

## Zika Virus Epidemic: Risk of Collateral Damage from Poorly Defined Risks

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## Introduction

In early 2015, an outbreak of *Zika virus*, a *flavivirus* transmitted by *Aedes* mosquitoes, was identified in northeast Brazil, an area where dengue virus was also circulating. By September, reports in the number of infants born with microcephaly in Zika virus affected areas increased and Zika virus RNA was identified in the amniotic fluid of two women whose fetuses were diagnosed with microcephaly by prenatal ultrasound. The natural long term incidence of microcephaly was only 1/20,000 [1]. Several months after the Zika virus outbreak a dramatic increase of new microcephaly cases was noted in women who were pregnant during the outbreak.

A short but comprehensive article was published in late February in the EC Gynaecology [2] journal instead of repeating this knowledge, this current article intends to raise questions regarding the risk of over reacting to the threat of fetal viral infection. There is strong evidence of association between fetal viral infection and microcephaly. However, evidence of causation is sparse and extensive research is urgently needed. The association of Zika virus and certain neurological diseases has been trumpeted in global mass media in a sensational way. It was only natural that social networks, online blogs and mass media have exploded with Zika virus related articles. This large amount of repetitive content has caused the number of searches for Zika virus on Google to increase by 3000% and reach panic levels. The statement by the Director- General of the WHO Margaret Chan who said "Zika virus now spreading explosively" has certainly made many to be concerned [3].

Microcephaly is a brain anomaly that can be caused by genetic causes, secondary to maternal infections with certain viruses, alcohol and drug abuse, environmental toxins and premature fusion of cranial bones (craniosynostosis) as well as certain metabolic disorders.

Microcephaly leads to severe undergrowth of the fetal/neonatal brain with abnormalities ranging from mild mental deficiencies to severe mental retardation and other neurological defects including but not limited to cerebral palsy [4]. The outbreak of Zika virus infections reported in Brazil in 2015 has been associated with a concurrent increase in the cases of microcephaly recorded by various Brazilian health organizations. There are however certain issues that make the information suspect. In Brazil, microcephaly was initially defined as head circumference below 33cm and later corrected to 32cm. In Pernambuco, the Brazilian state with the highest number of reported cases in Brazil, among 1373 cases reported, only 248 (18%) have been investigated and of those, only 138 (55%) confirmed as microcephaly associated with some infectious etiology, which may or may not include Zika virus. This became further complicated by the fact that there are at least three different reporting systems in Brazil using varying criteria. On the other hand, because some of the reporting requires microcephaly to be reported when there is some form of association with Zika virus, some researchers suspect that the Zika virus related cases of microcephaly might in reality be underestimated. Such magnitude of discordant information leads to confusion and in turn, confusion can easily lead to panic [3].

A concerted effort is in progress to coordinate the actions of various global and national health agencies in order to obtain valuable and definitive data that could effectively elucidate this global threat.

Until we find the answers to the questions listed in the text box and all questions that will arise during the research, as we gain further knowledge, we must be very cautious on how we interpret the results of recent reports. Microcephaly is defined as a head size that is 3 SD (standard deviations) below the mean. What is a doctor to tell the mother if the fetus head during the early second trimester is small but between 1SD and 2SD which is in the normal range? The fear that a small but normal head might become smaller as the pregnancy advances and become abnormal could prompt many parents to choose abortion as a preemptive action because of an unspecified probability of the fetus developing microcephaly by the time of birth.

Depending on cultural and religious societal influences, some patients might choose to continue the pregnancy regardless of fetal outcome while others might choose to terminate the pregnancy to avoid unwanted complications. This issue must be addressed very seriously by all concerned. Physicians will need to discuss any suspicious findings with the patients and try to educate them about the difficulty of prenatal diagnosis of microcephaly, the potential consequences, available treatments if any, and other alternative management choices, so that patients can make an informed decision free from fear and panic.

- 1. What is the rate of fetal transmission among all pregnancies infected during the time period under examination?
- 2. At what gestational age during pregnancy is the virus transmitted more readily through the placenta?
- 3. Is there any correlation between the gestational age at time of infection and the severity of microcephaly?
- 4. Are there other congenital defects that can be caused from Zika virus in addition to microcephaly? If yes, at what gestational age are other organs more vulnerable?
- 5. Does any of the existing antiviral medications decrease the risk of fetal damage in mothers that are actively infected during pregnancy?
- 6. Are there any environmental factors in the region of the outbreak that might have contributed to the occurrence of microcephaly?
- 7. Does previous maternal infection with Zika virus protect fetuses in subsequent pregnancies?
- 8. Identify all modes of transmission.

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