

# Could Serological Markers of the Dengue Viral Disease Predict the Outcomes in Pregnant South Asian Population?

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## Abstract

### ➤ *Background:*

A recent rise in the incidence of a vector borne viral disease, Dengue Disease, in South Asian countries has also shown an impact on the pregnant population in these regions. There are four known Dengue virus serotypes, the predominant ones being DENV- 2 and DENV-3, when present during pregnancy could be associated with complications like preterm birth, maternal mortality and morbidity and adverse neonatal outcomes.[1]. We aimed to study the outcomes in the pregnant patients that presented to our institution with the Dengue disease.

### ➤ *Methods:*

A 6-month (1/9/2019 – 29/2/2020) study was undertaken during the months of high prevalence of the Dengue disease in our region. Clinical, laboratory, maternal and foetal outcomes were studied among serologically positive dengue mothers treated at MGM Hospital, Aurangabad.

### ➤ *Results:*

A total of 25 patients were found to have Dengue disease during the study period. NS1Ag and IGM serological analysis results were used to achieve diagnosis and early management. 7 patients had symptomatic thrombocytopenia and needed platelet transfusions. Majority of our patients had favourable outcomes. 3 mothers died succumbing to the multi-organ failure.

### ➤ *Conclusion:*

Favourable maternal and foetal outcomes could be achieved with early diagnosis of suspected Dengue disease with both NS1Ag and IGM serological analysis.

**Keywords:-** Dengue in Pregnancy, Outcomes of Dengue Fever, Serological Markers in Dengue.

## I. INTRODUCTION

Dengue fever is a viral disease caused by any of the four closely related serotypes of genus Flavivirus, family Flaviviridae – a RNA virus. The four serotypes designated as DENV -1, DENV -2, DENV -3, DENV -4.[1] It is one of the most important vector borne diseases affecting countries like India, with the vector being the *Aedes aegyptis* mosquito. 40% of the world's population live in dengue prone zone, indicating the high risk and burden of carrying the disease. WHO estimates atleast 100 million infections occur every year including 5,00,000 dengue hemorrhagic fever cases and nearly 22,000 deaths.[2] The clinical severity of the disease has a wide spectrum and according to WHO Dengue classification there are four grades ranging from uncomplicated dengue fever (DF) to devastating Dengue Shock Syndrome (DSS). Infection by one serotype produces lifelong immunity to that specific serotype but only a few months of immunity to the others.[3]

Dengue infection in pregnancy carries the risk of haemorrhage for both the mother and the newborn. In addition, there is a risk of premature birth and fetal death and vertical transmission, which is well established, causing neonatal thrombocytopenia that necessitates platelet transfusions. [4-6]

Symptomatic dengue infection is a systemic and dynamic disease. The disease incubation period is around 2 weeks under favourable conditions. The clinical course of dengue infection passes through three phases -febrile phase, critical phase and recovery phase.[2] At parturition , severe bleeding may complicate delivery and/or surgical procedures performed on pregnant patients during critical phase of dengue i.e. marked thrombocytopenia . Literature search reveals that dengue is a significant factor for adverse pregnancy outcomes like preterm birth, Low birth weight, increased operative interference.[7] Diagnosis of dengue infection affects management and decisions of mode of delivery due to the hazardous risk of haemorrhage secondary to thrombocytopenia. Elevated liver enzymes, hemolysis, low platelet counts may be misleading and one might confuse it with HELLP syndrome. [9] Obstetrician being the frontline physician for a pregnant woman , should be able to identify , notify and manage cases of dengue fever in pregnancy.

There is insufficient data regarding the teratogenic power of the virus. As such dengue fever in pregnancy does not warrant termination of pregnancy.[10]

➤ *Aim and Objectives*

- To analyse the clinical presentation of dengue fever in pregnancy.
- To correlate the course of the disease with serological markers.
- To study various maternal and neonatal outcomes .

## II. MATERIALS AND METHODS

- Study design – Prospective Observational study
- Study period - September 2019 – February 2020. ( 6 months)
- Study place – MGM Medical College & Hospital, Aurangabad, Maharashtra.
- Sample size - 25
- Inclusion criteria - Pregnant females diagnosed and serologically confirmed to have dengue fever.
- Patients were included irrespective of the period of gestation.
- Exclusion criteria – other causes of fever among pregnant females.
- Data was collected from the patient case records and hospital records of the confirmed cases.
- A pre designed proforma was filled.
- Data was analysed and interpreted.

PARAMETER	NUMBER OF PATIENTS ( N = 25)
<b>PARITY STATUS</b>	
1. PRIMIGRAVIDA	18 (72%)
2. MULTIGRAVIDA	07 (28%)
<b>AGE OF THE MOTHER</b>	
1. < 19 YEARS	03 (12%)
2. 19 – 30 YEARS	21 (84%)
3. 30 – 35 YEARS	01 (4%)
<b>GESTATIONAL AGE AT DIAGNOSIS</b>	
1. <13 WEEKS	03 (12%)
2. 13 – 28 WEEKS	14 ( 56%)
3. > 28 WEEKS	08 (32%)

Table 1:- Demographic Profile of Mother (Patient)

72% of the patients were primigravida, since large number of patients booked at our hospital are primigravida. 84% of the patients were between 19-30 years of age, as it is mainly the reproductive age group. 56% of patients were in their second trimester followed by 32% in their third trimester. Almost all of these patients, diagnosed in second trimester could continue their pregnancy.

CLINICAL SIGNS AND SYMPTOMS	NUMBER OF PATIENTS (n = 25)
<b>SYMPTOMS</b>	
1. FEVER WITH CHILLS	23 (92%)
2. FEVER WITHOUT CHILLS	01 (4%)
3. MYALGIA	20 (80%)
4. HEADACHE	11 (44%)
5. PERSISTENT VOMITING	04 (16%)
6. ABDOMINAL PAIN	03 (12%)
7. BLEEDING DIATHESIS	02 (8%)
8. PETECHIAE	00 (0%)
9. SKIN RASH	02 (8%)
<b>SIGNS</b>	
1. FEVER ( TEMP > 100° F)	14 (56%)
2. TACHYCARDIA	19 (76%)
3. HYPOTENSION	03 (12%)
4. PRESENCE OF RASH	02 (8%)

Table 2:- Clinical Profile of Patients with Dengue Fever

The following table shows the clinical presentation of patients at the time of admission. In our study, 92% of mothers presented with fever with chills which was the most common presentation of dengue fever in pregnancy. Myalgia and headache were the next common symptoms with incidence of 80% and 44% respectively. In spite of 52% of patients having thrombocytopenia, only two patients presented with bleeding tendency in the form of malena and none of the patients presented with petechiae.

Clinically, at the time of admission, nearly 50% of the patients were documented to have fever with temperature above 100° F. Tachycardia was noted in 76% of the patients with a resting heart rate above 100 beats per minute, in those with or even without fever.

BIOLOGICAL TEST	NUMBER OF PATIENTS (n=25)
<b>SEROLOGICAL MARKERS</b>	14 (56%)
1. DENGUE NS1 + IgM -	6 (24%)
2. DENGUE NS1 – IgM +	5 (20%)
3. DENGUE NS1 + IgM +	
<b>SEVERITY OF THROMBOCYTOPENIA ( PLATELETS/CUMM)</b>	
1. < 20,000	7 (28%)
2. 20,000 – 50,000	3 (12%)
3. 50,000 – 1,00,000	3 (12%)
4. 1,00,000 – 1,50,000	3 (12%)
5. > 1,50,000	9 (36%)
<b>OTHER LABORATORY TEST</b>	
1. FALLING PLATELET COUNT	20 (80%)
2. RISING HEMATOCRIT	15 (60%)
3. LEUCOPENIA	08 (32%)
4. DERANGED LFT	07 (28%)

Table 3:- Laboratory Profile of Patients

76% of patients tested positive for Dengue NS1Ag. Out of these 76% patients, nearly 56% patients tested positive only for NS1Ag and the rest of them tested positive for Dengue IgM antibody as well. Only IgM positivity with negative results for NS1Ag was noted among 24% patients. Both tested positive in nearly 20% patients, who had more severe platelet falling trend but clinically remained unaffected.

Nearly 80% of our patients had falling trend of platelets, though they did not necessarily qualify for the definition of thrombocytopenia (<1,00,000/cumm). Although 28% of patients had deranged LFTs, six patients had ICU admission and one patient was clinically stable, monitored in the ward.

OUTCOME	NUMBER OF PATIENTS ( n=25)
<b>DELIVERY STATUS</b>	
1. VAGINALLY DELIVERED	04 (16%)
2. INTRAUTERINE DEATH	02 (8%)
3. PREGNANCY CONTINUED	20 (80%)
<b>MATERNAL OUTCOME</b>	
1. RECOVERED	22 (88%)
2. MULTIORGAN FAILURE	05 (25%)
3. DEATH DUE TO MULTIORGAN FAILURE	03 (12%)
<b>NEONATAL OUTCOME</b>	
1. NUMBER OF DELIVERIES	04 (16%)
2. NUMBER OF LIVEBIRTHS	03 (12%)
3. NUMBER OF IUD	02 (8%)

Table 4:- Outcome of Pregnancy and Neonates

Four patients (16%) who delivered vaginally, did not land up in Post Partum Hemorrhage due to strong anticipation, aggressive third stage management and prophylactic transfusion in two patients (8%). Strict fourth stage monitoring was done. But eventually two patients succumbed to multiorgan failure. One patient had IntraUterine Foetal Demise, succumbed before delivery.

➤ Flowchart

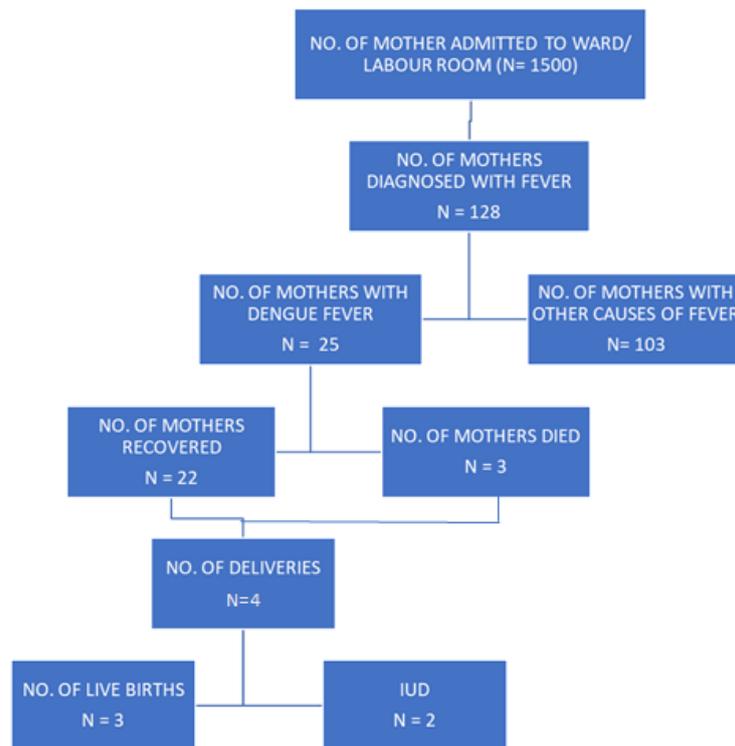


Fig 1

III. DISCUSSION

The outbreak of dengue is common during the monsoon and post monsoon season in the tropical belt. Dengue is endemic to the tropical areas and rare in temperate regions. Recently, there is rising epidemic potential of dengue. A high index of suspicion is needed in any pregnant female from these areas with fever during the

epidemics. As reported previously, most cases of dengue fever during pregnancy had favourable outcomes. Therefore, most of the mothers could continue their pregnancy similar to the study carried out by Sampath Kariyawasam et.al.,[7] Although our patients did not fulfil all the clinical and investigative criteria of dengue fever as defined by WHO, they had fever with thrombocytopenia. 56% of women in our study were in second trimester,

contradictory to previous studies like Gehlot H.et.al., in whom incidence was higher in third trimester. Almost all of these patients diagnosed in second trimester could continue pregnancy as they were remote from term and complications are expected when closer to term or in labour. As expected, four patients closer to their expected date of delivery had more severe clinical symptoms and landed up in multiorgan failure.[1] Most common symptoms included fever with chills(92%), followed by myalgia(80%) and arthralgia similar to other studies.[8] Though 76% of patients tested positive for NS1Ag which is highest among our patients, not all of them tested positive but 24% of patients tested positive only for IgM Antibodies, suggesting that the patients had recent infection with ending of viremic phase. In our study 25 pregnant females were included, after they serologically tested positive to the disease. So routine usage of NS1Ag testing as screening might not pick all the dengue positive patients, might give false negative results and hence, further coupling of testing by ELISA might be needed in patients with high index of suspicion. Out of the 25 patients, 7 patients had their platelets count dropped below 20,000 and needed platelet transfusions as they were symptomatic. All of the patients had a falling trend of the platelets, but values remained above critical level and 18 of them were asymptomatic. Fever with chills was noted to be the most common clinical presentation at the time of admission and maternal tachycardia with baseline heart rate above 100 beats per minute being the most common clinical sign noted in 76% patients. 6 (24%) patients needed ICU admission in view of dengue shock syndrome and needed critical care. All those (100%) who tested positive to both NS1Ag and IgM developed significant thrombocytopenia and multiorgan failure, including Acute Respiratory Distress Syndrome (ARDS) similar to that described by Lum et.al. Hence, these serological markers might aid in predicting the clinical course of the disease amongst pregnant females, and aid in better anticipation of complications and preparedness of the attending medical team. Four patients who delivered vaginally did not land up in PPH due to strong anticipation and aggressive management of third stage of labour. Elective LSCS was avoided in these patients to avoid any invasive procedures during the critical phase of dengue. One of the mothers had an Intrauterine death of the foetus and succumbed before delivery. There were a total of three live births and all three babies required NICU admission for observation and platelet monitoring. Stringent postpartum care, Hydration and supportive care reduce the maternal mortality and morbidity as shown by other studies

#### IV. CONCLUSION

This study highlights the clinical pattern and the natural course of dengue in pregnancy. The clinical presentation of dengue in pregnancy is almost similar to dengue in non – pregnant adults but the clinical course might be dreadful with complications like Post Partum Haemorrhage, Disseminated Intravascular Coagulation, shock. Most of our patients could continue their pregnancy with better maternal outcomes due to proper monitoring

during the antenatal period as well as intranatal period and adequate care offered at our centre. Easy and quick availability of blood and blood products, anticipation and adequate preparedness helped in achieving better outcomes. Dengue affection with serious consequences was seen in last trimester, as it complicated labour and was associated with both NS1Ag as well as IgM positivity. Hence serological markers could be used to predict severity of clinical course of dengue fever in pregnancy. Conservative management to be done unless there are complications or indications and till the critical phase of dengue is passed. Availability of Intensive care and efficient team work, aid in reducing the maternal morbidity and mortality and improved neonatal outcomes. Health care providers should consider dengue in differential diagnosis of pregnant women with fever during epidemics in endemic areas.

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