

Informal Expert consultation on Surveillance, Diagnosis and Risk Reduction of Leptospirosis

Chennai, 17-18 September 2009



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Objective of the consultation

- (1) To review existing epidemiological situation of leptospirosis in SEA Region including the impact of climate change
- (2) To review existing case definition and agree on revised case definition in the context of changing epidemiology and clinical picture of leptospirosis
- (3) To advice on capacity building for leptospirosis diagnosis in Member countries including laboratory networking

Introduction

Leptospirosis, also known as “rat-urine fever” in some countries, is transmitted by the urine of an infected animal and is contagious as long as it is still moist. Although rats, mice and other rodents are important primary hosts, a wide range of other mammals including dogs, deer, rabbits, cattle, buffaloes, sheep, and pigs also carry and transmit the disease as secondary hosts. Humans get infected through skin contact with water or soil containing urine from infected animals or consuming contaminated food or water. The disease is not known to be spread from human to human.

Leptospirosis is still widely overlooked and underreported. One of the possible reasons for this is that the clinical features are non-specific, with signs and symptoms similar to those seen in many other infectious diseases. Furthermore, confirmation of leptospirosis requires laboratory tests that are not always available and rapid diagnostic tests are not reliable.

Leptospirosis is an emerging public health problem in a number of countries of South-East Asia (SEA) region. Most countries in the SEA region are endemic to leptospirosis. The eleven countries in the SEA region together have a population of over 1.7 billion and a work force of about 774 million with more than 447 million people engaged in agriculture.

In India outbreaks of leptospirosis have often been reported from coastal areas of Kerala, Gujarat, Tamil Nadu, Karnataka, Goa and Andhra Pradesh. Thailand too has seen a dramatic rise in incidence of leptospirosis, mostly in its Northeast which experiences frequent flooding. The disease is also endemic in Indonesia. There is a direct correlation between the amount of rainfall and the incidence of leptospirosis, making it seasonal in temperate climates and year-round in tropical climates.



Outbreaks often occur after flash floods

Summary

The informal expert consultation was organized by WHO Regional Office for South-East Asia and hosted by National Institute of Epidemiology, Chennai. The consultation was attended by experts from Thailand, India, Indonesia, Sri Lanka, WHO Collaborating Center (CC) for Leptospirosis, Amsterdam and Port Blair. The experts reviewed leptospirosis situation in the region and there were presentation of country situation and control activities from high burden countries. Discussion was focused on case definition, estimation of burden of disease, surveillance and laboratory diagnosis including networking, chemoprophylaxis, case management, prevention and control.

It has been recognized that leptospirosis is an emerging and reemerging disease of public health importance in the region. Flash flooding is reported frequently from countries of South-East Asia region which is responsible for leptospirosis epidemics in past two decades. It is still not notifiable disease in many countries with high burden of leptospirosis. Although large numbers of pyrexia of unknown origin (PUO) are reported, investigation for leptospirosis is not carried out partly due to poor knowledge of clinical manifestation of leptospirosis or lack of laboratory diagnostic facilities. Leptospirosis is not considered for differential diagnosis of infectious diseases.

There is no systematic collection of data and information which is a major barrier for estimation of burden of disease. As a result, it is difficult to convince policy makers to prioritize leptospirosis as a major public health issue and convince potential donors and partners to support leptospirosis risk reduction activities in resource poor countries. WHO has taken a bold step to coordinate Leptospirosis Epidemiology Reference Group for estimation of burden of leptospirosis.

Surveillance of leptospirosis in rodents and domestic animals is important for developing appropriate risk reduction strategies, but it is neglected in most countries. It is not a priority disease in animal health sector and there is no institutional arrangement for study of leptospirosis and other rodent diseases of public health importance in most countries of the region.

Case definition was developed considering the field conditions and availability of laboratory facilities for clinical pathology and laboratory investigation. We agreed on sensitive case definition in the context of regional clinico-epidemiological situation.

The experience of mass chemoprophylaxis in endemic area of Gujarat of India was discussed in details. Thailand has been practicing early treatment of suspected patients in endemic areas. Chemoprophylaxis in new outbreak area has given good result in the past.

Leptospirosis risk reduction is a multidimensional and multidisciplinary activity which requires multisectoral coordination and cooperation. Although local technology has been developed in India and Thailand to minimize the risk of leptospirosis transmission in paddy fields and agricultural activities, more operational research is needed for practical application of new techniques.

The conclusions and recommendations of the consultation are as follows:

Conclusions and recommendations

Case definition

Considering the changing clinical manifestation of leptospirosis, limitation of available diagnostic test methods and need of early case detection and early treatment, the following case definition has been adopted;

Suspect case:

- Acute febrile illness ($\geq 38.50C$) and/or severe headache with
 - Myalgia
 - Prostration AND/OR
 - Conjunctival suffusion, AND
 - History of exposure to leptospira-contaminated environment

Probable (At primary health care level)

Suspect case with any **two** of the following:

- Calf tenderness
- Cough with or without hemoptysis
- Jaundice
- Haemorrhagic manifestations
- Meningeal irritation

- Anuria/ oliguria and/ or proteinuria
- Breathlessness
- Cardiac arrhythmias
- Skin rashes

Probable (At secondary and tertiary health care levels)

- Based on availability of laboratory facilities a probable case of Leptospirosis is a suspect case with a positive rapid IgM test

AND/ OR

- Supportive serologic findings (i.e., a MAT titre equal to 200 in a single sample)

AND/ OR

Any three of the following:

- Urinary findings: proteinuria, pus cells, blood
- Relative neutrophilia (>80%) with lymphopenia
- Platelets < 100,000 / cu mm
- Elevated serum bilirubin > 2 mg% ; liver enzymes moderately raised (Serum Alkaline Phosphatase, S amylase, CPK)

Confirmed

A confirmed case of Leptospirosis is a suspect or probable case with any one of the following:

- Isolation of leptospire from clinical specimens
- Positive PCR result
- Sero-conversion from a negative to positive or four-fold rise in titre by MAT
- Titre by MAT of 400 and greater in a single sample

Where Laboratory capacity not well established:

Positive by two different rapid diagnostic tests could be considered as laboratory confirmed case.

Surveillance

Considering the diverse disease surveillance system in countries of the South-East Asia Region and existence of systematic recording of clinical and laboratory confirmed leptospirosis cases in few countries, it is recommended to;

- include leptospirosis case reporting into the existing disease surveillance system with minimum data elements such as case, death, age, gender, location, basis of diagnosis and occupational linkage.
- carry out animal and rodent surveys and characterization of laboratory confirmed leptospira to identify circulating serovars and select candidate vaccine strains if deemed it necessary.
- improve disease surveillance in SEA Region through reporting and training.

Estimation of burden of disease (BoD)

Considering the importance of estimation of disease burden in SEA region for advocacy, prioritization and resource mobilization and understanding the complex nature of BoD in the absence of reliable and complete disease recording and reporting mechanism in the region, it is necessary to;

- establish a regional core group of experts by WHO SEARO with the following tasks;
 - Systematic review of epidemiological data
 - Epidemiological tools for BoD assessment: from LERG to be adapted to SEA Region
 - Execution of burden assessment – together with LERG
 - Identify gaps for research
 - Look for funding

Advocacy, awareness and education

Considering the protean nature of manifestation of disease, lack of laboratory diagnostic facilities, reporting of large number of PUO cases from flood affected areas, it is recommended to

- provide orientation to health professionals, community health workers on clinical diagnosis, case management, risk reduction measures of leptospirosis.
- organize public awareness campaign at community and school levels for recognition, prevention and control of leptospirosis in endemic areas.
- develop appropriate model IEC materials on recognition, prevention and control of leptospirosis considering disease characteristics, locality specific situation and community needs.
- organize meeting of major stakeholders (human and animal health, agriculture, education, civic bodies) for coordination of awareness campaign and control activities.

Diagnosis

Considering the fact that the performance (Sensitivity and specificity) of commercially available rapid diagnostic kits may differ from geographical region to other, and weak laboratory diagnostic facilities, the following points should be taken into consideration;

- Any new diagnostic tests must be validated before introduction and interpretation in the laboratory.
- Dark field microscopy should not be used for routine diagnosis as a sole test.
- Microscopic Agglutination Test is a gold standard which should be established at least in a National Referral Laboratory.
- ELISA test is a good option in a situation where MAT can not be introduced, performed and/or validated.
- PCR test has been proven as an effective diagnostic tool in early stage of illness.
- The following prescribed or alternate transport medium should be used for transportation and/or preservation of leptospires depending on availability:
 - 5ml EMJH or Fletcher's Medium (also the culture medium) -Prescribed
 - 5 ml Ringer lactate solution with 10% foetal calf or rabbit or horse serum (if no.1 not available). Immediately after reaching lab subculture to EMJH.
 - (If no. 1 and 2 not available) Unchlorinated tap water/well water (sterile) with 10 % rabbit or other serum can be used as transport medium.

Vaccination

Considering the fact that the efficacy of leptospiral vaccine produced in other geographical region is unknown due to local variability in serovars of endemic leptospiral strains in South-East Asia region and vaccination against one *Leptospira* serovar is not cross-protective against the other serovars, the following strategy should be taken into consideration;

- survey followed by continuous epidemiological monitoring of the prevalence of *Leptospira* serovars in a zone or region is crucial to select the correct serovars for incorporating into the vaccine.
- decision on vaccination should only be taken after well designed clinico-epidemiological studies of vaccines.

Chemoprophylaxis

Considering the results of efficacy of chemoprophylaxis in outbreak situation and endemic conditions in countries of South-East Asia region, it is recommended to consider post-exposure chemoprophylaxis;

- in case of laboratory accidents, capsule Doxycycline 100 mg twice daily for seven days or Amoxicillin or Ampicillin 2g daily for seven days.
- conduct well designed operational research on the use of chemoprophylaxis in endemic areas to ensure better compliance at the community level.

Case management

Considering the importance of early treatment of leptospirosis patients to reduce the case fatality rate, the following treatment regimen and possible transfer of severe and/or complicated cases needs to be taken;

- Mild illness (suspect case)
 - Cap Doxycycline 100 mg twice daily for 7 days OR
 - Amoxicillin or Ampicillin 2 g daily for seven days
- Mild illness (Probable case)/ Severe case
 - Inj Cry Penicillin G 2 MU IV 6 hourly after ST for 7 days , OR
 - Inj Ceftriaxone 1 gm IV OD for 7 days
- Shift patient to referral healthcare centre when any indication of organ dysfunction is noticed:
 - Renal
 - Hepatic
 - Pulmonary
 - Haemorrhagic
 - Neurological

Regional activities and capacity building

Considering the multisectoral and multidisciplinary nature of leptospirosis surveillance, diagnosis and risk reduction measures and the need of a regionally coordinated approach for capacity building at country level, the following action should be considered;

- Develop a regional strategic framework for surveillance, diagnosis and risk reduction of leptospirosis and discuss the document in a meeting of Programme Managers for consensus.
- Training modules should be developed in four specific areas considering the following training needs;
 - Epigroup: Surveillance, estimation of disease burden, outbreak response, sample collection at field (Rodent, animals, human), transportation, prevention and control
 - Labgroup: Laboratory diagnosis, quality control, quality assessment
 - Case management: Clinical diagnosis at peripheral and referral hospitals, individual case investigation, treatment of mild and severe cases, chemoprophylaxis
 - Programme management: Advocacy, health education, intersectoral cooperation (Public health, animal health, agriculture, local government), community mobilization, policy and project development, media communication
- Develop combined training programme for epidemiology and laboratory groups with the involvement of public health and animal health professionals for five to seven working days (Epigroup and labgroup together for basics and separate for specific areas such as hand-on training, estimation of disease burden, risk reduction strategies)
- Organize standard Training of Trainers at the regional level and provide support for country level training particularly for field level professionals.

Rodent control

Considering the fact that rodents are the major reservoirs of pathogenic leptospira. Hence controlling these reservoir species with proper strategy planning will reduce the incident of the disease in the affected areas. The strategy planning should cover the following:

- Identify the reservoir species of affected area
- Delineate areas for anti rodent activities
- Limit the operations to pre monsoon months
- Adopt appropriate technology for anti rodent operations which includes correct inputs and appropriate application technology.
- Capacity building among all involved personal and
- Create awareness among public to bring community involvement.

Programme schedule

Presentations (17 th September 2009)		
Session I		
Estimates of leptospirosis burden		
Chairman: Dr Rudy Hartskeerl		
08.15-08.35	1. Regional overview of leptospirosis in South-East Asia Region Country experience in surveillance, prevention and control of leptospirosis	Dr Gongal
08.35-09.00	a. India	Dr UVS Rana
09.00-09.20	b. Indonesia	Dr Rita Kusriastuti
09.20-09.40	c. Sri Lanka	Dr Pranitha Somaratne
09.40-10.00	d. Thailand	Dr Teerasak Chuxnum
10.00-10.30	1. Estimation of burden of leptospirosis in South-East Asia	Dr Sugunan
10.30-11.00	2. Utility of surveillance data for estimation of burden of disease due to leptospirosis	Dr Rudy Hartskeerl
Session II		
Laboratory Diagnosis and Networking		
Chairman: Dr Subhash Sehgal		
11.30-12.00	1. Laboratory diagnosis, new trends, laboratory diagnostic criteria, quality control and external quality assurance	Dr Vijayachari
12.00-12.15	2. Regional networking of laboratories- Nodal, regional ,peripheral laboratories and role of WHO CC as coordinating lab	Dr Gongal + Dr Vijayachari
Session III		
Surveillance framework and case management		
Chairman: Dr Pravit Choomkasien		
12.15-12.45	1. Case definition for surveillance, diagnosis and case management	Dr. Subhash Sehgal
12.45-13.15	2. Integration into existing multi-disease surveillance systems	Dr Sampath Krishnan
13.15-14.00	3. Case management at different levels and specialized care for complicated cases	Dr Gasem
Session IV		
Risk reduction strategies		
Chairman: Dr Rita Kusriastuti		
15.00-15.30	1. Source reduction strategies targeting domestic animals, rodents	Dr UVS Rana
15.30-16.00	2. Exposure reduction – High risk occupations, workplace practices, environment management	Dr Pravit Choomkasien
16.30-17.00	3. Vaccines for humans and animals	Dr Gongal
17.00-17.30	4. Role of chemoprophylaxis	Dr Sudhir Gandhi

Group discussions (18th September 2009)

Group I Surveillance framework and risk reduction

The structural framework of the surveillance system including functional units such as case detection units, data collating and analysing centres and decision support systems needs to be specified. Functions including case detection, bottom-up transmission of disease occurrence data and top-down dissemination of feedback information, analysis methods, initiation of public health action at various levels and in-built mechanisms for evaluation of the system need to be described. The attributes of the system including timeliness, flexibility, acceptability to state holders, ability to be integrated into existing surveillance set up and robustness to adapt to unanticipated situations have to be set and their feasibility needs to be assessed. Other related functions such as periodic surveys, surveillance of animal leptospirosis, rodent activity need to be discussed. Specific points to be discussed include: -

- Case definition
- Reporting units and channels
- Minimum data elements required
- Laboratory surveillance
- Periodic surveys
- Animal and rodent surveillance
- Case management and chemoprophylaxis

Group II Laboratory procedures and diagnostic criteria

The panel of laboratory test that could be used for the diagnosis needs to be made after assessing the merits and demerits of each test. Criteria for categorizing a test result as positive or negative in the case of tests with quantitative results need to be set. The advantages and disadvantages of using a single test or a combination of tests for diagnosis have to be discussed. Different tests to be used in different situations such as for routine surveillance for detecting sporadic cases and during epidemics and applying a diagnostic criteria to categorize a case as definite or probable case of leptospirosis are the other points that need to be discussed. The need to set uniform diagnostic standard and the method to achieve this are also important points of discussion. Modalities for networking, sharing information and QA and QC activities also need to be discussed. Specific points could be: -

- Laboratory tests
- Diagnostic criteria
- Diagnosis in different situations (sporadic cases, epidemics)
- Diagnosis with different strengths of confirmation
- Uniform standards
- Networking for sharing information, quality control testing

Group III	Disease burden estimation
	<p>Aiding in public health prioritization is an important function of surveillance system. Quantitative data indicating the relative importance of the disease to the overall disease scenario needs to be generated for this. The widely accepted method for this is to estimate the burden of disease in terms of composite indicators such as disability adjusted life-years (DALY) lost. Reliable morbidity and mortality data are prerequisites for DALY estimation. So is an estimate of the disability coefficient for leptospirosis. There is a need to explore the possibility of generating data on burden of disease due to leptospirosis in the region as well as in each of the member countries. The data requirements and methods for estimating disease burden due to leptospirosis may be discussed. The desirability of entrusting the responsibility of developing a method for this to a working group may also be considered.</p> <ul style="list-style-type: none"> • Availability of essential indicators • Disability coefficient estimation • Working group to develop methodology and integration to surveillance system • Study group to estimate current burden of disease due to leptospirosis from surveillance data • Incorporating data collection methods for disease burden estimation to the curriculum of periodic training
Group IV	Training Format
	<p>There is a necessity to conduct regular training for laboratory personnel and other professionals for strengthening the diagnosis, surveillance and preventive measures. Training is often conducted targeting specific professional/technical groups. However, a comprehensive training to the team of professionals that would be involved in surveillance, prevention and control of leptospirosis could be more effective as it would encourage team work and an understanding of the roles of all the disciplines involved in surveillance, prevention and control. A team comprising of a clinician, veterinarian , public health specialist, microbiologist and technician could be an ideal training candidate. The possibility of such a training format could be discussed. Target professionals/ health workers, training content and methodology and follow up action are other important areas that need to be discussed.</p> <ul style="list-style-type: none"> • Target needs • Target group • Training content • Training methods • Follow up action
Presentation of group discussion reports	
Draft document	
Summing up	

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