



SERIES OF DENGUE CASES IN PREGNANCY AND ITS OUTCOMES

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ABSTRACT

Dengue is a vector-borne viral disease. It is a disease caused by any one of the four closely related viruses (DEN-1, DEN-2, DEN-3, or DEN-4). The viruses are transmitted to humans by the bite of an infected mosquito (*Aedes aegypti*). Recently, there is an increase in the incidence of dengue fever in adult population in South Asian countries. With an increasing rate of adult dengue fever victims, the number of pregnant women infected with dengue has also increased. Dengue, during pregnancy may be associated with various complications, including abortions, preterm delivery, maternal mortality, low birth weight, neonatal admissions, and fetal anomalies. Timely intervention can improve the maternal as well as fetal outcome. This study was aimed to assess the clinical profile, maternal and fetal outcome of dengue fever during pregnancy and post-delivery. This study shows various outcomes in different trimesters of pregnancy.

KEYWORDS : Dengue, dengue in pregnancy, Dengue Shock Syndrome (DSS), Dengue Hemorrhagic Fever (DHF).

INTRODUCTION

Dengue is a disease caused by one of the four closely related viruses (DEN-1, DEN-2, DEN-3, or DEN-4). The viruses are transmitted to humans by the bite of an infected mosquito (*Aedes aegypti*) (World Health Organization., 1997). The *Aedes aegypti* mosquito is the vector of dengue/ Dengue Hemorrhagic Fever (DHF). Even though the dengue virus comprises four distinct serotypes (DEN 1-4) but DEN-3 is frequently associated with severe disease. The RNA virus belongs to the genus *Flavivirus*, (family *Flaviviridae*). Majority of dengue patients have a mild self-limiting illness and a few progresses to severe disease. As the incidence of dengue in adults increases, the incidence in pregnant women also increases. It has been estimated that there are over 100 million cases of Dengue worldwide each year. The major symptoms of dengue are high fever, headache, nausea, vomiting, arthropathy, eye pain, and rash development. Generally, younger children are more affected than older children and adults ("Dengue - Directorate of Public Health & Preventive Medicine," 2006). After the incubation period, the illness begins abruptly followed by the three phases 1) febrile, 2) critical and 3) recovery.

In Dengue, DHF is characterized by a fever that lasts from 2 to 7 days, with general signs and symptoms (e.g., headache, nausea, vomiting, and abdominal pain), followed by hemorrhagic manifestations, tendency to bruise easily, bleeding nose or gums, and possibly internal bleeding. The capillaries become excessively permeable ("leaky"), allowing the fluid component to escape from the blood vessels. This condition may lead to failure of the circulatory system and shock, followed by death, if circulatory failure is not corrected (Dale Carroll, Toovey, & Gompel, 2007; "Dengue - Directorate of Public Health & Preventive Medicine," 2006; World Health Organization., 1997).

Another fatal complication of Dengue is Dengue Shock Syndrome (DSS) which is associated with high mortality rate. The onset of DSS in dengue can be dramatic, and its progression is relentless. The pathogenesis of DSS in dengue is complex process associated with endothelial dysfunction induced by cytokines and chemical mediators. The diagnosis of DSS in dengue is largely clinical and is supported by serology and identification of viral load in blood. Careful fluid

management and supportive therapy is the mainstay of DSS management (Rohit Bansal, Priya Bansal, 2015).

Dengue poses a significant threat to pregnant women. In the present study, we have studied the pattern of dengue in pregnancy and the impact of dengue on the natural course of pregnancy. The maternal and fetal outcomes were also analyzed.

METHODS

The study was carried out in the department of obstetrics and gynecology, a tertiary care maternal and child health care hospital in Chennai, India. All the pregnant women who presented with fever and serologically confirmed as dengue fever were included in the study, irrespective of their gestational age. The age, weight, gestational age, parity, detailed history, clinical features, complete blood count, liver function test, and renal function test, coagulation profiles were recorded on admission and were repeated serially.

The severity grading of the dengue infection was done according to WHO classification and case definitions (WHO, 1999). The key differentiating feature between Dengue Fever (DF) and Dengue Hemorrhagic Fever (DHF) is the presence of plasma leakage in DHF (Kariyawasam & Senanayake, 2010). The presence of thrombocytopenia with concurrent hemoconcentration is to differentiate grades I and grade II DHF from DF (Kariyawasam & Senanayake, 2010). DHF is classified into four grades as per the severity: Grade I: fever accompanied by non-specific constitutional symptoms; the only hemorrhagic manifestation is a positive tourniquet test and/or easy bruising; Grade II: the presence of spontaneous bleeding manifestations, usually in the forms of the skin or other hemorrhages. Grades III and IV (profound shock) are considered to be DSS (WHO, 1999) ("WHO | Dengue haemorrhagic fever: diagnosis, treatment, prevention and control. 2nd edition. Geneva : World Health Organization.," 2015). Dengue was diagnosed using the ELISA method by detection of dengue virus-specific NS-1 antigen and IgM, IgG antibody. The impact of dengue on the natural course of pregnancy and labor and the maternal and fetal outcomes were noted.

RESULTS

All six pregnant women are seropositive for dengue (Table 1).

The patient's age range between 22-31 years. Predominantly all patients are presented with classical constitutional features such as myalgia and fever. Among six pregnant patients, one is in 1st trimester, one is in 2nd trimester, and the other four were in 3rd trimester. Only one patient had secondary dengue infection with positive IgM and IgG. All the others had only IgM positive. Two patients had dengue fever without any hemorrhagic manifestations. Other four patients diagnosed with DHF out of which two patients are DHF grade II and the other two patients developed DSS (grade III and IV). In both primary and secondary infections, the lower platelet count was observed.

Out of six patients, two patients required intensive care treatment with supportive care (inotropes and electrolyte correction). The other four patients with a milder clinical course (DF, DHF grade II) had uncomplicated deliveries. One patient (case #01) developed DSS, DHF grade III, was successfully resuscitated due to timely diagnosis and management of DSS. Her platelet count dropped to 29000 for which she was transfused with six units of platelet-rich plasma. She was under surveillance in the critical phase with adequate hydration and inotropic support. She delivered through cesarean section. The maternal and fetal outcome was good.

In one case we encountered multiorgan failure leading to the abortion of the fetus and maternal death (Case #04). This patient was a 24-year old, primigravida at eight-week gestation period presented with high-grade fever, malaise, and myalgia for one week. At the time of admission, she had stable vital signs, and there were no bleeding manifestations. The investigations showed a platelet count of 1.15 lakh/mm³ and positive serology (NS1Ag & IgM). She was under IV fluids, and her platelets were monitored. After four days she had an episode of giddiness following which patient developed capillary leak syndrome. Ultrasound examination confirmed missed abortion (5th day after the admission). Within two days the patient developed vascular leakage (ascites and pleural effusion) and bleeding manifestations, with hemoconcentration (hematocrit increased from 38% to 50%). Furthermore, the patient rapidly developed hepatorenal failure, cardiac failure and acute respiratory distress which needed CPAP with 100% oxygen. Despite transfusing 20 units of platelet-rich plasma (along with fresh frozen plasma and whole blood) the patient's condition deteriorated and eventually died due to DSS.

Fetal outcomes were satisfactory in all cases except for one case which was complicated with DSS went in for an abortion. None of the deliveries were complicated with postpartum hemorrhage. All the women and newborn who were discharged from the hospital were reviewed after one month in antenatal/postnatal clinic and pediatric clinic. None of the babies showed clinical evidence of ill health or failure to thrive.

DISCUSSION

Dengue fever in pregnancy creates anxiety amongst the treating obstetrician and also amongst the patients and their relatives for the fear of bleeding tendencies (Friedman et al., 2014). The outbreak of dengue is common during the monsoon and post-monsoon season. Dengue in pregnancy requires early diagnosis and treatment. Dengue should be considered among the differential diagnosis of fever during epidemics (Dale Carroll et al., 2007). A high index of clinical suspicion is essential in any pregnant woman with fever during epidemics, especially in endemic areas. The age of patients ranged from 22-31 years and one patient presented with dengue in the second-trimester, one in first-trimester and other four in third-trimester. The number of pregnant women who presented with primary dengue infection was higher (84% cases) than the number of secondary dengue infection (16% cases). Most common presenting symptom other than fever was myalgia followed by headache and skin rash. Our study includes six pregnant women with dengue. All patients had fever with a temperature between 99°F-104.1°F during the first 1-5 days of the illness. Fever with generalized myalgia was present in all six patients. Two patients had dengue fever without any hemorrhagic manifestations. Low platelet counts were seen in both primary and secondary infections. Out of six patients, one patient died due to DSS. Overall, the fetal outcome was satisfactory.

CONCLUSION

Dengue in pregnancy requires early diagnosis, treatment, and effective management. Dengue should be considered among the differential diagnosis of fever during epidemics. Early diagnosis is challenging for treating physicians due to ambiguity of clinical findings and pregnancy-related physiological changes. Absence of fetomaternal complications, infection by itself is not an indication for obstetric interference. Further studies are mandatory to develop specific guidelines for pregnant patients.

Table 1: Clinical and laboratory characteristics with fetomaternal outcomes.

PATIENT	AGE	GESTATIONAL AGE	DENGUE NS1Ag, IgM, IgG	PLATELET COUNT (10 ³ /CU MM)	HEMATOCRIT	AST/ALT	PRESENTING COMPLAINTS	HEMORRHAGIC MANIFESTATIONS	PLEURAL EFFUSION/ASCITES	SEVERITY	ICU	PLATELET TRANSFUSION	MATERNAL OUTCOME	MOD	FETAL OUTCOME
01	25	35+1	NS1Ag + IgM + IgG +	29	40.3	150/79	FEVER MYALGIA	P	N	DHF3	Y	Y	NORMAL	CS	NORMAL
02	26	26+1	NS1Ag + IgM+ IgG-	50	39	50/45	FEVER MYALGIA	P	N	DHF 2	N	N	NORMAL		PREGNANCY CONTINUING
03	28	39+5	NS1Ag + IgM + IgG-	45	40	69/65	FEVER MYALGIA	P	N	DHF 2	N	N	NORMAL	VD	NORMAL

04	24	8+2	NS1Ag + IgM + IgG -	4	50	8790 2185	FEVER MYAL GIA RASHE S	P	Y	DHF 4	Y	Y	MOF DEATH		ABORTI ON
05	31	39+4	NS1Ag- IgM + IgG -	80	35	35 40	FEVER MYAL GIA	N	N	DF	N	N	NORM AL	CS	NORMA L
06	22	38+5	NS1Ag + IgM+ IgG-	75	36	45 50	FEVER MYAL GIA	N	N	DF	N	N	NORM AL	CS	NORMA L

MOD-Mode of Delivery; VD- Vaginal Delivery; CS-Caesarean delivery; Plt-Platelet; P- Petechiae; DF-Dengue Fever; DHF-Dengue hemorrhagic Fever; PE - Pleural effusion; MOF- Multi-Organ Failure; IUD-Intra Uterine Death; Y- Yes and N-No.

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