

# Dengue Fever during Pregnancy: Maternal and Fetal Complications

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## ABSTRACT

**Introduction:** Dengue fever is the most rapidly spreading arthropod-borne self-limiting febrile illness. During pregnancy, it causes maternal complications, such as hemorrhage, abortion, and fetal complications like preterm babies, intrauterine death, low birthweight babies.

**Objectives:** To study the prevalence of dengue fever in pregnant women. To study the maternal and fetal complications in women infected with dengue fever during pregnancy.

**Materials and methods:** This was a 2-year retrospective study conducted at RajaRajeswari Medical College & Hospital, Bengaluru, India, from June 2013 to June 2015. In this study, pregnant women affected with dengue fever were included irrespective of gestational age. Women with dengue nonstructural protein 1 antigen positive or dengue immunoglobulin (Ig)M and IgG positive were diagnosed to have dengue fever. Maternal and fetal complications were studied.

**Results:** During the study period, there were 4,137 deliveries, of which 15 women had dengue fever. Incidence and prevalence of dengue was 0.36 and 0.72% respectively. Dengue fever without complications was noted in 66.6% pregnant women, dengue with complications was noted in 20% women, while 6.6% (n = 1) women developed dengue shock syndrome that resulted in maternal death due to multiorgan failure. Dengue hemorrhagic fever was seen in 13.3% women. In our study, 33.3% of women had preterm delivery, 40% had small for gestational age babies, and 6.6% had intrauterine fetal demise.

**Conclusion:** Dengue fever is endemic in our country. Pregnant women are vulnerable to this disease. It is associated with maternal and neonatal morbidity and mortality. Early diagnosis and maintenance of hydration and symptomatic treatment will avoid related complications.

**Keywords:** Dengue fever, Intrauterine growth restriction, Preterm, Thrombocytopenia.

**How to cite this article:** Pavanaganga A, Sailakshmi MPA, Rekha BR, Nagarathnamma R. Dengue Fever during Pregnancy: Maternal and Fetal Complications. J South Asian Feder Obst Gynae 2017;9(2):88-91.

**Source of support:** Nil

**Conflict of interest:** None

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**Date of received:** 16 December 2016

**Date of acceptance:** 21 January 2017

**Date of publication:** March 2017

## INTRODUCTION

Dengue fever is the most rapidly spreading arthropod-borne disease in the world. It is caused by single-stranded ribonucleic acid flavivirus. There are four serotypes of dengue virus, DEN1, DEN2, DEN3, and DEN4. It is transmitted by the *Aedes aegypti* mosquito.

Dengue fever is associated with severe human morbidity and mortality. The World Health Organization (WHO) has estimated that 2.5 billion people live in countries with high risk for dengue fever, 50 million people are infected annually, and 22,000 deaths result from dengue fever.<sup>1</sup> Over the past six decades, the Indian subcontinent has evidenced a tremendous change in the epidemiology of dengue fever in terms of prevalent strains, affected geographical areas, and severity of the disease.<sup>2</sup> These epidemiological changes are due to rapid changes in the environment due to urbanization. According to statistics by the National Vector Board, India had 40,571 and 99,913 cases of dengue fever in the years 2014 and 2015 respectively. Deaths due to dengue fever were 137 and 220.<sup>3</sup> Karnataka state had 3,358 and 5,077 cases of dengue fever, deaths due to dengue fever were 2 and 9 in the years 2014 and 2015 respectively.

Dengue is a self-limiting febrile illness; lack of early recognition and symptomatic treatment causes complications like dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).

Pregnancy is a very vulnerable period, and it is associated with several physiological changes. Dengue fever during pregnancy causes maternal complications like hemorrhage and abortion and fetal complications like preterm babies, intrauterine death (IUD), and low birthweight babies.<sup>4</sup> Very few studies have been done on the effect of dengue fever during pregnancy and its associated complications. This study aims to know the effect of dengue fever on pregnancy.

## OBJECTIVES

To study the prevalence of dengue fever in pregnant women. To study the maternal and fetal complications in women infected with dengue fever during pregnancy.

## MATERIALS AND METHODS

This was a 2-year retrospective study conducted at RajaRajeswari Medical College & Hospital, Bengaluru, India, from June 2013 to June 2015. In this study, pregnant women affected with dengue fever were included irrespective of gestational age. Pregnant women with febrile illness were subjected to a battery of investigations, which included dengue nonstructural protein 1 (NS1) antigen and immunoglobulin (Ig)M and IgG antibodies. Women with dengue NS1 antigen positive or dengue IgM and IgG positive were diagnosed to have dengue fever.

Dengue NS1 antigen and IgM and IgG antibodies were tested using the SD BIOLINE Dengue Duo rapid test. It is an *in vitro* immunochromatographic one-step assay designed to detect both dengue virus NS1 Ag and differential IgM/IgG antibody to dengue virus in human sera. The test has a sensitivity of 92.4% and a specificity of 98.4%. Laboratory investigations like complete blood count, liver function test (LFT), renal function test (RFT), prothrombin time (PT), activated partial thromboplastin time (APTT), and ultrasonography (USG) of abdomen and pelvis were included in the study. Maternal and fetal outcomes were studied.

The Centers for Disease Control and Prevention and WHO classification was applied to classify dengue cases.<sup>5</sup>

Criteria include the following:

- Dengue fever (without warning signs): Fever with two other symptoms like nausea, vomiting, rashes, myalgia, leukopenia, positive Tourniquet test.
  - Dengue with warning signs: Abdominal pain, persistent vomiting, ascites, pleural effusion, mucosal bleeding, hepatosplenomegaly, decrease in platelet count, increased hematocrit.
  - Severe dengue fever includes DSS and DHF.
- Criteria for severe dengue:
- Severe plasma leakage leading to shock (DSS), fluid accumulation with respiratory distress.
  - Severe bleeding.
  - Severe organ involvement.
    - Liver: Aspartate aminotransferase or alanine aminotransferase >1,000
    - Central nervous system: Impaired consciousness
    - Heart and other organs

## RESULTS

This was a 2-year retrospective study conducted at RajaRajeswari Medical College & Hospital, Bengaluru, India, from June 2013 to June 2015. There were 4,137 deliveries during the study period, 15 pregnant women were affected by dengue fever.

Table 1 shows demographic variables. Most women in the study belonged to the age group of 18 to 25 years

**Table 1:** Demographic variables

	Variables	Number	Percentage
Age (years)	18–25	10	66.7
	25–30	3	20
	> 30	2	13.3
Parity	Primi	8	53.3
	Multi	7	46.7
Gestational age at onset of dengue	First trimester	0	0
	Second trimester	5	33.3
	Third trimester	9	60
	Postnatal	1	6.7

(66.7%). Both primigravida and multigravida women were affected, 53.3 and 46.7% respectively. In this study, 60% women were affected in the third trimester.

Table 2 shows the maternal laboratory parameters and complications; 11 women tested positive for dengue NS1 antigen, 5 women were IgM and IgG positive. All women in the study had thrombocytopenia, altered LFT was seen in five women, and deranged coagulation profile was seen in one woman, leukopenia was seen in four women. Hepatosplenomegaly and ascites were seen 11 women.

Dengue fever was diagnosed in 10 women (66.6%); 3 women (20%) had dengue fever with complications, 2 women (13.3%) had DHF, and 1 woman (6.6%) had DSS. Woman with DSS had maternal death. Intensive care unit (ICU) admission was needed for five women (33.3%) and platelet transfusion was done in nine women (60%).

Table 3 shows mode of delivery. A total of five women (33.3%) had full-term normal delivery (FTND), 3 women (20%) had emergency lower (uterine) segment cesarean section (LSCS), five women (33.3%) had preterm delivery, and two women (13.3%) had instrumental delivery.

Table 4 shows neonatal outcome, small for gestational age (SGA) was seen in six cases (40%), and five cases (33.3%) had preterm babies. There was one (6.6%) IUD.

## DISCUSSION

Dengue fever is the most rapidly spreading vector-borne disease causing severe morbidity and mortality. It presents with symptoms of fever, retro-orbital pain, headache, abdomen pain, prostration, myalgia, rashes, and hemorrhagic manifestations.<sup>5</sup> Dengue fever may be due to primary or secondary infection. A primary infection is characterized by a slow and low titer antibody response. The IgM antibody is the first Ig isotype to appear. In contrast, during a secondary infection, antibody titers rise extremely rapidly and antibody reacts broadly with many flaviviruses. High levels of IgG are detectable even in the acute phase and they rise dramatically over the preceding 2 weeks.<sup>6</sup>

Table 2: Maternal laboratory values and complications

Sl. no.	NS1 Ag	Dengue IgM	Dengue IgG	Platelet count	Total count	LFT	RFT	USG	Platelets transfused	Maternal complications	ICU admission	PT, APTT
1	Positive	Positive	Negative	28,000	3,800	Altered	Altered	Ascites, pleural effusion, hepatosplenomegaly	10	DSS, maternal death	Yes	Normal
2	Positive	Positive	Negative	60,000	4,500	Normal	Normal	Normal	No	DF with PIH	No	Normal
3	Positive	Positive	Negative	29,000	7,000	Normal	Normal	Ascites, hepatosplenomegaly	4	DF with complication	No	Normal
4	Negative	Negative	Positive	56,000	5,500	Normal	Normal	Normal	No	DF	No	Normal
5	Positive	Negative	Negative	10,000	2,800	Altered	Normal	Ascites, hepatosplenomegaly	20	DF with complications	Yes	Normal
6	Positive	Positive	Positive	15,000	4,200	Altered	Normal	Ascites, hematuria	14	DHF	Yes	Altered
7	Positive	Positive	Negative	48,000	8,000	Normal	Normal	Hepatosplenomegaly	No	DF	No	Normal
8	Negative	Negative	Positive	56,000	7,500	Normal	Normal	Normal	No	DF	No	Normal
9	Positive	Positive	Negative	14,000	3,400	Altered	Normal	Ascites, hepatosplenomegaly	4	DF with complication	Yes	Normal
10	Positive	Positive	Negative	20,000	5,500	Altered	Normal	Normal	6	DF	No	Normal
11	Negative	Negative	Positive	32,000	8,700	Normal	Normal	Hepatosplenomegaly	No	DF	No	Normal
12	Positive	Negative	Negative	28,000	6,700	Normal	Normal	Normal	4	DF	No	Normal
13	Positive	Positive	Negative	13,000	5,500	Altered	Altered	Hepatosplenomegaly, ascites	6	DHF	Yes	Normal
14	Negative	Positive	Positive	56,000	110,000	Normal	Normal	Normal	No	DF, impaired GTT	No	Normal
15	Positive	Negative	Negative	70,000	3,500	Normal	Normal	Normal	Nil	DF	No	Normal

DF: Dengue fever; PIH: Pregnancy-induced hypertension; GTT: Glucose tolerance test

Table 3: Mode of delivery

Mode of delivery	Number	Percentage
FTND	5	33.3
LSCS	3	20
Instrumental delivery	2	13.3
Preterm	5	33.3

Table 4: Neonatal outcome

Neonatal outcome	Number	Percentage
SGA	6	40
AGA	3	20
Preterm	5	33.3
IUD	1	6.6

AGA: Appropriate for gestational age

Dengue fever during pregnancy can cause severe maternal and fetal morbidity and mortality. It causes fetal complications like abortion, prematurity, SGA babies, fetal distress, and maternal complications like bleeding diathesis, increased operative intervention, postpartum hemorrhage, and shock.<sup>4</sup>

Physiological variations during pregnancy like hemodilution, thrombocytopenia, and hypercoagulability mask thrombocytopenia, raised hematocrit, and leukopenia caused by dengue fever and cause delay in diagnosis. Hepatic dysfunction due to other obstetric complications like hemolysis, elevated liver enzyme levels, and low platelet levels syndrome; idiopathic thrombocytopenia of pregnancy; and antiphospholipid antibody syndrome mimic dengue fever and cause delay in diagnosing and treating dengue fever.<sup>7,8</sup>

Prevalence and incidence of dengue fever was 0.72 and 0.36% respectively, in our study. Most cases in the study were primary dengue cases, 60% (n = 9). Studies of Tan et al<sup>7</sup> showed a prevalence rate of 2.5%. Studies of Singla et al<sup>9</sup> showed an incidence of 7.5%. In our study, 60% of the women were affected in the third trimester; similar results were seen in studies of Adam et al<sup>10</sup> and Ismail et al.<sup>11</sup>

Dengue fever without complications was noted in 66.6% pregnant women, all had thrombocytopenia. Dengue with complications was noted in 20% women, they had thrombocytopenia with hepatosplenomegaly, and no fluid leakage was noted. One (6.6%) woman developed DSS 1 week after delivery and resulted in maternal death due to multiorgan failure. The DHF was seen in two women (13.3%). One woman had hematuria, altered LFT, and ascites with pleural effusion and delivered normally; she had postpartum hemorrhage and needed ICU admission and 14 units platelet transfusion. Another woman had excessive bleeding, altered LFT and RFT, and ascites with hepatosplenomegaly; she had an intrauterine fetal demise, and needed six units platelet transfusion and

ICU admission. Similar results were seen in studies of Kariaswamy and Senanayake.<sup>12</sup>

Studies of Chitra et al showed similar results.<sup>15</sup> In our study, 33.3% of women had preterm delivery, 40% had SGA babies, and 6.6% had intrauterine fetal demise. Studies of Pouliot et al<sup>13</sup> showed 16% women had preterm delivery. Studies of Hanf et al<sup>14</sup> showed 17.4% had preterm delivery, 19.8% had SGA, and 3.5% had IUD. Studies of Adam et al<sup>10</sup> showed 17.9% had preterm delivery and 24% had low birthweight.<sup>16</sup>

## CONCLUSION

Dengue is an emerging vector-borne disease. Pregnant women are vulnerable to this disease. It is associated with maternal and neonatal morbidity and mortality. As dengue is endemic in our country, in any febrile illness during pregnancy, dengue fever should be one of the differential diagnoses. Early diagnosis and maintenance of hydration and symptomatic treatment will avoid hemorrhagic complications. Availability of platelets and blood products is very essential for treating complications of dengue fever. Platelet transfusion is done only when platelet is less than 20,000 or when patient has hemorrhagic manifestations. Preventive measures should be taken to avoid dengue fever. Public awareness regarding dengue fever and its related complications helps reduce the morbidity.

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