women of low socioeconomic status to give birth in health facilities. This, in turn, was intended to help reduce the MMR.

The scheme was guided by the previous National Maternity Benefit Scheme,⁴ under which a provision was made for the payment of Rs 500 (US$ 9.41) per pregnancy to women from poor households for prenatal and postnatal maternity care up to the first two live births.⁵ In the 10 focus states (Assam, Bihar, Chhattisgarh, Jammu and Kashmir, Jharkhand, Madhya Pradesh, Orissa, Rajasthan, Uttarakhand, and Uttar Pradesh), the JSY promised cash incentives to a woman if the delivery was conducted in a government or accredited private health facility.⁴ According to JSY’s guidelines, after delivery in one of these facilities, the eligible woman would receive Rs 600 (US$ 11.30) in urban areas and Rs 700 (US$ 13.18) in rural areas.⁴ The cash incentive was higher in the 10 focus states – Rs 1000 (US$ 18.83) in urban areas and Rs 1400 (US$ 26.36) in rural areas. In the non-focus states, women were eligible for the cash benefit for their first two livebirths, and if they had a government-issued below-the-poverty-line card or were from a Scheduled (low) Caste or Tribe.⁴ Against this background, we argue that the purpose of JSY was not well designed and that it cannot be considered as an effective pathway to reduce maternal deaths. We have proposed an alternative way forward to reduce maternal mortality.

Causes of maternal mortality: where JSY stands

Among the direct causes of maternal deaths in India, haemorrhage is the leading cause (38%), followed by sepsis (11%), hypertensive disorders (5%), obstructed labour (5%), abortion (8%), and other conditions (33%).⁶ The conceptual framework of delays proposed by Thaddeus and Maine focuses on socioeconomic/cultural factors (women’s status in household and society, educational and economic status of women, etc.), access to facilities (distance, transportation, etc.) and availability of quality of care (staff and equipment in health centre) as the crucial factors behind maternal morbidity and mortality.⁷ However, this model was debated because of its oversimplification of each level of care.⁸

Haemorrhage remains one of the top three preventable obstetrics-related causes of maternal mortality worldwide, with most deaths occurring within 24–48 hours of delivery.⁹ Indeed, in 2010 the World Health Organization estimated that 77% of maternal deaths in developing countries occurred within two days of delivery.¹⁰ The latest nationally representative District Level Household and Facility Survey 2007–2008 (DLHS-3)¹¹ revealed that in India, where most maternal deaths occur due to postpartum haemorrhage (PPH),¹² around 48% of women aged 15–49 years reported receiving postnatal care within 48 hours of delivery.
due to PPH is preventable through risk factor identification, rapid diagnosis and timely management of postnatal care; therefore, poor performance in postnatal care in India remains a daunting challenge for programme managers and policy-makers.

On the other hand, as per the estimates from DLHS-3, almost 50% of women aged 15–49 years had at least three antenatal care visits; the lowest performance was 22% in Uttar Pradesh. Only 47% of women reported that they underwent institutional delivery, and only 13% of eligible women had received JSY assistance.

The experiment of introducing incentives for physicians to perform delivery to reduce maternal mortality was deemed fruitless. For instance, the Government of Gujarat (western India) launched a public-private partnership scheme called ‘Chiranjeevi Yojana’ or “plan for a long life” to bridge the gap in the availability of quality maternal health-care services for below-the-poverty-line families in rural areas by collaborating with private practitioners in small towns. The state government paid private gynaecologists Rs 1795 (US$ 33.75) per delivery – including Rs 200 (US$ 3.76) to the patient for transportation costs to the place of delivery and Rs 50 (US$ 0.94) to the person accompanying the patient to compensate for loss of wages. But, contrary to expectation, there was no appreciable progress in the overall reduction of MMR in Gujarat in 2004–2006 (160/100 000 live births) or 2007–2009 (148/100 000 live births). In contrast, the reduction was more impressive in Uttarakhand/Uttar Pradesh, and even in Bihar/Jharkhand, which are recognized as underdeveloped states.

The argument for this is that the promotion of institutional delivery through JSY is not the only way to reduce maternal deaths. According to 2010 estimates, only 19% women received full antenatal care (at least three visits for antenatal check-up, one tetanus toxoid injection and 100+ iron folate acid tablets/syrup), indicating the possibility of poor demand or provision of antenatal care. In addition, 26% of women aged 15–49 did not undergo any antenatal care, and almost half (48%) of the eligible women did not receive safe delivery care (either institutional delivery or home delivery assisted by skilled person). Moreover, while 37% women experienced post-delivery complications, nearly 45% of them did not seek any post-delivery treatment at national level. The reported post-delivery complications were nearly 50% in states such as Bihar, Jharkhand, and Uttar Pradesh.

**The way forward**

The statistics documented above lead us to believe that incentives attached to institutional delivery are insufficient to defer maternal deaths. In the last few years, there has been a gradual decline in the country’s MMR overall. This has been the outcome of efforts to reduce delays in seeking medical help, timely use of medical facilities and provision of adequate care. Moreover, behavioural factors such as improved women’s education, as well as mass media exposure, awareness and use of health services, availability of, and access to health facilities, are some of the key factors that have led to increased maternal health-care use. In addition, it is clear that institutional delivery has increased due to JSY. However, what should be prioritized to help attain MDG5? We propose a two-fold approach.

First, the priority areas of the maternal health-care programme should be reoriented to postnatal care. The proposition of offering a cash incentive, especially within 48 hours
of delivery, needs to be evaluated and the effectiveness of the programme checked on a pilot basis. Delivery in an institution must be encouraged as well as supervision by qualified physicians as long as is necessary, i.e. the programme should not be limited to discharging women automatically from the institution within 48 hours of delivery. Clearly, this needs physical facilities and human resources to enhance the currently overburdened public health infrastructure.

Second, the focus should be on the continuum of maternal health care as well as on "packages", which include integrated services for potential mothers from adolescence and pre-pregnancy period to delivery and immediate postnatal and maternal health care. Such care is provided by families and communities through outpatient services, clinics and other health facilities. As far as the package is concerned, a recent review of ongoing research has proposed packages of care for delivery at the community, health-centre or hospital level, where the package of maternal care includes:

- general supportive care (cessation of smoking during pregnancy, prevention of intimate partner violence, prevention of maternal drug abuse during pregnancy, recognition and treatment of postnatal depression, and family planning);
- maternal nutritional (supplementation of multiple micronutrients, balanced protein energy, periconceptual folic acid and iron-folic acid during pregnancy, and calcium supplementation in pregnant women with low/inadequate intake);
- improved quality of basic antenatal care (at least four visits of focused antenatal care, screening and management of sexually transmitted infections and prevention and management of malaria in pregnancy);
- expanded antenatal care (treatment and management of maternal diabetes, management of HIV, anti-platelet agents in high-risk pregnancies, antihypertensives for mild to moderate hypertension during pregnancy, magnesium sulphate for treatment of pregnancy-induced hypertension/eclampsia, influenza and pneumococcal vaccination);
- community-based interventions (emergency transport funds, cash transfers, supportive care during childbirth, etc.);
- childbirth care (basic obstetrics, emergency obstetrics [lower segment caesarean section, active induction of post-term pregnancy], treatment of pre-term pre-labour rupture of membranes, training traditional birth attendants in clean delivery and referral);
- postnatal care (birth spacing/family planning, postnatal visits).

It is encouraging that the High Level Expert Group Report on Universal Health Coverage for India, instituted by the Planning Commission, Government of India, suggested that the ‘National Health Package’ cover essential health at primary, secondary, as well as tertiary level care for all citizens of India by 2022. Here, it is imperative to suggest a comprehensive “package” for maternal healthcare that follows a continuum of care to avert maternal deaths in India. The role of the NRHM in promoting such a comprehensive package cannot be underestimated. Since its launch in 2005, it has provided the key strategy to India’s current public health system, has influenced the development of new guidelines to strengthening prenatal, natal and postnatal service delivery, and promoted the extended use of available health infrastructure, particularly human resources, at facility and non-facility levels. As far as the facility level is concerned, mandatory
counselling on the benefits of postnatal care could help in raising awareness on post-delivery health. However, non-facility initiatives under NRHM could reach eligible women through community health workers to provide appropriate counselling to women and other household members, particularly husbands, on the importance of postnatal care and on the adverse consequences of ignoring postnatal health check-ups.

Although the continuum of care has recently been highlighted as central for reproductive, maternal, newborn, and child health (RMNCH), and a means to reduce the burden of maternal and child deaths globally, the main barrier to increased coverage of the integrated package in most developing countries is inadequate operational management, especially at district and community level. Since the concept of continuum of care in RMNCH is quite recent, there is little evidence of its effective integration in more global programmes.

Neighbour initiatives

Two recent initiatives from Ethiopia (Health Service Extension Package) and Mexico (Seguro Popular Program) could be helpful for policy-makers and programme managers in India to initiate an integrated RMNCH approach. In 2003, the Government of Ethiopia and its partners analysed selected maternal and child health interventions and the country's Health Sector Development Programme. The results of the analysis indicated the need to shift from a facility-based model to an approach that extended access to basic health services to communities. In response, the Government of Ethiopia developed a new Health Service Extension Package (HSEP), which posted two female health workers in every community, supported by health centres and several thousand new medical officers. During the following year, the Child Survival Partnership expanded its focus to include maternal and newborn health strategies, with newborns serving as a bridge between child and maternal health interventions and strategies. Since 2004, Ethiopia has developed an in-country coordination process, RMNCH survival strategies, and has incorporated these strategies into its major policy initiatives, like the Poverty Reduction Strategy Programme.

Likewise in Mexico, a national health insurance programme called Seguro Popular, introduced in 2003, provides access to a package of comprehensive health services with financial protection for more than 50 million people previously excluded from insurance. Since its inception, there is evidence that Seguro Popular has improved access to health services and reduced the prevalence of catastrophic and impoverishing health expenditure, especially for the poor. The reduction of maternal and child deaths, and coverage of maternal and child healthcare services, have been pragmatic during the past few years. These efforts can be adapted and translated for countries seeking to provide universal coverage against threats to the health security of individuals and populations. Learning from this experience – its successes and its challenges – will not only help to improve health conditions and financial protection for all people in Mexico, but will contribute to the global movement towards universal health coverage.

Conclusions and recommendations

Given our analysis of the institutional delivery of cash through JSY, it is proposed to rethink the cash incentive system to reduce maternal mortality and reconsider maternal health care as a continuum of care. According to the budgetary provision in the Twelfth Five Year Plan, the Government of India allocated
nearly 2% of its Gross Domestic Product to healthcare. Some of this could be used to design an effective package of maternal care. Reduction in maternal mortality and associated issues should be high on the political agenda, especially of a developing country like India as a clearly rising power in the global economic situation.

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Pandemic influenza preparedness planning: lessons from Cambodia
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Introduction
Experts have estimated that a pandemic influenza outbreak could cost more than 60 million lives worldwide.\textsuperscript{1} When considered in combination with recent research demonstrating human-to-human transmission potential of the highly pathogenic strain of avian influenza A(H5N1),\textsuperscript{2} this highlights the growing need for public health officials to review their pandemic influenza preparedness strategy. This is especially true for South-East Asia which is predicted to be the likely epicentre of future pandemics.\textsuperscript{3}

Following the 2009 H1N1 swine flu pandemic, many governments drew upon guidance from the World Health Organization (WHO) pandemic influenza preparedness framework\textsuperscript{4} to revise their national pandemic influenza plans. Cambodia was no different and the government updated its National Comprehensive Avian and Human Influenza Plan by producing three further pandemic influenza strategies.\textsuperscript{5–7}

Interventions can be separated into pharmaceutical and non-pharmaceutical categories. Pharmaceutical options include antiviral stockpiling, the use of vaccines, which would take six months to produce, and there is now early evidence that certain immunemodulatory pharmaceuticals, including off-patent statins, may be effective in reducing influenza-related mortality.\textsuperscript{8} Non-pharmaceutical approaches are varied, but include investing in improved surveillance by way of sentinel sites and a network of approved laboratories, social distancing by risk communication, the closure of schools and workplaces, and the use of protective personal equipment (PPE).

One drawback of these guidance documents is that they hold a neutral perspective on which policy options might be the most beneficial, and furthermore do not give any indication on how best to allocate resources. It should be a priority to ensure that the US$ 2.7 billion that has been invested globally in the past seven years into pandemic preparedness\textsuperscript{9} is spent effectively.

As part of a wider project evaluating pandemic influenza mitigation investment options in Cambodia, we conducted semi-structured interviews with members of Cambodia’s pandemic influenza national coordinating committees to assess current beliefs. Informants were chosen from the...
National Pandemic Planning and Response Committee, National Committee for Disaster Management, National Pandemic Vaccine Committee, and the Joint Partners Interface Group. Of the 33 identified members, 14 (42%) responded and took part. Informants were first asked to score the 10 pandemic policy areas, as listed above, based on importance and their willingness to invest resources, on a scale of one to five (with five meaning 'very important'). Participants were permitted to use each number more than once in order to gain a more reflective estimate of how the different interventions compared with each other. They were then invited to comment on how they reached their decision for each area. Using basic statistical methods and Grounded Theory, two main themes emerged from the analysis of the transcripts, i.e. difficulties in prioritizing the different pandemic preparedness interventions, and a lack of consensus on certain interventions. We believe these problems are also likely to exist in other South-East Asian countries that share similar attributes.

Difficulties in prioritization

Given that the ability to prioritize different policy areas or interventions is a key part of the health planning process, it was surprising that all but one of the policy areas scored between four and five, which we interpreted as ‘important’ to ‘very important’. This highlighted an inability to differentiate adequately between policy areas. The single policy area that did not receive all-round acknowledgement of its importance was, unsurprisingly, generic immunemodulatory pharmaceuticals, due to the current paucity of evidence. The results are shown in Table 1.

Contrasting concerns

Despite the overarching importance placed upon all of the WHO-backed interventions in the first instance, some informants raised concerns that were not held consistently across the group. This was observed with both pharmaceutical and non-pharmaceutical approaches.

Pharmaceutical interventions

Many informants spoke of the need to stockpile antivirals, with the majority of informants opening with a line similar to this participant:

“It is very critical to have a stockpile for Tamiflu.”

Yet in contrast to this stated need for Tamiflu, some informants raised concerns about the associated costs of antiviral stockpiling, including storage and distribution, as well as the assumptions made about the drug’s efficacy. These concerns are illustrated by the following comments:

“[We] need to spend a lot of money and the duration of use is short thus stockpiling is not important... if we stock it, we waste money... It is not necessary for a developing country like us.”

“[We make an] assumption that antivirals are good...we assume that the virus is sensitive to antivirals... and that antivirals decrease mortality, and decrease the period of transmissibility.”

Vaccination strategies also appeared to invoke mixed concerns among the informants. All informants commented on at least one of the following issues: speed and capacity of vaccine manufacturing, unknown efficacy, and cost. Yet despite these legitimate concerns, investment for this policy option remained popular among respondents.
Non-pharmaceutical interventions

All 14 respondents agreed on the importance of governance, diagnostic capacity, and human resources, and that all medical staff must receive suitable PPE. Justifications included the International Health Regulations and healthworkers’ faith in the equipment. The general impression of PPE among informants was captured by this informant:

“without [PPE] we can’t do anything."

In contrast, another stated:

“Our country is poor and the PPE is expensive and... if we wait for PPE we can’t do anything else.”

The policy option for critical care equipment generated even more polarized results. Some informants firmly stated the importance of having life-saving critical care equipment, perhaps over-stating their efficacy, while others made comments about their being costly and potentially non-cost-effective. Social distancing raised similar mixed responses: four informants stated that it was a valid policy option, while five others raised concerns about efficacy and difficulties with implementation.

Why does this matter?

These interviews highlight the difficulties that policy-makers face when allocating resources to pandemic influenza preparedness in Cambodia, and may also reflect difficulties faced by their counterparts throughout South-East Asia. Our findings also show that drawing concrete conclusions from the current evidence base is challenging, possibly because the evidence has largely been generated in high-income settings. While high-income countries are able to allay the uncertainties by investing across the board, countries with limited resources may inadvertently invest in less cost-effective measures. This could in effect result in unnecessary loss of life in the event of a future pandemic.

What next?

In order to support the decision-making process in pandemic influenza policy, we suggest need for better research on two counts. First, there needs to be better evidence on the effectiveness of interventions, especially in low-income countries. Second, appropriate economic evaluation needs to complement these studies in order to guide decisions on implementation. While we recognize the inherent difficulties in pandemic influenza modelling due to its uncertain timing, and viral virulence and response to interventions, having a better grasp of the relative differences between the interventions described in the WHO pandemic influenza preparedness framework would allow for more intelligent decision-making by public health officials.

In order to facilitate this process of generating better evidence, we make two recommendations. First, pre-approved clinical trials, where ethical approval and funding would be confirmed ahead of the next pandemic, may be able to generate more reliable strain-specific data that could be used as events unfold. Second, improved communication could enable researchers to help policy-makers interpret their results in the context of pandemic uncertainty, and conversely, it is crucial that in such a challenging area of decision-making, policy-makers should liaise with researchers to help direct their work.

Acknowledgements

We would like to thank the informants for their time in conducting these interviews. This work was supported through Deutsche Gesellschaft
Table 1: Fourteen key pandemic influenza informants in Cambodia were asked to score each pandemic influenza policy based on importance and their willingness to invest

<table>
<thead>
<tr>
<th>Health facility resources</th>
<th>Key informant</th>
<th>Mean score [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human resources (e.g. doctors, nurses, laboratory technicians)</td>
<td>5 5 5 5 5 4.5 4 4 5 5 4 5 5</td>
<td>4.8 [3.8-5.0]</td>
</tr>
<tr>
<td>Personal protective equipment (e.g. masks, gloves)</td>
<td>5 5 5 5 5 3 2.5 4 3.5 5</td>
<td>No score</td>
</tr>
<tr>
<td>Critical care equipment and training (e.g. ventilators)</td>
<td>5 5 5 5 4 1.5 3 4.5 5 3.5 4 5 4</td>
<td>4.2 [3.2-4.7]</td>
</tr>
<tr>
<td>Influenza diagnostic capacity</td>
<td>5 5 5 5 4.5 5 4 4 3 5</td>
<td>No comment</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stockpiling</th>
<th>Antiviral stockpiling</th>
<th>Mean score [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stockpiling</td>
<td>4.5 5 3 4 5 5 4.5 5 3 3 2 4 4 4</td>
<td>4.0 [3.0-4.5]</td>
</tr>
<tr>
<td>Personal protective equipment stockpiling (e.g. masks, gloves)</td>
<td>5 5 4 5 5 3</td>
<td>No comment</td>
</tr>
</tbody>
</table>

| Vaccination (assuming an effective vaccine can be produced approximately 6 months after the pandemic strain is identified) | 5 5 4 4 5 5 4.5 2.5 5 4.5 5 3 | No score | 5 | 4.4 [3.4-4.9] |

| Generic immune-modulators – developing a framework to support the use of statins or other immune-modulators | No comment | 4 1 No comment | 4 No comment | 1.5 3 No comment | 3 No comment | 3 No comment | 2.8 [1.8-3.8] |

| Governance (including strategies for cooperation and legal frameworks) | 5 5 5 5 5 4.5 5 5 5 4 4.5 5 | 4.9 [3.9-5.0] |

| Measures to temporarily reduce social contact (including school or work closure) | 5 5 4 3.5 4 | 3.75 2 5 No score | 4 5 4.5 No score | 4 4.1 [3.1-4.9] |

Scores were given from one to five (with five being the most important). 'No comment' was used when the informant had insufficient knowledge of the policy area to give a score. 'No score' was used when an opinion was expressed but no score was provided.
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References


A review of Japanese encephalitis in Uttar Pradesh, India
Roop Kumaria, Pyare L Joshi

**Background:** Japanese encephalitis (JE) is a major public health problem in India. When the first case was reported in 1955, the disease was restricted to south India. The disease spread to north India in 1978 from where extensive and recurrent outbreaks of JE have been reported ever since. An attempt has been made to review the epidemiology of JE over the past 30 years and suggestions made for its prevention and control.

**Methods:** An epidemiological profile of JE (1978–2009) has been compiled and analysed to understand the trend and status of the disease.

**Results:** In India, while 24 states are endemic for JE, Uttar Pradesh contributed more than 75% of cases during the recent past. Over the years, the seasonal trend has changed and the epidemic peak of the disease has advanced by one month.

**Conclusion:** JE is closely associated with the pattern of precipitation, flooding and rice production systems. Analysis of trends and influencing factors will help in designing suitable strategies for the prevention and control of JE in the country. Continuous monitoring of vector populations and JE virus infection rates in vector mosquitoes will help in predicting an outbreak and in taking effective intervention measures.

**Key words:** Japanese encephalitis, epidemiology, Uttar Pradesh, India, vector, high-risk districts

**Introduction**

Japanese encephalitis (JE), a vector-borne viral disease, is endemic to large parts of Asia and the Pacific regions. An estimated 3 billion people are at risk, and the disease has recently spread to new territories globally. JE is a major public health challenge due to its high epidemic potential, high case–fatality and neuropsychiatric sequelae among survivors. JE was first recognized in Japan in 1924. Since the late 1960s, the size of epidemics in Japan and the People’s Republic of China has steadily declined. In contrast, new epidemic foci of JE were reported in the parts of tropical southeastern Asia as late as 1969.

In India, the first human case was reported from North Arcot district of Tamil Nadu in 1955. Until 1973, the disease was confined to southern parts of India, with low prevalence; subsequently the disease spread to various other parts of India. The first outbreak of
JE was recorded in 1973 from Burdwan and Bankura districts of West Bengal. In 1978, suspected outbreaks of JE were reported from 18 states and 24 states and Union Territories have reported suspected JE cases till recent past.

The State of Uttar Pradesh (UP) is highly endemic; since the first report of a JE epidemic in 1978, extensive and recurrent outbreaks have been reported from the eastern parts of the State. An attempt has been made in this article to review the epidemiology of JE since 1978, particularly in UP, and to make recommendations for its prevention and control.

**Study area**

Uttar Pradesh, 241 000 km², is the most populous State in India with over 199 million people as of 2011. The majority of the population is engaged in agriculture, which contributes to 41% of the State’s economy. Since its division in 2000 into two states, UP has 71 districts, 106 thousand villages, 3640 primary health centres and 18565 sub-centres.

Climatically, while the State experiences tropical monsoons, weather conditions change significantly as per the location and onset of the season. UP has three broad seasons – winter from October to February (minimum temperatures of 3–4 °C), summer from March to mid-June (temperatures up to 45 °C), and the rainy season from June to September (85% of average annual rainfall of 99cm and temperatures of 30–45 °C). The entire region is prone to annual flooding due to its topography. Five districts in Eastern UP (Gorakhpur, Kushinagar, Maharajganj, Sant Kabir Nagar and Siddarth Nagar), a region surrounded by embankments and drainage structures, are the most affected by floods as they are traversed by major rivers originating in the Nepali hills. Regular flooding is devastating for the crops, life and property of the farming community, and to a large extent determines their socioeconomic and political lives.

**Domestic animals**

The common domestic animals include cows, buffaloes, goats, pigs, dogs and horses. The pig is known to be the amplifier host of the JE virus (JEV). Despite this knowledge, unorganized piggeries are common in most districts in the region.

**Methodology**

**Surveillance and case definitions**

Clinical diagnosis is made by the respective medical officers of the health centres/hospitals who attend the JE cases in outpatient or inpatient departments, using standard case definitions as per national guidelines. Serum and cerebrospinal fluid samples of suspected cases are tested by IgM enzyme-linked immunosorbent assay (ELISA) for confirmation of JE. Previously, laboratory and treatment facilities were only available at Baba Raghav Das (BRD) Medical College, Gorakhpur; King George Medical College, Lucknow (now Shahuji Maharaj Medical University) and Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow. Since 2005, district hospitals are being strengthened for diagnosis of JE cases. Eastern districts of UP are highly endemic, and most JE patients from these areas have been treated at BRD Medical College, along with JE patients from border districts of Bihar and even neighbouring Nepal.

In 2006, the National Vector Borne Disease Control Programme (NVBDCP) modified the case definition of JE. Since then, epidemiological surveillance for acute encephalitis syndrome (AES) was initiated...
Japanese encephalitis in Uttar Pradesh, India  
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and suspected JE cases are now reported as follows: “Clinically, a case of AES is defined as a person of any age, at any time of year with the acute onset of fever and a change in mental status (including symptoms such as confusion, disorientation, coma, or inability to talk) AND/OR new onset of seizures (excluding simple febrile seizures). Other early clinical findings may include an increase in irritability, somnolence or abnormal behaviour greater than that seen with usual febrile illness”.

JE surveillance therefore aims to identify patients with AES and thereafter confirm JEV infection using IgM ELISA test.

Methods

Epidemiological data for JE over the past 32 years (1978–2009) as reported by State Health Authorities and from published and unpublished documents were collected and analysed for the purpose of this study. The burden of JE morbidity, annual incidence rate (number of cases per 100,000 risk area populations) and case–fatality rate (proportion of deaths against the total number of cases reported per year) were estimated.

Results

As compared with the total number of JE cases reported in the country, UP contributed a fifth of the disease burden (20.4% of cases and 18.7% of deaths) during 1978–1987 (Figures 1A and 1B). Its contribution increased between 1988 and 1997 to 24.3% cases and 20.9% deaths, and represented well over half of the total cases and deaths reported in the country between 1998 and 2009. While the proportion of JE cases reported from Uttar Pradesh in 1997 was only 14%, it started increasing dramatically from 1998 and in 2005, a major outbreak in UP contributed over 90% of all suspected JE cases (6061) – and over 89% deaths (1501) – in the country. During the four following years, 2006–2009, 80.8%, 73.6%, 78.5% and 77.0% of cases, respectively, were contributed by the State of Uttar Pradesh (Figure 1C).

Figure 1A: Proportion of Japanese encephalitis cases contributed by Uttar Pradesh in national figures by decade, 1978–2007
Figure 1B: Proportion of Japanese encephalitis deaths contributed by Uttar Pradesh in national figures by decade, 1978–2007

Figure 1C: Contribution of Japanese encephalitis cases by Uttar Pradesh in national figures by year, 1997–2009
**Trend of JE cases and deaths in Uttar Pradesh**

Figure 2 shows that, despite year-to-year fluctuation, there was no definite trend of JE cases and deaths in the State since 1978. In the first decade (1978–1987), a total 9299 reported JE cases, and 3103 deaths attributed to suspected JE cases, were reported from 46 districts. The first outbreak of suspected JE was recorded in UP in 1978, during which 3550 cases and 1117 deaths were reported from 40 districts. While in 1979 only 150 cases were reported, this number again increased in 1980 to 1604 cases reported from 15 districts. Thereafter, the incidence of JE declined until 1985. In the second decade (1988–1997), the total number of reported cases and deaths were 10 064 and 3194, respectively, from 25 districts. During 1998–2009, the burden of JE was much higher than the previous decades, at 18 760 cases and 4189 deaths, reported from 40 districts in the State.

**Case–fatality rate**

The annual case–fatality rate (CFR) of reported suspected cases shown in Figure 2 was higher in the beginning (1978–1987), ranging from 31.2% to 48.0%, before declining in 1988–1997 (range 21.0–39.9%) and 1998–2007 (18.6–24.9%). In the 2005 JE outbreak, the overall CFR was 24.9% as compared with earlier outbreaks in 1978 (31.5%), 1985 (34.5%) and 1988 (31.5%). This indicates an improvement in the management of JE cases over time.

**Seasonal variation**

Monthly reported JE cases from 1998 to 2007 indicate that sporadic cases occurred in the month of June and reached a peak in September before declining thereafter.
Seasonal peaks of JE cases have occurred during the months of August to October in the State; data also indicate that maximum cases were concentrated in the period from July to October, coinciding with rainy and post-rainy seasons. With the onset of winter, JE incidence declined substantially.

Average AES/JE cases in recent years compared with data of 1988 (Figure 3) show some variation in seasonal trends and cyclic patterns of the disease. For example, cases have started to increase from early July, peaking in October as opposed to September (cases also peaked in October in the 1970s and 1980s). During the outbreak in UP in 2005, weekly data indicated that cases started occurring in July with a sharp peak in end August/early September. In contrast, the 1988 outbreak in Gorakhpur and Deoria districts witnessed JE cases starting in September and reaching a peak in the second week of October, before subsiding in November. The entire course of the disease during the 1985 outbreak was of 8 to 9 weeks’ duration from mid September to mid November. However, the 1978 outbreak reported cases reported from mid October until November. Thus, over three decades, the peak of the epidemic has advanced by one month approximately.

**Districts with repeated occurrence of JE cases**

Figure 4 shows the districts where JE cases occurred repeatedly from 1978 to 2007. Of the total 72 districts in the State, 17 districts have reported only sporadic cases of suspected JE (not laboratory confirmed) at one time in 30 years. Of these districts, 7 (Bijnor, Bulandshahr, Etah, Kaushambi, Deharadun, Pauri and Mainpuri) reported only 1 or 2 cases of suspected JE, 6 districts (Agra, Etawah, Hamirpur, Badaun, Ormoi...
Japanese encephalitis in Uttar Pradesh, India

During the second decade under review (1987–1997), JE emerged for the first time as a problem in Siddharth Nagar district in 1989, in Maharajganj in 1990 and in Kushinagar in 1997. Since then, these districts have regularly reported JE cases every year. An in-depth review of the origins of these districts indicates that Siddharth Nagar was created in 1988 out of Basti district; Maharajganj was carved out from Gorakhpur district in 1989, and Kushinagar emerged in 1994 from Deoria district. Thus, the high incidence of JE reported in the newly created districts was due to their geographic affinity with their highly JE endemic parent districts since 1978. However, in 1995 and 1996, no case was reported by the state, therefore, there was less number of districts affected.

The three new districts that emerged in the decade 1998–2007 – Balrampur, Sant Kabir Nagar and Shravasti – have also reported JE...

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**Figure 4: Map showing frequency of Japanese encephalitis cases reported annually from each district in Uttar Pradesh, 1978–2007**

![Map showing frequency of Japanese encephalitis cases reported annually from each district in Uttar Pradesh, 1978–2007](image-url)
cases since their creation. Sant Kabir Nagar emerged in September 1997 from Basti district, while Balrampur was created from Gonda district in 1997. Shravasti became a new district in 2000 carved out from the districts of Bahraich and Gonda. All these parent districts were highly endemic for JE. Figure 5 shows the increasing number of districts affected by JE in Uttar Pradesh.

**Disease burden by district**

Figures 6A–C indicate the distribution of cases in different districts from 1978 to 2007. The incidence rates appear to be higher in eastern districts of UP. The district-wise estimation of JE cases per 100 000 population (annual incidence rate) from 1978 to 1987 ranged from 0.01 to 9.87. Deoria district had the maximum average annual incidence rate (9.87) followed by Gorakhpur (9.40), Pilibhit (3.14), Azamgarh (2.01), Ballia (1.66) and Kheri (1.19). The remaining districts (Lakhimpur, Bahraich, Gonda, Gazipur, Lucknow, Bareilly and Sultanpur) showed a sporadic distribution of cases from 0.5 to 1.0 per 100 000 population.

From 1988 to 1997, like the earlier decade, the highest incidence rate was reported from Deoria (11.90 cases per 100 000 population) followed by Gorakhpur (11.59). It is important to highlight that during this decade, a serious JE problem emerged for the first time in the two newly created districts of Maharajganj (847 cases and an attack rate of 3.84 per 100 000 population) and Siddarth Nagar (274 cases with an attack rate of 1.38 per 100 000). Since then, these districts have reported JE cases every year.

First time JE incidence was reported from Kushinagar district immediately after its creation, which has since emerged as the most problematic district in the State with the highest average annual incidence rate (29.90 per 100 000 population), followed by

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**Figure 5: Shifting scenario of Japanese encephalitis in Uttar Pradesh by year showing annual number of affected districts and trends in incidence rate**

![Chart showing annual number of affected districts and trends in incidence rate](chart)
Figure 6: Distribution of reported Japanese encephalitis cases in Uttar Pradesh


Maharajganj (21.80), Gorakhpur (10.01), Siddharth Nagar (7.60), Deoria (6.59) and Bahraich (3.62).

During the period from 1998 to 2007, Kushinagar, Maharajganj, Gorakhpur, Siddharth Nagar, Deoria and Bahraich were the most JE problematic districts in the State. Data indicate that Azamgarh, Ballia, Kheri and Pilibhit districts had been highly endemic from 1978 to 1988, after which time the disease burden declined.

Besides increased disease burdens in some districts, new epidemic foci of JE have also been emerging in Uttar Pradesh. During the second decade of study from 1988 to 1997 (Figure 6B) first-time JE problems emerged in the new districts of Maharajganj (1990), Siddharth Nagar (1989), and Kushinagar (1997). Since these districts were part of the old endemic districts, they also reported JE cases every year since their creation.

Kushinagar district has become the most high-risk district in the State with an average annual incidence rate over 10 years of 29.90 per 100,000 population, followed by Maharajganj (21.80). The incidence rate was comparatively less in Gorakhpur (10.01) and Deoria (6.59) districts, where a high proportion of JE had been reported repeatedly since 1978.

**Age distribution of JE cases**

Analysis of age distribution of JE cases from Gorakhpur division in outbreaks in 1985, 1988, 2005 and 2009 (Figure 7) show that children were more susceptible than adults. The average age of affected children in eastern UP was 6.8 years between 2004 and 2006. The highest number of cases occurred in children aged between 0 and 10 years: 47% in 1985, 60% in 1988, 88% in 2004, and 94% in 2006 outbreaks, respectively.
Figure 7: Distribution of Japanese encephalitis cases by age and sex, Gorakhpur division, Uttar Pradesh

7A: Distribution of JE cases by age/sex, Gorakhpur, 2009

7B: Distribution of JE cases by age/sex, Gorakhpur, 2005
7C: Distribution of JE cases by age/sex, Gorakhpur, 1988

7D: Distribution of JE cases by age/sex, Gorakhpur, 1985
Analysis of 3887 JE cases reported in 2005 from Gorakhpur and Basti divisions indicated that the maximum cases (58%) were reported in the age group of 4 to 6 years, while 18% of cases were reported in the age group 15 years and above. Age distribution of JE seropositive cases reported by BRD Medical College during 2009 shows that 75.1% of confirmed JE cases were reported in the age group below 15 years. In earlier outbreaks in 1985 and 1988, the proportion of adults was higher – 25% and 22%, respectively – which then declined by 3% in 2004. After JE vaccination in children up to 15 years, the proportion of cases in adults slightly increased in 2009 (24.87%) in 2006.

**Sex distribution of JE cases**

The 2005 JE outbreak in UP reported a case breakdown of 61% males and 39% females (deaths attributed to disease were 59% in males and 41% in females). However, in Gorakhpur division, a line listing of 1087 cases showed a ratio of 56.0% males to 43.8% females. A year later in 2006, a line listing of 249 cases revealed 155 (62.3%) males against 94 (37.7%) females. From 2007 to 2009, line listings showed steady average of male to female cases of JE (68 (57.1%) males and 51 (42.9%) females, and 122 (59.5%) males and 83 (40.5% females, respectively).

**JE vaccination**

In 2006, the Government of India launched a JE vaccination campaign for children from 1 to 15 years of age. This was followed by immunization of new cohorts as an integral component of the Universal Immunization Programme with single dose of live attenuated JE vaccine (SA–14-14-2) in 11 highly endemic districts of four states (Assam, Karnataka, Uttar Pradesh and West Bengal). Of the 11 districts, 7 (Deoria, Gorakhpur, Kheri, Kushinagar, Maharajganj, Sant Kabir Nagar and Siddharth Nagar) reported coverage of above 95% of the estimated target. This success led to the JE vaccination programme being extended in a phased manner to the other endemic districts. During 2007, an additional seven endemic districts (Bahraich, Balrampur, Basti, Gonda, Rae Bareli, Saharanpur and Shravasti) were covered. A further 16 districts were included in 2008 and 2009. Sustained high coverage of JE vaccination is clearly required to bring down the disease burden. The percentage coverage of JE vaccination in Uttar Pradesh from 2006 to 2009 is given in Table 1.

Although the reported coverage was very high, an independent evaluation by UNICEF in 2008 showed that only 51% of eligible children received JE vaccination during the campaign. However, it may be said that the proportion of JE sero positive cases in Gorakhpur did not cease to occur but there was decline, from 38.8% in 2005 to 14.2% in 2006, 12% in 2007, 8% in 2008 and 10.8% in 2009 after introduction of JE vaccination in 2006 in high endemic districts (Report of the National Institute of Virology Field Unit, Gorakhpur).

Figure 8 shows that JE cases usually appear in the third month after onset of the monsoon. For example, in 2005 JE cases were reported from August following the monsoon in May, while in 2006 and 2007, the monsoon started in April and cases started being reported in July. Vector mosquitoes proliferate profusely subsequent to a monsoon, stimulating an increase of virus activity in mosquitoes and human–mosquito contacts and thus transmission, followed by JE cases. This preparatory phase of 2–3 months should be used to prepare for the prevention of an outbreak. The reason for the 2005 outbreak may have been caused by prolonged rainfall: as seen in Figure 8, the pattern of rainfall was different in that year, which had two peaks of rainfall – one in July and another in October – with a prolonged rainy season from May to
### Table 1: Coverage of Japanese encephalitis vaccine (SA 14-14-A) in Uttar Pradesh

<table>
<thead>
<tr>
<th>Sl No</th>
<th>Year</th>
<th>District</th>
<th>Target (1–15 year olds)</th>
<th>Total vaccinated children</th>
<th>Total coverage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2006</td>
<td>Gorakhpur</td>
<td>1 390 307</td>
<td>1 349 047</td>
<td>97.03</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>Deoria</td>
<td>1 074 219</td>
<td>1 072 683</td>
<td>99.86</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>Kushinagar</td>
<td>1 095 877</td>
<td>1 085 055</td>
<td>99.01</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>Maharajganj</td>
<td>776 500</td>
<td>806 996</td>
<td>103.93</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>Kheri</td>
<td>1 183 481</td>
<td>1 218 364</td>
<td>102.95</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>Sant Kabir Nagar</td>
<td>542 062</td>
<td>511 417</td>
<td>94.35</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>Siddarth Nagar</td>
<td>775 934</td>
<td>792 944</td>
<td>102.19</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Total</strong></td>
<td><strong>6 838 380</strong></td>
<td><strong>6 836 506</strong></td>
<td><strong>99.97</strong></td>
</tr>
<tr>
<td>1</td>
<td>2007</td>
<td>Ambedkar Nagar</td>
<td>764 068</td>
<td>741 354</td>
<td>97.03</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>Bahraich</td>
<td>990 327</td>
<td>992 254</td>
<td>100.19</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>Balrampur</td>
<td>623 020</td>
<td>622 963</td>
<td>99.99</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>Barabanki</td>
<td>1 074 154</td>
<td>1 063 815</td>
<td>99.04</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>Basti</td>
<td>774 322</td>
<td>750 262</td>
<td>96.89</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>Gonda</td>
<td>1 040 501</td>
<td>1 045 957</td>
<td>100.52</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>Mau</td>
<td>719 800</td>
<td>691 341</td>
<td>96.05</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>Raebareli</td>
<td>1 058 987</td>
<td>1 029 154</td>
<td>97.18</td>
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<tr>
<td>9</td>
<td></td>
<td>Saharanpur</td>
<td>1 056 185</td>
<td>923 246</td>
<td>87.41</td>
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<tr>
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<td></td>
<td>Sitapur</td>
<td>1 385 606</td>
<td>1 312 326</td>
<td>94.71</td>
</tr>
<tr>
<td>11</td>
<td></td>
<td>Shravasti</td>
<td>331 903</td>
<td>326 485</td>
<td>98.37</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Total</strong></td>
<td><strong>9 818 873</strong></td>
<td><strong>9 499 157</strong></td>
<td><strong>96.74</strong></td>
</tr>
<tr>
<td>1</td>
<td>2008</td>
<td>Azamgarh</td>
<td>1 400 000</td>
<td>1 329 471</td>
<td>94.96</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>Ballia</td>
<td>1 067 337</td>
<td>1 040 948</td>
<td>97.53</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>Bareilly</td>
<td>1 337 392</td>
<td>1 399 552</td>
<td>104.65</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>Faizabad</td>
<td>649 634</td>
<td>641 736</td>
<td>98.78</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>Hardoi</td>
<td>1 270 372</td>
<td>1 296 593</td>
<td>102.06</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>Lucknow</td>
<td>1 506 695</td>
<td>1 477 852</td>
<td>98.09</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>Muzzafar Nagar</td>
<td>1 340 232</td>
<td>1 243 694</td>
<td>92.80</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>Sultanpur</td>
<td>1 234 068</td>
<td>1 229 295</td>
<td>99.61</td>
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<tr>
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Source: NVBDCP
November. Other years had only one peak of rainfall.

**Discussion**

In India, 24 States/UTs were affected with JE but the State of UP contributed more than 75 per cent of JE cases to the country (Figure 1). In Uttar Pradesh, out of total of 71 districts, 7 eastern districts were highly affected due to JE and contributed about 78.27% of the total cases of the State during the recent decade. Gorakhpur, Deoria and Basti have been found to be high risk districts for JE since 1978, and other four districts which were carved out from these three districts namely Maharajganj, Kushinagar, Siddhath Nagar and Sant Kabir Nagar also remained high JE endemic since their inception. The eastern districts are the most prone to JE than western districts. Eastern district’s proneness to floods is attributed, among other things, to heavy rainfall, low and flat topography and the silting of river beds which make river levels to rise and have impact on temperature and humidity. Flood problems of eastern UP were due to reduction in the absorptive capacity of the soil. This ‘reduction’ has been magnified with the development of intensive canal irrigation during the past five decades. Due to construction of unlined canal networks and embankment; ground water table increased in this area resulting more flood and more water stagnations after the monsoon rains. As in Eastern UP, Bihar’s flood-prone area too tripled from 2.5 m ha in 1954 to 6.8 m ha in 1994. Flood proneness and water logging hit the lives and livelihoods of people in several ways including the growth of the vector mosquito population. Between 1951 and 1981, the area cultivated in kharif which fell from 214 000 ha to 68 000 ha due to annual flooding and
surface water logging; as a result, in these areas, farmers clung to traditional mixed-crop farming technologies. The tradition of animal husbandry too has been undergoing change due to waterlogging; as grazing lands remain submerged in water for long periods, large bovines have declined in population. Marginal farmers and landless have increasingly taken to piggery. All these factors contribute to increase of JE incidence in the eastern districts during the past decades.

Studies from peninsular and eastern parts of India indicate that pigs are the main vertebrate host of JEV and the major reservoir of the infection. Because infected pigs act as amplifying hosts, domestic pig rearing is an important risk factor in the transmission of JE to humans. In different parts of the country, 12–44% of the pig population have been found to be positive for JE antibodies, particularly in endemic areas. Pigs play an important role in the natural cycle and serve as an amplifier host since they allow manifold virus multiplication without suffering from disease and maintain prolonged viraemia. Thus, mosquitoes biting pigs can be dangerous for humans. In India, the population of pigs is reported to be more than 135 million, 31.7% (42.84 million) of which are in Uttar Pradesh. As per the last 17th livestock census, UP has the largest pig population in the country. Unorganized piggeries are plenty: the rural population who rear pigs virtually co-exist with these animals. Hence, the chance of human infection is high. The probability of vector mosquito species getting infected with JEV is higher when infected mosquito populations dramatically increase and the human biting rate increases. During the transmission season, when vector density is abundant, infected mosquitoes transmit infection to human beings as incidental, dead-end hosts in the transmission cycle due to low and short-lived viraemia.

Although the burden of disease in Uttar Pradesh has increased, CFRs of JE cases have declined over the years from 31.5% in 1978 to 18.0% in 2009. This is as a result of early detection, better case management and early referral of patients to treatment centres. In contrast in Nepal, overall mortality from JE was 9.8% in the year 2000 and 20.9% in 2003. A similar trend in CFR (7–30%) was reported in Philippines from 1972 to 1985.

An in-depth review of various outbreaks reported from Uttar Pradesh shows that in the 1985 outbreak of JE, the attack rate was 0.08 and 0.16 per thousand population in Gorakhpur and Deoria districts, respectively. The average number of cases per village was 1.1 in Gorakhpur and 1.2 in Deoria. Three years later in the 1988 outbreak, these averages rose to 1.6 cases per affected village in Deoria, and 2.4 in Gorakhpur. This difference may be attributed to variance in the population size and demographic profile of the villages.

Eight UP districts were affected by the 1988 outbreak: Gorakhpur, Deoria, Azamgarh, Basti, Gonda, Bahraich, Ballia and Faizabad. Nearly half of the cases and deaths were recorded from Gorakhpur alone, which was the worst affected district in the entire country. This outbreak became the largest epidemic recorded in any state in India to date, with 4544 cases and 1413 deaths. The next major JE outbreak to affect eastern was in 2005 and was the longest and most severe epidemic in three decades: 6061 persons were affected, 1501 of whom died. The etiologic agent was confirmed to be Japanese Encephalitis virus in 2005 outbreak of viral encephalitis in UP. Analysis of epidemic peaks of JE outbreaks shows that the duration of outbreaks is getting longer. Uttar Pradesh experienced its first outbreak in 1978 from mid October to November, i.e. a duration of 6–7 weeks.
In 1985, an outbreak\textsuperscript{16} started in the second and third week of September with an explosive rise in incidence in the subsequent 4 weeks followed by a decline over the next 2–3 weeks. The entire course of the epidemic was of 8 to 9 weeks duration. Thus, while the duration of epidemics in the 1970s and 1980s was 6–9 weeks,\textsuperscript{16} the 2005 JE epidemic lasted for about 17 weeks. Note that the first JE outbreak in Karnal, Haryana in 1990 continued for about 10 weeks.\textsuperscript{20}

In all outbreaks until 1988, seasonality of the disease was recorded from September to November, the post-monsoon season, which coincides with paddy cultivation and the period of peak mosquito density.\textsuperscript{11,23} The maximum number of cases was generally reported in October.\textsuperscript{22} However, monthly JE cases for the decade 1997 to 2007 indicate that sporadic JE incidence was reported in the month of June, gradually increasing from July and peaking in September before declining (Figure 3). Maximum cases were concentrated in the period August to October, coinciding with the rainy and post-rainy season. With onset of winter, JE incidence subsided. It was also reported that JE cases reached a peak during August/September in the Nepalese districts bordering UP in 2004.\textsuperscript{14} The results reveal that between 1978 and 2009 in UP, the peak of the epidemic season moved forward by approximately one month from October to September, and since 1997, seasonality of the disease has started in July instead of September.

About 90\% of the rainfall occurs during the south-west monsoon, lasting from about June to September. Flooding usually occurs from July to August during the rainy season and is a recurrent problem that creates an excellent breeding ground for JE vectors. Comparison of rainfall data with JE incidence indicates vector density, and subsequently JE cases increase one month after the peak rainy months. Relative to the 2005 outbreak, the duration of rainfall was longer compared with other years, starting in May, then peaking in July and August before its decline (Figure 8). However, a second peak of rain occurred in October, which explains the longest duration of JE outbreak (August to November) in that year: incidence increased rapidly in August and reached a peak in the first week of September, but the epidemic peak was not until November due to the prolonged rainy season.

Thus, seasonality of the disease and a shift in epidemic peak may be attributed to the pattern of monsoons, floods and change of weather in the State.\textsuperscript{24} It is also observed that JE cases usually appear in the third month after onset of the monsoon; thus the pattern of rainfall influences vector breeding and occurrence of JE cases. As per studies carried out from 1990 to 1996 in Gorakhpur, vector density increased after onset of the monsoon and reached its peak in September.\textsuperscript{25} However, the peak of JE cases was reported in October when the vector population, particularly \textit{Culex tritaeniorhynchus}, was on the decline.\textsuperscript{25} Such a relationship between the epidemic and declining vector population has also been observed in Japan, where this type of pattern was attributed to the differences in total and infected populations of vector species.\textsuperscript{26}

The present analysis shows that, though both sexes were affected, males usually outnumbered females. The female to male ratio in 2007 was 1:1.3. The 2005 outbreak showed female to male ratios of 1:1.28 and 1:1.58 while it was 1:1.7 in 1988\textsuperscript{27} and 1:1.5 in 1985.\textsuperscript{16} Male predominance was also seen in the first JE outbreak in 1978. Previous reports and recent analyses clearly indicate that in general men are more prone to JE infection than women, which could be attributed to more outdoor activity by the male population during the peak biting time of exophilic vectors and more exposed body parts, especially the
lower extremities, to mosquito bites, while women tend to be fully covered by dresses.

Data also reveal that, in the first JE epidemic in 1978 in UP, while no age group was spared more cases (42.5%) occurred in children below 10 years of age. A high number of cases in children was also reported in the 1988 outbreak (adults 22%, children >10 years,60% of total cases). In contrast, the number of adult cases was higher in the 1985 and 1987 outbreaks. Similar observations were made in the Indian states of Assam, Bihar and West Bengal. An analysis of age distribution in 1990–1996 revealed that the maximum number of cases occurred in children aged between 1 and 15 years, with the highest occurrence in the age group 6–10 years in Gorakhpur region. In 2004, of the total 115 cases analysed from Gorakhpur, 105 (91.3%) were among children below 15 years of age. In 1988, 22% cases occurred in adult age groups: This figure declined to 16% in 2005, largely because most adults in the area were immune to JEV, and the majority of cases were seen in children from 3 months to 15 years of age. Since introduction of JE SA14-14-2 vaccine in 2006, JE cases reported in upper age groups, including from Uttar Pradesh, have increased from 3% in 2006 to 25% in 2009. Similarly in Japan, JE has become a disease of older age groups since 1967, the CFR being higher in the elderly. A gradual decrease of herd immunity in older persons has been taking place, creating a potential for future disease outbreaks.

Over the years, children in UP have become a more susceptible group to JE. However, those with debilitating chronic illness or immunosuppression are at greater risk of disease, with symptoms ranging from malaise to meningo encephalitis with seizures and death. The attack rate decreases with age in endemic populations due to the presence of neutralizing antibodies as a result of natural exposure and subclinical infections in such individuals. The estimated population at risk in endemic areas is 45.1%. However; in relatively non-endemic areas where the virus is introduced for the first time, individuals of all age groups are susceptible.

After vaccination in 2006, the proportion of JE laboratory-confirmed positive cases declined in the Uttar Pradesh (NVBDCP Report). However, the virus remains a major and consistent cause of outbreaks in the eastern region of the State, accounting for approximately 10%–15% of total AES cases annually. Since introduction of JE SA14-14-2 vaccine in 2006, JE cases reported in upper age groups, including from Uttar Pradesh, have increased from 3% in 2006 to 25% in 2009. Similarly in Japan, JE has become a disease of older age groups since 1967, the CFR being higher in the elderly. A gradual decrease of herd immunity in older persons has been taking place, creating a potential for future disease outbreaks. In Uttar Pradesh, based on the elevated density and infection with JEV, Cx.tritaeniorhynchus considered responsible for causing epidemics in the area. Cx. pseudovishnui, Cx. whitmorei, Cx. gelidus, Cx. epidesmus, Anopheles subpictus, An. Peditaeniatus and Mansonia uniformis are suspected to play some role in the epidemiology of JE in the region. In Gorakhpur area, JEV infection was detected in female Cx. tritaeniorhynchus and Cx. epidesmus tested by ELISA. But JEV could be isolated only from Cx. tritaeniorhynchus by the Toxorhynchites splendens inoculation-indirect immunofluorescence (Toxo-IFA) insect bioassay. Isolation of JEV from Cx. epidesmus has been reported in Bankura, West Bengal. During the 1991 outbreak in
Gorakhpur, JEV was isolated from wild caught Cx. tritaeniorhynchus. However, JEV has since been detected by ELISA at the National Centre for Disease Control from adult Cx. gelidus, Cx. pseudovishnui, Cx. b. tritaeniorhynchus, in addition to Cx. tritaeniorhynchus reared from wild caught immature mosquitoes from Gorakhpur region (2009). JEV was detected in adult mosquitoes raised from wild caught immatures and males of the following vector species: Cx. tritaeniorhynchus, Cx. vishnui, Cx. infula, Cx. gelidus, Cx. fuscocephala and Ma. indiana. Vertical transmission of JEV occurred in both hot and cool seasons, and is thus regularly maintained in nature during the non-transmission season as well. The presence of a wide variety of vector species, their different bionomics and vectorial capacity, therefore needs to be studied. The monitoring of virus infection in vector mosquitoes should form an essential component of a surveillance system to assess monthly infection rates of vectors to predict disease outbreaks and to develop an early warning system in order to take remedial measures in the State of Uttar Pradesh.

The larval habitat of Cx. tritaeniorhynchus is primarily low lying flooded areas containing grasses and rice paddies. Eastern Uttar Pradesh is mainly a paddy growing area, with clay soil and a very high water table. The ecosystem comprising rivers, lakes, irrigation canals, ponds, reservoirs and rice fields favour vector breeding. Surface water bodies are perennial breeding sources in UP and provide a wintering and staging ground for a number of migratory waterfowls and a breeding ground for resident birds. They also act as mother foci for vector mosquitoes. After the monsoon, vectors spread to other water stagnation areas and rice fields. Thus breeding control with appropriate larvicides or using larvivorous fishin all permanent water bodies, before the start of monsoon and paddy irrigation, may check proliferation of breeding of Cx. tritaeniorhynchus and other JE vectors and even contain the vector population during JE transmission season. In addition, rice fields support waterfowl, especially egrets and herons, which are the reservoirs of JEV. Surveillance should be strengthened during the lean season to map breeding sites of vector mosquitoes in order to plan appropriate control measures.

Rice fields being the most productive breeding sites of Cx. tritaeniorhynchus, its population dynamics is closely associated with paddy cultivation. In Gorakhpur, a single paddy crop is grown per year and the majority of JE vectors show one peak a year, i.e. in September. The occurrence of JE in the region has therefore been closely associated with this peak. Interestingly, two peaks of JE vectors were recorded when double paddy crops were cultivated in Tamil Nadu.

The steady spread of JE confirmed cases to new areas in India is a serious public health concern. Eastern districts of Uttar Pradesh have been highly endemic since 1978; in 1990, the disease spread to the west, affecting neighbouring state Haryana for the first time, followed by Saharanpur and Muzaffarpur in western Uttar Pradesh in 2003 and 2005, respectively. Climate change may also influence the migration patterns of birds, which may result in the introduction of JEV to new areas. Since little is known about reservoir bird migration patterns, this is an important issue to investigate. Climate change is also affecting agricultural patterns, and the development of agriculture in the region has resulted in the vast expansion of water bodies and irrigation systems which support mosquito breeding, and in turn JEV.

Most of the JEV strains isolated in India belong to genotype III. However, JEV
Japanese encephalitis in Uttar Pradesh, India

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genotype I has recently been reported in human patients from Gorakhpur. Due to the evolution of new viral strains and/or re-emergence of older strains, children lack protective immunity. Although health management facilities have improved in UP (CFR reduced), concrete steps should be taken to combat JE, including the development of more efficient surveillance in human, vector and vertebrate hosts and strengthening of JE vaccination programme. In addition, first and secondary referral health facilities need to be reinforced for better management of JE cases.

Conclusion

Japanese encephalitis is still a major health problem in eastern Uttar Pradesh, north India. No antiviral drug against JEV is available. Chemical control of vector populations with insecticides plays a marginal role in control of the disease due to their exophilic behaviour. The use of larvicides is limited as vector mosquitoes prefer to breed in large water bodies. In some situations, e.g. during outbreaks of JE, space-spraying may interrupt the transmission cycle for a short time. Wider issues, including current agricultural practices, water management systems, and human behaviour patterns, need to be investigated. The most important long term strategy to fight flood-proneness is of rapid increase in groundwater irrigation which will not only lower water tables but also help reduce the intensity of floods which will further impact on public health and to improve the socioeconomic status of people in JE-affected areas. Awareness needs to be developed on personal protection against mosquito bites and the importance of early referral of cases.

In summary, JE could be controlled with effective surveillance systems, segregation of pigs, an integrated vector control approach, early detection of JE outbreaks, and high coverage of eligible children with JE vaccine. Continuous monitoring of vector populations and virus infection rates in vector mosquitoes would help to predict outbreaks more in advance and to implement proper control measures. To this end, a combination of strategies involving other sectors and the community would be required to instil the sense of urgency needed to accelerate effective control of JE in the country.

Acknowledgements

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References


A study on delay in treatment of kala-azar patients in Bangladesh

Syed M Arif, Ariful Basher, Mohammad R Rahman, Mohammad A Faiz

Visceral leishmaniasis (kala-azar) continues to be a major rural public health problem in Bangladesh. A cross-sectional study was carried out in two subdistricts of Mymensingh district from January 2006 to June 2007 to evaluate the delay kala-azar treatment. Suspected patients who attended to out patient department (OPD) were subjected to a dipstick test (RK39) for kala-azar. Sixty five from Bhaluka and 60 positive patients from Gafargaon subdistrict were enrolled. Most of the patients (80%) first visited nonqualified private practitioners, while only 15.2% consulted registered doctors. Fifty per cent were referred to the Upazilla health complex (UZHC) by the family members or relatives. About 49% and 43% patients required third and second health-care providers for kala-azar treatment, respectively. Patient delay ranged from 2 to 30 days; median 4 (IQR 3 to 7 days), the system delay ranged from 0 days to 225 days; median 54 (IQR 40–66 days). Residential status (p value <0.05) had impact on patient delay. Educational status and number of treatment providers had impact on system delay (p<0.05). System delay rather than patient delay is the important weakness of the kala-azar control programme in Bangladesh. Residence in rural areas, low educational background and treatment providers are associated with these delays. A proper educational programme may reduce the delay.

Key words: Visceral leishmaniasis, sand fly bite, health-seeking behaviour

Introduction

The Indian subcontinent has experienced a major resurgence of kala-azar (KA) which accounts for 60% of all reported cases of kala azar in the world.1,2 Kala-azar is caused by infection in the reticulo endothelial system by the protozoan Leishmania donovani acquired through sand fly bites.3,4,5 It carries a high mortality ranging from 80% to 100% in untreated cases.6 Even with treatment, case–fatality rates in excess of 10% are not uncommon.7 It is associated with about 2.4 million disability–adjusted life years and around 70 000 deaths per year.8

Kala-azar is one of the major public health problems in Bangladesh, and the disease has been endemic for many decades. In the late 1970s kala-azar emerged sporadically in Bangladesh. During 1981–1985 only
8 upazilas (subdistrict) reported kala-azar cases, which was increased to 105 upazilas in 2004. In the past few years, the kala-azar situation had assumed epidemic proportions with the number of reported cases increasing from 3978 in 1993 to 8505 in 2005. But, in 2010, the number of cases reported was less than 4000 and there was only 1 death. The actual number of cases might be a little higher due to incomplete reporting systems and late detection of PKDL cases. The hyperendemic zones in Bangladesh for kala-azar are mostly in Mymensingh district.

Social behaviour and economic consequences of kala-azar patients are still not well known, despite long standing occurrence of the disease and the implementation of various control programmes. This is due to inadequate information and the delay in diagnosis, social and community factors that influence care-seeking behaviour and the ability to control the disease etc. Delay in diagnosis and treatment of kala-azar leads to progression of disease, increase in the risk of complications and also augments the reservoir for further transmission. Factors associated with delay are not well addressed. The objectives of this study were to understand patient and system factors responsible for delay in seeking treatment and suggest intervention tools towards improving the kala-azar control programme.

**Methods**

The study was designed as hospital-based cross-sectional study; carried out at Gafforgaon and Bhaluka Upazilla Health Complex (UZHC); two Upazilla (subdistrict; lowest administrative unit and government 50 bed hospital) of Mymensingh district (highest prevalence of kala-azar by Upazilla in the country). Areas were selected purposively due to expediency of the investigators. Delay in receiving treatment for kala azar could be divided into “patient delay” (time from symptoms recognition to initial medical consultation) and “system delay” (time from first medical consultation to final treatment).

We approached 125 new patients of kala azar attending at the UZHC during the study period. The sample size was determined with a single population proportion formula by assuming that 50% of the patients will come early for kala azar treatment at a UZHC (to obtain minimum sample size) with 95% confidence interval.

Consecutive confirmed 65 patients from Bhaluka and 60 patients from Gafargaon upazilla were enrolled in this study. Patients attending to the out patient department (OPD) or in-patient facility with history of fever (Temp \(\geq 38 \, ^{\circ}C\)) for at least for 2 weeks with one or more of the followings criteria: (a) anaemia \((5<\text{Hb}<10 \, g/dl)\); (b) loss of weight; (c) splenomegaly were eligible to a RK 39 test for kala-azar. The patients were subjected to a detailed clinical evaluation by one of the investigators. Historical points as outlined in the CRF (case record form) were recorded through a face-to-face interview. Few of the physical examination findings (e.g. anaemia, hepatosplenomegaly) were also recorded.

The data were checked with logical explanations to ensure accuracy. Standard definitions of the different types of delays were followed. Both descriptive and inferential statistics were determined using SPSS-16. Frequencies and proportions were used for the descriptive analysis. The ANOVA test, 2 sample Student’s-t test, chi\(^2\) test were used to assess differences considering each group is approximately normal. Cross-tabulations and multiple logistic regression analysis was done to identify the most important predictors for kala-azar treatment delay.
Ethical clearance was obtained from the ethical committee of Bangladesh Medical Research Council (National Ethics Committee). Prior to study enrollment, written informed consent was obtained from each participating patient. Detailed study-related information was read out and explained in local language. Research assistants supplied a copy of the handout to the patient/his/her guardian. Signed written informed consent was obtained from the patient/ guardian. Finger impressions were obtained from participants, who could not sign. For subjects below 18 years, consent was taken from the eligible guardian. All patients were ensured treatment with Miltefosine tablets.

Results

General characteristics of patients

About 60% study subjects were less then 20 years of age with only of the 15.1% above 45 years (range 4–60 years). A majority 64% (80) were male and almost all (98.4%) were from the Muslim community. Most patients were from rural areas (80.8%) and half (42.2%) were married; 34.4% were farmers and 32.8% students. About half had monthly income < US$ 50, while 8% had income >US$ 100.00. Twenty four per cent had no formal education. Those educated up to the fifth grade were 52.8%, and only 23.2% were graduates. Splenomegaly was present in 87.2% patients, 8.8% patients were moderately anaemic while the rest were mildly anaemic (Table 1).

Knowledge about the disease

Only 15.2 % had no idea about the disease (Table 2). Almost all the respondents (84.8%) had heard the name kala-azar, and most (92.8%) knew that the disease was completely curable but only one person knew that it is an infectious disease transmitted by the bite of a sandfly. About 30.0% had family history of kala-azar. Most patients (85.6%) heard about the disease from hospital. According to the interviewees, about 60.8% always used mosquito nets at bedtime and 1.6% never used one. Approximately 96.8% fell asleep on a bed rather than the floor, and 56% slept during daytime (Table 2).

Type of facility first visited

One hundred and twenty five patients consulted with various types of health-care providers as the first place for seeking help with most visiting private health-care providers. About half (49.6%) went to village doctors, 27.2% to pharmacy personnel, 3.25% to the ‘Kabiraj’ (traditional health provider) and 2.4% to a medical assistant. Only 15.2% visited registered doctors and 2.4% directly reported to the Upazilla Health Complex (UZHC). Majority (85.6%) attended at UZHC as their third or fourth order treatment location. Many patients were referred to the UZHC by immediate family members or relatives (49.6%) for definite treatment. MBBS (registered) doctors referred 21% of patients to UZHC.

Determinants of pattern of delay

Patient delay ranged from 2 to 30 days with a median of 4 (IQR 3 to 7) days. The system delay ranged from 0 to 225 days, with a median duration of delay 54 (IQR 40 to 66) days. The median total delay was 55 (IQR 35 to 68) days. Seventy three per cent had patient delay below 7 days (73%). System delay over 2 months were experienced by 28% of patients (Table 5). Residential status had significant statistical association with patient delay. Educational status, number of treatment providers and first healthcare provider had statistical association with System delay ($p<0.05$). (Table 3)
### Table 1: General characteristics of the study population

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<td></td>
<td>&lt;64.10</td>
<td>47</td>
<td>37.6</td>
</tr>
<tr>
<td></td>
<td>&lt;128.21</td>
<td>14</td>
<td>12.2</td>
</tr>
<tr>
<td>Residential status</td>
<td>Urban</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>Semiurban</td>
<td>23</td>
<td>18.4</td>
</tr>
<tr>
<td></td>
<td>Rural</td>
<td>101</td>
<td>80.8</td>
</tr>
<tr>
<td>Marital status</td>
<td>Married</td>
<td>23</td>
<td>42.2</td>
</tr>
<tr>
<td></td>
<td>Single</td>
<td>39</td>
<td>32.2</td>
</tr>
<tr>
<td></td>
<td>Divorced</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td>32</td>
<td>25.6</td>
</tr>
<tr>
<td>Past family history of kala-azar</td>
<td>Yes</td>
<td>38</td>
<td>30.4</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>87</td>
<td>69.6</td>
</tr>
<tr>
<td>Clinical anaemia</td>
<td>Moderate anaemia (Hb-6–10g/dl)</td>
<td>11</td>
<td>8.8</td>
</tr>
<tr>
<td></td>
<td>Mild anaemia (Hb-10–12g/dl)</td>
<td>113</td>
<td>90.4</td>
</tr>
<tr>
<td></td>
<td>No anaemia</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>Yes</td>
<td>109</td>
<td>87.2</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>16</td>
<td>12.8</td>
</tr>
</tbody>
</table>
**Table 2: Knowledge of respondents about kala-azar in Baluka and Gafargaon**

<table>
<thead>
<tr>
<th>Items</th>
<th>Respondents</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heard the name kala-azar</td>
<td>Yes</td>
<td>106</td>
<td>84.8</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>19</td>
<td>15.2</td>
</tr>
<tr>
<td>Kala-azar is an infectious disease, transmitted by sand fly bite</td>
<td>Yes</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>124</td>
<td>99.2</td>
</tr>
<tr>
<td>Complete cure of the disease is possible</td>
<td>Yes</td>
<td>116</td>
<td>92.8</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>Not known</td>
<td>8</td>
<td>6.4</td>
</tr>
<tr>
<td>How kala-azar is known about</td>
<td>FM/Neighbour/Relative</td>
<td>3</td>
<td>2.4</td>
</tr>
<tr>
<td></td>
<td>Village doctor</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>MBBS doctor</td>
<td>14</td>
<td>11.2</td>
</tr>
<tr>
<td></td>
<td>Hospital</td>
<td>107</td>
<td>85.6</td>
</tr>
<tr>
<td>Frequency of using mosquito net</td>
<td>Always</td>
<td>76</td>
<td>60.8</td>
</tr>
<tr>
<td></td>
<td>Often</td>
<td>32</td>
<td>25.6</td>
</tr>
<tr>
<td></td>
<td>Never</td>
<td>2</td>
<td>1.6</td>
</tr>
<tr>
<td></td>
<td>Always</td>
<td>76</td>
<td>60.8</td>
</tr>
<tr>
<td>Sleeping in a bed</td>
<td>Bed</td>
<td>121</td>
<td>96.8</td>
</tr>
<tr>
<td></td>
<td>Floor</td>
<td>4</td>
<td>3.2</td>
</tr>
<tr>
<td>Habit of day-time sleeping</td>
<td>Regular</td>
<td>2</td>
<td>1.6</td>
</tr>
<tr>
<td></td>
<td>Occasional</td>
<td>38</td>
<td>30.4</td>
</tr>
<tr>
<td></td>
<td>Rarely</td>
<td>70</td>
<td>56.0</td>
</tr>
<tr>
<td></td>
<td>Not at all</td>
<td>15</td>
<td>12.0</td>
</tr>
</tbody>
</table>

**Table 3: Relationship between sociodemographic factors and patient delay and system delay (multiple linear regression analysis)**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Patient delay</th>
<th>System delay</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β-coefficient</td>
<td>(95% confidence interval)</td>
</tr>
<tr>
<td>Age</td>
<td>–0.086</td>
<td>(-0.918 – 0.345)</td>
</tr>
<tr>
<td>Sex</td>
<td>0.065</td>
<td>(-0.031–0.028)</td>
</tr>
<tr>
<td>Education</td>
<td>0.002</td>
<td>(-0.140–0.142)</td>
</tr>
<tr>
<td>Religion</td>
<td>-0.052</td>
<td>(-0.007–0.004)</td>
</tr>
<tr>
<td>Marital status</td>
<td>-0.049</td>
<td>(-0.066–0.038)</td>
</tr>
<tr>
<td>Monthly income</td>
<td>-0.048</td>
<td>(-96.963–55.661)</td>
</tr>
<tr>
<td>Residential status</td>
<td>-0.269</td>
<td>(-0.045–(-0.010)</td>
</tr>
<tr>
<td>No. treatment providers</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>First care provider</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

NA – not applicable
Discussion
Understanding the treatment-seeking behaviour of communities regarding kala-azar can be the key to the success of an elimination programme launched by the Government as Bangladesh along with India and Nepal have set the target of reducing the cases below 1 per 10 000 by the year 2015.1

Our data showed that most patients were below 40 years (82.2%) which is consistent with the studies.12,13 Awareness about the signs and symptoms of a disease can prompt patients to seek early treatment. However, in our study population, knowledge about the signs and symptoms of the disease was very poor despite the fact that the disease has been endemic for such a long time. Fever and splenomegaly were present in almost every kala-azar patient in Bangladesh. The majority of subjects lacked knowledge about the involvement of humans in the transmissibility and the infectious nature of the disease. There was an almost complete lack of knowledge about the transmitting vector (99.2%), which is a matter of concern for adaptation of preventive measures against the disease. Although most people were aware of the protective role of mosquito nets (Table 2), and many of households used bednets during sleeping, their acceptability and efficacy against kala-azar need more study.

The main health-seeking behaviour with the onset of fever was to visit a local health-care provider. People in the study community generally consult traditional healers due to a hierarchical system in their households. The majority of patients sought care at the village doctor or personnel at the pharmacy (76.8%) or private doctor (MBBS) (15.2%). This indicates that the traditional healers are considered important in the treatment of kala-azar. Only a small number preferred public health facilities for treatment because of their views of inadequacy of the health system. Only 2.4% rated public health facilities as their first choice. The care-seeking pattern for fever were more likely to be managed initially at low cost. Multiple care-seeking events and switching different types of providers were not uncommon. More than 50% patients required three or four health-care providers for their definitive treatment.

Sociodemographic factors have long been associated with delay in management of kala-azar patients. The results indicate the obvious existence of delay in diagnosis and treatment of kala-azar patients. System delay was the most frequent type of delay and the greatest contributor to total delay. Distance from patients’ home to a health facility is also important as it affects health-care seeking and follow-up of diagnostic procedures. As most patients were from rural areas, distance between their homes to the health-care service had contributed to the delay in the diagnosis. This is consistent with the studies done in TB patients in Uganda and Ethiopia.18,19 Patients who tried their first consultation at rural areas experienced a longer patient delay than those who first sought care in urban facilities. Our data suggested that the first health-care provider plays an important role in determining the duration of system delay. A major finding of this study was that about 50% of the study subjects who soughted final treatment at UZHC were referred by their immediate family members or relatives. Village doctors referred only 5.6% patient although they play a significant role as first-care providers. This exposes a very weak point in our health care system. Therefore, by raising awareness among health-care providers and field staff, we can strengthen the referral system and thus shorten system delay. Eighty per cent of patients soughted medical care from village doctors, pharmacies and ‘kabiraj’, so health campaigns at the community level should be
conducted to raise awareness and to facilitate early referral. Educational status also had significant relationship with system delay ($p<0.05$). This may be due to fact that most of the patients of this study reside in rural areas (80.8%) (Table 1). They were illiterate and had to travel a long distance to consult with a qualified doctor to seek medical care and most rural people had no easy access to Government facilities. However educational status had no effect on delay to initiation of treatment (patient delay) as established in other studies.20,21 Other factors such as age, sex, marital status, economic status and religion were not associated with patient delay and system delay (Table 3), although other studies had confirmed prolonged delays with initiation of treatment.18-23

Further in this study, poor knowledge of the study subjects about symptoms, infectious nature, and mode of transmission emphasizes the need for health education campaigns.

A system delay in treatment of kala-azar appears to be the major determinant of a treatment delay in the selected highest kala-azar prevalent area of Bangladesh. The current National Kala-azar Elimination Programme should address this issue in attempts to improve patients’ access to early treatment. Residence in rural areas and treatment providers have contributed to both the patient delay and the system delay. The elimination programme should emphasize training and continued education program for the First level health-care providers, many of whom are private health-care providers, in addition to the general BCC (behaviour change communication) campaign, to effectively reduce the treatment delay in the early case management of kala-azar.

Although it is difficult to extrapolate these findings, the level of KAP (knowledge–attitude–practice) about Kala-azar is not likely to be substantially different in other parts, because the study area is the oldest focus of kala-azar in Bangladesh and the population is expected to have maximum awareness about the disease. Even after such a prolonged and incessant disease transmission in the area, this lack of knowledge, indifferent attitude, and incorrect practices are pointers about the poor commitment of health–policy planners for the disease. For optimal utilization, public health facilities should be fully equipped to deal with cases of kala-azar.

Reference


Factors associated with high prevalence of pulmonary tuberculosis in HIV-infected people visiting for assessment of eligibility for highly active antiretroviral therapy in Kathmandu, Nepal

Bishnu R Tiwaria, Surendra Karki, Prakash Ghimire, Bimala Sharma, Sarala Malla

Background: Tuberculosis is the leading cause of deaths among HIV patients. In this study, we estimated the prevalence of pulmonary tuberculosis (PTB) and identified the factors/co-morbidities associated with active PTB in HIV-infected people visiting the national public health laboratory to assess their eligibility to receive highly active antiretroviral therapy.

Methods: A cross-sectional study was conducted to measure the prevalence of pulmonary tuberculosis. Data on probable risk factors in patients with and without PTB were compared, calculating the odds ratio as a measure of association. Factors showing significant association in univariate analyses were included in a stepwise backward logistic regression model to adjust for confounding.

Results: The prevalence of pulmonary tuberculosis was 32.4 % (95% confidence interval (CI) 30.25–34.56). In the univariate analysis, patients with PTB were more likely to be older, married, and have a longer duration since the diagnosis of HIV, diarrhoea, parasitic infection, lower CD4 T-cell counts, and lower CD4/CD8 ratio. However, the backward stepwise logistic regression revealed that only the CD4 T-cell count < 200/µL (AOR 11.69, 95% CI 6.23–21.94), CD4 T-cell count 200–350/µL (AOR 2.52, 95% CI 1.30–4.89), diarrhoea (AOR 2.77, 95% CI 1.78–4.31), parasitic infection (AOR 3.34, 95% CI 2.02–5.50) and ‘sex with partner’ as probable modes of transmission (AOR 0.44, 95% CI 0.20–0.93) were independently associated with pulmonary tuberculosis.

Conclusion: A high prevalence of pulmonary tuberculosis was observed. Participants with tuberculosis were significantly more likely to have lower CD4 counts, diarrhoea, and parasitic infections. HIV treatment programmes should consider these factors for better outcomes.

Key words: HIV, CD4, pulmonary tuberculosis, diarrhoea, Nepal
Background

Tuberculosis (TB) is caused by bacteria belonging to Mycobacterium tuberculosis complex. About one third of the world’s population is latently infected with TB bacteria. HIV infection leads to immune deterioration, thus providing a platform for the activation of latently infected TB.1

TB is the leading cause of deaths in HIV-infected people in resource-limited settings. About one third of HIV-infected people are co-infected with TB, most of them living in low- and middle-income countries.2 In Nepal, 80 000 people have active TB infection at any one time, with about 40 000 new cases and 5000–7000 deaths per year.3 As many as 11% of newly detected TB cases are infected with HIV and up to 23% of newly detected HIV cases are co-infected with TB.4 5 A high prevalence of HIV/TB co-infection is described elsewhere.6–9

Estimating the magnitude of pulmonary tuberculosis (PTB), and the factors associated with it in HIV-infected people, may be useful at policy level as well as for management of individual patients for better outcomes. In resource-limited settings, HIV is often diagnosed in late stage of the disease and in association with other co-morbidities related to deterioration of the immune system. In this study, we aimed to estimate the prevalence of PTB and identify the factors associated with it in HIV-infected people visiting the national public health laboratory (NPHL) for assessing eligibility to highly active antiretroviral therapy (HAART).

Methods

Setting and study population

This study was conducted in people infected with HIV, attending NPHL for CD4 T-cell count in Kathmandu, Nepal, primarily for the purpose of assessing their eligibility for HAART. NPHL is the largest referral centre in the country, equipped with an automated CD4 T-cell count facility. Although the facility is located in the capital city, the participants came from various parts of the country as a CD4 T-cell count service was not available outside of Kathmandu until the middle of 2008. Nepal is a landlocked country in South Asia with a poorly functioning health system. During our study period, the country had widespread and violent civil war and high political instability.

Study design and data collection

We conducted a cross-sectional study to measure the proportion of active pulmonary tuberculosis and analysed the data comparing patients with PTB and without PTB, to identify the associated factors/co-morbidities. A total of 1807 participants were included in the study from March 2005 to December 2008. The median age of participants was 30 years (interquartile range, 25–35 years), 66% of whom were male, and 90% were married. The study was explained to participants, who were assured about the confidentiality and anonymity of the collected information. An informed verbal consent was obtained from all the volunteers.

Definition of study variables

Pulmonary tuberculosis was defined as a participant whose sputum specimen was positive for acid fast bacilli (AFB) by microscopic examination at NPHL; or who had a prior medical record of being diagnosed with PTB on the basis of other laboratory investigations (sputum smear examination or microbiological culture) from other health-care facilities. Participants with tuberculosis other than PTB were excluded from the study. Participants with pulmonary tuberculosis already receiving HAART were also excluded from the analysis. The status of diarrhoea was ascertained by self-reporting of participants having loose
Factors associated with high prevalence of pulmonary tuberculosis in HIV-infected people in Kathmandu  

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stools 3 or more times a day. Information on parasitic infection was collected from the examination of stool specimens from a random subset of the study sample. Information about age, sex, possible mode of transmission, and date of HIV diagnosis was collected from a patient register maintained at NPHL.

**Laboratory investigation**

The volunteers were instructed on appropriate sputum specimen collection. Briefly, all sputum smears were stained with gram stain and observed under low power (10x) objective. Samples having less than 10 epithelial cells and more than 25 pus cells per low-power field were accepted and those not meeting the criteria were requested to submit a repeat sample. Sputum specimens collected and stained following AFB staining methods were examined microscopically following the standard protocol. At least 200 fields were evaluated before reporting negative.10

Microscopic examination of stool samples was performed by wet mount, formal-ether sedimentation technique and modified acid fast staining.10 Three millilitres of blood from each participant was collected for CD4 T-cell count, performed using flow cytometry.11

**Statistical analysis**

Data were entered in a Microsoft Excel spreadsheet and statistical analysis was performed by STATA (version 10; StataCorp, College Station, United States of America). The measure of association between different explanatory variables and TB infection (outcome variable) was expressed in terms of odds ratio (OR) with corresponding 95% confidence interval. Factors significantly associated with TB infection at p<0.05 in univariate analysis were adjusted for confounders in a backward stepwise multiple logistic regression model. The independently associated variables were tested for statistical interaction by using a test of homogeneity. The chi-square test was used to test statistical significance in categorical variables and the Wilcoxon ranksum test was used for continuous variables. A p-value of < 0.05 was considered statistically significant.

**Ethics**

The study was approved by the Ethics Committee of Tribhuvan University, Kathmandu. Participation was fully voluntary based on informed verbal consent. Participants diagnosed with TB or being infected with intestinal parasites were referred appropriately for treatment.

**Results**

The median time since the first diagnosis of HIV was 23 weeks (inter-quartile range, 7–36 weeks). The major modes of transmission reported were injecting drug use (41.2%) and commercial sex (36.6%). The median CD4 and CD8 T-cell count was 257/µL (inter-quartile range, 132–419) and 1010/µL (inter-quartile range, 657–1432), respectively. About 86% of the participants had a CD4/CD8 cell ratio of ≤0.5.

Of the 1807 participants, 32.4% (95% CI, 30.25–34.56) were ascertained to have pulmonary tuberculosis infection. The proportion of TB was not significantly different among males (33.8%) and females (29.5%). Among patients with PTB, 82.7% had a CD4 T-cell count of less than < 200/µL and 73.9% had a CD4/CD8 T-cell ratio of < 0.25. In the univariate analysis, patients with PTB were more likely to be older, married, and have a longer duration since the diagnosis of HIV, diarrhoea, parasitic co-infection, lower CD4T-cell count, and lower CD4/CD8 ratio. The distribution of factors across patients with and without PTB, and the measure of association in terms of corresponding unadjusted odds ratios, are shown in Table 1.
Table 1: Factors associated with tuberculosis in univariate analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients with PTB (%)</th>
<th>Patients without PTB (%)</th>
<th>Unadjusted odds ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of participants</td>
<td>585</td>
<td>1222</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Median age (Q1, Q3)</td>
<td>32(28, 36)</td>
<td>29(24, 35)</td>
<td>-</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Marital status</td>
<td>561(96.1)</td>
<td>1071(87.6)</td>
<td>3.43(2.17–5.65)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male</td>
<td>403(68.89)</td>
<td>788(64.48)</td>
<td>1.21(0.98–1.51)</td>
<td>0.06</td>
</tr>
<tr>
<td>Median duration in weeks since HIV diagnosis (Q1, Q3)</td>
<td>24(12, 36)</td>
<td>21(6–36)*</td>
<td>-</td>
<td>0.01</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>271(59.2)</td>
<td>117(12.8)</td>
<td>9.92(7.51–13.11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Parasitic infection</td>
<td>112(64.7)</td>
<td>38(8.7)</td>
<td>9.21(5.95–14.36)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Possible mode of transmission</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother to child</td>
<td>17(2.9)</td>
<td>98(8.1)</td>
<td>1(Reference)</td>
<td></td>
</tr>
<tr>
<td>Sex with partner</td>
<td>75(12.8)</td>
<td>209(17.1)</td>
<td>2.07(1.13–3.94)</td>
<td>0.011</td>
</tr>
<tr>
<td>Injecting drug use</td>
<td>255(43.6)</td>
<td>490(40.1)</td>
<td>3.00(1.78–5.27)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Commercial sex</td>
<td>237(40.5)</td>
<td>425(34.8)</td>
<td>3.21(1.90–5.65)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age group (in years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than 11</td>
<td>21(3.6)</td>
<td>106(8.7)</td>
<td>1(Reference)</td>
<td></td>
</tr>
<tr>
<td>11–20</td>
<td>6(1.1)</td>
<td>37(3.1)</td>
<td>0.82(0.28–2.13)</td>
<td>0.72</td>
</tr>
<tr>
<td>21–30</td>
<td>227(38.8)</td>
<td>584(47.8)</td>
<td>1.96(1.21–3.28)</td>
<td>0.006</td>
</tr>
<tr>
<td>31–40</td>
<td>256(43.8)</td>
<td>413(33.8)</td>
<td>3.13(1.93–5.22)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>More than 40</td>
<td>75(12.8)</td>
<td>82(6.7)</td>
<td>4.62(2.64–8.20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median CD4 T-cell count (Q1, Q3)</td>
<td>107(52, 171)</td>
<td>347(232–487)</td>
<td>-</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median CD8 T-cell count (Q1, Q3)</td>
<td>710 (443, 1085)</td>
<td>1124(778–1526)</td>
<td>-</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CD4 T-cell</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;200</td>
<td>484(82.7)</td>
<td>211(17.3)</td>
<td>51.5(34.20–79.24)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>200–350</td>
<td>74(12.7)</td>
<td>405(33.1)</td>
<td>4.10(2.61–6.57)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;350</td>
<td>27(4.6)</td>
<td>606(49.6)</td>
<td>1(Reference)</td>
<td></td>
</tr>
<tr>
<td>CD4/CD8 T-cell count ratio</td>
<td>407</td>
<td>860</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.25</td>
<td>301(73.9)</td>
<td>290(33.7)</td>
<td>10.7(6.36–18.84)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>0.25–0.5</td>
<td>90(22.1)</td>
<td>405(47.1)</td>
<td>2.29(1.33–4.13)</td>
<td>0.002</td>
</tr>
<tr>
<td>&gt;0.5</td>
<td>16(3.9)</td>
<td>165(19.2)</td>
<td>1(Reference)</td>
<td></td>
</tr>
</tbody>
</table>

* CI, confidence interval; Q1=25th quartile, Q3=75th quartile.
All the factors significantly associated with PTB in univariate analysis were included in the multiple logistic regression model. The backward stepwise logistic regression revealed that only the CD4 T-cell counts of < 200/µL and 200–350/µL, diarrhoea, parasitic infection and sex with partner as probable mode of transmission were independently associated. Participants with PTB were about 12 times more likely to have a CD4 T-cell count of < 200/µL and two-and-a-half times more likely to have a CD4 T-cell count of 200–350/µL compared with participants with a CD4 count of > 350/µL. Similarly, participants with TB were more than twice as likely to have diarrhoea and parasitic infection/infestation. However, participants with probable mode of transmission by “sex with partner” were significantly less likely to have active TB infection. The corresponding adjusted OR from multivariate analysis is shown in Table 2.

### Discussion

This is the largest study in the country to date involving participants from different risk groups to estimate the prevalence of PTB and associated factors and co-morbidities in HIV-infected people before the start of HAART. Our study revealed that about one third of the participants presenting at NPHL had a pulmonary tuberculosis infection, which suggests an alarming PTB epidemic among HIV-infected people in Nepal. Our finding is very high compared with similar studies done in Cambodia and the United Republic of Tanzania, although the Cambodian study involved active case-finding of TB in a home-care programme of HIV-infected people. It should be noted that in our study, cases of PTB included newly diagnosed as well as existing TB cases that had not commenced HAART. This may partly explain the higher prevalence observed in our study. Also, since our study participants were being assessed for HAART eligibility on the basis of CD4 T-cell count, it is clear that at least one third of HIV patients had already developed PTB before the start of HAART. Such a high TB burden adds complexity to HIV treatment as well as to treatment of TB itself. In addition, the finding has implications for the possible impact of HIV on a TB epidemic: since patients were diagnosed by positive sputum smear microscopy, it is probable that they are highly infectious and a powerful source of transmission to others in their close environment, particularly their families. Although it has been shown that patients with CD4 T-cell counts of < 200/µL may be less infectious, representing a lower risk of transmission, HIV-infected TB patients can be highly infectious in case of multi-drug resistant tuberculosis.

This study showed that the HIV-infected people attending for a CD4 T-cell count already had a very poor immune status. The median CD4 count was 257/µL and about 86% of all

### Table 2: Factors associated with tuberculosis infection (multivariate analysis)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted odds ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 T-cell count &lt;200/µL</td>
<td>11.69(6.23–21.94)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CD4 T-cell count 200–350/µL</td>
<td>2.52(1.30–4.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>2.77(1.78–4.31)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Parasitic infection</td>
<td>3.34(2.02–5.50)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>“Sex with partner” as possible mode of transmission</td>
<td>0.44(0.20–0.93)</td>
<td>0.03</td>
</tr>
</tbody>
</table>
participants had a CD4/CD8 ratio of ≤ 0.5. The fact that the median time since the diagnosis of HIV was less than six months indicates that the participants were diagnosed in late stages of the disease, which is not uncommon in resource-limited settings. The lower CD4 count was strongly associated with the higher odds of PTB. This finding suggests the extent of missed opportunity of preventing TB, probably due to a delayed start of HAART; earlier initiation, at a CD4 count of >350/µL, may have a significant effect on reducing the incidence of TB. Lower CD4 count is a well-established risk factor for development of active TB among HIV-infected people. The guideline of the World Health Organization to initiate HAART at CD4 T-cell count ≤ 350/µL should therefore be followed strictly to prevent TB or other opportunistic infections.

The lower CD4 count was strongly associated with the higher odds of PTB. This finding suggests the extent of missed opportunity of preventing TB, probably due to a delayed start of HAART; earlier initiation, at a CD4 count of >350/µL, may have a significant effect on reducing the incidence of TB. Lower CD4 count is a well-established risk factor for development of active TB among HIV-infected people. The guideline of the World Health Organization to initiate HAART at CD4 T-cell count ≤ 350/µL should therefore be followed strictly to prevent TB or other opportunistic infections.

One limitation of the study was that the PTB status in most of the participants was ascertained on the basis of sputum smear microscopy. Microscopy is a less sensitive method than culture when the bacterial load in the sputum is lower. The prevalence of PTB may therefore be marginally underestimated. In addition, we do not have data on the status of anti-tuberculosis treatment or its duration. In the scenario of treatment of TB for more than 3–4 weeks, the patient may convert to smear negative, thus leading to a further underestimation of true prevalence. Since the study was of cross-sectional nature, we have no information on the temporal relationship between diarrhoea and parasitic infection with active PTB; these variables should therefore be considered as co-morbidities rather than any indication of risk of developing TB. Data on possible modes of transmission are based on patient information. However, one of the strengths of our study is that it is based on real world observed settings.

Conclusions

We conclude that the prevalence of pulmonary tuberculosis is alarmingly high in our study population. The majority of participants had a very poor immune status as assessed on the basis of the CD4/CD8 ratio before the
initiation of HAART. The odds of PTBs were higher in participants with lower CD4 T-cell counts, diarrhoea, and intestinal parasitic infection. These findings may be useful for formulating better strategies for HIV and TB treatment programmes in the country. For example, early diagnosis of HIV infection; motivation of patients to visit CD4 T-cell count facilities as early as possible; initiation of HAART on higher threshold values of CD4 T-cell counts; and treatment of intestinal parasitic infection as an integral part of HIV programmes, may prove beneficial for better treatment outcomes.

Acknowledgements
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References
Factors associated with high prevalence of pulmonary tuberculosis in HIV-infected people in Kathmandu


Compliance of off-premise alcohol retailers with the minimum purchase age law
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\textbf{Background:} In Thailand, the 2008 Alcoholic Beverages Control Act set the minimum purchase age (MPA) at 20 years old in order to limit new drinkers as part of the overall alcohol control effort. This study aims to assess the compliance of off-premise alcohol retailers with MPA restrictions and to identify factors affecting sales to adolescents.

\textbf{Methods:} A decoy protocol was used to quantify compliance of 417 alcohol retailers from three categories, namely grocers, modern minimarts and department stores. Multi-stage sampling was applied to obtain the samples in four provinces: Bangkok, Nakorn Sawan, Songkhla and Surin. Each alcohol retailer was visited twice by 17–19 year-old male and female adolescents who tried to buy alcohol. Information collected from focus groups and in-depth interviews with vendors and management officers were analysed for the qualitative methodology.

\textbf{Results:} Of all 834 buying attempts undertaken by the underage adolescent, 98.7\% were successful in buying alcohol. Only 0.9\% were asked for age and 0.1\% were requested to show an ID card. Age and ID verifications were statistically significant to buying success as well as province, while number of vendors, gender and age of vendors and buyers, type of outlet, law cautions and advertisement signs in the outlet demonstrated no significant association.

\textbf{Conclusions:} The results showed that vendors fail to comply with the law despite the fact that they know the law. Enforcement needs to be strengthened to effectively limit new drinkers.

\textbf{Key words:} sting or decoy operation, alcohol purchase survey, law compliance, minimum purchase age (MPA).

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\textbf{Introduction}
Alcohol consumption has become more common and accepted in Thailand. The most worrisome trend is the rise in the number of new drinkers. A study in 2008 revealed that Thailand has approximately 260 000 new drinkers each year.\textsuperscript{1} Among the 12.8\% of adolescents aged 15–19 years who have become regular drinkers, 21.6\% are binge
drinkers and 40.4% are intoxicated youth drinkers. These figures have drawn the attention of concerned parties as drinking among adolescents leads to many related problems other than health, such as drug use, premature sexual intercourse, low educational performance, crime and suicide.1

The Alcoholic Beverages Control Act, in effect since 2008, attempts to deter youths from drinking by restricting the minimum purchase age (MPA) to 20 years.3 The law does not impose penalties on purchasers but instead on vendors. In fact, the responsible government authorities have been trying to promote the law and its enforcement, and civil society has increasingly launched special campaigns to emphasize its enforcement in parallel to their usual educational and awareness-raising campaigns. However, in a number of recent surveys, vendors in many provinces reported that 17–31% of their customers in the three months prior to being surveyed seemed to be underage1,4,5 and more than 50% of the general public had witnessed sales made to underage customers.6 This led to research questions about whether vendors consciously sell alcoholic beverages to underage customers and whether there are any factors that influence such illegal sales. Previous studies that evaluated law enforcement in Thailand through self-report methodologies4,5 are not able to answer these questions due to methodological limitations. An unobtrusive test purchase methodology, which has been applied in studies in other countries,7-13 is an alternative research methodology available. This study used test purchases to assess the compliance of off-premise alcohol vendors on MPA restrictions in naturalistic settings.

Methods
This study applied mixed methods of both quantitative and qualitative methodologies. To represent the population of 579,413 outlet licensees in Thailand in 2009,14 a sample size of 385 was calculated based on the assumption that 50% of retailers do sell alcohol to adolescents (95% confidence and 5% precision levels). The sample size was then increased by approximately 10% for any missing or incomplete cases, resulting in an adjusted sample size of 428. Multi-stage sampling was used to obtain the samples in four provinces. In the first-stage sampling, four provinces were purposively selected with different geographical locations and density of alcohol licensees per capita: Nakorn Sawan (northern) and Surin (north-east), with a high density of licensees per capita; and Bangkok (central) and Songkhla (south), with a low to middle density. The samples were distributed proportionally according to the number of licences registered in each province. In the second stage of sampling, main streets or business areas of these four provinces were purposively selected to increase the likelihood of achieving the specified number of samples and for feasibility of the survey.

Following several surveys conducted to enumerate and develop a map of the physical locations of the retailers, a total of 417 samples were used in this study. These were broken down as follows: Bangkok, 163 (39.2%); Nakorn Sawan, 63 (15%); Songkhla, 74 (17.8%) and Surin, 117 (28%). Alcohol retailers were classified into three categories, namely grocers, modern mini-marts and department stores. Temporary or canvas outlets, mobile sales units, restaurants and pharmacies that sold alcohol were excluded.

Independent variables in this study included province, gender of buyer and vendor, age of buyer and vendor, number of vendors, age check, ID card check, type of outlet, law caution and advertisement signs. The dependent variable was the result of a purchase attempt.
For the qualitative methodology, 29 key informants who were vendors or owners, including management staff from all outlet categories, were selected purposively from all provinces for focus groups (n=26, 13 vendors or owners and 13 management staff) and in-depth interviews (n=3, 2 vendors or owners and 1 management staff).

**Purchase protocol**

A purchase protocol was designed based on guidance from the Pacific Institute for Research and Evaluation and a data collection form was also developed. Both the protocol and the form were tested and adjusted prior to the actual purchase survey.

Recruitment of the adolescent volunteers, purchase procedure, particular brand and type of alcoholic beverage, timing of purchase and conversation dialogue were strategically and purposely planned. A total of 40 adolescents – 20 male and 20 female – who met the selection criteria were recruited. The adolescents were 17–19 years old with an appearance that matched their age. Their racial and/or ethnic characteristics were also harmonious with those of the local residents in the purchase survey sites. The adolescents received permission from their parents or guardians and submitted written consent for participation in the survey. The minimum number of adolescents participating in the survey was four males and four females and the total number varied according to the sample size in each province. A local partner organization facilitated the recruitment of the adolescents, except in Bangkok where the adolescents were recruited by the researchers. The adolescents and adult volunteers or assistant researchers were trained to note the information required for the data collection form and undertook role-play rehearsals to become acquainted with purchase procedures and dialogue before they undertook the fieldwork.

Each adolescent had a different code and was paired with an adult volunteer or assistant researcher. The adolescent volunteer was assigned to buy a particular beer brand from a particular number of alcohol outlets appearing on the map. The adult volunteer was instructed to enter the outlet before the adolescent to help observe the protocol and necessary information required for the data collection form, record the conversation between vendors and the adolescent and for security purposes. The adolescents were trained to tell the truth when challenged about their age, to carry their ID cards and to show them if requested. When the vendor sold alcohol to the adolescent, even with age or ID card verification, that purchase attempt was considered successful. If the vendor did not sell alcohol, even if they had asked for age or ID, that purchase attempt was considered unsuccessful. The adolescents were instructed to leave without complaint. Each adult/adolescent pair had to complete the data collection form immediately after each purchase attempt, in a place far from the vendor’s sight and from that of the next outlet on the list. Each outlet was visited twice by different gender adolescent volunteers.

**Ethical considerations**

The covert test purchase of alcohol and use of underage adolescents raised some significant ethical issues. The rights of the vendors were well respected although advance survey notice was not provided. The results of the study would have been invalid or distorted without the use of underage adolescents in a natural setting. This principle is in line with the International Ethical Guidelines for Biomedical Research Involving Human Subjects. Prosecution was not brought against vendors who sold alcohol to underage customers. To allay the concerns of researchers that the survey might encourage the test purchasing
adolescents to initiate future alcohol use, orientation and training were provided. In addition to permission from their parents or guardians and their written consent, the adolescents could withdraw their participation at any time. The names of all volunteers, alcohol retailers, vendors, and key informants remain confidential. This study was approved by the Ethical Committee of the Institute for the Development of Human Research Protections, Ministry of Public Health.

Data analysis
Categorical variables were descriptively analysed using simple frequencies and percentages for general information obtained from the survey such as purchase success, age and ID card verifications, category of alcohol outlet, gender, age and number of vendors. To examine associations among categorical variables, chi-square and Fisher’s exact tests were performed. Statistical significance was assessed at $p<0.05$. SPSS version 15 and STATA version 10 for Windows were used for the analysis. Content analysis of the qualitative findings of the focus groups and in-depth interviews were conducted.

Results

Characteristics of alcohol retailers
When classified into the three different outlet categories, there were 253 (60.7%) conventional grocers, 17 (4.0%) department stores and 147 (35.3%) mini-marts. At the time of purchase, 68% of the alcohol outlets had only one vendor, 32% had two or more vendors, and 67% of all vendors were female. The estimated age of a third of vendors (35%) from observation was under 30 years old. In 0.1% ($n=1$) were asked to show an ID card. 27.1% of the alcohol retailers placed alcoholic beverages in front of the outlet, 33.1% at the side, 16.5% at the back and 23.3% in other areas. The majority of the alcohol outlets did not display relevant law cautions and advertisement signs (Table 1).

Overall results of the purchase survey
Overall, 98.7% ($n=808$) of purchase attempts were successful. While three provinces had a very small proportion of sales refusals, 100% of purchase attempts in Songkhla province were successful. The proportion of successful attempts made in different outlet categories, outlets with a different number of vendors and outlets displaying law cautions and advertisement signs presented similar results (Figure 1).

Association between variables and purchase success
The study results demonstrated that the proportion of successful and unsuccessful purchases in the four provinces were statistically different. When vendors checked the age of the adolescent, the proportion of successful purchases dropped significantly from 99.3% to 28.6%. The purchase attempt was unsuccessful (0%) when the volunteer’s ID card was verified. As a consequence, the verification of age and ID card had a statistically strong association with purchase success (Table 2).

Factors that had no significant association with purchase success were the gender and age of the adolescent and the gender, age and number of vendors. The proportion of sales to adolescent girls and boys was almost equal. A similar result was found across the different ages of test-purchasing adolescents. When considering the characteristics of the vendors, the proportion of successful
### Table 1: Characteristics of alcohol retailers

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Alcohol retailers by province</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bangkok</td>
<td>163</td>
<td>39.2</td>
</tr>
<tr>
<td>Nakorn Sawan</td>
<td>63</td>
<td>15.0</td>
</tr>
<tr>
<td>Songkhla</td>
<td>74</td>
<td>17.8</td>
</tr>
<tr>
<td>Surin</td>
<td>117</td>
<td>28.0</td>
</tr>
<tr>
<td>Total</td>
<td>417</td>
<td>100.0</td>
</tr>
<tr>
<td>2. Alcohol retailers by category</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Department store</td>
<td>17</td>
<td>4.0</td>
</tr>
<tr>
<td>Grocer</td>
<td>253</td>
<td>60.7</td>
</tr>
<tr>
<td>Mini-mart</td>
<td>147</td>
<td>35.3</td>
</tr>
<tr>
<td>Total</td>
<td>417</td>
<td>100.0</td>
</tr>
<tr>
<td>3. Number of vendors in the outlet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>567</td>
<td>68.0</td>
</tr>
<tr>
<td>2</td>
<td>203</td>
<td>24.3</td>
</tr>
<tr>
<td>3</td>
<td>64</td>
<td>7.7</td>
</tr>
<tr>
<td>Total</td>
<td>834</td>
<td>100.0</td>
</tr>
<tr>
<td>4. Gender of vendor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>561</td>
<td>67.3</td>
</tr>
<tr>
<td>Male</td>
<td>273</td>
<td>32.7</td>
</tr>
<tr>
<td>Total</td>
<td>834</td>
<td>100.0</td>
</tr>
<tr>
<td>5. Estimated age of vendor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 30 years old</td>
<td>292</td>
<td>35.0</td>
</tr>
<tr>
<td>30–45 years old</td>
<td>272</td>
<td>32.6</td>
</tr>
<tr>
<td>46–60 years old</td>
<td>189</td>
<td>22.7</td>
</tr>
<tr>
<td>&gt; 60 years old</td>
<td>81</td>
<td>9.7</td>
</tr>
<tr>
<td>Total</td>
<td>834</td>
<td>100.0</td>
</tr>
<tr>
<td>6. Placement of alcohol in the outlet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Front</td>
<td>226</td>
<td>27.1</td>
</tr>
<tr>
<td>Side (left or right)</td>
<td>276</td>
<td>33.1</td>
</tr>
<tr>
<td>Back</td>
<td>138</td>
<td>16.5</td>
</tr>
<tr>
<td>Other</td>
<td>194</td>
<td>23.3</td>
</tr>
<tr>
<td>Total</td>
<td>834</td>
<td>100.0</td>
</tr>
<tr>
<td>7. Law caution in the outlet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>277</td>
<td>33.2</td>
</tr>
<tr>
<td>No</td>
<td>557</td>
<td>66.8</td>
</tr>
<tr>
<td>Total</td>
<td>834</td>
<td>100.0</td>
</tr>
<tr>
<td>8. Content of the law caution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restriction on time of sales</td>
<td>106</td>
<td>38.3</td>
</tr>
<tr>
<td>Restriction on minimum purchase age</td>
<td>170</td>
<td>61.3</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>Total</td>
<td>277</td>
<td>100.0</td>
</tr>
<tr>
<td>9. Alcohol advertisements in the outlet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>102</td>
<td>12.2</td>
</tr>
<tr>
<td>No</td>
<td>732</td>
<td>87.8</td>
</tr>
<tr>
<td>Total</td>
<td>834</td>
<td>100.0</td>
</tr>
</tbody>
</table>
purchases from male and female vendors was virtually the same (98.9% vs 98.5%) as was the percentage of sales made by vendors who appeared below 60 years old. Sales occurred in every instance when the underage adolescents bought an alcoholic beverage from vendors who were older than 60. The number of vendors in an outlet was not associated with purchase outcome; neither were the presence of law cautions or advertisement signs at the outlet.

**Highlighted findings from the qualitative method**

**Knowledge of the law**

The information collected from focus groups and in-depth interviews with vendors or owners, including management staff of alcohol outlets, revealed that most vendors knew of restrictions on the sale of alcohol, but not of the latest age restriction. Most vendors thought the MPA was still 18 years and were uncertain about penalties. On the other hand, management staff of department stores and modern mini-mart chains had a more precise knowledge of the law and reported paying serious attention to compliance with the law pertaining to the sale of alcoholic beverages. Their vendor employees were strictly instructed not to sell alcoholic beverages to underage customers.

**Reasons for illegal sales and sale refusals**

Most vendors reported that they sold alcoholic beverages to underage customers because there was no legal comeback for doing so. One vendor said that he might as well sell it to adolescents because if he didn’t, they could easily buy it from another outlet with total impunity. Sometimes, vendors asked for age if they suspected that the customer was underage, but still sold them alcoholic beverages.
### Table 2: Association between variables and purchase success

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Successful</th>
<th>Unsuccessful</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purchase attempt (%)</td>
<td>819</td>
<td>808 (98.7)</td>
<td>11 (1.3)</td>
<td>0.042*</td>
</tr>
<tr>
<td>Province</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bangkok</td>
<td>320</td>
<td>314 (98.1)</td>
<td>6 (1.9)</td>
<td></td>
</tr>
<tr>
<td>Nakorn Sawan</td>
<td>118</td>
<td>114 (96.6)</td>
<td>4 (3.4)</td>
<td></td>
</tr>
<tr>
<td>Surin</td>
<td>233</td>
<td>232 (99.6)</td>
<td>1 (0.4)</td>
<td></td>
</tr>
<tr>
<td>Songkhla</td>
<td>148</td>
<td>148 (100.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Gender of buyer</td>
<td></td>
<td></td>
<td></td>
<td>0.752</td>
</tr>
<tr>
<td>Female</td>
<td>408</td>
<td>402 (98.5)</td>
<td>6 (1.5)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>411</td>
<td>406 (98.8)</td>
<td>5 (1.2)</td>
<td></td>
</tr>
<tr>
<td>Age of buyer</td>
<td></td>
<td></td>
<td></td>
<td>0.544</td>
</tr>
<tr>
<td>17 years old</td>
<td>83</td>
<td>81 (97.6)</td>
<td>2 (2.4)</td>
<td></td>
</tr>
<tr>
<td>18 years old</td>
<td>282</td>
<td>279 (98.9)</td>
<td>3 (1.1)</td>
<td></td>
</tr>
<tr>
<td>19 years old</td>
<td>454</td>
<td>448 (98.7)</td>
<td>6 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Gender of vendor</td>
<td></td>
<td></td>
<td></td>
<td>1.000</td>
</tr>
<tr>
<td>Female</td>
<td>554</td>
<td>546 (98.6)</td>
<td>8 (1.4)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>265</td>
<td>262 (98.9)</td>
<td>3 (1.1)</td>
<td></td>
</tr>
<tr>
<td>Estimated age of vendor</td>
<td></td>
<td></td>
<td></td>
<td>0.768</td>
</tr>
<tr>
<td>&lt;30 years old</td>
<td>280</td>
<td>277 (98.9)</td>
<td>3 (1.1)</td>
<td></td>
</tr>
<tr>
<td>30–45 years old</td>
<td>271</td>
<td>266 (98.2)</td>
<td>5 (1.8)</td>
<td></td>
</tr>
<tr>
<td>46–60 years old</td>
<td>188</td>
<td>185 (98.4)</td>
<td>3 (1.6)</td>
<td></td>
</tr>
<tr>
<td>&gt;60 years old</td>
<td>80</td>
<td>80 (100.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Number of vendors present</td>
<td></td>
<td></td>
<td></td>
<td>0.386</td>
</tr>
<tr>
<td>1</td>
<td>561</td>
<td>551 (98.2)</td>
<td>10 (1.8)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>194</td>
<td>193 (99.5)</td>
<td>1 (0.5)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>64</td>
<td>64 (100.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Age check</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Not asked</td>
<td>811</td>
<td>805 (99.3)</td>
<td>6 (0.7)</td>
<td></td>
</tr>
<tr>
<td>Asked</td>
<td>7</td>
<td>2 (28.6)</td>
<td>5 (71.4)</td>
<td></td>
</tr>
<tr>
<td>ID card verification</td>
<td></td>
<td></td>
<td></td>
<td>0.013*</td>
</tr>
<tr>
<td>Not asked</td>
<td>817</td>
<td>807 (98.8)</td>
<td>10 (1.2)</td>
<td></td>
</tr>
<tr>
<td>Asked</td>
<td>1</td>
<td>0 (0.00)</td>
<td>1 (100.0)</td>
<td></td>
</tr>
<tr>
<td>Type of outlet</td>
<td></td>
<td></td>
<td></td>
<td>0.084</td>
</tr>
<tr>
<td>Department store</td>
<td>32</td>
<td>32 (100.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Grocer</td>
<td>501</td>
<td>493 (98.4)</td>
<td>8 (1.6)</td>
<td></td>
</tr>
<tr>
<td>Mini-Mart</td>
<td>286</td>
<td>283 (99.0)</td>
<td>3 (1.0)</td>
<td></td>
</tr>
<tr>
<td>Law caution</td>
<td></td>
<td></td>
<td></td>
<td>0.354</td>
</tr>
<tr>
<td>None</td>
<td>550</td>
<td>544 (98.9)</td>
<td>6 (1.1)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>269</td>
<td>264 (98.1)</td>
<td>5 (1.9)</td>
<td></td>
</tr>
<tr>
<td>Advertisement sign</td>
<td></td>
<td></td>
<td></td>
<td>0.633</td>
</tr>
<tr>
<td>None</td>
<td>719</td>
<td>710 (98.7)</td>
<td>9 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>100</td>
<td>98 (98.0)</td>
<td>2 (2.0)</td>
<td></td>
</tr>
</tbody>
</table>

*Statistically significant \( P<0.05 \) at 95% confidence level.
It was also found that illegal sales were partially related to culture. Parents or senior staff often instruct their children or subordinates to perform tasks for them, including buying alcoholic beverages. Vendors of local grocers reported that they sold alcoholic beverages to children because they knew the adult drinker, were familiar with their family members, and believed that the alcohol was not intended for the child or adolescent in question.

The main reason cited for refusing a sale was apprehension regarding the law. However, inconsistencies in practice were found for vendors who asked for age and ID. During peak time, age and ID verification was not performed. Almost all vendors believed that the decision to sell was primarily based on the morals of the vendor.

**Perspectives on enforcement of the law and suggested measures to prevent illegal sales**

Most vendors had a relatively positive attitude toward MPA. They strongly supported law enforcement but felt that awareness of its importance, equity, wider coverage of enforcement and more stringent penalties were necessary. Random checks by authorized entities would encourage compliance. Advertisements and public campaigns run on a regular basis could help stimulate vendors to be cautious when selling alcoholic beverages to young customers.

Vendors did not consider themselves a cause, but rather a consequence of youth drinking. Therefore, they suggested a law against alcohol purchase and possession by adolescents, and reflected that the law should impose penalties on the adolescents, as well as their parents, to prevent illegal purchase. It was also noted that while basic knowledge of the relevant law should be provided, the authorities concerned should work more proactively to ensure that all vendors – particularly those in remote areas – are aware of this law. This would also facilitate the imposition of penalties.

**Discussion**

The primary aim of this study was to assess the compliance of alcohol retailers with the law in different outlet categories and in naturalistic situations. As a consequence, the methodology and findings of the study are unique among the limited pool of research into law enforcement and illegal sales to underage customers in Thailand. Our study also provides the results of test purchases in cases when law cautions and advertisements were displayed in the outlet, whereas other studies, both locally and internationally, have not paid attention to these two variables. Thus, there were no comparable data.

The findings of this study have similarities and disparities with other international studies. Generally, the proportion of purchase success is consistent with the results of studies in other countries although the figures in Thailand are much higher. The underage adolescents had very little difficulty in obtaining alcoholic beverages, with a very low risk of being challenged for proof of age. This is similar to the results of studies in São Paulo, Brazil, and Washington, DC, United States of America where the proportions of purchase success were as high as 80% and 97% respectively. The findings of the study in Brazil were also consistent with our study in that the age and gender of the adolescent and the type of alcohol outlet did not influence purchase success, while a study in the Netherlands found that underage female adolescents were more successful with alcohol purchases than males. It would be interesting to study further the effectiveness of MPA in different countries and characteristics of interventions that could promote sustainable enforcement of this particular restriction.
With regards to the age of the adolescent and the vendors, this study did not show any significant relationship of these two variables with purchase success, while the study in Brazil found that vendors older than 30 years were seven times more likely to refuse sales to underage customers. Concerning the number of vendors in the outlet, one study observed that sales to underage customers were more likely when the vendor was alone. In contrast, this study found that sales were less likely when there was only one vendor in the outlet, although this relationship is not statistically significant.

We also reflected on the unexpected result in Surin. Despite major campaigns and strong networks of civil society organizations working actively for alcohol control at the provincial level, the purchase success in Surin was very high at 99.6%. A preliminary recommendation would be for such campaigns and networks to try to focus on promoting law enforcement, rather than raise public awareness of the harms of alcohol and to change people’s attitudes towards drinking alcohol in general. This proposal is in line with a report from an evaluation of the status and direction of alcohol control campaigns in Bangkok during 2010–2011.

Limitations of the study
A major difficulty was being able to identify whether or not the samples (alcohol outlets) studied actually held a sales licence. Inclusion and exclusion criteria were clearly established to increase the chance of having a proper sample. Moreover, it was considered that alcohol outlets in certain physical locations would normally hold sales licences. In addition, we could not use the physical addresses of the alcohol outlets officially registered because it could not be proved that they were actually operating at the registered address and in what category. Thus, a map of the physical locations of alcohol outlets was created, based on an enumeration survey undertaken by the researchers. Lastly, it is quite common for grocers to provide a few tables for their customers, but this is for occasional use and not mainly for on-premise alcohol consumption. These grocers were therefore included in the survey, but were very small in number. Thus, the study limitations were dealt with effectively to reduce any possible influence on the results.

Conclusions and recommendations
The results of our study reflect that law enforcement, in respect of MPA restrictions, still needs to be strengthened despite the fact that the Alcoholic Beverages Control Act has been in effect since 2008. Age and ID card verifications are effective interventions to limit access to alcoholic beverages of underage adolescents. When the vendors asked for age, sales of alcohol to the adolescents dropped to approximately one third, whereas ID card verification led to a complete sales refusal. Alcohol retailers should therefore be encouraged to perform age and ID card verifications when faced with young customers to help prevent youth drinking.

This study also suggests that many parties concerned with law enforcement should cooperate to reduce sales to adolescents. The potential benefits of enforcement of MPA restrictions are substantial and the costs are low. The Excise Department could contribute by emphasizing the restriction on sales to underage persons when a licence is granted. A range of practical interventions ranging from simple to complex should be considered, such as enclosure of law caution stickers and leaflets with the licence, brief verbal introductions to the law, guidance on what to do when encountering young customers and
licensee meetings. A short training course as a prerequisite for alcohol sales licensees would also help promote and raise awareness of the law. In addition to the existing penalties under the Alcoholic Beverages Control Act, the licence should be terminated when alcohol retailers infringe the law. Increased monitoring and enforcement activities, such as random visits and warning letters, by enforcement or regulatory-related authorities could also lead to positive changes in age and ID card verification practices. Campaigners, communities, mass media and civil society could also contribute actively to reducing illegal sales to minors. Campaigns specifically addressing the MPA, community-based interventions with multisectoral partnerships, and media advocacy can all be part of the overall effort to prevent underage alcohol sales and related problems. References


External quality assessment in blood group serology in the World Health Organization South-East Asia Region

Patravee Soisangwana

**Background:** The quality of blood transfusion services (BTS) is essential for the treatment of patients who need blood or blood products. BTS involve several steps, including the acquisition of the donor’s blood, blood grouping, unexpected antibody screening, blood storage, transfusion, etc. There is a need to check the effectiveness of all elements in the BTS can be assessed and monitored by an external quality assessment.

**Aim:** To assess and evaluate the performance of ABO and Rh(D) blood grouping and unexpected antibody screening of the selected World Health Organization (WHO) South-East Asia Region Member country laboratories.

**Methods:** WHO Collaborating Centre on Strengthening Quality of Health Laboratories (Thailand) organized a regional external quality assessment scheme for blood group serology (REQAS-BGS) between 2002 and 2008 for laboratories in countries of the WHO South-East Asia Region. Test items for ABO and Rh(D) blood groupings and unexpected antibody screening and identification were distributed three cycles per year to BTS laboratories in Bangladesh, Bhutan, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka and Thailand. By the end of the project, a total of 20 BTS laboratories had participated for differing lengths of time.

**Results:** It was found that 87.5%, 93.3%, 81.3%, 92.3%, 100% and 87.5% of laboratories returned the test results in 2002, 2003, 2004, 2006, 2007 and 2008, respectively. Laboratories with excellent quality or a trend of quality improvement for ABO and Rh(D) blood grouping, unexpected antibody screening and identification during the six years were 60% (12/20), 50% (10/20), 52.9% (9/17) and 81.8% (9/11), respectively. At the initiation of the scheme, most laboratories were using substandard methods for ABO and Rh blood groupings, i.e. performing only direct blood grouping alone but subsequently adopted the standard methods, i.e. performing both direct and reverse blood groupings.

**Conclusion:** REQAS-BGS in South-East Asia countries has been useful for assessing, monitoring and improving the quality of testing. Challenges such as high costs and regulatory requirements for international shipment of blood samples could be solved by amending the regulation(s) for shipment, or establishing a national EQAS.

**Key words:** Regional external quality assessment scheme (REQAS), blood transfusion services, laboratories, quality, ABO, Rh(D) blood grouping, unexpected antibody screening and identification.

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Introduction

The quality of laboratory investigation results is essential for the treatment of patients, monitoring the progress of disease, and disease prevention and surveillance. The quality of the results in the blood transfusion services (BTS) is critical since the human blood product is directly transfused to patients. Any error in the test result (false negative or false positive) can have serious consequences including death of the recipients. To achieve a continuous quality system in BTS, the effectiveness of all critical associated elements should be assessed, using both internal and external mechanisms. Internal assessment can be done by the use of batch controls, staff competency testing and audits. But evaluation of the whole process in a laboratory, requires an external quality assessment (EQA). EQA can be conducted by delivering test items of known compositions that closely simulate the clinical materials to participating health laboratories and subsequently comparing their results. EQA has several objectives: (i) assess laboratory performance and the ability to determine the correct results; (ii) identify any errors in the laboratory; (iii) stimulate laboratory personnel to improve their performance and the use of standard methods; and (iv) encourage the establishment and implementation of quality systems with the relevant standards.

To minimize errors in the blood banking procedures, the WHO’s Regional office for South-East Asia has been implementing effective quality assurance for BTS in Member countries since 1998. This external quality assessment scheme (EQAS) is recognized as an important tool for laboratory quality improvement. EQAS data are also recognized by accreditation bodies as important elements for meeting quality standards for laboratory quality as per ISO 15189 and ISO/IEC 17025.

WHO EQA schemes have been established in the main areas of testing in transfusion laboratory practice by the United Kingdom National External Quality Assessment Service (UK-NEQAS). Because of the absence of national EQAS in SEAR countries, a regional EQAS was initiated by WHO’s Regional office for South-East Asia to create awareness among the countries and to provide them with technical support to set up and improve the quality of their performance. Accordingly, a Regional External Quality Assessment Service in Blood Group Serology (REQAS-BGS) was organized in 2002 by the Bureau of Laboratory Quality Standards (BLQS), Department of Medical Sciences, Thailand (WHO Collaborating Centre on Strengthening Quality of Health Laboratories) to strengthen BTS in SEAR countries. All countries participated, except the Democratic People’s Republic of Korea and Timor-Leste since these two countries lacked BTS and experienced difficulties with the shipment route of the test items. The aim of the REQAS-BGS project was to evaluate the performance of the laboratories for ABO and Rh blood grouping and unexpected antibody screening and identification of the participating laboratories during 2002–2008.

Materials and methods

In this cross-sectional, retrospective study in a 20 laboratories from nine SEAR countries participated. Each laboratory was given a confidential code number, which was used for performance evaluation reporting of data results. Data on evaluation were made available only to the respective participating laboratory and to the coordinator at the WHO South-East Asia Regional Office (SEARO). A breakdown of the laboratories participating in the EQA scheme is shown in Table 1.
The packed red cells and converted sera used in the preparation of the test items were provided by the National Blood Center, Thai Red Cross Society (the WHO Collaborating Centre for Training in Blood Transfusion Medicine). They were tested negative for HBV, HCV and HIV infections and syphilis. The test items were prepared for samples of ABO and Rh(D) blood groupings and unexpected antibody screening test (screening) and identification.

For each distribution cycle, three sets of the test items (red blood cell suspensions and corresponding ABO blood group sera) were distributed to the designated laboratories. Three serum samples (negative or positive for a single or mixed unexpected antibody) for screening and identification were also sent in the same shipment. The test sets were dispatched 15 times, three distribution cycles per year during 2002–2008, to each laboratory by courier in non-cold package condition (Table 1). Participating laboratories in India received the test items through SEARO during distribution cycles 3–15. Details of the test items distributed are shown in Table 2.

The participating laboratories were requested to conduct only the tests currently available in their routine services. Laboratory performance evaluation was based on the status of report return within the closing date, completeness of the test data, the standard...
method for the test, patterns and degrees of cell agglutination, consistency of agglutination pattern, blood group interpretation and detection, and type of unexpected antibody. The results were compared with the consensus modes derived from the Thai-NEQAS results. Professional judgment by the Expert Committee (comprising the experts from the Thai National Red Cross Society, Deans of the Faculty of Medical Technology and Faculty of Allied Health Sciences of the Thai universities, etc.) was used for the final decision when consensus mode could not be calculated. The REQAS test items were the same sample sets organized for the Thai-NEQAS. The overall scores for performance evaluation of each testing were calculated from the results of the three test items in each distribution cycle. A full score for each testing was 4.0. Quality ranking was based on the full score, i.e. excellent (4.0), very good (3.5–3.99), good (3.0–3.49), borderline (2.5–2.99), and unacceptable (< 2.49).

A performance evaluation report for each distribution cycle with suggestions and comments for improvement was submitted to the individual participants. A summary report, which included the data of all participants’ performance and types of reagents, was also dispatched to all participants for review and comparison of their performance with the others. To ensure confidentiality, participating laboratories received a summary of the evaluation report without mentioning names of the laboratories.

### Table 2: Details of the test items distributed to participating laboratories

<table>
<thead>
<tr>
<th>Distribution cycle</th>
<th>ABO1</th>
<th>ABO2</th>
<th>ABO3</th>
<th>Rh 1</th>
<th>Rh 2</th>
<th>Rh 3</th>
<th>UnAb 1</th>
<th>UnAb 2</th>
<th>UnAb 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>AB</td>
<td>A</td>
<td>O</td>
<td>Pos</td>
<td>Neg</td>
<td>Pos</td>
<td>Neg</td>
<td>Anti-D</td>
<td>Neg</td>
</tr>
<tr>
<td>2</td>
<td>O</td>
<td>AB</td>
<td>A3</td>
<td>Pos</td>
<td>Neg</td>
<td>Pos</td>
<td>Anti-Mia</td>
<td>Neg</td>
<td>Neg</td>
</tr>
<tr>
<td>3</td>
<td>AB</td>
<td>O</td>
<td>A</td>
<td>Pos</td>
<td>Neg</td>
<td>Weak-D</td>
<td>Neg</td>
<td>Anti-D</td>
<td>Neg</td>
</tr>
<tr>
<td>4</td>
<td>Subgroup B</td>
<td>AB</td>
<td>O</td>
<td>Pos</td>
<td>Neg</td>
<td>Pos</td>
<td>Neg</td>
<td>Neg</td>
<td>Anti-E</td>
</tr>
<tr>
<td>5</td>
<td>O</td>
<td>B</td>
<td>A</td>
<td>Neg</td>
<td>Pos</td>
<td>Pos</td>
<td>Anti-D</td>
<td>Neg</td>
<td>Neg</td>
</tr>
<tr>
<td>6</td>
<td>B</td>
<td>AB</td>
<td>O</td>
<td>Pos</td>
<td>Neg</td>
<td>Pos</td>
<td>Neg</td>
<td>Anti-D</td>
<td>Neg</td>
</tr>
<tr>
<td>7</td>
<td>B</td>
<td>AB</td>
<td>O</td>
<td>Pos</td>
<td>Weak-D</td>
<td>Pos</td>
<td>Anti-Mia</td>
<td>Anti-D</td>
<td>Neg</td>
</tr>
<tr>
<td>8</td>
<td>A</td>
<td>A</td>
<td>O</td>
<td>Pos</td>
<td>Neg</td>
<td>Neg</td>
<td>Anti-E</td>
<td>Neg</td>
<td>Neg</td>
</tr>
<tr>
<td>9</td>
<td>A</td>
<td>B</td>
<td>O</td>
<td>Pos</td>
<td>Neg</td>
<td>Weak-D</td>
<td>Neg</td>
<td>Neg</td>
<td>Anti-E+ Anti-C</td>
</tr>
<tr>
<td>10</td>
<td>A</td>
<td>B</td>
<td>O</td>
<td>Neg</td>
<td>Pos</td>
<td>Pos</td>
<td>Anti-Mia</td>
<td>Neg</td>
<td>Neg</td>
</tr>
<tr>
<td>11</td>
<td>O</td>
<td>O</td>
<td>A</td>
<td>Pos</td>
<td>Neg</td>
<td>Pos</td>
<td>Anti-Mia</td>
<td>Anti-D</td>
<td>Anti-E</td>
</tr>
<tr>
<td>12</td>
<td>O</td>
<td>B</td>
<td>AB</td>
<td>Weak-D</td>
<td>Neg</td>
<td>Pos</td>
<td>Neg</td>
<td>Anti-D</td>
<td>Anti-D</td>
</tr>
<tr>
<td>13</td>
<td>A</td>
<td>B</td>
<td>O</td>
<td>Neg</td>
<td>Pos</td>
<td>Neg</td>
<td>Neg</td>
<td>Anti-D</td>
<td>Anti-Mia+anti-Leb</td>
</tr>
<tr>
<td>14</td>
<td>B</td>
<td>O</td>
<td>AB</td>
<td>Neg</td>
<td>Pos</td>
<td>Pos</td>
<td>Neg</td>
<td>Anti-D</td>
<td>Neg</td>
</tr>
<tr>
<td>15</td>
<td>A</td>
<td>A</td>
<td>O</td>
<td>Pos</td>
<td>Neg</td>
<td>Weak-D</td>
<td>Anti-D</td>
<td>Anti-D</td>
<td>Neg</td>
</tr>
</tbody>
</table>

Neg, negative; Pos, positive; UnAb, unexpected antibody screening test and identification.
Results

At the beginning of the project, 15 laboratories from nine countries participated. Two additional laboratories from Bangladesh and one from Maldives joined the project to replace those that withdrew at the 8th, 9th and 10th cycle. The total number of participating laboratories in the REQAS-BGS project was 20 (Table 1). Because certain laboratories did not always receive the test items, mainly due to customs clearance problems, the percentage of laboratories that returned reports was calculated based on those that received the test items, not on the total number of delivery cycles. It was found that 14 of 20 (70%) laboratories returned results for every set of tests received. Two laboratories reported on two tests (ABO and Rh blood grouping), 7 laboratories reported on three tests (ABO, Rh blood grouping and unexpected antibody screening) and 11 reported on all four tests (ABO, Rh blood grouping, unexpected antibody screening and identification) (Table 3).

Test items showing mixed-field agglutination, i.e. A3 and B subgroups, were sent to participating laboratories. Only 1 of 14 laboratories reported the correct A3 subgroup result, the remainder reporting A blood group without the mixed-field agglutination, and while all laboratories identified B blood group, only 2 reported the correct subgroup.

Performance evaluation was calculated based on the system used for the Thai national EQAS in blood group serology currently conducted by BLQS for individual testing. The evaluation method was developed by the Bureau of Laboratory Standards accredited according to ISO/IEC 17043 by NATA, Australia. Participating laboratories followed testing manual. For ABO blood grouping, three laboratories showed consistently excellent quality for all cycles while four had unacceptable performance in at least one distribution cycle caused by either the use of a substandard method (cell grouping only), incorrect ABO blood grouping, inconsistent results between cell and serum groupings, or incomplete records of the results in the report form. For Rh(D) blood grouping, two laboratories showed consistently excellent quality for all cycles, whereas 11 had unacceptable performance in at least one distribution cycle. The main causes of the errors were the use of a substandard method to identify weak-D, incorrect Rh(D) blood group, or incomplete records of the results (Table 4).

Performance evaluation for unexpected antibody screening showed that 3, 6 and 11 laboratories reported on no, some and all distribution cycles, respectively. Of the 11 complete reports, the results of 3 laboratories were excellent and 8 were

<table>
<thead>
<tr>
<th>No. of tests</th>
<th>Type of test</th>
<th>No. of countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>ABO and Rh(D) blood grouping</td>
<td>2 Maldives (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nepal (1)</td>
</tr>
<tr>
<td>3</td>
<td>ABO, Rh(D) blood grouping and unexpected antigen screening</td>
<td>7 Bangladesh (3), Maldives (2), Myanmar (1), Nepal (1)</td>
</tr>
<tr>
<td>4</td>
<td>ABO, Rh(D) blood grouping, unexpected antigen screening and identification</td>
<td>11 Bangladesh (1), Bhutan (1), India (4), Indonesia (2), Myanmar (1), Sri Lanka (1), Thailand (1)</td>
</tr>
</tbody>
</table>

Table 3: Details of tests reported by participating laboratories for the performance evaluation
of unacceptable quality. The major cause of errors was false-negative results. The ratio of negative to false positive in all errors was 21:4. Only three laboratories successfully identified the unexpected antibody for all distribution cycles, 8 laboratories reported for some distribution cycles and 9 did not report. Four of the 6 laboratories that only returned reports in certain distribution cycles had excellent quality for all returned results. The unacceptable quality was due to false-positive, false-negative, unidentified and reported mixed types of antibody reports.

The status of the quality system in each laboratory was determined by analysing the quality ranking of each testing. The status was classified into three groups, i.e. excellent quality for all cycles; showed a trend of quality improvement; and showed no significant quality improvement. The number of laboratories classified into each group is shown in Table 5.

**Discussion**

The REQAS-BGS project was first initiated in SEAR in 2002 under the auspices of SEARO. A major challenge encountered was the shipment of the test items to certain countries due to regulations relating to the importation of potentially infectious materials, and to infrequent flights from Bangkok to the destination. In addition, multiple steps to clear the test samples from customs, despite prior arrangement of the delivery process in accordance with the International Air Transport Association (IATA) regulations, resulted in delayed deliveries, non-deliveries and deterioration of the test samples. These delays were reduced in later cycles, which may have been due to better planning and management of the delivery schedules and more awareness and experience of the individuals involved. Moreover, the delivery of batch materials to a designated collaborator for forwarding to participating laboratories in the same country would significantly reduce transportation costs as well as the delivery time.

Although the test items were shipped outside the cold chain, we carried out random checks on the homogeneity and stability of the aliquots stored or transported at room temperature in all 15 distribution cycles, to ensure that the samples were still acceptable if they reached their destination five days after dispatch.

**Table 4: Number of laboratories with unacceptable quality and the main causes of the errors**

<table>
<thead>
<tr>
<th>ABO</th>
<th>Rh</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unacceptable quality at least in 1 of 15 distribution cycles</td>
<td>4</td>
</tr>
<tr>
<td>Cause of error</td>
<td>• use of substandard method (cell grouping only)</td>
</tr>
<tr>
<td></td>
<td>• reported incorrect ABO blood grouping</td>
</tr>
<tr>
<td></td>
<td>• inconsistent results between cell and serum groupings</td>
</tr>
<tr>
<td></td>
<td>• incomplete record of results in report form</td>
</tr>
</tbody>
</table>
All the 20 BTS laboratories nominated to participate in the project were well-established with responsibility for the supply of blood products within their respective countries. However, they are not representative of all laboratories in the country in the majority of cases. Their performance evaluation in the REQAS-BGS project reflects their current and potential competency in BTS, and should be used to promote a fully functioning quality system for the acquisition and transfusion of the blood products needed by the patients.

The REQAS-BGS project involved the performance evaluation of four routine tests in BTS, i.e. ABO and Rh(D) blood grouping, and unexpected antibody screening and identification. Only 11 of 20 laboratories from seven Member countries – Bangladesh, Bhutan, India, Indonesia, Myanmar, Sri Lanka and Thailand – provided results on all the four tests. Furthermore, not all laboratories performed the standard ABO blood grouping procedures (both cell and serum grouping), either because they lacked the standard cells or because they were unable to differentiate the weak-D grouping. The latter is essential to prevent the transfusion of weak-D blood to a Rh-negative patient which would result in production of the corresponding antibodies.\(^7\)

Since the five laboratories that could not correctly identify the weak-D blood group probably performed only the immediate spin method, it is recommended that the indirect antiglobulin test be used for correct blood group identification. This test is needed for cross-matching in all BTS laboratories.

With regard to the test items with mixed-field agglutination, initially only 1 reported the correct A3 and 2 laboratories reported the correct B subgroups. However, after receiving the evaluation results, most laboratories reported the correct results in subsequent delivery cycles. This showed that the BTS laboratories could improve their competency for blood groups with irregular reactions.

BTS laboratories must be able to screen and identify unexpected antibodies in patients in order to select blood products without the corresponding antigen. This is essential to avoid any transfusion reaction or antibody responses that may result in further difficulty in selecting blood products, especially for patients with thalassemia.\(^8,9\) In this study, unexpected antibody screening test could be performed by 18 participating laboratories, among which 11 could perform the antibody identification. Nine laboratories prepared

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**Table 5: Summary of the quality status of laboratories from the performance evaluation results (Answer: right)**

<table>
<thead>
<tr>
<th></th>
<th>ABO blood grouping</th>
<th>Rh blood grouping</th>
<th>Unexpected antibody screening</th>
<th>Unexpected antibody identification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent quality for all cycles</td>
<td>4 (20.0%)</td>
<td>2 (10.0%)</td>
<td>4 (23.5%)</td>
<td>5 (45.4%)</td>
</tr>
<tr>
<td>Trend of quality improvement</td>
<td>8 (40.0%)</td>
<td>8 (40%)</td>
<td>5 (29.4%)</td>
<td>4 (36.4%)</td>
</tr>
<tr>
<td>No significant trend of quality improvement</td>
<td>8 (40.0%)</td>
<td>10 (50%)</td>
<td>8 (47.1%)</td>
<td>2 (18.2%)</td>
</tr>
<tr>
<td>Total number of laboratories</td>
<td>20</td>
<td>20</td>
<td>17</td>
<td>11</td>
</tr>
</tbody>
</table>
their own screening cells but only 2 of them reported the correct results. False-negative results, especially anti-Mia, were reported by laboratories that did not have the screening cells for the antibody. Since anti-Mia is common in Asian populations, screening cells that can detect the antibody should be available in BTS laboratories in SEAR.\textsuperscript{10–12} The REQAS-BGS project stimulated laboratory quality in the participating BTS since many of them have started to procure the appropriate screening and panel cells for their routine use, and have improved the quality of their services by evaluating the root causes of error.\textsuperscript{13} However, it is expected that the cost would be significantly reduced if laboratories could prepare their own cells since commercial cells are expensive and normally short-lived. The preparation of standardized cells should be obtainable from the selected local donor panel and this would facilitate the use of the standard method of blood grouping and provide an easy and low-cost supply of the standard cells.

Even though some laboratories reported the correct BGS results, the number of test items was small compared with the number of the samples routinely tested in which an error could occur. Samples that give inclusive results by cell grouping alone need to be retested with the serum grouping technique. Therefore, an appropriate quality system must be established for most accurate and efficient laboratories.

Continuous training in both quality and academic aspects of BTS has been provided to laboratories since the initiation of the quality management training project by SEARO in 2001. However, a number of BTS still require quality improvement. Indeed, the WHO global database on blood safety summary report 2011 indicates that 47% of donations are tested in laboratories without quality assurance.\textsuperscript{14}

Since 2002, BTS staff from 9 of the 11 SEAR Member countries have received WHO grants for training on the establishment of EQAS in BGS and laboratory quality systems. These countries should thus have sufficient knowledge and experience to establish their own EQAS rather than relying on regional or international quality assessment networks. This would not only provide all local laboratories with quality performance assessment and an overall BTS quality management record at the national level, but also future planning of quality improvement by policy-makers.

Presently, Bhutan has begun to provide national EQAS in BGS. India has EQAS for blood banking, although this service is available only for transfusion-transmitted infectious markers.\textsuperscript{15} Some Member countries, such as India, Indonesia and Thailand, have already established strong laboratory quality systems as well as an accreditation body, which could facilitate and promote the improvement of quality systems in sister countries.

WHO has been promoting quality assurance in countries of the Region since the 1980s. Several consultations and workshops have stimulated countries to practise quality assurance with emphasis on internal quality control and EQAS.\textsuperscript{16}

**Conclusions**

The results of our project point to the importance of quality systems and continuous quality assessment, both internal and external, in BTS laboratories. The limitations and obstacles in organizing REQAS should encourage policymakers and responsible institutions to initiate EQAS at the national instead of the regional level. The retrospective data can also be used to follow up improvements in the BTS quality systems to sustain the success of participating laboratories in the REQAS-BGS project.
External quality assessment in blood group serology in the
WHO South-East Asia Region

References


Jeevan B Sherchanda, W William Schluter, Jatan B Sherchan, Sarmila Tandukar, Jyoti R Dhakwa, Ganga R Choudhary, Chandeshwar Mahaseth

Background: Rotavirus as a causative agent of childhood diarrhea is known to cause serious illness among children less than 5 years of age. This study examined the epidemiology of rotavirus disease burden and diversity of G and P genotypes of rotavirus in Nepal.

Methods: Stool samples were tested for rotavirus by Enzyme Immuno Assay and Group A rotaviruses were detected by using both ELISA and RT-PCR in 2718 samples between 2009 and 2011.

Results: Rotavirus was more frequently detected among inpatients (28.5%) than outpatients (15.2%). Over the three-year study period, 653 (24.4%) cases were positive for rotavirus by ELISA. Genotyping by RT-PCR was done on 638 samples. The most prevalent genotype was G12P [6] (60.4%). Mixed infections were not uncommon (14% in 2009, 29% in 2010 an 7% in 2011). However, 41 were partially typed and 23 were completely untyped over the study period.

Conclusions: This study highlights the rotavirus disease burden and diversity of rotavirus strains circulating in Nepal. Continued sentinel surveillance will provide useful information to policy makers with regard to rotavirus vaccine introduction.

Keywords: Human rotavirus, prevalence, genotype, RT-PCR

Introduction

Worldwide, rotavirus is the most common cause of severe gastroenteritis among infants and young children.1,2 While diarrhea is the second most common cause of fatal childhood illness, about 1.34 million deaths occur worldwide among children aged less than 5 years due to rotavirus.3,4 Though the incidence of rotavirus infection among children in developed and developing countries is similar; outcomes vary widely with 82% of fatalities estimated to occur in developing countries.5 Each year, rotavirus causes approximately 111 million episodes of acute gastroenteritis requiring home care, 25 million clinic visits, and 2 million hospitalizations5 in the U.S. and Europe.3

Rotavirus belongs to the Reoviridae virus family and the virion comprises of three concentric protein layers. The outer capsid consists of two proteins, VP7 and VP4 that are used to classify rotavirus strains into G (glycoprotein) and P (protease sensitive)
genotypes, respectively. Of the 12 G and 15 P genotypes known to infect humans, genotypes G1P[8], G2P[4], G3P[8], G4P[8] and G9P[8] cause over 90% of rotavirus disease worldwide.9

Two effective rotavirus vaccines, a single-strain attenuated human rotavirus vaccine (Rotarix, GlaxoSmithKline Biological) and a multi-strain bovine-human reassortant vaccine (RotaTeq, Merck and Company) are now available. WHO recommends the inclusion of rotavirus vaccines in all national routine immunization schedules. In countries where diarrheal deaths account for ≥10% of mortality among children <5 years of age, the introduction of rotavirus vaccine is strongly recommended.10 Efficacy of these vaccines has ranged from 80% to 98% in industrialized countries, including Latin America, and 39% to 77% in developing countries, such as Africa and Asia.3,4

The present study summarizes the findings from three years of hospital-based rotavirus sentinel surveillance in Nepal and the epidemiology of rotavirus gastroenteritis and characterizes circulating rotavirus strains among children aged less than five years in Nepal.

**Material and methods**

**Clinical methods**

Children presenting to the pediatric emergency unit of Kanti Children’s hospital were screened for diarrhea by the treating medical officer or nurse. Children aged less than 60 months with acute diarrhea and from whom stool sample could be recovered within 24 hours of hospitalization were recruited. Ethical approval was obtained from the Institutional Review Board (IRB), Institute of Medicine, Tribhuvan University, Kathmandu, Nepal. The study was explained to the caregivers and written informed consent obtained.

**Study setting, sample and data collection:** This study was conducted between January 2009 to December 2011 in Tribhuvan University, Institute of Medicine, Public Health Research Laboratory, Maharajgunj, Kathmandu, Nepal.

Case enrollment was done on the basis of inclusion and exclusion criteria among children visiting Kanti Children’s hospital with symptoms of acute watery diarrhea, fever, vomiting, and abdominal pain. All children less than five years of age who were admitted for treatment of acute gastroenteritis diarrhoea and/or vomiting with or without intake of medications were included. Diarrhoea was defined by the occurrence of three or more liquid stools in a 24-hour period and presence of diarrhea at the time of clinical presentation with admission to the inpatient diarrheal treatment unit. The exclusion criteria were as follows: Hospital-acquired diarrhea, which was defined as onset of diarrhea more than 48 hours after hospitalization; bloody diarrhea; and chronic and/or persistent diarrhea, which was defined as diarrhea that lasted for more than two weeks.

**Sampling:** A total of 2718 stool samples were collected. Specimens were stored at −70°C until analysed using ELISA and molecular methods. All case-based data and clinical information was recorded on a standardized questionnaire and was analyzed using EPI-Info software.

**Measurement variables:** Data were collected using a pre-coded data collection tool. Variables included child’s age, sex, symptoms, and duration of symptoms, water source, and home hand washing practices, diarrhea contacts, housing facilities, education
and occupation of the caregiver, temperature of the child, hydration status, and rotavirus results.

**Rotavirus detection:** The specimens were tested by a solid-phase sandwich-type enzyme immunoassay method (Rotavirus Ag ELISA, Pro Spect, USA).

**Rotavirus Genotyping**
Detection of rotaviruses in clinical specimens and determination of the G-type and P-type was accomplished by extraction of the viral RNA from fecal specimens and analysis by reverse-transcription polymerase chain reaction (RT-PCR) with primers specific for the VP7 genes of G serotypes 1, 2, 3, 4, 8, 9, 10, and 12 and VP4 genes of P serotypes 4, 6, 8, 9, 10 and 11. Rotavirus genotyping was done in collaboration with Christian Medical College, Vellore – Rotavirus Regional Reference Laboratory and WHO Collaborating Centre, India. A total of 638 samples were rotavirus positive [2009 (n=221), 2010 (n=151), and 2011 (n= 266)] and were analyzed by RT-PCR method described by Gouvea et al. and Gunasena et al.12

**Results**

**Epidemiology of Rotavirus**
From January 2009 to December 2011, 2718 cases meeting the enrollment criteria were evaluated for rotavirus. Of these 653 (24.0%) cases were positive for rotavirus by EIA, among the positive cases, 638 samples were processed for genotyping by RT-PCR.

**Clinical Presentation among Hospitalized Children**
Abdominal pain was the most common symptom among the 2718 children with diarrhea. (See Table 1). Approximately 25% of cases with each of the evaluated symptoms were found to be positive for rotavirus. The degree of dehydration among rotavirus cases was more likely to be moderate to severe rather than mild.

**Distribution of rotavirus by EIA**
Rotavirus was detected by EIA among 25.4% (230/906) in 2009, among 23.9% (195/815) in 2010 and among 22.7% (228/997) in 2011. The predominant strain was G12P [6] during all three years of the study period, (45.7% in

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**Table 1: Clinical presentation in hospitalized patients**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>No. cases</th>
<th>Rotavirus positive cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>2439 (98.7%)</td>
<td>583 (23.9%)</td>
</tr>
<tr>
<td>Fever</td>
<td>1392 (51.2%)</td>
<td>327 (23.4%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>1310 (48.1%)</td>
<td>352 (26.8%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1315 (48.3%)</td>
<td>367 (27.9%)</td>
</tr>
<tr>
<td><strong>Degree of dehydration</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>261 (9.6%)</td>
<td>34 (13.02%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>1881 (66.7%)</td>
<td>487 (25.8%)</td>
</tr>
<tr>
<td>Severe</td>
<td>535 (19.7%)</td>
<td>123 (22.9%)</td>
</tr>
</tbody>
</table>

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Figure 1: Month-wise distribution of rotavirus from 2009 to 2011

Month wise distribution of rotavirus positive in hospitalized children

Rotavirus among hospitalized children showed a seasonal distribution with the highest percent of diarrhea cases caused by rotavirus during the winter months from December to March. The month with the highest percentage of rotavirus positive cases was January (38.5%) in 2009, February (53.4%) in 2010, and April (34.9%) in 2011.

Age and year-wise distribution of rotavirus positive cases in hospitalized children

Hospitalization and enrollment of children 0 to 11 months was more common than among older aged children. In 2009, rotavirus was most commonly identified (28.1%) among children 0 to 11 months, whereas the rates of rotavirus as the cause of diarrhea among hospitalized children was more common among children 12–23 months of age in 2009 (35.5%) and in 2011 (26.7%).

Distribution of major combination of G and P types of rotavirus in hospitalized children

The most common circulating genotype in the population under surveillance was G12P [6] (45.7% in 2009, 28.5% in 2010 and 30% in 2011) over the three-year investigation, though the mixed type was slightly higher in 2010 (29.8%).
Discussion

Diarrhea continues to be a major public health problem and leading cause of death in developing countries.\textsuperscript{11-16} The present study is a continuation of a prospective study among children less than five years of age with diarrhea evaluated at Kanti Children’s Hospital, which is the only government-supported children’s hospital in Nepal. The majority of the children who tested positive for rotavirus antigen had clinical features of diarrhea, vomiting, and moderate to severe dehydration. Overall, the prevalence of rotavirus during the three-year study period was 24.0\% which is similar to previously published studies from the same institution,\textsuperscript{17-22} but comparatively lower than evaluations at other study sites.\textsuperscript{2,5,7,8} Fever and vomiting were more often associated with rotavirus infection compared to other causes of diarrhea.\textsuperscript{11} Rotavirus was a major cause of pediatric gastroenteritis and was the underlying etiology of diarrhea for one-fourth of children 6 to 24 months of age hospitalized with an acute diarrheal illness.\textsuperscript{23}

The present study found a clear seasonal pattern of acute rotavirus gastroenteritis that peaked in winter, i.e., December to February (31.3\%, 35.4\%, and 30.6\% in year 2009, 2010, and 2011, respectively) followed by early spring i.e. March to May, (31.3\%, 32.9\%, and 26.1\% in 2009, 2010, and 2011, respectively) with only 15.3\% in both summer (June to August) and autumn (September to November), which is in contrast to similar study conducted in Nepal 2006.\textsuperscript{19}
Global epidemiologic surveys have identified G1P [8], G2P [4], G3P [8], G4P [8], and G9P [8] as the most common G/P genotype combinations associated with diarrhea in humans. However, recent studies in developing countries have shown increased identification of a high proportion of rotavirus strains with unusual G/P combinations, which may have implications for vaccine efficacy.24,25 The genotypic distribution pattern from this study identified G12P[6] as the predominant strain (35.1%), with G2P[4] strains as the second most common genotype identified (17.7%) over the three years study. G1P[8], which is the single strain present in the licensed Rotrix oral vaccine9 was the third most common strain identified among 8.3% of all specimens. This strain was uncommon in 2009 (2.7%). G1P [6] was the fourth most common type identified but was uncommon in 2010 (2.0%), but relatively more common in 2011 (10.2%). Thus, variations were found to occur in genotype distribution from year to year over the three-year study period. Results from other countries differ from ours.2,3,6,8,26 In this study, the strain G9P6 that occurred only in year 2010 (6.6%) and was the predominant strain in a study from India in 1996.27 The incidence of G9 with either P[8] or P[6] was also reported by Jain et al in 2001 to be 17% in stool samples collected from hospitals in Bhopal, New Delhi, Davengere, Lucknow, Nagpur and Shimla from 1996 to 1998.28

<table>
<thead>
<tr>
<th>Genotypes</th>
<th>Year</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2009</td>
<td>2010</td>
</tr>
<tr>
<td>G1P[8]</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>G12P[4]</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>G12P[6]</td>
<td>101</td>
<td>43</td>
</tr>
<tr>
<td>G12P[8]</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>G2P[4]</td>
<td>32</td>
<td>7</td>
</tr>
<tr>
<td>G1[4]</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>G1P[6]</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>G2P[8]</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>G2P[6]</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>G3P[8]</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>G9P[8]</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>G9P[4]</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>G9P[6]</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Mixed</td>
<td>31</td>
<td>45</td>
</tr>
<tr>
<td>Partially typed</td>
<td>16</td>
<td>19</td>
</tr>
<tr>
<td>Untyped</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>221</td>
<td>151</td>
</tr>
</tbody>
</table>
G12 genotype was first detected in the Philippines,\textsuperscript{6} and appears to be more prevalent in recent years in developing countries.\textsuperscript{29} This study demonstrates that a variety of different rotavirus types circulate simultaneously in Nepal.

The observation of G and P strains identified in this study suggests the circulation of various rotavirus strains in Nepal and may help to characterize the antigenic variation of the rotavirus. In the present study, the third most frequent circulating genotypes in the population under surveillance were mixed genotypes. High mixed infection with different rotavirus strains may reflect frequent contamination of water sources with rotavirus strains that facilitate generation of novel rotavirus strains through a re-assortment process.\textsuperscript{29} Non-typeable rotavirus strains were present in 3.6\% over the three-year study period. Partially typed virus strains were identified in 6.4\% of children with acute diarrhea. The presence of mixed genotypes may indicate infection because of poor sanitation or transmission of recombinant strains transferred from animals to humans.\textsuperscript{30, 31}

Our study has some limitations. Firstly, in the laboratory, we did not examine for all pathogens but only for rotavirus and enteric adenoviruses in addition to pathogens for which routine screening is performed according to hospital protocols. Results of these investigations have provided evidence of the burden of disease associated with rotavirus, but did not determine an etiology for nearly half of all diarrheal cases. Additional examinations for noroviruses, sapoviruses, astroviruses, and a variety of enteric bacteria would be needed to complete this picture. Secondly, the sentinel-hospitals the only government children’s hospital in the country and may not be representative of admissions to smaller or private hospitals. It is possible that children with uncomplicated diarrhea are admitted less often to referral centers. Thirdly, this study was based on a single sentinel site representing a catchment population of about three million, which does not represent complete scenario of the nation to ward rotavirus disease burden in Nepal.

This year-round surveillance of rotavirus genotypes will contribute to identifying important and emerging strains of rotavirus among Nepalese children. Continuation and expansion of laboratory-based rotavirus sentinel surveillance in other areas of Nepal is likely to yield important information for improved public health control of rotavirus associated outbreaks, as well as aid in the tracking of changes in strains that cause serious diarrhea among infants and young children.

**Conclusions**

There is high disease burden of rotavirus gastroenteritis among children less than five years of age. Genotyping analysis highlights that the existence of significant diversity of rotavirus strains with unusual G and P combinations. Therefore, rotavirus sentinel surveillance and genotyping will provide important background information for decision-making about whether to introduce rotavirus vaccine into Nepal National Immunization Program.

**Recommendation**

In Nepal, we have no information about the medical and social costs either to parents, for treatment of their children when they are ill with rotavirus diarrhea, or to the health sector, for the direct medical care provided by the government. Such an analysis might help advance the case for a rotavirus vaccine and establish the economic value of routine immunization. In addition, we have no exact information about the cost of
vaccines currently licensing (Rota Teq; Merck and RotaRix; GlaxoSmithKline) and their effectiveness in developing Asian countries like Nepal. Hence, we recommend continuing the rotavirus surveillance in other sentinel site of Nepal to obtain more information and to represent national scenario of rotavirus disease burden estimation, which can strongly support-evidence based decision making on vaccine introduction, monitor serotype/genotype distribution, and allow evaluation of vaccine impact after vaccine introduction.

Acknowledgements
We express our profound gratitude to WHO for supporting this study. We are also grateful to WHO Collaborating Center, CMC Vellore for confirmation of genotyping samples.

Conflict of interest
None to declare

References

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Research brief

Evidence of HPV subtypes linked with cervical cancer in Nepal

Chop L Bhusal, Sulochana Manandhar, Meeta Singh, Aarati Shah, Sushharma Neupane, Dibesh Karmacharya, Kate Cuschieri, Heather Cubie, Duncan C Gilbert, Sameer M Dixit

Objectives: Cervical cancer is the commonest malignancy among women in Nepal but data are limited on which subtypes of human papillomavirus (HPV) are associated with cancer in this population. Now that vaccines against HPV types 16 and 18 are available, this evidence is of vital importance in obtaining further support for a vaccination programme.

Methods: Cervical swabs from 44 histologically confirmed invasive cervical cancer cases were obtained from two tertiary referral hospitals in Nepal. Evidence of HPV subtypes was identified using an HPV multiplex polymerase chain reaction (PCR), and confirmed at the Scottish HPV Virus Reference Laboratory.

Results: HPV types 16 and 18 were present in 70% of samples, along with other high-risk subtypes. HPV 6 and 11 were not observed. Epidemiological data assessment appeared to indicate that patient age, age of marriage and age of first pregnancy were associated with increased HPV infection in patients.

Conclusions: This study provides further evidence of the importance of HPV types 16 and 18 in cervical cancer in Nepal and adds support to a nationwide vaccination programme and the use of HPV detection in screening programmes.

Key words: Cervical cancer, HPV, Nepal, multiplex polymerase chain reaction

Introduction

Cancer of the cervix is responsible for the greatest number of cancer deaths among women in Nepal, with up to 2000 deaths per annum. Unlike in more developed countries, where comprehensive screening programmes have contributed to reduced incidence and mortality, cancers in Nepal tend to present at advanced stage with significant associated morbidity and mortality.

It is appreciated that worldwide the majority of cervical cancers are associated with infection with high-risk, oncogenic subtypes...
of human papillomavirus (HPV), acquired through sexual contact. Viral oncogenes E6 and E7 downregulate p53 and pRb, respectively, resulting in cellular proliferation and a malignant phenotype.

The development of vaccines for HPV has brought into focus the precise nature of this association in terms of which subtypes are prevalent in which populations. Preliminary data from Nepal from 54 women with invasive cervical cancer demonstrated HPV-16 in 68.5% and HPV-18 in 22.2%, the next most frequent subtype being HPV-45 (in 5.6% patients). This is broadly in keeping with similar population studies from India and Pakistan and in a wider context the United States of America and the United Kingdom. Provisional experiences of instigating an HPV vaccination programme in Nepal have been encouraging with 99.3% of 1096 girls completing the course of 3 doses of Gardasil®.

To further support the introduction of HPV vaccination in Nepal, we present here data on the presence of oncogenic high-risk HPV subtypes from 44 invasive squamous cell carcinomas of the uterine cervix from Nepal.

Methods

This work has approval from the Ethical Review Board of the Nepal Health Research Council, Ministry of Health and Population, Government of Nepal.

Cervical swab samples were collected from the cervix of women fulfilling inclusion criteria using sterile cytobrushes and immediately inserted into a container containing phosphate buffer saline (PBS) as transport medium and stored at 4–8 °C. Sample vials were brought to room temperature and vortexed vigorously to detach the exfoliated cells. Deoxyribonucleic acid (DNA) was extracted using the GeneALLRibo-Spin VRD Kit (GeneAll, China). Briefly cells were lysed by lysis buffer followed by vortexing. DNA was precipitated and captured on spin columns, then washed with buffers RBW and RNW, each followed by centrifugation. Finally the purified DNA was eluted in DNase/RNase free water. The DNA was stored at -20 °C until used for polymerase chain reaction (PCR).

HPV-specific multiplex PCR was carried out using Seeplex HPV4A ACE screening kit. Following the manufacturer’s instructions, 3 μl of undiluted extracted DNA was used as template DNA in sample tubes to make the final volume of 20 μl. Negative and positive controls provided were included in each assay. PCR thermocycling was performed: 5 μl of each PCR product was electrophoresed in 2% agarose gel along with the DNA marker provided with the kit. The result was visualized under ultraviolet illumination and the bands were analysed in the reference of marker DNA (Figure 1). The result was considered valid only in the presence of the distinct band of the internal control indicating PCR success.

Results for HPV types 16 and 18 were validated and samples further genotyped at the Scottish HPV Virus Reference Laboratory, Edinburgh. Samples were assessed using a multimetrix HPV genotyping kit.

Results

Of the 44 cervical samples analysed, 82% (36) showed HPV infection by PCR, of which 80% were HPV-16 or 18. Eleven HPV types, including nine high-risk groups, were observed in this study. Types 42 and 43 are not considered high-risk but were identified in the samples. HPV 16 and 18 DNA was identified in 68% of the total sample and 83% of HPV positive samples. The prevalence of other types in the population were observed at a much lower percentage (Table 1).
In terms of histological subtypes, 35 of 44 were squamous cell carcinomas. Of these, 78% were positive for HPV DNA while for adenocarcinoma \((n=9)\), HPV infection rates were 22%. The majority of cases in this cohort \((n=39)\) were stage I or II with only five cases in advanced stage (III/IV) carcinoma.

The majority of patients in this study had married at an early age with 29 of the 41 patients, where data were available, having been married prior to the age of 18 (Nepal’s legal age of marriage until 2002 was 16). Out of these 29 patients, 25 had evidence of HPV (86%). Eight of the 12 respondents who reported marrying later than aged 18 showed evidence of HPV (67%), though this does not reach statistical significance (Fisher’s exact test \(p=0.2\)). More respondents reported having a child under \((n=22)\), as opposed to
Evidence of HPV subtypes linked with cervical cancer in Nepal

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older (n=19) than 18 years of age. Within the two groups, those that became pregnant at an earlier age had a higher HPV infection prevalence (61%) than those in the second group (39%).

Discussion

The data presented here confirm earlier findings that the majority of cancers of the cervix in Nepal are associated with HPV infection, and furthermore that HPV-16 and -18 represent the major subtypes responsible. Specifically, 36 of 44 (82%) cases demonstrated the presence of HPV infection. HPV-16 was present in 22 cases (61% of HPV-positive tumours) and HPV-18 in 8 cases (22%); the remaining cases demonstrated the involvement of multiple subtypes.

Combined with the limited previous data, this comprises 98 cases of invasive cervical cancer from Nepal. Of these, 83 (85%) were associated with HPV infection, namely HPV-16 in 59 cases (71% HPV positive, 60% all cervical cancers) and HPV-18 in 20 cases (24% and 20% respectively). Therefore, 80% of cervical cancers in Nepal are theoretically preventable with currently available vaccines.

Marriage and pregnancy at an early age both appear to be linked to a higher likelihood of HPV infection in cervical cancer cases in this study. This concurs with data from a previous publication, where early age at first sexual intercourse (AFSI), early age at first marriage (AFM) and early age at first pregnancy (AFP) were linked to higher incidence of HPV infection and cervical carcinoma in women of developing countries.

While effective screening programmes have reduced morbidity and mortality from cancer of the cervix in the developed world, a multitude of challenges beset the introduction of such a programme across Nepal. Indeed, a previous study reported low rates of compliance with colposcopy following abnormal screening results. As a result, mortality and morbidity from cervical cancer remain unacceptably high. The development and successful clinical introduction of HPV vaccines, however, present a major opportunity to make inroads into cancer prevention in Nepal.

Furthermore, HPV DNA typing can benefit screening programmes. DNA typing in cervical cancer screening is used in many countries; results from large randomized controlled trials testing for HPV DNA suggest that most women with cervical cytologic abnormalities should be assessed using this form of screening. The role of HPV screening in neighbouring India has been widely discussed.

In summary, these results are consistent with those from elsewhere in South Asia and the wider world and should provide further support for the introduction of an HPV vaccination programme across Nepal. Work to assess HPV infection rates in the healthy female population of Nepal should be extended to identify high-risk HPV types in the population and facilitate early screening to achieve comprehensive prevention of cancer of the cervix.

Acknowledgements

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References


Institutionalizing district level infant death review: an experience from southern India
Sanjeev Upadhyaya\textsuperscript{a}, Sudeep Shetty\textsuperscript{b}, Selva S Kumar\textsuperscript{c}, Amol Dongre\textsuperscript{d}, Pradeep Deshmukh\textsuperscript{e}

\textbf{Background:} An Infant Death Review (IDR) programme was developed and implemented in two districts of Karnataka.

\textbf{Objective:} We explored the processes that led to the development of the IDR programme with a view to improving the existing pilot programme and to ensuring its sustainability.

\textbf{Methods:} A sequential mixed-methods design was followed in which quantitative data collection (secondary data) was followed by qualitative data collection (in-depth interviews). Quantitative data were entered using EpiInfo (version 3.5.1) software and qualitative data were analysed manually.

\textbf{Results:} Apart from ascertaining the cause of infant deaths, the IDR Committee discusses social, economic, behavioural and health system issues that potentially contribute to the deaths. As a result of the IDR programme, key actors perceived an improvement in infant death reporting at district level, the development of a rapport with the local community, and elaboration of a feedback system for corrective actions. This has led to improved health care during pregnancy.

\textbf{Conclusions:} We found that involvement of the different stakeholders in planning and implementing the IDR programme offered a platform for collective learning and action. Impediments to the success of the programme need to be addressed by corrective actions at all levels for its future sustainability.

\textbf{Key words:} Verbal autopsy, infant death, rural, district, India.

\textbf{Introduction}

The infant mortality rate (IMR) is universally regarded as an important indicator of the health and economic status of communities, and the effectiveness of maternal and child health services. According to the Sample Registration System (SRS) of India, IMR in Karnataka, a southern state of India, was 38 per 1000 live births in 2010.\textsuperscript{1} India’s National Population Policy (2000) envisions reducing IMR to less than 30 per 1000 live births,\textsuperscript{2} echoing Millennium Development Goal 4 to reduce under-five mortality by two thirds between 1990 and 2015.\textsuperscript{3} Cause-of-death data are critical to formulating good public health programmes; developing national, regional, and global policies; and implementing

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and evaluating public health action.\textsuperscript{4,5} In developing countries, most deaths are neither attended by physicians nor certified medically, so two thirds to three quarters of the world’s population remain outside any systematic mortality surveillance.\textsuperscript{6–10} Studies in Asia and Africa in the 1950s and 1960s used systematic interviews with physicians to assess causes of death,\textsuperscript{11} a technique that the Narangwal project in India later labelled verbal autopsy (VA); the method subsequently evolved, particularly during the 1970s when the World Health Organization (WHO) discussed lay reporting of health information by people with no medical background.\textsuperscript{11–14} Today, VA remains the best available approach to assess the cause of death in communities in which most deaths occur at home. Separate questionnaires for neonatal, child, maternal, and other adult deaths have been suggested.\textsuperscript{15} The need for an infant death audit system was therefore crucial to map the rise or decline in infant deaths, to identify common causes of death, as well as for prioritization of actions, fund allocation and monitoring and evaluation.

The United Nations Children’s Fund (UNICEF), Hyderabad, India in partnership with the Department of Health and Family Welfare Services, Karnataka, has been implementing a pilot Infant Death Review (IDR) programme to strengthen the district health system review of infant deaths. So far, the research on verbal autopsy has focused on technical aspects such as the development of standardized tools, validated algorithms and computerized algorithms.\textsuperscript{14,16} However, for VA methods to extend their reach successfully from research to routine application, feasibility demonstration at local level and implementation research have been suggested to resolve emerging challenges as the programme develops.\textsuperscript{17} Hence, we explored the processes leading to the development of the IDR programme within the health system, and the perspectives of key programme actors at various levels. We hope that our findings may be useful to refine the pilot programme, and for health-care systems that wish to implement a similar programme in a developing country context.

Material and methods

Setting

The present study on the Infant Death Review programme was carried out in Raichur and Dakshina Kannada districts of Karnataka. These two districts were chosen in consultation with the Director of the National Rural Health Mission, Karnataka, based on the performance of its health system. Raichur district, located 413 km north of the state capital Bangalore with a population of 1 924 773, has poor health indicators and a female literacy rate of 49.6%. On the other hand, Dakshina Kannada, 347 km west of Bangalore, has a population of 2 083 625 with better health indicators and 84% female literacy. The crude birth rate of Karnataka was 19.2 per 1000 population with 34.1% home deliveries.\textsuperscript{1,18} This review was done during February and March 2012.

Method

A sequential mixed-methods design was followed where quantitative data collection (secondary data) was followed by qualitative data collection (in-depth interviews).

To begin with, verbal autopsy forms and the minutes of meetings and reports related to the programme were reviewed. Reports from 566 infant deaths from both districts from January to June 2011 were obtained from the district health system. Following quantitative analysis of the verbal autopsy records, 38 in-depth interviews (IDI) were conducted at district and sub-district level with health-care providers who were actively involved in programme activities and willing to participate freely.
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(Table 1). Semi-structured guidelines were used to conduct the interviews, the purpose of which was to explore the respondents’ experiences related to the IDR programme. Interviews were conducted at a date, time and place convenient for the respondents. With their permission, interviews were audio recorded and transcribed verbatim. The interviewer (second author) was sensitized to qualitative data collection.

**Data analysis**

Quantitative data was entered using Epi-Info (version 3.4.3) software. The proportional mortality was calculated for neonatal and post-neonatal periods. The inter-observer reliability between the Medical Officer and the district Infant Death Review Committee for causes of death was assessed by kappa statistics. This measures the agreement between two or more observers taking into account that they may agree or disagree purely by chance. For qualitative data analysis, structural coding was done using codes such as process, questionnaire design, its administration, mortality classification, ascertainment of cause of death and forces ‘for’ and ‘against’ the IDR programme. Transcripts were reviewed and a list of codes worked out. Manual content analysis was done and text data were presented under each coding category. Data collection and analysis was supervised by a public health expert who was trained in handling qualitative data. Findings of the analysis were reviewed by other authors to ensure their completeness and trustworthiness. Statements ‘for’ and ‘against’ the programme were calculated for different levels of health-care providers.

Informed consent was obtained from the respondents of the IDI. Permission for this review was obtained from the Director of the National Rural Health Mission, Karnataka.

**Results**

**Analysis of verbal autopsy records**

Based on the prevalent infant mortality rates applied by the state to the rural district of

### Table 1: Category of respondents and number of in-depth interviews conducted

<table>
<thead>
<tr>
<th>Respondents</th>
<th>Dakshina Kannada</th>
<th>Raichur</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>District level</strong> – District Health Officer, Reproductive and Child Health (RCH) Officer, District RCH Programme Assistant, members of faculties of Community Medicine and Paediatrics of affiliated medical colleges</td>
<td>3</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td><strong>Peripheral health institutions</strong> – Medical officers, lady health visitors, auxiliary nurse midwives</td>
<td>10</td>
<td>9</td>
<td>19</td>
</tr>
<tr>
<td><strong>Village level</strong> – Accredited social health activists, anganwadi workers</td>
<td>4</td>
<td>7</td>
<td>11</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>17</td>
<td>21</td>
<td>38</td>
</tr>
</tbody>
</table>
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We expected 1208 infant deaths to be reported during January to June 2011. However, only 566 infant deaths were reported – 447 (79%) from Raichur and 119 (21%) from Dakshina Kannada – for which we obtained verbal autopsy information.

Of the 556 infant deaths, 316 (55.8%) were male and 250 (44.2%) were female; 451 (79.7%) belonged to parents who had below-poverty-line cards provided by the state government. Scheduled castes/scheduled tribes (SC/ST) accounted for 239 (42.2%) of the deceased infants, more than half of whom occurred in Raichur. Noteworthy is the breakdown between the two districts: 42% infant deaths in Raichur took place at home, the next highest proportions being in private health facilities (28.8%), government health facilities (19.9%) and in transit (9.6%). In Dakshina Kannada, 36.2% infant deaths took place in government health facilities followed by private health care facilities (32.8%), at home (18.9%) and in transit (12.1%) (Table 2).

Regarding the category of infant deaths in each district from January to June 2011, Dakshina Kannada reported 83 (69.7%) neonatal and 36 (30.3%) post-neonatal deaths, while Raichur reported 294 (65.8%) neonatal and 153 (34.2%) post-neonatal deaths (Tables 2 and 3).

As ascertained by the district IDR Committee, the most common causes of infant deaths in Dakshina Kannada were pneumonia (19.3%), birth asphyxia/injury (13.4%), congenital malformations (12.6%), low birth weight (9.2%) and prematurity (8.5%). Overall, the inter-code reliability between cause of death as ascertained by medical officers and the District IDR sub-

### Table 2: Sociodemographic characteristics of deceased infants in Raichur and Dakshina Kannada districts, January to June 2011

<table>
<thead>
<tr>
<th>Socio demographic characteristics</th>
<th>Raichur (n=447)(%)</th>
<th>Dakshina Kannada (n=119)(%)</th>
<th>Total (n=566)(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>241 (53.9)</td>
<td>75 (63.0)</td>
<td>316 (55.8)</td>
</tr>
<tr>
<td>Female</td>
<td>206 (46.1)</td>
<td>44 (37.0)</td>
<td>250 (44.2)</td>
</tr>
<tr>
<td><strong>Socioeconomic status (colour of ration card)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Above poverty line</td>
<td>72 (16.1)</td>
<td>43 (36.1)</td>
<td>115 (20.3)</td>
</tr>
<tr>
<td>Below poverty line</td>
<td>375 (83.9)</td>
<td>76 (63.9)</td>
<td>451 (79.7)</td>
</tr>
<tr>
<td><strong>Caste</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>109 (24.4)</td>
<td>31 (26.1)</td>
<td>140 (24.7)</td>
</tr>
<tr>
<td>Scheduled caste/Scheduled tribe</td>
<td>207 (46.3)</td>
<td>32 (26.9)</td>
<td>239 (42.2)</td>
</tr>
<tr>
<td>Other backward classes</td>
<td>70 (15.7)</td>
<td>21 (17.6)</td>
<td>91 (16.1)</td>
</tr>
<tr>
<td>Others</td>
<td>61 (13.6)</td>
<td>35 (29.4)</td>
<td>96 (17.0)</td>
</tr>
<tr>
<td><strong>Place of death (n=543; n₁=427 and n₂=116)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>178 (41.7)</td>
<td>22 (18.9)</td>
<td>200 (36.8)</td>
</tr>
<tr>
<td>Government health facility</td>
<td>85 (19.9)</td>
<td>42 (36.2)</td>
<td>127 (23.4)</td>
</tr>
<tr>
<td>Private health facility</td>
<td>123 (28.8)</td>
<td>38 (32.8)</td>
<td>161 (29.7)</td>
</tr>
<tr>
<td>Transit</td>
<td>41 (9.6)</td>
<td>14 (12.1)</td>
<td>55 (10.1)</td>
</tr>
</tbody>
</table>
In Raichur, the most common causes of death as ascertained by medical officers were birth asphyxia/injury (26.2%), pneumonia (17.4%), and congenital malformations (11%) (Table 4).

**Processes leading to the development of the IDR programme**

(i) Preparatory process: In March 2010, UNICEF Hyderabad organized a national consultative workshop on Infant Death...
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Review in Bangalore in collaboration with the Government of Karnataka. Experts at the workshop discussed the VA questionnaire, mortality classification and developed guidelines for IDR implementation at district level, and in July 2010 the programme was initiated. This involved government health-care providers; programme managers from RCH and the department of Women and Child Development; paediatrics and community medicine specialists from medical colleges; and representatives from private hospitals involved in the planning process of the IDR programme. The workshop participants finalized the verbal autopsy tool and guidelines for the IDR programme.

(ii) Questionnaire design: a comprehensive verbal autopsy questionnaire for neonatal and post-neonatal deaths was developed in consultation with experts as a checklist with filters based on existing tools and literature. It was a simple colour-coded questionnaire (pink for newborn deaths and yellow for post-neonatal deaths) in the local language Kannada. The questionnaire was pre-tested on a sample of 12 deaths to incorporate local words and terms. The VA tool consisted of 17 pages including 3 pages for writing descriptive notes such as case summaries. It covered comprehensive information on socio-demographic characteristics, antenatal, natal and postnatal care and health-care seeking

Table 4: Causes of death ascertained by Medical Officer in Raichur, Karnataka

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Neonatal period No. (%)</th>
<th>Post-neonatal period No. (%)</th>
<th>Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth asphyxia/injury</td>
<td>116 (39.5)</td>
<td>1 (0.7)</td>
<td>117 (26.2)</td>
</tr>
<tr>
<td>Congenital malformations</td>
<td>28 (9.5)</td>
<td>21 (13.7)</td>
<td>49 (11.0)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>1 (0.3)</td>
<td>6 (3.9)</td>
<td>7 (1.5)</td>
</tr>
<tr>
<td>Feeding problem</td>
<td>4 (1.4)</td>
<td>3 (2.0)</td>
<td>7 (1.5)</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>5 (1.7)</td>
<td>0 (0)</td>
<td>5 (1.1)</td>
</tr>
<tr>
<td>Infection of central nervous system</td>
<td>0 (0)</td>
<td>12 (7.8)</td>
<td>12 (2.7)</td>
</tr>
<tr>
<td>Low birth weight</td>
<td>18 (6.1)</td>
<td>1 (0.7)</td>
<td>19 (4.3)</td>
</tr>
<tr>
<td>Malnutrition related death</td>
<td>0 (0)</td>
<td>7 (4.6)</td>
<td>7 (1.6)</td>
</tr>
<tr>
<td>Neonatal sepsis</td>
<td>39 (13.3)</td>
<td>2 (1.3)</td>
<td>41 (9.2)</td>
</tr>
<tr>
<td>Others</td>
<td>4 (1.4)</td>
<td>13 (8.5)</td>
<td>17 (3.8)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>22 (7.5)</td>
<td>56 (36.6)</td>
<td>78 (17.4)</td>
</tr>
<tr>
<td>Postnatal aspiration</td>
<td>3 (1.0)</td>
<td>3 (2.0)</td>
<td>6 (1.3)</td>
</tr>
<tr>
<td>Prematurity</td>
<td>14 (4.8)</td>
<td>1 (0.6)</td>
<td>15 (3.4)</td>
</tr>
<tr>
<td>Respiratory distress syndrome</td>
<td>26 (8.8)</td>
<td>0 (0)</td>
<td>26 (5.8)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sudden death</td>
<td>3 (1.0)</td>
<td>8 (5.2)</td>
<td>11 (2.5)</td>
</tr>
<tr>
<td>Unknown</td>
<td>11 (3.7)</td>
<td>19 (12.4)</td>
<td>30 (6.7)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>294 (65.7)</strong></td>
<td><strong>153 (34.3)</strong></td>
<td><strong>447 (100)</strong></td>
</tr>
</tbody>
</table>

*Others include accidents, homicide, and severe form of kernicterus
behaviour to capture the context in which the death occurred.

(iii) Capacity-building at various levels: Training started with a consultation of officials from the State Directorate and a few districts, followed by rapid training courses at district and sub district levels. At district level, an initial launch meeting was conducted to sensitize all stakeholders, including medical colleges, professional bodies, and other public service departments (e.g. Women and Child Development) in both districts. A separate sensitization programme on modalities of reporting infant deaths at the community and facility level was conducted for the Indian Academy of Paediatrics chapter in Dakshina Kannada and for the Indian Medical Association in Raichur. A one-day training programme was organized for all medical officers separately in each district on administration of verbal autopsy and ascertainment of cause of death.

Skill-building was carried out by reviewing all verbal autopsy questions in an interview in the local language, with illustrations on how to ascertain the cause of death based on diagnostic criteria. Following this, a few trained, skilled and motivated medical officers were identified by the district RCH officer to conduct further training for auxiliary nurse midwives, lady health visitors and other paramedical staff at taluk level. Medical officers of primary health centres sensitized anganwadi workers (AWW) and accredited social health activists (ASHA) under their service area. In order to create awareness of the IDR programme, Gram-panchayat (local self-government) members, leaders of women’s self-help groups, and representatives from local nongovernmental organizations were sensitized in specific training sessions.

(iv) Information on infant deaths: Village workers such as AWW and ASHA were asked to report details of infant deaths to the Medical Officer of the Primary Health Centre (PHC) on a short form called the First Information Report (FIR). In addition, they should send a Short Message Service (SMS) to a unique mobile number at district headquarters. In one Raichur district block, the district health system with support from UNICEF provided self-addressed and printed postal envelopes for reporting FIR.

(v) VA administration and cause of death ascertainment: The Medical Officer was asked to pay a home visit and interview the close carer of the deceased infant within 15 days of its reporting to ascertain the cause of death. The completed VA forms were then forwarded to the district Infant Death Review subcommittee (IDRSC). This committee consisted of the District Health Officer, district RCH officer, paediatricians from regional medical colleges, public health experts, district programme managers from the department of Women and Child Development, and medical officers from peripheral health centres.

In Dakshina Kannada, during monthly IDR Committee meetings, all the submitted VA forms and clinical case records of the deceased infants available from parents were discussed. In addition to ascertaining the cause of death, IDRSC discussed socioeconomic factors and events related to pregnancy, delivery, postnatal period, health-care seeking, gaps in the health system and health-care services. In Raichur, IDRSC reviewed only selected cases of infant deaths from community and hospital settings. The cases were selected on the basis of completeness of records, geographical location and cause of death. IDRSC provided feedback to peripheral health institutions regarding common causes of infant deaths and implementation of strategies tailored to local needs. The proceedings of IDRSC were submitted to the district IDR Committee to refine needs-based strategies to prevent infant deaths.
(vi) Positive and negative effects of the Infant Death Review system and options for improvement

Positive elements of the IDR system for the district health authorities and medical college faculties were their new partnership and the involvement of regional medical colleges in planning, implementation and training. This created a rapport with the local community and improved infant death reporting. Forces ‘against’ the programme were an initial lack of motivation at district and peripheral level to the new initiative, incomplete information in verbal autopsy reports, late reporting, lengthy form, and overburdened staff. Options suggested for future sustainability were to make the VA reporting form more concise, to train district level staff and medical officers and to improve health-care facilities.

Health workers of peripheral health institutions reported that the identification of gaps in the health-care system and financial incentives for AWW and ASHA to report deaths had contributed to infant death reporting. They also saw an opportunity to educate family members on the prevention of infant deaths. On the negative side, these health workers felt overburdened with their existing workload, and suffered from poor cooperation from caregivers and a lack of transport facilities. Options to redress this situation included financial incentives for medical officers to complete verbal autopsies, improved logistics, and forming sub district committees where infant deaths are high.

Anganwadi and ASHA workers noted that, as a result of the IDR programme, they had more information on the causes of infant deaths, and had feedback. This in turn had improved antenatal care. However, they have to face poor cooperation from caregivers, including occasional anger. These village workers considered that the arrival of a medical officer in the village to conduct verbal autopsy confers a sense of importance to issues related to infant deaths (Table 5).

Discussion

Decision-makers and programme managers need simple data that can be linked to improving the provision of care. These potential users of verbal autopsy methods have different perspectives from researchers, tending to prefer simple VA instruments for their feasibility and programme relevance over technical performance. Our study explored the different perspectives of district health authorities, staff of the Primary Health Centre and village-level staff as key actors in the IDR programme. This contextual knowledge is useful for health-care managers and planners for ensuring programme sustainability. In particular, we noted that health system managers sought concrete and programme-relevant data, implying an interest in the socioeconomic determinants of mortality.

The Survey of Causes of Death by the Registrar General of India has been merged with the Sample Registration System, resulting in a modified verbal autopsy method with physician review. The current SRS sample size does not allow sub district level estimation of IMR, which varies across districts. Thus, a reduction in the average IMR in a State does not provide a complete picture of mortality decline, necessitating identification of high mortality-prone areas and planning innovative strategies for IMR reduction in these areas. Hence the need for sub-district ‘infant death audit systems’ to gain accurate and reliable estimates for planning at the district and sub-district level.

Our study proposes a feasible approach to strengthen the existing health-care system at district level. We found that the involvement of stakeholders – the
Table 5: Forces ‘for’ and ‘against’ the IDR programme at various levels

<table>
<thead>
<tr>
<th>Stakeholder</th>
<th>Perceived advantage</th>
<th>Perceived impediment</th>
<th>Options for sustainability</th>
</tr>
</thead>
<tbody>
<tr>
<td>District level authorities and medical</td>
<td>Public–private partnership (private medical colleges)</td>
<td>Incomplete information in verbal autopsy forms</td>
<td>Make reporting form concise</td>
</tr>
<tr>
<td>college faculties</td>
<td>Involvement of pediatricians</td>
<td>Late reporting and poor feedback</td>
<td>Provide repeated training and feedback to medical officers</td>
</tr>
<tr>
<td></td>
<td>Involvement of partners in planning, implementation and training</td>
<td>Lack of motivation</td>
<td>Improve health-care facilities</td>
</tr>
<tr>
<td></td>
<td>Closer rapport with the community</td>
<td>Lack of interest in peripheral staff</td>
<td>Train district level staff</td>
</tr>
<tr>
<td></td>
<td>Improved reporting and ensuing actions</td>
<td>Lengthy VA; staff do not always understand the technical content</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Form in local language</td>
<td>Overburdened staff</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary health care staff</td>
<td>Gaps in health service identified and rectified</td>
<td>Overburdened with existing national health programme</td>
<td>Financial incentives for medical officers to complete VA</td>
</tr>
<tr>
<td></td>
<td>Improved reporting of infant deaths</td>
<td>Coordination of many meetings</td>
<td>Regular supply of forms</td>
</tr>
<tr>
<td></td>
<td>Financial incentives for village level <em>anganwadi</em> or ASHA workers to report deaths</td>
<td>Non-availability of, and incomplete information from caregivers, requiring more than</td>
<td>Taluk (sub-district) level committee may be formed if number of deaths</td>
</tr>
<tr>
<td></td>
<td>Opportunity to educate family members for prevention of infant deaths</td>
<td>two visits</td>
<td>reported is high</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Transport problems to access remote villages</td>
<td></td>
</tr>
<tr>
<td>Village-level workers</td>
<td>Improved quality of antenatal care</td>
<td>Poor cooperation from caregivers (as they believe village workers are paid for VA)</td>
<td>Medical officers visiting the family of the deceased would confer the</td>
</tr>
<tr>
<td></td>
<td>Move from just reporting to finding out cause of infant death and events leading to it</td>
<td>Anger faced from family members for deficiency in health care (if death happens at</td>
<td>seriousness of the issue; including for neighbours</td>
</tr>
<tr>
<td></td>
<td></td>
<td>health-care delivery centre</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Forms, or some terms therein, in English</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cost of using mobile phone to send SMS to announce infant death</td>
<td></td>
</tr>
</tbody>
</table>
Department of Health, Department of Women and Child Development, local medical colleges, district hospital authority, peripheral health institutions, local representatives from WHO and UNICEF – in planning and implementing the IDR programme provided a platform for collective learning and action. The causes of deaths derived from verbal autopsies may not be as reliable as hospital-based certification, but information on risk factors and the health care sought prior to death made health-care providers more aware of the causes of infant deaths. The potential impediments identified to the success of the IDR programme need to be addressed by corrective actions at the relevant level by policy-makers and programmers for its sustainability.

**Conclusion**

Involving the different stakeholders such as government health departments and private health-care providers in the IDR programme creates synergy and is essential for its sustainability. In addition to ascertaining the cause of infant deaths, the IDR Committee discusses social, economic, behavioural and health system issues that may have contributed to the death. As a result of the IDR programme, respondents perceived an improvement in infant death reporting at the district level, a closer rapport with the local community, and the welcome development of a feedback system for corrective actions. This has led to improved quality of care during pregnancy as perceived by health service providers.

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The authors thank Dr Arun Aggarwal, Professor of Community Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, for his critical review and comments. We are grateful to the Directorate of Health and Family Welfare Services, Karnataka, for the opportunity to pilot this study in two districts in the state. We also thank the District Health and Family Welfare Officers and District Reproductive and Child Health Officers in Raichur and Dakshina Kannada for allowing this study to be conducted in their districts. Finally, we express our appreciation to all staff and expert members of the IDR Committee who volunteered information, as well as to all individuals whose contributions made the work possible.

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Policy and practice

Health systems responsiveness and its correlates: evidence from family planning service provision in Sri Lanka

W L S P Perera, Lillian Mwanri, Rohini de A Seneviratne, Thushara Fernando

Background: The World Health Organization has described health systems responsiveness (HSR) as a multi-domain concept encompassing eight non-medical expectations of health-care service seekers. HSR is a valuable measure of health systems performance, providing policy-makers and service providers much information to improve services. This paper presents findings of a cross-sectional survey conducted to assess HSR and its correlates through family planning (FP) services in Colombo district, Sri Lanka.

Methods: A Health Systems Responsiveness Assessment Questionnaire, developed and validated in Sri Lanka, was used. Trained interviewers administered the questionnaire in 38 FP clinics randomly selected to sample 1520 clients.

Results: The rating of responsiveness as ‘good’ for six domains ranged from 88% (n=1338) to 72% (n=1094). The overall HSR was rated to be ‘good’ by 83.4% (1268). Ethnicity being majority Sinhalese, persons who were currently employed and those using oral contraceptive pills (OCP) or condoms were negatively associated with rating of HSR. Positive associations with the HSR assessment were a family income of less than Rs 40 000 (US$ 303) per month, satisfaction with current FP method, use of only one method within the past year, use of only one FP clinic within the past year, health service provider being a medical officer, intention to use the FP clinic services in future, and satisfaction with overall services of the clinic.

Conclusions: Though overall HSR was rated by the majority as ‘good’, some aspects need more attention in delivering FP services.

Key words: health systems responsiveness, family planning, Sri Lanka.

Introduction

Health systems responsiveness

The 2000 World health report (WHR), published by the World Health Organization (WHO), identified three main goals to improve the performance of health-care systems.1 The degree to which the legitimate non-
medical expectations of people were met was one of these goals, named health systems’ responsiveness (HSR).1,2

Assessment of HSR

The need to assess and improve national HSR has been documented. The assessment, essentially, has to be made by the service seeker who is in the best position to state how non-medical expectations were met.1,2 Assessments based on individual perspectives are influenced by sociodemographic factors of the respondents as well as the sociocultural milieu. Nevertheless, this approach can provide valuable information on the performance of health-care systems, especially if the assessment tool is tailored to the specific sociocultural context of the country.2,3

WHO assessed HSR in 71 Member States in 2002–2004 during the World Health Survey (WHS).4 Inpatient and outpatient ‘modules’ were used for the assessment, which covered the entire health system of the country and included government, private and traditional medicine systems. Results were presented as a percentage of respondents, rating each item of the modules as moderate, bad or very bad. Table 1 describes the published data on patient services for Sri Lanka.

While assessing the responsiveness of the entire health system is important, assessing a specific service or institution would have much practical value.2 In line with this recommendation, a tool has been developed and validated in the Sri Lankan setting to assess HSR of family planning services.5,6

<table>
<thead>
<tr>
<th>Table 1: Health system responsiveness in Sri Lanka</th>
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</thead>
<tbody>
<tr>
<td><strong>Domain/item of responsiveness</strong></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Prompt attention</td>
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<tr>
<td></td>
</tr>
<tr>
<td>Dignity</td>
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<tr>
<td></td>
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<tr>
<td>Communication</td>
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<td></td>
</tr>
<tr>
<td>Autonomy</td>
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<tr>
<td></td>
</tr>
<tr>
<td>Confidentiality</td>
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<tr>
<td></td>
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<tr>
<td>Choice</td>
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<tr>
<td>Basic amenities</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Social support</td>
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<td></td>
</tr>
</tbody>
</table>

Correlates of HSR

Many factors – related to both the health sector as well as the sociocultural context – determine people’s assessment of HSR. These correlates play an important role in the assessment and could provide insight for policy-makers and service providers to improve service provision. To our knowledge, these factors have not been scientifically appraised and published.

Family planning services in Sri Lanka

Family planning (FP) services were introduced to Sri Lanka in 1953 and were well accepted.7 Today, they are a key component of the maternal and child health (MCH) package provided by the Government with the objective of improving the health and quality of life of families.7–8 The Family Health Bureau of the Ministry of Health coordinates provision of services within the government sector and registers FP clinics. Five methods of FP are provided through these registered clinics.

Though applicable to every facet of health-care delivery, HSR is especially relevant for services that are sought repeatedly over many years, e.g. long-term use of FP. Family planning is a sensitive topic in Sri Lanka where non-medical expectations of clients often determine their willingness to use services, even if they are widely available. Also, the satisfaction of clients plays a critical role in ensuring the proper use of FP methods, and minimizing method failure. This paper describes the findings of a cross-sectional survey conducted to assess the responsiveness of FP services of the public health sector through examination of HSR correlates.

Methodology

Sri Lanka, with an estimated population of 20.86 million, is divided into 25 administrative districts.9 The Colombo district houses approximately 20% of this population and has a network of public as well as private health-care institutions providing FP services. The public health sector runs 64 registered FP clinics in 12 Medical Officer of Health (MOH) divisions.7,8

A cross-sectional study was conducted on clients seeking services from FP clinics of MOH divisions in Colombo district. Sample size was calculated using the formula for estimating prevalence for descriptive studies.10 Prevalence of ‘good’ HSR was taken as 60% as it was the lowest estimation made in the country to ensure maximum sampling size.4,10 Estimated sample size was 753 for a precision of 3.5%. Cluster sampling was used: clients attending one clinic session comprised a cluster. Cluster size was 40 patients13 and the sample size was multiplied by two to account for design effect.11–12 Thirty-eight clinics were randomly selected from the list of registered FP clinics and within the clinic, systematic sampling was used to identify study participants.13 The calculated sample size was 1506 and a total of 1520 was taken as final.

We developed and validated the Health Systems Responsiveness Assessment Questionnaire (HESRAQ) in Sri Lanka to assess the HSR of FP services.5,6 Since correlates of HSR had not been identified earlier, focus group discussions and in-depth interviews were conducted with clients and non-users of FP, service providers and policy-makers to identify possible correlates. Twenty-five factors were identified and assessed in the cross-sectional survey. The tool was administered by trained research assistants who were pre-intern medical officers to persons as they left the FP clinics.

The results of the rating of HSR were categorized into three groups. Group 1 combined ‘very good’ and ‘good’ and indicated
good HSR; Group 2 contained the ‘moderate’
responses, indicating neutrality; and Group 3
consolidated ‘bad’ and ‘very bad’, signifying
that the HSR was bad. Correlates were
identified using logistic regression analysis.
First, bivariate analysis was performed using
chi square test followed by logistic regression
with significant variables. SPSS version 16
was used to determine the odds ratios (OR)
and 95% confidence intervals (95% CI) of
the correlates for rating the overall HSR as
‘good’ or ‘bad’.

Results
Response rate was 100%. All respondents
were married females and came from
different socioeconomic backgrounds.
The sociodemographic characteristics of
respondents and their FP use are presented
in Table 2.

The findings of the assessment carried out
using HESRAQ are given in Table 3.

Although the vast majority (83.4%) of
participants stated that the overall HSR of
FP services was good, 3.8% were unhappy
and a further 12.8% remained neutral in
their assessment. The highest rated domain
was ‘being treated with dignity’ (88%).
Regarding the confidentiality maintained on
medical information, and the ease of access
to FP services, 84% and 83% of respondents
were happy, respectively. On the other hand,
almost one fifth expressed dissatisfaction or
remained neutral about the state of the clinic
environment, with another 23.9% stating
the same regarding adequate communication
during medical encounters. ‘Client choice’ was
rated lowest with 28% of respondents stating
they were either unhappy or neutral on the
adequacy of choice given to them on the clinic,
provider and FP method.

Though 25 correlates were identified, only
10 were found to be associated with an HSR
rating. Logistic regression analysis of a rating
being ‘good’ is summarized in Table 4.

Domains that had negative HSR outcomes
were Sinhalese ethnicity (OR=0.189, CI
0.062−0.579), being employed (OR=0.247,
CI 0.104−0.587) and using OCP/condoms
as contraception (OR=0.09, CI 0.02−0.31).
On the other hand, factors associated with
positive HSR were a family income of less than
Rs 40 000 (US$ 303) per month (OR=19.31,
CI 4.70−79.27), satisfaction with current FP
method (OR=10.68, CI 4.80−23.74), use of
only one method in the past year (OR=6.69,
CI 2.74−16.33), use of only one FP clinic in
the past year (OR=9.91, CI 3.87−25.36),
health service provider being a medical officer
(OR=19.77, CI 3.59−108.88), intention to use
the clinic for FP services in future (OR=14.24,
CI 4.13−49.08) and satisfaction with overall
services of the clinic (OR=69.07, CI 20.31−
234.87).

Discussion
Our study showed that the majority of
respondents were happy with the HSR in
relation to FP services provided by the
Government. This is consistent with findings
of the only other local assessment on HSR in
the WHS. Since the WHS only published the
percentage of respondents rating each item
as ‘moderate/bad/very bad’, and only on a
five-point Likert-like scale, the percentage
rating of each item as ‘good/very good’ would
be reasonably interpreted as the balance
percentage of respondents. This percentage
would reasonably compare with the percentage
rating items as ‘very good/good’ in the present
study. Other studies conducted in Sri Lanka on
patient satisfaction and quality of health care
– two concepts with similarities to HSR –also
reveal a high rating of non-medical aspects of
health-care delivery by the Government. Though
the overall rating was high, there was
much variation in different domains of HSR.
### Table 2: Sociodemographic characteristics and use of modern family planning methods among respondents

<table>
<thead>
<tr>
<th>Sociodemographic characteristic</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 25</td>
<td>334</td>
<td>22.0</td>
</tr>
<tr>
<td>25–34</td>
<td>984</td>
<td>64.7</td>
</tr>
<tr>
<td>≥ 35</td>
<td>202</td>
<td>13.3</td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Currently married</td>
<td>1520</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sinhala</td>
<td>1240</td>
<td>81.6</td>
</tr>
<tr>
<td>Sri Lankan Tamil</td>
<td>128</td>
<td>8.4</td>
</tr>
<tr>
<td>Indian Tamil</td>
<td>14</td>
<td>0.9</td>
</tr>
<tr>
<td>Muslim</td>
<td>138</td>
<td>9.1</td>
</tr>
<tr>
<td><strong>Religion</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buddhist</td>
<td>1152</td>
<td>75.8</td>
</tr>
<tr>
<td>Hindu</td>
<td>120</td>
<td>7.9</td>
</tr>
<tr>
<td>Roman Catholic/Christian</td>
<td>110</td>
<td>7.2</td>
</tr>
<tr>
<td>Islam</td>
<td>138</td>
<td>9.1</td>
</tr>
<tr>
<td><strong>Level of education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No schooling</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Grade 1–5</td>
<td>186</td>
<td>12.2</td>
</tr>
<tr>
<td>Grade 6–10</td>
<td>806</td>
<td>53.0</td>
</tr>
<tr>
<td>Passed GCE O/L</td>
<td>278</td>
<td>18.3</td>
</tr>
<tr>
<td>Grade 12 – 13</td>
<td>66</td>
<td>4.4</td>
</tr>
<tr>
<td>Passed GCE A/L*</td>
<td>148</td>
<td>9.7</td>
</tr>
<tr>
<td>Above GCE A/L qualifications</td>
<td>36</td>
<td>2.4</td>
</tr>
<tr>
<td><strong>Current employment status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Currently employed</td>
<td>378</td>
<td>24.9</td>
</tr>
<tr>
<td>Currently unemployed</td>
<td>1142</td>
<td>75.1</td>
</tr>
<tr>
<td><strong>Method of family planning</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral contraceptive pill</td>
<td>74</td>
<td>4.9</td>
</tr>
<tr>
<td>Condoms</td>
<td>10</td>
<td>0.7</td>
</tr>
<tr>
<td>Depot-medroxyprogesterone acetate (DMPA)</td>
<td>1168</td>
<td>76.8</td>
</tr>
<tr>
<td>Implant</td>
<td>56</td>
<td>3.7</td>
</tr>
<tr>
<td>Intrauterine contraceptive device (IUD)</td>
<td>212</td>
<td>13.9</td>
</tr>
</tbody>
</table>

*GCE O/L – General Certificate of Education Ordinary Level.
**GCE A/L – General Certificate of Education Advanced Level.
Table 3: Health systems responsiveness assessment of family planning services

<table>
<thead>
<tr>
<th>Domain</th>
<th>Rating</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Good (%)</td>
<td>Moderate (%)</td>
</tr>
<tr>
<td>Being treated with dignity</td>
<td>1338 (88.0)</td>
<td>125 (8.2)</td>
</tr>
<tr>
<td>Confidentiality</td>
<td>1277 (84.0)</td>
<td>185 (12.2)</td>
</tr>
<tr>
<td>Ease of access to services</td>
<td>1262 (83.0)</td>
<td>200 (13.2)</td>
</tr>
<tr>
<td>Clinic environment</td>
<td>1218 (80.1)</td>
<td>244 (16.1)</td>
</tr>
<tr>
<td>Communication</td>
<td>1157 (76.1)</td>
<td>301 (19.8)</td>
</tr>
<tr>
<td>Client choice</td>
<td>1094 (72.0)</td>
<td>356 (23.4)</td>
</tr>
<tr>
<td>Overall HSR</td>
<td>1268 (83.4)</td>
<td>194 (12.8)</td>
</tr>
</tbody>
</table>

Table 4: Correlates of ‘good’ health systems responsiveness

<table>
<thead>
<tr>
<th>Correlate</th>
<th>95% CI for Exp (β)</th>
<th>Exp (β)</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>very good/good</td>
<td>Sig.</td>
<td>Exp (β)</td>
<td>Lower</td>
<td>Upper</td>
</tr>
<tr>
<td>1 Sinhalese in ethnicity</td>
<td>0.004</td>
<td>0.189</td>
<td>0.062</td>
<td>0.579</td>
</tr>
<tr>
<td>2 Currently employed</td>
<td>0.002</td>
<td>0.247</td>
<td>0.104</td>
<td>0.587</td>
</tr>
<tr>
<td>3 Family income less than Rs 40 000 (US$ 303)/month</td>
<td>0.000</td>
<td>19.31</td>
<td>4.70</td>
<td>79.27</td>
</tr>
<tr>
<td>4 Current method of FP: OCP/condoms</td>
<td>0.000</td>
<td>0.09</td>
<td>0.02</td>
<td>0.31</td>
</tr>
<tr>
<td>5 Satisfied with current method of FP</td>
<td>0.000</td>
<td>10.68</td>
<td>4.80</td>
<td>23.74</td>
</tr>
<tr>
<td>6 Used only one FP method in past year</td>
<td>0.000</td>
<td>6.69</td>
<td>2.74</td>
<td>16.33</td>
</tr>
<tr>
<td>7 Used FP services from only one clinic in past year</td>
<td>0.000</td>
<td>9.91</td>
<td>3.87</td>
<td>25.36</td>
</tr>
<tr>
<td>8 Service provider is a medical officer</td>
<td>0.001</td>
<td>19.77</td>
<td>3.59</td>
<td>108.88</td>
</tr>
<tr>
<td>9 Intent to use the clinic for FP services in the future</td>
<td>0.000</td>
<td>14.24</td>
<td>4.13</td>
<td>49.08</td>
</tr>
<tr>
<td>10 Satisfied with overall services of the clinic</td>
<td>0.000</td>
<td>69.07</td>
<td>20.31</td>
<td>234.87</td>
</tr>
<tr>
<td>Constant</td>
<td>0.000</td>
<td></td>
<td></td>
<td></td>
</tr>
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</table>

Exp (β) – Odds ratio
Respondents expressed satisfaction on being treated with dignity in clinics. The domain 'dignity' of the WHS module assessing outpatient department (OPD) settings is comparable with the domain in the present study.\textsuperscript{4} The two items comprising the domain in WHS were rated as very good/good by 86.9% and 76.8% of respondents respectively, while the rating in the present study was 88%.\textsuperscript{4} There is much respect for dignity of mothers attending MCH clinics in the local culture compared with general medical services.\textsuperscript{14} Also, the closeness of clients to service providers, who are mainly public health midwives, leads to much respect between the client and service provider in the field.\textsuperscript{5}

Confidentiality was the second highest rated domain. The ratings in the WHS were lower, i.e. 75.7% against 76.7% in the present study.\textsuperscript{4} Since the WHS was a general OPD assessment, the higher rating in the present study could be explained by the cultural respect for mothers seeking FP services in relation to their confidentiality, in addition to there being very little medical information collected at the FP clinic as opposed to OPD settings.\textsuperscript{5,19}

Ease of access to services was rated by 83.0% as being good. The domain 'prompt attention' was comparable with this domain in our study.\textsuperscript{4–5} Both elements were rated as very good and good in the WHS (70.2% and 62%, respectively). The WHS was an overall assessment on OPD services where the time travelling to larger but far-away hospitals and the longer waiting time in overcrowded hospital settings is reflected in the results. FP services, which are provided at smaller institutions and outreach clinics, offer services closer to home, and reduce the waiting time, given that mothers are generally given a specific time to attend the clinic.\textsuperscript{5}

The majority of respondents expressed satisfaction with the environment of FP clinics. The WHS assessed OPD facilities under the domain 'basic amenities', where the items were rated very good and good by 69.4% and 59.3%. The higher levels of rating in our study could be explained because the setting was an FP clinic at which a limited number of mothers attend, unlike OPD settings which are generally overcrowded, especially in larger hospitals where most people go for outpatient services. Therefore, it is evident that the FP clinic setup – the general MCH setup in the public health sector – offers a better environment than the general OPD facilities.\textsuperscript{5}

Communication in the WHS was assessed on two items: clear explanations and time for questions, rating very good or good at 82.6% and 70.8% respectively. Only 76.1% of respondents in our study said that their expectations had been met with regard to communication. The reason for this may be a lack of explanation on the more technical aspects of FP methods and even the side effects of FP methods.\textsuperscript{6} On the contrary, the time given for questions was rated lower in the WHS, given the general overcrowding and thus waiting time in OPD settings for patients to receive clarifications.

The client choice was rated lowest, i.e. either bad or average, at 28%. The WHS assessed the aspect of choice in two domains, namely autonomy and choice of provider.\textsuperscript{4–5} The choice of provider in the WHS study met the expectations of 69.1% of people, which largely matched the finding of our study. Autonomy, or the involvement of patients in making decisions in OPD settings was rated lower in the WHS, assessed on providing treatment information and involvement in deciding treatment. Only 66.9% and 70.4% rated these aspects very
good/good respectively. Involving the patient in decision-making was similar in the present study, although the provision of treatment information was lower in the WHS. This could reflect a lack of attention to informing patients adequately on their medical condition in the general outpatient settings.  

**Correlates**

Regarding the analysis of ethnicity, the Sinhalese (the majority in Sri Lanka) rated the HSR lower. However, qualitative research on HSR by the Principal Investigator in Sri Lanka showed that non-Sinhalese respondents had lower levels of expectations. Literature presumes that minority ethnic groups may have lower expectations of government services when the majority of the workforce comprises the ethnic majority. Some literature suggests that minorities could be discriminated against and marginalized in health-care delivery and that they could rate HSR poorly; this was not supported in the present study.  

Being currently employed showed a negative association with the rating of HSR. This could be explained by the fact that the employed have less time to visit clinics, which are generally open only during working hours. This observation is supported in the literature, which states that respondents in the labour force might have higher non-medical expectations, especially regarding efficient services. Literature on patient satisfaction suggests that currently employed respondents may be more educated with a higher monthly income and a higher level of expectations. In our study, the majority of the currently employed had a lower family income level than those who were employed on a daily basis, and many had to lose a day’s work to seek services.

Monthly family income was analysed on two levels, with a cut-off based on the median income. A monthly family income of less than Rs 40 000 (US$ 303) had a positive effect on the HSR rating. Respondents with a higher family income may have higher expectations and hence tend to be ‘harsher raters’. Though respondents with high income have the option of obtaining services from the private sector, there was more confidence in the government public health services despite the inconvenience.  

Contraceptive methods were categorized into two groups; methods that can be obtained during domiciliary services (OCP/condoms) and methods that can only be obtained from an FP clinic (DMPA/implant/IUD). Use of OCP and condoms showed a negative association with rating of HSR. The present study revealed that, though the clinics have to provide all five methods of FP, users generally seek DMPA, implant and IUD services. Service providers expect OCP and condom users to use public health midwives and are not well received at clinics, as providing these FP methods is sometimes treated as adding to the already overburdened clinics.  

Satisfaction with the current method was positively associated with the HSR rating. As already shown, this matches the satisfaction expressed by this group with all aspects of care in clinics. The main objective of visiting the clinic was to obtain a method of choice that would satisfy the respondent. Therefore, obtaining a satisfactory method ‘free at the point of delivery’ in the local context was adequate, and shortcomings in other aspects were secondary issues. The literature supports the findings that, irrespective of the level of expectation, the service seeker’s satisfaction with medication, etc. could lead to a higher rating.
Having used only one method within the previous year was positively associated with HSR rating. The literature states that experimenters and frequent changers are the hardest to satisfy during any health-care provision, and that the personality of the client plays a role in the satisfaction with the care received. This was not taken into consideration in our study. Some respondents had to change method due to the unavailability of another at some point. These clients were unsatisfied with the general medical services of the clinic due to such shortages.

Obtaining services from only one clinic over the previous year was associated with a positive rating of HSR. The literature suggests that doctor shoppers are harder to please. Local literature also confirms that clients who visit several places are unhappier with their medical and non-medical care. In addition, regular service seekers are generally from the surrounding area and know the public health midwife and other health providers, making the clinic environment more friendly.

Attendance by a medical officer showed a positive association with rating of HSR and was an expectation of many when seeking any form of health service. In addition, female clients often had more confidence in a male medical officers, who were thought to be more skilled. In relation to invasive procedures such as implants and IUDs, medical officers were believed to be more trained compared with even the most experienced nursing officer.

Intention to use the clinic for FP services in the future had a positive association with HSR. In addition to noting satisfaction, such respondents did not wish to make a lower assessment of HSR for fear of discrimination in case the health-care providers became aware of their response, despite assurance of confidentiality.

The strongest positive association was being satisfied with the overall clinic services. The literature emphasizes that patients’ assessment of the health-care delivery system is mainly dependent on their satisfaction with the medical care provided.

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Challenges faced by skilled birth attendants in providing antenatal and intrapartum care in selected rural areas of Myanmar

Kyaw Ooa, Le Le Wina, Saw Sawa, Myo Myo Mona, Yin Thet Nu Ooa, Thae Maung Maunga, Su Latt Tun Myinta, Theingi Myintb

Background: In Myanmar a large proportion of antenatal and intrapartum care in rural areas is provided by skilled birth attendants (SBAs), this study assessed the coverage by these health workers of all births, their adherence to service guidelines, and community opinion on the antenatal and delivery care they give in two rural health centres in Pathein Township, Ayeyarwaddy Region to identify the challenges and improve antenatal and intrapartum service delivery provided by the SBAs.

Method: A structured questionnaire was used to interview 304 women who had infants under one year of age, and in-depth interviews were held with 12 SBAs and 10 community members.

Results: Of the 304 pregnancies, 93% had received antenatal care (ANC); 97% of these were covered by SBAs at an average 15 weeks' gestation. The average frequency of ANC visits was 9. Rates of home and hospital deliveries were 84.5% and 13.8% respectively. Among home deliveries, use rate of SBA was 51.4%, while for postnatal care, 31.3% was given by unskilled providers (traditional birth attendants (TBAs) 17.5%, auxiliary midwives (AMWs), 13.8%). Multivariate analysis showed that interviewees aged 30 years and below (OR=0.468, \( P = 0.046 \)), with an education at primary level and below that of husband (OR=0.391, \( P = 0.007 \)) or not residing in the village of the rural/station health centre (OR=0.457, \( P = 0.011 \)) were significantly less likely to use SBAs. The categories of supervision, referral, and health education activities of SBAs were not in line with service guidelines. The main reasons were lack of access and community acceptance of TBAs.

Conclusion: Heavy workload, geographical location, transportation and financial concerns were major challenges for SBAs, along with community compliance and mutual coordination. Good communication and service management skills were important to overcome these challenges.

Key words: antenatal care, maternal and child health, Myanmar, skilled birth attendant (SBA), home delivery.

Introduction

In Myanmar, maternal and child health, including newborn care, has been prioritized with the aim of reducing morbidity and mortality of mothers and children. Safe motherhood initiatives have expanded into a national movement focusing on the rural...
population. Approximately 1.3 million women give birth each year in Myanmar. The chance that a woman will die from pregnancy-related causes is 1 in 33 and skilled birth attendants (SBA) are present at only 40% of deliveries and just over 20% of institutional deliveries.\(^1\) Although improvements in the health status of mothers and children have been made, much more needs to be done to sustain the gains.\(^2\)

Even though mothers tend to deliver more children in rural than in urban areas, 80% of deliveries are at home,\(^3\) of which the majority are by unskilled birth attendants. High home delivery rates and low use of skilled providers are addressed in the country’s strategic plans, which comprise improved skills and capacity of providers, family and community practice, and service delivery systems. Information on challenges in improving these three major pillars would support Myanmar’s strategy for more effective implementation of a reduction in the maternal mortality ratio (MMR). Thus, this study tried to identify the challenges and ways to improve antenatal and intrapartum service delivery provided by skilled birth attendants in rural area.

**Methodology**

The study was conducted at Pathein Township in Ayeyarwaddy Region, which was selected because of its low township coverage by SBAs compared with the national average (51% in Pathein, 63.6% national coverage).\(^4\) Two rural health centres – Thalakkhwar Station Health Unit and Kyetpaung Rural Health Centre – were be selected for their relatively high and low SBA rate respectively. A sample of 300 mothers who had given birth in the previous 12 months were interviewed with a structured questionnaire exploring antenatal and delivery care-seeking practice. User opinions and community perspectives on services provided were explored by key informant interviews with 10 community members including TBAs and local community leaders. Providers’ adherence to service delivery guidelines was assessed by reviewing records and carrying out in-depth interviews with 12 basic health staff (BHS) in the selected health centres.

Quantitative data were entered by EpiData\(^{tm}\) and analysed by SPSS version 16. Qualitative data were processed in content analysis to address compliance, satisfaction and choice of services. Matrix analysis was also made to identify existing challenges in skilled attendance.

**Findings**

**Profile of study area**

Pathein Township had a population of 380,460 and an urban–rural ratio of 1.01:1. The number of women of reproductive age was 87,505. Its nine health centres count 126 BHS spread over six rural health centres (RHC) and three station hospitals. There were 85 functioning AMWs and 66 trained TBAs, and in 2009, ANC coverage was 59.6%, SBA rate was 51% and referral rate was 5.6%. Delivery rate attended by AMWs was 12.6% with a 9.7% referral rate, while deliveries attended by trained TBAs were 7.3%, with a 7.4% referral rate. Rates for maternal mortality, infant mortality and neonatal mortality were 2.4, 15.1 and 4.7 per 1000 live births respectively. The abortion rate was 3.04.\(^5\)

**Past obstetric history and care-seeking practice**

A total of 304 women were interviewed. Their age ranged from 17 to 45 years with a mean (SD) of 29.4 ±6.5 years. The average family size was five, two of whom were earning members; 30% of women and 60% of husbands were daily wagers and 42% of women were dependent. About 90% of women
and their husbands were of low to middle-level education. The ethnic group Bamar accounted for 65% of the population, the remaining being Kayin. The ratio of Buddhist to Christian was 2:1. Half of housing is built from wood and bamboo, and 35% are made from bamboo and thatch.

The route to the nearest health centre for 60% of subjects was on foot, and for 24% by bicycle. The median duration to reach the health centre was 20 minutes. Some 50% of women needed 10–30 minutes to reach the nearest health centre. Travel expenses varied from an average 1000 kyats to a maximum of 4000 kyats (equivalent to 5 US$).

The median number of children of the study group was 2. Of a total 776 previous pregnancies, 84.4% had registered at the antenatal clinic. Stillbirth and abortion rates of these pregnancies were 0.7% and 1.8% respectively. Antenatal booking rates tapered with later order of parity (Figure 1). The location of the antenatal booking for first parity was mostly at health centres or general practitioner clinics.

Recent antenatal, intranatal and postnatal care practice

Antenatal booking rates for last pregnancies was 93%, 97% of which occurred with skilled health personnel. The average gestational period of antenatal bookings was 15 weeks. The average frequency of ANC visits was 9 (median=6). Half of women made antenatal bookings between 12–20 weeks of gestation and visited 4–10 times for ANC. One third of pregnancies experienced oedema and 18% noticed high blood pressure.

The last pregnancies were delivered on average in the 37th gestational week. Half of

![Figure 1: Percentage of antenatal booking by parities](image-url)
women delivered between 36 and 38 weeks’ gestation. The rate of SBAs used was 59.1%. Delivery rates at home and hospital were 84.5% and 13.8% respectively. Among home deliveries, use rate of SBA was 51.4%. During delivery, 2.6% of cases changed birth place, mainly to hospitals to receive the services of skilled providers. The referrals were mainly made by midwives, TBAs, AMWs and medical doctors (Figure 2). The major problem faced after delivery was haemorrhage. SBA rates at the start of labour, during delivery and after delivery were 52%, 53% and 52.9%, indicating no significant difference in birth attendance per phase of labour. Rates of skilled attendance at home delivery for all pregnancies was high – 91% at the start of labour – showing that most births were planned at home. However, given that 88% of deliveries actually occurred at home, 3% of deliveries had changed location between first labour pains and birth.

Nearly one-third (31.3%) of postnatal care was provided by unskilled workers (TBA=17.5% and AMW=13.8%). Postnatal problems occurred among 5.6% of cases after their last deliveries. Most problems were minor medical illnesses that were not referred.

Factors associated with the use of skilled birth attendants

The use of SBA, operationally defined as “use at delivery”, was grouped into three categories: never use, sometimes use and always use. Bivariate analysis showed that the following indicators were associated with higher use of SBAs: better access to a health

Figure 2: Proportion of basic health services that need support to meet the set guidelines
centre, i.e. residing in RHC main village (46% vs 35%, \(P=0.005\)), higher education level of women (58% vs 36%, \(P=0.002\)) and husbands (57% vs 34%, \(P<0.001\)), good housing status (\(P=0.04\)), younger age of woman (44% vs 37%, \(P=0.001\)) and husband (48% vs 35%, \(P=0.003\)) (Table 1). Multivariate analysis ( multinomial logistic regression) showed that younger women, i.e. 30 years and below (OR=0.468, \(P=0.046\)), low level of husband’s education, i.e. primary and below (OR=0.391, \(P=0.007\)), not residing near RHC (OR=0.457, \(P=0.011\)) were significant factors for lower use of SBA (Table 2).

**Adherence to service delivery guidelines**

The 12 BHS interviewed had an average total service of 15 years (range 3.5–29 year). Nine BHS were graduates and the remaining three had passed high school. A variety of registries and report books were reviewed during the interview.

Activities that deviated most frequently from the guideline instruction laid down by the Department of Health\(^6\) were related to providing antenatal care, providing delivery care, and service management. Others were supervisory, referral and health education activities (Figure 2).

Regarding delivery care, most deviations were due to difficult access and community acceptance and use of TBA services, as illustrated below.

_We could not go to them because they are staying in the middle of a paddy field alone and there was no road._

_We could not avoid TBA because they are more accessible and have better relationship_

_TBAs are over there since long, long ago. They can give service for uncomplicated cases...Accessibility is their priority._

Deviations from antenatal care guidelines were the inability to cover 100% of cases, non-provision of some antenatal examinations (especially height measurement, urine albumin test), and some inadequate antenatal visits, exemplified as follows.

_Many women did not come regularly and for those women, we cannot give antenatal care service for full frequency._

...we have no time to check urine of all women. Thus we check only those who have high blood pressure... Height measuring also could not be done for all women. Only if we suspect she is short we measure and record.

...sometimes we have to skip some procedure stated in the guideline ...to get satisfaction of clients, to save their time, and to get their compliance...

Among the three types of BHS, most deviations were found in the provision of services by lady health visitors (LHV), and the least in the activities of midwives (Figure 6). Most frequent reasons were deficient facilities/equipment/materials, lack of accessibility and low compliance of the client. The next most frequent reasons were time constraints, weak supervision system and community compliance or use of TBA services (Figure 3).

Regarding ANC service provision, improving management skills (including planning, prioritizing and adapting to the situation) is the first priority for BHS in order to be able to face and overcome challenges. Secondly, improved skills in cooperation mechanisms with TBAs, AMWs and local authorities were considered important (Figure 4).

_We could not avoid TBA because they are more accessible and have better relationship_
### Table 1: Factors associated with use of SBA in previous and last pregnancies (bivariate analysis)

<table>
<thead>
<tr>
<th>Factor</th>
<th>Use of skilled birth attendant</th>
<th>Total</th>
<th>$\chi^2$ (df)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Never</td>
<td>Sometimes</td>
<td>Always</td>
<td>Freq</td>
</tr>
<tr>
<td>Residing at or near to HC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residing at subcentre</td>
<td>60</td>
<td>28</td>
<td>48</td>
<td>136</td>
</tr>
<tr>
<td>Residing at HC</td>
<td>44</td>
<td>47</td>
<td>77</td>
<td>168</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;= 30</td>
<td>69</td>
<td>30</td>
<td>77</td>
<td>176</td>
</tr>
<tr>
<td>31+</td>
<td>35</td>
<td>45</td>
<td>48</td>
<td>128</td>
</tr>
<tr>
<td>Age (years) husband</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;= 30</td>
<td>54</td>
<td>25</td>
<td>72</td>
<td>151</td>
</tr>
<tr>
<td>31+</td>
<td>50</td>
<td>50</td>
<td>53</td>
<td>153</td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illit+Pri</td>
<td>87</td>
<td>58</td>
<td>80</td>
<td>225</td>
</tr>
<tr>
<td>Middle or above</td>
<td>16</td>
<td>17</td>
<td>45</td>
<td>78</td>
</tr>
<tr>
<td>Husband's education level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illit+Pri</td>
<td>84</td>
<td>50</td>
<td>68</td>
<td>202</td>
</tr>
<tr>
<td>Middle or above</td>
<td>20</td>
<td>23</td>
<td>57</td>
<td>100</td>
</tr>
<tr>
<td>Housing status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bamboo</td>
<td>49</td>
<td>49</td>
<td>62</td>
<td>160</td>
</tr>
<tr>
<td>Wooden or Brick</td>
<td>8</td>
<td>5</td>
<td>20</td>
<td>33</td>
</tr>
<tr>
<td>Other</td>
<td>46</td>
<td>21</td>
<td>40</td>
<td>107</td>
</tr>
</tbody>
</table>

Freq=frequency; HC= health centre; Illit+Pri= grouping from illiterate to primary education. Other non-significant factors not described in the table are health centre ($P=0.996$); occupation ($P=0.657$); race ($P=0.708$); religion ($P=0.537$); family monthly income ($P=0.74$); husband’s occupation ($P=0.21$)
### Table 2: Multivariate analysis of significant factors for use of SBA (multinomial logistic regression)

<table>
<thead>
<tr>
<th>Use of SBA (Ref: Never use)</th>
<th>( P ) value</th>
<th>OR</th>
<th>95% CI of OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \text{Lower} )</td>
<td>( \text{Upper} )</td>
<td></td>
</tr>
<tr>
<td><strong>Always used</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (( \leq 30 \text{ vs } &gt;30 ))</td>
<td>0.046</td>
<td>0.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Age of husband (( \leq 30 \text{ vs } &gt;30 ))</td>
<td>0.104</td>
<td>1.8</td>
<td>0.9</td>
</tr>
<tr>
<td>Education (( \leq \text{primary vs &gt;primary} ))</td>
<td>0.163</td>
<td>0.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Education of husband (( \leq \text{primary vs &gt;primary} ))</td>
<td>0.006</td>
<td>0.4</td>
<td>0.2</td>
</tr>
<tr>
<td>Housing (bamboo vs wood/brick)</td>
<td>0.718</td>
<td>0.8</td>
<td>0.3</td>
</tr>
<tr>
<td>Housing (other vs wood/brick)</td>
<td>0.284</td>
<td>0.6</td>
<td>0.2</td>
</tr>
<tr>
<td>Health Centre (RHC vs SHU)</td>
<td>0.585</td>
<td>1.2</td>
<td>0.7</td>
</tr>
<tr>
<td>Residence (sub-centre vs main)</td>
<td>0.011</td>
<td>0.5</td>
<td>0.2</td>
</tr>
</tbody>
</table>

OR, odds ratio; RHC, rural health centre; SHU, station health unit;
Results for “sometimes used” category were omitted since the factors for use of SBA were similar to the results for “always used” category.

### Figure 3: Reasons for deviation of service provision from the guideline

[Diagram showing reasons for deviation]
with local people. In hard to reach areas, we have to cooperate with them. If we cooperate, risk cases will be more access to us and be referred.

**Community opinion towards skilled providers**

Community informants felt that midwives could cover about two thirds of all deliveries and almost all antenatal activities and immunization, including tetanus toxoid vaccination. The remaining deliveries were carried out by AMWs and sometimes, especially in hard-to-reach areas, by TBAs. Community informants noted that midwives would try to assume all deliveries in their responsible area but are unable to cover everything, which the community appreciated.

*We see midwives frequently in our village ... especially for vaccination.*

*People know that midwives are more skilful but could not always be available ...[they] stay far away and thus more costly.*

Key informants estimated home delivery to be about 90%, with hospital delivery only in cases of emergency. All respondents agreed that the main challenge for midwives was overburden of their workload. A midwife cannot rapidly reach all patients if she is responsible for 7–10 villages. In addition, midwives sometimes need to go to town for a meeting or training.

Client access to health providers was low. Half of villages under SBA coverage were too far away from the sub-centre to reach in time. Emergency situations made clients more inclined to use a health provider who was nearer and could respond rapidly whether or not s/he was skilful enough. Pregnant women who were residing in less accessible areas could not use the skilled provider due to geographical barriers, or transportation difficulties, occurring seasonally in the outreach areas covered by midwives. Seasonal fluctuations affect access to roads and diurnal variation of waterways in the delta area. Thus, in an emergency, the inability to travel means that clients cannot use a skilled provider even if they wanted to.

A further challenge for skilled providers was poor cooperation of local people and authorities to encourage clients to use skilled personnel and to comply with referrals. They stated that community support was low, especially in delivery care.

The last challenge, essential for referral, was coordination between skilled providers of health centres from different levels. Poor coordination by the providers and financial concerns of the health centre makes the provider reluctant to refer, and leads to client non-compliance.

Usually, local voluntary providers cooperate with midwife ANC and immunization services by making arrangements for the location, transportation and organization of clients. In some instances, cooperation between AMWs, trained TBAs and midwives was supportive for midwives to develop a close relationship with local authorities and to gain client compliance. Cooperation was indirectly supportive for midwives’ intrapartum care services in being informed of problem cases, compliance with referral, transportation assistance and the resolution of financial issues.

**Discussion**

Unpredictable obstetric complications are developing in 15–20% of pregnancies. A major proportion of deaths resulting from these complications occur either at home or in transit. Increased access to, and quality and quantity of health facilities in the country...
could reduce maternal mortality dramatically, according to SriLanka experiences.\textsuperscript{7,8} Though safe motherhood is a high priority programme, 90\% of deliveries still occur at home and 50\% are attended by TBAs.\textsuperscript{2}

Specific challenges remain for Myanmar to reduce its MMR. Low education and economic status, and lack of access influence the client’s decision to use skilled providers in pregnancy care. Providers also highlighted accessibility as a challenging factor to increase SBA use. This challenge was reiterated by community key informants for skilled providers to be able to provide full coverage. Accessibility means all geographical, managerial and financial aspects both by clients and providers. For some midwives, their area of responsibility and the size of the population were too large for them to meet their targets for full coverage of ANC and SBA. Geographical barriers can prevent both clients and providers from meeting their needs. Deviations of skilled providers’ services from the guideline were mainly caused by having responsibility for too wide area and too large population size, little time and lack of facilities. Service manuals were not found in all BHS hands. Many descriptions in the manuals confuse them. The role of lady health visitors in rural areas should be emphasized with practical service-provision and supervisory activities over the midwives, especially for coordination between BHS and the community.

Furthermore, all perspectives considered that clients’ habitual use of unskilled providers was due to a low level of education and because unskilled providers were more accessible than skilled providers.

**Conclusion**

Skilled attendance for all births is the only way to ensure emergency obstetric care for all pregnancies with complications. The percentage of births attended by skilled health workers is considered to be the most appropriate process indicator. Current estimates indicate that globally, only 56\% of births are assisted by a skilled person.\textsuperscript{9}

Although communities suggested more skilled staff in their areas, manpower and resources are scarce. The country’s strategic plans should therefore focus on improving the capacity of current health providers, especially in management and communication; and improving family and community practice through close coordination with community authorities and health volunteers. Regarding cooperation, the delegation of some services, accompanied by close and supportive supervision, good communication and motivation with positive attitudes, would be effective. This study highlights the major challenges and suggests priorities and ways to overcome them. The objective would be to implement a more effective national strategic plan, with the ultimate goal of reducing MMR.

**Acknowledgements**

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**References**

Challenges faced by skilled birth attendants in providing antenatal and intrapartum care in selected rural areas of Myanmar

Kyaw Oo et al.


**Epidemiologic investigation of excess maternal and neonatal deaths and evidence-based low-cost public health interventions – Ignaz Semmelweis: the etiology, concept and prophylaxis of child bed fever**¹

S D Gupta²

**Introduction**

_When I look back upon the past, I can only dispel the sadness which fall upon me by gazing into that happy future when the infection will be banished .... The conviction that such a time must inevitably sooner than later arrive will cheer my dying hour._ So wrote Ignaz Semmelweis in his last days while he suffered depression due to continued criticism by medical professionals and colleagues. Semmelweis suggested that simple hand-washing with chlorinated water could prevent the spread of infection and save the lives of women in maternity.² His methods showed that maternal deaths due to puerperal fever reduced from 12.2% to 2.4% in maternity wards. He expanded his methods to washing of instruments, which altogether removed puerperal infection in the hospital. However, his observations were in serious conflict with contemporary scientific and medical opinions, which rejected his observations. His suggestion that doctors should wash their hands with chlorinated lime even offended some doctors and his colleagues. They refused to accept that they could be responsible for spreading infection. Semmelweis’s claims were thought to lack scientific basis and his practice of antiseptic use only gained acceptance years after his death, when Louis Pasteur³ invented the germ theory of disease in 1862, and Joseph Lister⁴ invented methods for antiseptic surgery in 1867.

Ignaz Semmelweis’s investigations of maternal and neonatal deaths laid the foundation of modern public health and epidemiological investigations, and prevention of avoidable deaths through hand-washing with chlorine and lime before clinical examination of patients. Semmelweis’s classic approach not only contributed to our knowledge of causal hypothesis, but discovery of appropriate interventions supported by evidence that led to a reduction in maternal and neonatal deaths.

Semmelweis’s insights are a brilliant example of translation of research into action for wider human well-being. Today,

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¹Indian Institute of Health Management Research, Jaipur, India. Correspondence to S D Gupta (e-mail: sdgupta@iihmr.org)
the prevention of puerperal sepsis and infections resulting from deliveries conducted in unhygienic conditions and unsafe abortions is a major approach to reduce maternal and neonatal mortality all over the world. The impact of Semmelweis’s discovery on human health was so immense that millions of maternal deaths have been averted since the initiation of such a simple intervention as the adoption of aseptic procedures during childbirth. Globally, the estimated 526 000 maternal deaths in 1980 are reported to have been reduced to 342 000 in 2008, a reduction of almost one third. Yet a large number of maternal deaths, about 90%, are easily preventable through simple technical and social interventions. Incidentally, 99% of maternal deaths globally occur in developing countries where home deliveries are still common and infection control measures are not adhered to. Puerperal sepsis thus is still prevalent in developing countries and continues to present a significant risk of obstetric morbidity and mortality for women in these regions.

We briefly describe below the investigations of Ignaz Semmelweis and prophylaxis measures that enabled him to demonstrate the significant reduction in maternal and neonatal deaths.

**Investigations of childbed fever (puerperal fever)**

Semmelweis’s investigation on excess maternal and neonatal deaths is a testimony of modern concepts and approaches of epidemiological investigations. His work demonstrated how simple observations and comparison of frequency of events could help develop causal hypothesis and testing to draw conclusive evidence of cause and effect relationships. He laid the foundation of the modern-day epidemiologic approach: identify and define problem; define research question and develop hypothesis causation and mode of transmission; collect and analyse data; establish cause and effect relationship; develop and design intervention; and evaluate impact.

Semmelweis observed excess maternal deaths among women who gave birth in Vienna Maternity Hospital. Of the two maternity clinics operated by the hospital, he found that maternal deaths were higher in the first. His data collected data on maternal deaths over a period of six years since 1841 showed that, on average, the mortality rate was three times higher in the first clinic over the second clinic. He also noted that the mortality rate was five times higher in the first clinic in 1846 (Table 1).

Semmelweis further observed that the deaths in the first clinic would have been higher as the serious patients were transferred to Vienna General Hospital. When these patients died, they were included in the mortality data of general hospital rather than the first clinic. He also observed that the referral rates of patients in first clinic were higher than the second clinic due to higher frequency of serious patients.

He ascribed these deaths to childbed fever. He defined childbed fever “as a disease...
characteristic of and limited to maternity patients, for whose origin the puerperal state and specific causal moments were necessary'. He also observed higher mortality among newborns delivered by women and also died in the first clinic due to similar clinical and pathological characteristics (Table 2).

**Research questions and hypotheses**

The prime research question he had in his mind was why there was higher maternal mortality in the first clinic? What caused excess maternal and newborn deaths? What was the source and how did these women acquire that causative agent?

In order to address his research questions, Semmelweis explored whether the women admitted to the first clinic were different to those in the second clinic (now called selection bias). He reviewed the admission process of the maternity hospital selection bias, if any.

*The admission of maternity patients was regulated as follows: Monday afternoon...*
at four o'clock admissions began in the first clinic and continued until Tuesday afternoon at four. Admission then began in second clinic and continued until Wednesday afternoon at four o'clock. At that time admissions resumed in the first clinic until Thursday afternoon, etc. On Friday afternoon at four o'clock admissions began in the first clinic and continued through forty-eight hours until Sunday afternoon, at which time again admissions began in the second clinic. Admissions alternated between two clinics through twenty-four periods, and only once a week did admissions continue in the first clinic for forty-eight hours\(^1\).

He found that the admissions were done regularly without any predetermined criteria; he concluded that there was no selection bias that would render women admitted to the first clinic more susceptible.

He considered several factors that could possibly be associated with excess maternal deaths in the first clinic, included various clinical conditions, prolonged dilation and other delivery-related characteristics. He also considered environmental factors and the geographic location of the clinics and arrangement of maternity beds in the wards. He found no conclusive difference in maternal deaths.

The authorities were also concerned with disturbing differences in maternal deaths in the two clinics. In order to reduce deaths, several measures were adopted such as transfer of patients to the general hospital, change of physician and medical procedures, environmental conditions and rooms from time to time. Various other measures were also adopted. However, the maternity patients continued to die of childbed fever.

Semmelweis then discovered that mortality was consistently greater in the first clinic since 1940 when it started training only obstetricians, while the second clinic trained only midwives, and wondered whether this could be the reason for the discrepancy. Did obstetricians cause more damage to the birth canal during examination? As most of the physicians were foreigners, it was also posited whether they were rougher than the natives? Incidentally, mortality rates declined when foreigner doctors were excluded from examinations in late 1846 and early 1847; however, they remained higher in the first clinic, and climbed back to higher levels in the months that followed (Figure 1). It did not seem logical that examination by obstetricians, especially foreigners, was associated with higher mortality in the first clinic.

These observations astounded the hospital authorities and Semmelweis. The mystery of higher maternal deaths in the first clinic remained unresolved.

It is interesting to learn how exceptional incidents can play a crucial role in epidemiological investigations of causes and mode of transmission of a disease. Semmelweis left for England to study English in the winter of 1846, returning to Vienna in March 1847. On his return, he learnt that Professor Jakob Kolletschka, who he admired, had died of symptoms similar to those of maternity patients in his clinic. He described his case history as follows:

\textit{Kolletschka, Professor of Forensic Medicine, often conducted autopsies for legal purposes in the company of students. During one such exercise, his finger was pricked by a student with same knife that was being used in the autopsy... Professor Kolletschka contracted lymphangitis and phlebitis in the upper extremity... He died of bilateral pleurisy, pericarditis, peritonitis, and meningitis. A few days before he died, a metastasis also formed in...}
one eye. ... I was haunted by Kolletschka’s disease and was forced to recognize, even more decisively, that the disease from which Kolletschka died was identical to that from which so many maternity patients died.

It proved to be clinching evidence for the cause of childbed fever.

Semmelweis had earlier shown from autopsies that the cause of newborn deaths were identical to those of women who had died from childbed fever, and thus concluded that they died of the same disease. The same results were found in Kolletschka’s autopsy, confirming that he died of the same disease. Semmelweis thus notes:

The exciting cause of Professor Kolletschka’s death was known; it was the wound by autopsy knife that had been contaminated by cadaverous particles ... Kolletschka was not the first to have died in this way. I was forced to admit that if his disease was identical with the disease that killed so many maternity patients, then it must have originated from the same cause that brought it on in Kolletschka.

In Kolletschka, the specific causal factor was cadaverous particles that were introduced into his vascular system. I was compelled to ask whether cadaverous particles had been introduced into vascular systems of those patients whom I had seen die of this identical disease. I was forced to answer affirmatively.

In order to answer yet another important question, i.e. how cadaver particles were transferred to maternity patients, Semmelweis analysed the chain of sequences and circumstances in which these particles could have contaminated the wounds.

The obstetrics students were assigned only to the first clinic and the midwives to the second clinic. The obstetrics students were required to carry out anatomical orientation on cadavers as a part of their training. They washed their hands with soap and water, but this did not destroy the cadaverous particles on their hands. They then examined maternity patients and thus contaminated the genitals of pregnant and delivering patients with cadaverous particles. These particles were
subsequently introduced into the vascular systems of maternity patients, producing a similar disease to that which killed Kolletschka. On the other hand, the trainee midwives in the second clinic were not required to carry out anatomical interventions on cadavers and hence did not visit the mortuary. The assistants, too, in the second clinic seldom visited the mortuary. These observations led Semmelweis to infer that the students whose hands were contaminated with cadaver particles were responsible for transmission of childbed fever.

**Intervention**

History was made. The cause of childbed fever (puerperal sepsis) was discovered which still kills tens of thousands of women during pregnancy and childbirth in developing countries today. Semmelweis went forward to discover an intervention to prevent the spread of the disease. He hypothesized that, if the cadaverous particles are destroyed chemically, the disease must reduce or be prevented. He instituted hand-washing with chlorine solution before examining maternity patients (Figure 1):

_To destroy cadaverous matter adhering to hands, I used Chlorina Liquida. This practice began in middle of May 1847... Both students and I were required to wash (hands) before examinations. After a time I ceased to use Chlorina Liquida because its high price, and I adopted the less expensive chlorinated lime. In May 1847, during the second half of which chlorine washings were first introduced, 36 patients died – this was 12.24 percent of 294 deliveries. In the remaining seven months of 1847, the mortality rate was below that of the second clinic._

**Monitoring and evaluation of intervention**

Semmelweis evaluated the effect of chlorine washing of hands and equipment, and demonstrated that chlorine prevented the transmission and spread of childbed fever as observed from reduction in mortality rates among maternity patients in the first maternity clinic compared with the mortality levels in the second maternity clinic (Table 3).

_In these seven months, of 1841 maternity patients cared for, 56 died (3.04%). In 1846, before washing with chlorine was introduced, 4010 patients cared for, 459 died (11.4%). In the second clinic in_

<table>
<thead>
<tr>
<th></th>
<th>First clinic</th>
<th>Second clinic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Year</strong></td>
<td><strong>Births</strong></td>
<td><strong>Deaths</strong></td>
</tr>
<tr>
<td>Pre-training year</td>
<td>1839</td>
<td>2781</td>
</tr>
<tr>
<td>Obstetric training permitted</td>
<td>1840</td>
<td>2789</td>
</tr>
<tr>
<td>Before chlorine washing</td>
<td>1846</td>
<td>4010</td>
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<tr>
<td>Chlorine washing introduced</td>
<td>1847</td>
<td>3490</td>
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<tr>
<td>After chlorine washing</td>
<td>1848</td>
<td>3556</td>
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**Table 3: Annual births, deaths, and mortality rates for all maternity patients at the clinics of the Vienna Maternity Hospital for 1839, 1840, 1846–1948**
1846, of 3754 patients, 105 died (2.7%). In 1847, when approximately the middle of May I instituted washing with chlorine, in the first clinic of 3490 patients, 176 died (5%). In the second clinic, of 3306 patients 36 died (1%). In 1948, chlorine washings were employed throughout the year and of 3556 patients, 45 died (1.3%). In the second clinic in the year 1948, of 3219 patients 43 died (1.3%).

Replication of interventions
Semmelweis was convinced that hand-washing with chlorinated lime before examining the patient by doctors would reduce maternal and neonatal deaths. He suffered ignominy at the hands of his fellow colleagues and seniors. He left the Vienna hospital as he could no longer endure the frustrations of dealing with the Viennese medical establishment, and returned to Pest in Hungary. Despite being criticized by the medical community and fellow colleagues, Semmelweis replicated his intervention by introducing hand-washing with chlorine water in Pest’s small St Rochus Hospital where childbed fever was rampant. From 1851 to 1855, only eight patients died of childbed fever out of 933 births (0.85%). The results he demonstrated in Vienna Hospital were thus reproducible. He repeated the same interventions in 1857 when he took over as Professor at the University of Pest maternity clinic, where the results were once again impressive.

Research for action
Research remains impotent unless it is used to protect and improve human health and promote welfare through public health action. Semmelweis’s research is a salient example of how research was employed to improve human health. His observations and experiments formed the basis of modern-day infection control measures in hospitals and health care in general. Infection control measures, especially disinfection of hands and equipment have saved the lives of millions of pregnant and childbearing women who may have died of puerperal sepsis all over the world, thanks to the great discovery of Semmelweis. Hospital infection control is the hallmark of patient safety today.

Semmelweis’s seminal observations led the way for modern epidemiologic thinking and approach. Observations of disease trends and making comparisons are critical components of modern-day epidemiological approaches for initiating investigations and testing causal hypotheses. Semmelweis systematically observed maternal death trends in the maternity hospital and developed a causal hypothesis. Though he could not explain the causal agent, he successfully investigated the source of infection and mode of spread of puerperal fever among women who gave birth in his hospital. He also successfully demonstrated that if the chain of spread was blocked, the disease could be prevented. Nevertheless, Semmelweis could not provide scientific evidence to prove his hypothesis that cadaveric particles produced puerperal fever. He was severely criticized by his contemporary medical professionals and scientists for bruising their ego and for his statements that doctors were responsible for the spread of infection.

Semmelweis was reluctant to publish his work and disseminate the results among the scientific community until 1861 when he published his book on Concepts, Etiology and Prophylaxis of Childbed Fever, 16 years after his discovery. Dissemination of research is critical to create awareness, advocacy and acceptance of its results, in order to further its applications as evidence for policy and action. However, there are several barriers that obstruct meaningful dissemination and uptake of the results. Research evidence is one of many inputs to acceptance and
decision-making by peers, fellow professional groups and clinicians, health-care managers, and health-care policy-makers. Translating research into action requires intellectual rigour, discipline, creativity, clinical judgment and skills, a favourable organizational climate, and above all endurance and tolerance towards contemporary scientific reviews and comments. Semmelweis was academically brilliant and made a seminal discovery, but lacked leadership skills. He was arrogant, severe on his critics, calling them murderers and medical ‘Neros’, and accused his superiors of causing the deaths of mothers. He became frustrated and angry with himself, but refused to publish his monumental discovery.

He was denied recognition in his lifetime and finished his days in a mental asylum in ignominy, dying at the very young age of 47 years. His work was recognized only after about two decades of his demise with the advent of germ theory and the value of antiseptic techniques in preventing spread of infection. He was described as the saviour of mothers. His discovery of hand-washing with antiseptic solution left a legacy in modern medicine and infection control, thus saving the lives of millions of women; not only averting deaths from nosocomial infections, but reducing the cost of health care the world over. The Austrian Government issued a commemorative 50 euro coin in 2008 in his honour; and libraries, museums and universities have been named Semmelweis in recognition of his discovery and contribution to medical science.

References


Recent WHO publications

Achieving the health-related millennium development goals in the South-East Asia Region: measuring indicators 2012

This publication presents the achievements on MDGs by Member States of the WHO South-East Asia Region gauged only at the national level. It depicts the road covered by countries in the past 10 years and the gaps that have to be bridged in the remaining five years, along with ascertaining the likelihood of reaching each of the targets by 2015. The report also highlights the bottlenecks, the most intense challenges and the constraints faced by each country in its strategic actions and interventions.

South-East Asia Regional Strategic Framework for Improving Neonatal & Child Health and Development
Publisher: World Health Organization, Regional Office for South-East Asia. New Delhi: 2012. 83 pages. DOC NO.- SEA/CAH/09

Despite a significant improvement in child mortality, the South-East Asia (SEA) Region is unlikely to achieve the Millennium Development Goal (MDG) 4 target and needs significant improvement in maternal, newborn and child health (MNCH) programmes in Member States. The broad objective of the WHO-UNICEF joint South-East Asia Regional Strategic Framework for Improving Neonatal & Child Health and Development is to guide and assist Member States to develop or strengthen their national strategies and plans to improve newborn and child survival, reduce the burden of child morbidity and disability and promote child health and development. The Strategic Framework encourages Member States to incorporate an equitable child health and development perspective into policies and actions within the health system and emphasizes that the implementation requires multisectoral collaboration. Member States are encouraged to use local situation assessment, improve convergence within Health Programmes, and to strengthen health systems and enhance the capacity in planning and management of the child health programmes for the scaling up of evidence-based interventions for child health and development. The Framework presents a brief Regional situational analysis that has been used to form the basis for appropriate strategies for child and neonatal health. A brief analysis of the broader determinants beyond the health system such as safe drinking-water, sanitation and hygiene, education, gender, is also included, as well as an analysis of coverage levels of existing interventions that helps identify gaps and missed opportunities for strengthening health systems. The Framework is based upon principles of child rights and equity. It highlights the need to think about the whole child, not just their health. The Framework uses the principle of continuum of care across the life-course, from pre-conception.
through pregnancy, childbirth, the postnatal period, infancy, childhood and adolescence. Such a holistic approach is important since maternal, neonatal and child health are closely linked with each other, not only intrinsically, but also programmatically. It emphasizes that the services must be organized through a process that preserves functional continuity across different levels of health-care delivery from home/community to first-level health centres and referral hospitals. This Framework is intended to be the basis for subsequent joint WHO-UNICEF country support for Member States in the WHO SEA Region for newborn and child health and development.
Guidelines for contributors

Original research articles on public health, primary health care, epidemiology, health administration, health systems, health economics, health promotion, public health nutrition, communicable and non-communicable diseases, maternal and child health, occupational and environmental health, social and preventive medicine are invited which have potential to promote public health in the South-East Asia Region. We also publish editorial commentaries, perspectives, state of the art reviews, research briefs, report from the field, policy and practice, letter to the editor and book reviews etc.

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The tables/figures must be self explanatory and must not duplicate information in the text. Each table and figure must have a title and should be numbered with Arabic numerals. Each table should be typed in double space on a separate sheet of paper. Figures should be black and white glossy photographs or drawn by artist or prepared using standard computer software. A descriptive legend must accompany each figure which should define all abbreviations used. All tables and figures should be cited in the text.
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