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Commentary

Seroprevalence of dengue virus infection and its detrimental effects on pregnant women in wake of the recent floods

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INTRODUCTION

Dengue infections are caused by four genetically related but antigenically distinct dengue virus serotypes (DENV-1,2,3,4).[1] Spread via the female Aedes mosquito, the disease is highly widespread in tropical and subtropical areas, where the climate allows ideal breeding grounds for *Aedes aegypti* the primary vector for dengue infections.[2] Moreover, *Aedes albopictus* has emerged as an important secondary vector, especially in countries not susceptible to *Aedes aegypti*, further increasing the worldwide incidence of the disease.[3] As a result of these developments and vectors, adapting well to urban areas, dengue is rapidly transforming into a global burden. Endemic in 129 countries, a study claims that an alarming 3.9 billion people worldwide are at risk of contracting dengue infection.[4] Furthermore, data shows that the incidence of dengue infections is rising drastically, with the number of cases increasing from 2.4 million in 2010 to 5.2 million in 2019.[3]

Despite the worldwide spread, Asia still has 70% of the burden.[5] Pakistan, in particular, has a high incidence of dengue. The recent history of rampant floods and the rapid increase in population, supplemented by the lack of proper healthcare facilities, provides an ideal environment for the growth of the virus. Stagnant rainwater on roads and rooftops has provided the vector with suitable breeding grounds, while the lack of effective antivirals and vaccines, especially in now-isolated rural areas, has further fostered its spread in the form of fevers.[6] The wide spectrum of manifestations, ranging from a mild fever, without accompanying symptoms, to severe hemorrhagic fever or potentially lethal dengue shock syndrome, makes it more challenging to effectively track and monitor the spread of this disease.[3] Though the primary method of transmission for dengue virus is mosquito bites, there is concrete evidence of vertical transmission when pregnant women are infected.[7]

MODE OF TRANSMISSION

Upon being bitten by *Aedes aegypti*, the non-structural protein of the dengue virus, NS-1, is secreted into the individual's sera and co-localizes with dsRNA and other components of replication complexes, playing an essential role in virus replication.[8] Hence, presence of NS-1 indicates DENV infection, making it an important diagnostic marker. In case of a negative result, the patient is checked for presence of IgM antibodies, which can confirm recent exposure to the virus. In pregnant women, DENV activates the innate immune system which stimulates the upregulation of pro-inflammatory cytokines, interleukin 6 (IL-6) and interleukin 8 (IL-8), raising their concentration in the maternal serum. IL-6 and IL-8 act symbiotically to activate the endothelium, causing endothelial cell dysfunction, followed by vascular leakage, contraction of intravascular volume, and fluid loss. This depletion of volume can result in hypo-perfusion, leading to hypoxia and eventually multi-organ dysfunction.[9] Moreover, complications to the fetus can arise via vertical transmission when clinical manifestations like thrombocytopenia and plasma leakage impair placental circulation, allowing DENV to cross the placental barrier.

ADVERSE EFFECTS OF DENGUE ON THE INFANT AND MOTHER

Due to the transmission of DENV from the mother to child, shortly after birth, the neonate suffers from fever,

respiratory distress, and thrombocytopenia; diminution of symptoms requiring platelet transfusions.[10] A systematic review of 30 published articles by Pouliot et al found that offsprings of DENV-infected women have a lower birth weight in comparison to those of uninfected women. In addition, women, infected with DENV during pregnancy, are more likely to have cesarean deliveries, as well as pre-eclampsia.[7] Pre-eclampsia is detrimental to the patient's health and can cause preterm birth, since it is advised that delivery be no later than 34 weeks of gestation, for safety of both, the mother and the infant.[11] Furthermore, pre-eclampsia results in thrombocytopenia, increasing the probability of the mother developing HELLP syndrome, as approximately 1 in every 5 women, suffering from pre-eclampsia or eclampsia, acquire this disease.[12] An observational study conducted in 2021 observed 44 pregnant women, who suffered from DENV. Out of these women, post-partum hemorrhage occurred in ten women while eight experienced acute kidney injury, and two were in need of dialysis. Eight developed ARDS, seven called for mechanical ventilation, four suffered from acute liver failure, and eighteen women showed proof of shock. An additional seven were near-miss cases and a total of fifteen deaths were reported; two miscarriages, four stillbirths, seven maternal and two neonatal deaths.[9] This study ascertains the potential risk, dengue carries, for pregnant women.[13-15]

CONCLUSION

The disastrous monsoon rainfall in Pakistan since mid-July 2022 has put 33 million people at risk of dengue infection, which is a third of the country. Along with more than 1.7 million houses, approximately 2000 health facilities have been destroyed in 81 tragedy-stricken districts. The flooding has reportedly caused 8.0 million affected individuals in need of health assistance, 12,867 causalities, 1739 deaths, and 64,767 reported cases of dengue fever. With no proper assistance, every victim of these floods has become susceptible to contracting dengue including 650,000 pregnant women, with more than 130,000 requiring emergency care and 2000 births occurring daily. Increase in stagnant water, due to flooding, has resulted in a drastic rise in dengue cases. Without proper health care and lack of action from relevant bodies, victims of dengue have been neglected, with pregnant women unable to have a safe delivery. A better method of tackling this situation would be to modify the relief boxes, being provided to affected areas by NGOs. Addition of dengue medications, plus mosquito repellents as basic necessities should be considered. An informant should be sent to these areas, in order to raise awareness of dengue's potential threats and vulnerability of pregnant women so, more caution can be taken. Medical camps, catering to these areas, should be equipped with relevant medications and technology to alleviate problems, with childbirth, induced by dengue. With this commentary, we hope to raise awareness and initiate plans to mitigate the adversities so that the potential casualties of this generation and the ones to come, can be minimized. This is no less than a humanitarian crisis and we hope to convey the need for help.

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