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Review article

Dengue in pregnancy

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ABSTRACT

Dengue fever is a febrile disease found in the tropics and is a major health concern for Southeast Asian countries. The obstetrician's concern regarding the effect of dengue infection revolves around the maternal and foetal effect of infection in different trimesters of pregnancy and labour, risk of transplacental transfer, confusion with other co-morbidities and the management. Most common foetal outcomes related with dengue infection during pregnancy are preterm birth and low birth weight babies. Dengue fever in pregnancy most often is treated conservatively with a careful watch on complete blood count.

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1. Introduction

Dengue fever (DF) is a febrile disease found in the tropics and is endemic in more than 100 countries. It is one of the fastest spreading viral infections and remains a major health concern for Southeast Asian countries with cyclic epidemics [1]. It is caused by one of the four closely related virus serotypes of the genus flavivirus, family flaviviridae. Infection with one serotype provides long lasting immunity against that serotype but cross reactivity against the other serotype is temporary. The risk of severe dengue increases with subsequent infections [2]. In India multiple viral serotypes are circulating and some regions have case fatality rates of 3–5% in general population, which is much higher than other Southeast Asian regions (1%) [3]. Whether dengue infection is associated with adverse maternal and neonatal outcome, is still a dilemma. There is a paucity of literature on effects of dengue infection on pregnancy outcome.

2. Concerns

Management of dengue infection in pregnancy should be taken seriously to reduce morbidity and mortality in mother as well as foetus. Early detection and access to proper medical care reduces case fatality from 20% to below 1% in DF [4]. The obstetrician

concern regarding the effect of dengue infection revolves around the maternal and foetal effect of infection in different trimesters of pregnancy and labour, risk of transplacental transfer, confusion with other co-morbidities and the management. Baseline tachycardia, lower baseline blood pressure and lower hematocrit of pregnancy may give rise to confusion in the diagnosis of dengue. In this reviews, original articles and case reports were identified by searching PUBMED from 1994 to July 2016 using the keywords 'dengue, pregnancy, maternal and foetal outcome' and finally 29 articles have been refereed to. Evidences suggest that the symptomatic dengue infection is associated with poor foetal outcome [5]. In view of poor obstetric outcomes dengue infection during pregnancy warrants early admission and prompt management [6].

3. Clinical presentation of dengue in pregnancy

The clinical manifestations of dengue in pregnant women are similar to those of non-pregnant women but with some important differences [7]. Patients generally present with:

- Fever with myalgia (most common).
- Abdominal pain (important to differentiate from threatened abortion/preterm labour).
- Dehydration and loss of taste for food.
- Severe headache (important to differentiate from severe preclampsia) and body pain.
- Nausea and vomiting (to be differentiated from hyperemesis gravidarum).

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- Bleeding from the gums.
- Rashes on upper body (to be differentiated from pruritic urticarial papules and plaques of pregnancy (PUPP)).
- Pleural effusion, ascites and hypotension (to be differentiated from amniotic fluid embolism if patient in labour).
- Foetal death.
- Involvement of lungs and liver (high SGOT/SGPT) (to be differentiated from HELLP syndrome).

4. Impact of dengue on pregnancy

Adverse effects of dengue virus infection depend on the different stages of pregnancy, i.e., early and late pregnancy, peripartum and postpartum period (Table 1).

4.1. Effect of dengue infection in early pregnancy

The teratogenic and abortifacient effects of dengue infections on pregnant women before 20 weeks of pregnancy are unclear. Prevalence of miscarriage associated with dengue infection during pregnancy has been reported from case series, which ranged from 3.8% in Sri Lanka to 16% in India [8,9]. There are few case reports of congenital anomalies after dengue infection in early gestation but they may be unrelated with infection [10].

4.2. Effects of dengue infection in late pregnancy

Although most common foetal outcomes related with dengue infection during pregnancy are preterm birth and low birth weight babies but the results from one of the meta-analyses published in Lancet in 2016 showed no significant association between the infection during pregnancy and preterm birth and low birth weight babies [5].

The possible hypothesis for adverse foetal outcome in pregnancies with dengue infection has been attributed to increased production of proinflammatory cytokines including IL6, IL 8 and TNF alpha which can affect the uterus through the increased production of uterine activation proteins thereby causing preterm delivery [11,12]. The prevalence of preterm birth ranged from 3% to 17% and low birth-weight babies ranged from 9 to 19% in various cohort studies [7,13].

There are few case series where stillbirths had been reported in dengue infection. Prevalence of stillbirth in pregnant women who had dengue infection during pregnancy varied between 4.7% and 13% [9,14,15]. The stillbirths in these case series occurred mostly only in women who had severe dengue infection. It has been postulated that thrombocytopenia, plasma leakage or bleeding tendency by dengue infection can affect the placental circulation and foetal death [16]. Moreover presence of virus in the placental tissue can also cause stromal oedema, increased formation of

syncytial knots and chorangiosis which can lead to foetal growth retardation, hypoxia and also foetal death [17,18].

Dengue myocarditis have also been reported which highlights the need to consider the dengue infection in pregnant patient living or travelling to endemic areas who presents with cardiopulmonary failure [19]. Another possible effect of DF and dengue haemorrhagic fever (DHF) in pregnancy is bleeding due to severe thrombocytopenia especially in high-risk cases, such as placenta previa.

4.3. Vertical transmission of dengue infection

The risk of vertical transmission is well established among women with dengue during the perinatal period [20,21]. Perinatal transmission of dengue virus is confirmed when the dengue virus is identified in placenta and newborn serum. It is most commonly seen in cases where infection occurred at or near the time of delivery. Those infants had common clinical features of thrombocytopenia, fever, hepatomegaly and varying degrees of circulatory insufficiency [22]. The reason of transplacental transfer of virus can be due to endothelial damage and increased vascular permeability in cases of severe dengue infection [23]. It is important to know that dengue infection may cause disease in neonates born to infected mothers, even if mother experiences asymptomatic infection which can commonly occur in endemic areas [24]. It is well known that after dengue infection a long lasting serotype specific immunity is acquired and high antibody titres of one dengue type are protective against another serotype but if the antibody titres have decreased this may enhance the immune response (immune enhancement) causing DHF [25]. These maternal antibodies which are transferred transplacentally in term babies are thought to protect infants from dengue infection when the antibody titres are high. It is important to note that the mother infected early in pregnancy and the mothers of preterm babies do not transfer the antibodies to their neonates due to immature placenta lacking Fcγ II receptors which develop in the third trimester [24]. Moreover the half-life of these maternal antibodies is 2.6 months, thus after 3 months when these antibodies are reduced to minimum, immunological enhancement may cause DHF in the infants. A study in Thailand on placental antibodies during maternal infection suggested that if the time interval between maternal infection and delivery were long enough, the newborn would be protected against severe neonatal dengue by maternal IgG antibodies [24]. Various studies have given different neonatal outcomes in the dengue infected pregnant females which could be due to the beneficial role of an early platelet transfusion for severe thrombocytopenia or a clotting disorder and the length of time between infection and birth and whether the baby was protected by antibodies [26]. Dengue should be included in the differential diagnosis of neonatal sepsis in neonates of babies where dengue is endemic [27].

4.4. Impact of dengue at parturition

Severe bleeding may complicate delivery and surgical procedures during the critical phase, i.e., the period coinciding with marked thrombocytopenia with or without plasma leak. The risk of maternal haemorrhage remains the major concern in the term pregnancy or during labour in patients with dengue infection. The anaesthesia in these patients with DHF is also a major concern. General anaesthesia is a preferred choice in the absence of hypertension and central nervous system manifestations, as risk of spinal haematoma due to damage of a non-compressible vessels can occur in spinal anaesthesia [28]. Dengue fever does not warrant termination of pregnancy.

Table 1
Fetomaternal complications of dengue in pregnancy [25].

Maternal complications
Miscarriages
Premature labour
Still birth
Haemorrhage during labour
Retroplacental haematoma

Foetal consequences
Prematurity
Low birth weight/intrauterine growth retardation
Foetal death in utero
Acute foetal distress during labour
Maternal-foetal transmission
Neonatal thrombocytopenia

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