Assessment of Microcephaly in context of Zika Virus
February 25, 2016

What is microcephaly?
Microcephaly is a birth defect where the head size of the baby is much smaller than other babies of the same age and sex\(^1\). This is often accompanied by other anomalies such as intellectual disability in addition to higher risk for mortality/morbidity at birth and other physical (visual, hearing) and mental disabilities as the babies grow older. The severity of microcephaly itself ranges from mild to severe\(^2\).

Microcephaly is a rare birth defect which has gained a lot of importance due to suspected associations with Zika virus (ZIKV) infection during pregnancy\(^3\).

How common is microcephaly?
Prevalence of microcephaly ranges from 2 - 12 babies per 10,000 live births in the Unites States\(^4\). Birth prevalence of microcephaly, estimated through a recent systematic review and meta-analysis of 55 studies reporting the prevalence of congenital anomalies in India was 2.3 per 10,000 births which was similar to reports by the European surveillance of congenital anomalies (EUROCAT) \(^5\).

Microcephaly and Zika virus
On the 1st of February 2016, the World Health Organization (WHO) declared Zika virus disease a Public Health Emergency of International Concern, after reports of increased cases of microcephaly in specific geographic areas of Brazil reporting ZIKV transmission\(^3\).

WHO is developing guidelines that include standard case definitions, standard testing and diagnostic techniques; and standard research protocols to support the vulnerable countries in SEAR.

Potential adverse effects of exposure to Zika virus in utero may not be restricted to microcephaly alone. Surveillance approaches should also identify changes in rates of spontaneous abortion, stillbirths, low birth weight and small for gestational age. Postpartum prevalence of visual, hearing or other neurological and developmental abnormalities should also be looked for and monitored.

NBBD Surveillance network
The WHO SEARO New born and birth defect (NBBD) surveillance network is an initiative in partnership with US-CDC, operational since July, 2014 to ascertain the prevalence of birth defects and study newborn health and stillbirths in the South East Asia region.

The birth defects component of the online surveillance system is currently capturing externally visible birth defects, from selected participating hospitals in 8 SEAR countries. We are working to upgrade the system in response to the recent Zika virus Public Health Emergency to monitor occurrence of microcephaly and detect any unusual increase and clustering of cases in the region.

In case of a baby reported with microcephaly the mother needs to be investigated for any evidence of Zika virus infection as per the standard testing guidelines.

What causes microcephaly?
There are many potential causes of microcephaly, but they often remain unknown. The most common causes include:\(^2\):

- **infections in the womb**: toxoplasmosis (caused by a parasite found in undercooked meat), rubella, herpes, syphilis, cytomegalovirus and HIV;
- **exposure to toxic chemicals**: maternal exposure to heavy metals like arsenic and mercury, alcohol, radiation, and smoking;
- **genetic abnormalities** such as Down syndrome; and
- **severe malnutrition during fetal life**, amongst others.

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Interim guidance

- Increased rates of congenital microcephaly have been reported in the context of the Zika virus outbreak in Brazil, beginning in late 2015. However, different anthropometric cut-offs of microcephaly i.e. the measurement used to determine if a newborn has a small head or not; it will take time and effort to understand the exact nature and biological basis of the association.
- Ministries of Health and public service delivery centers in the SEAR region are encouraged to increase surveillance and administer mandatory reporting of possible cases of either Zika Virus and/or birth defect/microcephaly.

What can you do?
- We encourage all member countries to document Head Circumference (HC) of all live births.
- You can log in to our database- click here to register
  - **Head circumference (HC),** the measurement of the baby’s head around its largest area, it is the best measure for assessing microcephaly at birth. It should be measured using standardized technique and equipment at least 24 hours after birth.
    - **Technique:** Maximum circumference through the supraorbital ridge to the occiput
    - **Equipment:** Use a flexible but non-stretchable tape
    - **Measurement:** Health care providers need to measure head circumference and interpret it according to the WHO standards using Standard Deviation (SD) scores specific for sex and gestational age.
- WHO has Growth Standards for term newborns and Intergrowth standards for preterm newborns (boys and girls) that should be used to classify microcephaly
  - To calculate head circumference (HC) current and expected for age, use this [online tool](#).

What are the reporting standards and cut-off values?

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Interpretation</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HC less than -2SD</td>
<td>Microcephaly</td>
<td>Head circumference of less than -2 SD should be considered to have microcephaly</td>
</tr>
<tr>
<td>HC between -2SD</td>
<td>Microcephaly</td>
<td>Regular clinical follow up during infancy which includes rate of head growth, maternal and family history to assess for genetic or other causes, and physical and neurological examinations for associated disabilities. A significant proportion of these children could have normal neurological development.</td>
</tr>
<tr>
<td>and -3SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HC less than -3SD</td>
<td>Severe Microcephaly</td>
<td>CT scan or MRI; and perhaps ultrasound if the fontanelle is of a reasonable size, to detect congenital brain malformations.</td>
</tr>
</tbody>
</table>

*Newborns with microcephaly and structural brain abnormalities defined by neuroimaging or neurological or functional disabilities should be considered to have microcephaly of major importance.

How can you manage microcephaly?
- Microcephaly is a lifelong condition with no known cure or standard treatment.
- Options range as babies with mild microcephaly often don’t have any other problems besides small head size.
- They need routine check-ups to monitor their growth and development.

We recommend the Network hospitals to maintain their capacity to detect and confirm cases of microcephaly in all newborns delivered in the hospitals using the standard technique and classified as described above.

For more information, contact us at secah@who.int
Basic Assessment

Are you aware of the recent Zika virus outbreak?

No

Refer to WHO Zika Fact sheet

Yes

Are you doing any outbreak surveillance/documentation?

No

Refer to WHO Reporting Standards

Yes

Are there any new reports of ‘fever with rash’?
Are any of them reported in pregnant women?
Is there an unusual increased incidence of microcephaly?

No

Yes

Measure Head Circumference of all Live Births-Intergrowth21 Standards Classify Microcephaly
Report to NBBD Surveillance network

Investigate the Mother for Zika virus infection (Refer national guidelines)

Additional Reporting to WHO-SEARO
Contact: secah@who.int
Global Response

WHO has activated its Emergency Operations incident management system to coordinate the international response. The guidelines for Strategic Response and Joint Operations Plan aims to provide support to affected countries, build capacity to prevent further outbreaks and control them when they do occur, and to facilitate research that will help us better understand this virus and its effects.

1. SURVEILLANCE

- Provide up to date and accurate epidemiological information on Zika virus disease, neurological syndromes and congenital malformations.

2. RESPONSE

- Engage communities to communicate the risks associated with Zika virus disease and promote protective behaviors, reduce anxiety, address stigma, dispel rumors and cultural misperceptions.
- Increase efforts to control the spread of the Aedes and potentially other mosquito species as well as provide access to personal protection measures equipment and supplies.
- Provide guidance and mitigate the potential impact on women of childbearing age and those who are pregnant, as well as families with children affected by Zika virus.

3. RESEARCH

- Investigate the reported increase in incidence of microcephaly and neurological syndromes including their possible association with Zika virus infection.
- Fast-track the research and development (R&D) of new products (e.g. diagnostics, vaccines, therapeutics).

Resources

This document assesses the possible risk of transmission, plausibility between the increased incidence in newborns with microcephaly and Zikavirus infection gathered from the limited sources. Detailed information on the epidemiology of the Zikavirus as well as microcephaly can be found in the factsheets via related links:

Zika virus
- Fact sheet: Zika virus (English version)
- Zika virus disease: Questions and answers
- WHO’s work on Zika virus

Microcephaly
- Q&A: Women, microcephaly and Zikavirus (English version)
- WHO’s work on Microcephaly
- Head circumference for age
References
1. INTERGROWTH-21st very preterm size at birth reference charts, Villar, José et al. The Lancet, Volume 0, Issue 0, Published Online: 18 February 2016 DOI: http://dx.doi.org/10.1016/S0140-6736(16)00384-6
4. CDC, 2016- Facts about Microcephaly, Birth Defects, NCBDDD, CDC www.cdc.gov/ncbddd/birthdefects/microcephaly.html
5. WHO- ZIKA STRATEGIC RESPONSE FRAMEWORK & JOINT OPERATIONS PLAN, JANUARY-JUNE 2016 http://apps.who.int/iris/bitstream/10665/204420/1/ZikaResponseFramework_JanJun16_en g.pdf?ua=1