International Journal of Medicine Research
ISSN: 2455-7404; Impact Factor: RJIF 5.42
Received: 16-01-2019; Accepted: 23-02-2019
www.medicinesjournal.com
Volume 4; Issue 2; April 2019; Page No. 31-34

A retrospective study of dengue fever in pregnancy on maternal and fetal outcome in a tertiary center

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Abstract
Background: The increasing incidence of adult dengue fever has led to the increase in number of infected pregnant women. Dengue, during pregnancy may be associated with various complications like preterm delivery, fetal death, low birth weight, neonatal admissions, fetal anomalies, and miscarriage. Timely intervention can improve the maternal as well as fetal outcome. The aim of the study was to assess the clinical profile, maternal and fetal outcome of dengue fever during pregnancy.
Methods: A retrospective study was carried out, among the antenatal patients who were diagnosed with serologically confirmed dengue fever during a period of 12 months (Jsan 2017 to Dec 2017); at a Tertiary care Hospital in Coimbatore, Tamil Nadu. Patients were included irrespective of period of gestation of contracting the disease and were followed up till delivery and all babies were followed up to six weeks post-partum.
Results: Thrombocytopenia(<1.5L/mm3) was found in 66.6%(n=40) patients, of which 8.2%(n=5) patients had Platelet count below 25,000 cells/mm3 and 8.2% patients required platelet transfusion. Other complications observed were spontaneous abortions (6.5%); preterm birth (9.5%), oligohydramnios (8.2%).Fetal distress and meconium stained amniotic fluid were observed in 7.6% Adverse fetal outcome observed were low birth weight (27.3%), prematurity (23%)
Conclusions: The gestational age at presentation of dengue fever appeared to be significant. Early onset or late onset in pregnancy appeared to have a bad prognosis. A high suspicion is essential in any pregnant female with fever during epidemics especially in endemic areas like Tamil Nadu. Conservative medical and obstetrical management is the treatment of choice.

Keywords: dengue fever, dengue hemorrhagic fever, dengue shock syndrome thrombocytopenia

1. Introduction

Dengue is an acute mosquito-borne viral infection that places a significant socioeconomic and disease burden in India. The recent outbreak in India in 2015 there where about 1 lakh cases were reported of which there were 220 deaths as reported by national vector borne disease control programme [1].

Dengue fever is a viral disease spread by *Aedes aegypti* (Diptera: Culicidae) mosquito. It is caused by a single stranded RNA virus belonging to the family Flavivirus. There are four serotypes DEN1, DEN2, DEN3, and DEN4 [2].

It is more common in children but with increasing rate of adult dengue fever victims, the number of infected pregnant women has also increased. In most of the cases of dengue fever in pregnancy, no serious harm has been noted. Treatment includes proper hydration, antipyretics and careful monitoring [3].

Dengue fever in pregnancy can be associated with various complications like haemorrhage, abortion and maternal mortality and in fetal complications like preterm delivery, low birth weight, fetal anomalies and intrauterine death. Timely intervention can improve the maternal as well as fetal outcome.

Classic dengue fever (DF) is defined by the World Health Organization as an acute febrile illness with two or more of the following signs or symptoms: intense headache, retro-orbital pain, myalgia, arthralgia, rash, leukopenia and hemorrhagic manifestations. The clinical severity of disease has a wide spectrum, and according to the World Health Organization (WHO) dengue classification scheme, there are four grades ranging from uncomplicated dengue fever (DF) to dengue hemorrhagic fever (DHF) and devastating dengue shock syndrome (DSS)[2]. DHF is currently defined by the following four World Health Organization (WHO) criteria:
Fever or recent history of fever lasting 2-7 days

Any hemorrhagic manifestation
Thrombocytopenia (platelet count of <100,000/mm3)
Aim was to assess the clinical profile, maternal and fetal outcome of dengue fever during pregnancy.

Materials and Methods

A retrospective study was carried out, among the antenatal patients who were diagnosed with serologically confirmed dengue fever during a period of 12 months (jan 2017-Dec 2017) at KOVAI medical center and hospital a Tertiary care Hospital in Coimbatore TN, India. Patients were included irrespective of period of gestation of contracting the disease and were followed up till delivery and all babies were followed up to six weeks post-partum.

Methods

Every consecutive antenatal patient diagnosed with dengue fever clinically and serologically during the study period were included in the study, irrespective of the gestational age. Antenatal patients who presented to the OPD and casualty with clinical features of dengue fever during the study period were examined and Laboratory investigations like Dengue IgM ELISA were used to confirm the diagnosis of Dengue fever.60 patients were included in this study after informed consent.

Neonates of mothers who presented with dengue fever near

term were monitored closely for clinical features of dengue fever and thrombocytopenia.

Results

During the study period, 60 cases of maternal dengue were diagnosed and confirmed biologically.

Table 1: Distribution of subjects - gestational age at diagnosis

Gestational age at diagnosis	Percentage
<12 weeks	8.3%(n=5)
12-20 weeks	21.4%(n=13)
20-28wks	15%(n=9)
28-34 wks	25%(n=15)
34-37wks	10%(n=6)
>37wks	20%(n=12)

Table 2: Trimester wise frequency

Trimester	Frequency	percentage
1	5	8.3%
2	22	36.6%
3	33	55%

Table 3: Variation in platelets

Platlet count	Number of patients
>1.5 lakh	20
>1-1.5 lakh	26
< 50000	14 (3 pateints had severe thrombocytopenia)

Results from mothers

The cases were recruited during a period of one year. The mean age of the women included in our study was 26.07 ± 4.38 year, the youngest being 18 yrs and the oldest being 35 yr. We had only 5 cases who had dengue fever in the first trimester of pregnancy while 36.6% presented in the second trimester and 55% in the third trimester (Table 1, 2).

Clinical and biological findings

This study had 85% patients presenting with fever, 40% with headache, and 18.9% with diffuse muscle pain or arthralgia as their predominant symptom.

There were 5 cases (8.3%) of DHF and 2 cases (3.2%) of DSS. Of the 60 pregnant women, 6 patients (10%) had an increase in liver enzymes AST (Aspartate aminotransferase) and ALT (Alanine aminotransferase) ranging from 2 to 7 times the normal level. 70.4% patients had Thrombocytopenia of which 13.3% had severe thrombocytopenia (<50,000cells/mm3) at the time of diagnosis, and 5% patients had platelet count less than 20,000 cells/mm3. 8% of the patients needed transfusion (Table 3). Of the 60 cases of maternal dengue, 91.3% of the patients were found to have Dengue IgM positive whereas 8.7% patient were found to have both Dengue IgM and IgG seropositivity.

Obstetric consequences

This study included 5 patients with dengue fever before 12 weeks of gestation of which one patient had a spontaneous miscarriage at 11 weeks while the other three patients had an uneventful pregnancy and a full term delivery. One patient lost for follow up. All of these patients had platelet count between 1-1.5 lakhs. However, the number of patients are too less to come to any conclusion.

There were 13 patients who contracted the infection during aperiod of 12 to 20 weeks of gestation. Of these 2 patients had spontaneous miscarriage. Among the two patients who had spontaneous abortion both had platelet count less than 20,000 per cc3 and required platelet transfusion. Another 4 patients had platelet counts less than 50,000/cc3 of which 2 patients developed preeclampsia later in pregnancy and required termination of pregnancy before 37 weeks. All the other patients had otherwise uncomplicated pregnancy and term delivery.

We had 9 patients who developed dengue fever during a period of 20 to 28 weeks of gestation. Of these two patients developed preterm labour, Four patients had platelet counts less than 1.5 L (of which one had DSS), 3 patients had term delivery,

In our study 15 patients presented between 28 to 34 weeks of gestation, and among these patients, 5 of them (41.6%) had preterm deliveries, all others had term deliveries. One patient had DHF and one patient had DSS she was shifted to ICU and recovered well.

Between 34 weeks and 37 weeks, 6 patients were included, of which 2 patients had preterm deliveries rest had an uneventful pregnancy.

12 patients were infected after 37 weeks 3 patients had intrapartum complications like fetal distress and Meconium stained amniotic fluid were more among these patients. No cases of APH or PPH were reported in our study.

One patient was referred from periphery in very severe form of DSS with MODS and succumbed to the disease.

Neonatal consequences

Birth weights were between 2500 and 3500 g in 30/48 cases (62.5%). Birth weights less than 2,500 g were observed in 10(16.4%) new borns, Only 20% of the babies were preterm. 10 Babies (16.6%) required NICU admission. Neonatal thrombocytopenia was found in 6 of babies. There were no cases of neonatal malformation.

Discussion

The WHO criteria were strictly applied to define cases of DF. Our Study included 60 confirmed cases of Dengue fever of which 2 patients developed Dengue Hemorrhagic Fever and 2 patient had Dengue Shock Syndrome.

Maternal outcomes

One of the striking feature observed in the study by S Panicker *et al.* [4] at Coimbatore was the severe thrombocytopenia (platelet count of <50,000 cell/mm3) which was seen in 78.5% of their women of which two women had platelet counts <10,000 cell/mm3. The fall in platelet count was rapid and progressive initially. Our study also found thrombocytopenia in 43/60 patients (71.6%) of which 4 patients had counts less than 20,000 cells/mm3 similar to observations in the above mentioned study.

2 cases of DHF and 2 cases of DSS required multiple platelet transfusion.

Most of our patients had a normal clinical presentation of acute dengue fever, 2 of the women had the signs and symptoms of DHF, with persistent thrombocytopenia, rising hematocrit, and fluid collection in the third space. Correction of fluid and electrolyte imbalance as well as multiple platelet transfusions was helpful and the patient recovered after treatment. Chanana C *et al*. [5] also described a similar case which was mistakenly diagnosed with hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome.

We observed a case of Dengue Shock Syndrome in

pregnancy which was successfully managed with fluid and ionotrope supports. Patient was a 24 year old primigravida referred at 34 weeks of gestation as a case of fever with hypotension and dyspnea. Her platelet count was 1.2 lakh initially which fell to 45,000. She had positive Dengue NS1 antigen and positive IgM. Later she developed pulmonary edema, hemoptysis and severe hypotension. She was intubated and started on dopamine and Noradrenaline. Patient recovered with supportive management and was extubated. She had intra uterine fetal demise and delivered vaginally. Post expulsion period was uneventful. She recovered completely and was discharged.

Raised serum hepatic transaminases (AST and ALT) levels were seen in all 15 patients with DHF in the study done by Kariyawasam S *et al*. [6] in Srilanka. 100% of DHF and 60% DF patients had elevated liver enzymes in the study by Waduge *et al*[7].In our study 7 patients had elevated liver enzymes which included both DHF patients, 2 DSS patient and three patients with Dengue fever. Liver enzymes normalised after the acute phase of the disease. Only one patient had DIC.

The gestational age at presentation of dengue fever also appeared to be significant. Early onset and late onset in pregnancy appeared to have a bad prognosis. In our study, two patients had spontaneous miscarriage of which one patient presented at11 weeks of gestation. Of the 13 patients who got infected between 12 and 20 weeks, one patients had spontaneous miscarriage. This study shows similar results to one study done by carles *et al*. [8]

In our study there were no cases of intracranial bleed or medical termination of pregnancy due to foetal anomaly most commonly skeletal dysplasia which was reported by other studies

Five patients (8.2%) developed intrapartum fetal distress and three of them required emergency LSCS. One patient had instrumental delivery and another had a normal vaginal delivery. Two of these patients were near term and went into spontaneous labour during dengue infection. Fetal distress was noted in previous studies also. Basurko C *et al.* [9] also observed fetal distress in 7.5% patients similar to our study whereas Garg R *et al*. [9] noted a higher rate 16% in their study conducted at Agra.

There were 4 cases (16.7%) of meconium stained amniotic fluid (MSAF). Among these, 3 patients presented with dengue infection near term. Another patient with dengue infection presented with preterm labour and was done an emergency LSCS for moderate MSAF.

Another possible effect of DF during pregnancy is bleeding due to severe thrombocytopenia in some highrisk pregnancies, such as placenta previa or retro placental hematoma. Antepartum hemorrhage was not noted in any of our cases Another was a patient with placenta praevia who presented at 36weeks of gestation with bleeding per vaginum which got controlled with supportive care and platelet transfusion for a platelet count of 30, 000. She underwent elective LSCS at 38 weeks.

There were no cases of PPH in our study. Basurko C *et al.* [9] also reported postpartum haemorrhage in 9.8% cases, one of which had DIC.

There was one case of maternal death who was referred from primary health center she was a case of primigravida in ? weeks with DSS and MODS. Ismail *et al.* [10] in a recent review reported three maternal deaths out of 16 cases (2.6%) and also noted a 50% prematurity rate.

Fetal and neonatal outcomes

Data from other authors also showed an increase in the rate of prematurity. Carles *et al.* in their review of 38 cases in French Guiana indicate a significant increase in prematurity and fetal death The main obstetric consequences of infection were an increase in premature births (19.6%) and an increased risk of preterm labour (41%) cases in the study by Basurko C *et al*.

In our study 12 patients (20%) had preterm labour and premature babies

There were one case of Intra Uterine fetal Death in our study. There was one patient who lost for follow up who dengue at 13+ wks of gestation.

Fetomaternal transmission

We observed 6 cases of neonatal thrombocytopenia. In all cases the maternal infection occurred around the time of delivery. all babies were admitted to NICU, they developed fever with thrombocytopenia on postnatal day 3 and Dengue IgM was found to be positive. One of the baby required platelet transfusion, all babies recovered and was discharged by postnatal day 14. Similar case of vertical transmission in the neonate presenting with MSAF have been described previously as well.

Conclusion

Pregnancies complicated by dengue infection require close monitoring for potential maternal and fetal complications. Dengue Haemorrhagic fever may present with features similar to Preeclampsia and HELLP. Serological tests aid in confirming the diagnosis of DHF. Effects on the fetus or new-born seem to be variable, with apparently less fetal harm occurring earlier in pregnancy. In near term disease, severe fetal or neonatal illness or death may occur. Such illness may also predispose the new-born to subsequent DHF. A high index of clinical suspicion is essential in any pregnant female with fever during epidemics especially in endemic areas like Tamil Nadu. Conservative medical and obstetrical management is the treatment of choice Further studies and systemic reviews are necessary as there is no evidence based data available for management of dengue patients in pregnancy.

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