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Dengue Fever in Pregnancy and Its Maternal and Fetal Outcome

Ronak R. Bhankhar*, Sushma R Shah, Ami V. Mehta,
Payal P. Panchal, Manthan U. Sojitra
Department of Obstetrics and Gynaecology, Smt. NHL Municipal medical college, SVPIMSR, Ahmedabad, Gujarat, India. (M) 9429380729
**Corresponding Author: Dr. Ronak R. Bhankhar*

ABSTRACT:-
BACKGROUND: As the rate of dengue fever is increasing in the general population rate of pregnant women being infected with dengue virus and its associated complication like miscarriage, preterm delivery, low birth weight, maternal mortality has also increased, yet an appropriate intervention can improve both maternal and fetal outcome
METHODS: A retrospective study was carried out among 30 antenatal patients diagnosed to have serologically confirmed Dengue Fever during period of 12 months. Patients were selected irrespective of period of gestation of contracting the infection and were followed till delivery and 6 weeks postpartum to see maternal and fetal outcome. Patients were defined and categorized as per the World Health Organization (WHO) Dengue classification
RESULTS: Amongst 30 cases of Dengue Fever, 4 were classified as Dengue Hemorrhagic Fever and 1 as Dengue Shock Syndrome. From 21(70%) patients infected in third trimester 6 had preterm labour. Thrombocytopenia (platelet <1.5 lakhs) was present in 25(83.3%) patients of which 6(20%) had platelet <50000 and 1(3.3%) had platelet <20000. other complications like oligohydroamnios (13.3%), meconium stained liquor(26.7%) fetal distress(16.67%) and hemorrhagic complications like ante partum hemorrhage(6.67%) and intracranial hemorrhage(3.33%) were seen. Fetal complications like Intrauterine Fetal Death (IUFD), prematurity (21.4%),low birth weight(17.8%) and (35.7%) requiring NICU admission were seen.
CONCLUSION: The gestational age at diagnosis of Dengue Fever appeared to be significant. Early or late onset in pregnancy appeared to have poor prognosis. The Dengue Fever in pregnancy increases risk of premature birth and the effect on fetus remains variable from severe neonatal illness to even death. Management of Dengue Fever in pregnancy is mainly conservative like in non pregnant patients. Hence conservative medical and obstetrical management is the treatment of choice.

Keywords: Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF), Dengue shock Syndrome (DSS), Thrombocytopenia, preterm birth.

I. INTRODUCTION:

Dengue is an acute mosquito borne viral infection caused by single stranded RNA virus with 4 subtypes: DEN-1,DEN-2,DEN-3,DEN-4.The vector being female Aedes Aegypti mosquito which typically breeds near human habitation in fresh water collection[1]. With increasing infection in adult population the incidence of dengue in pregnancy is also increased and has a significant disease burden in India[2]. The disease spectrum ranges from Uncomplicated Dengue fever to Dengue hemorrhagic fever to Dengue shock syndrome.
As per WHO Classic Dengue Fever (DF) is defined as acute febrile illness with 2 or more of the following signs or symptoms: headache, ocular pain, myalgia, arthralgia, rash, leukopenia
Dengue Hemorrhagic Fever (DHF) is defined as:
1-Fever or recent history of fever lasting for 2-7 days.
2- Thrombocytopenia (platelet count<100,000/mm^3).
3- Hemorrhagic manifestations like patachie, epistaxis, bleeding gums, hematemesis, vaginal bleeding.
4- Evidence of increased vascular permeability.
Plasma leakage due to increased vascular permeability is evidenced by at least one of the following:

- Presence of fluid in third space such as pleural effusion or ascites detected by radiological study.
- Hematocrit >20% above mean hematocrit of population for age and sex.
- Hypoproteinemia or hypoalbuminemia detected by serological tests.

Signs of shock are:
Tachpnea, tachycardia, cold and cyanosed extremities, blood pressure unstable or pulse pressure <20 mmhg.

As pregnancy is a decreased immune state of a female, the risk of Dengue fever in pregnancy increases especially in highly endemic areas. Dengue in pregnancy carries an increased risk of preterm delivery, low birth weight, hemorrhage for both mother and fetus. Hence adequate rehydration therapy either by oral or intravenous route along with blood and blood products transfusion has shown to improve maternal outcome[1].

The clinical manifestations, treatment and outcome in pregnant women are similar to non pregnant women. Misdiagnosis or delayed diagnosis can be due to some overlapping clinical or laboratory features with better recognized conditions of pregnancy like HELLP syndrome, pulmonary embolism,various obstetric causes of per-vaginal bleeding. Hence we conducted a retrospective study at our institution among the antenatal women who presented with or newly diagnosed with serologically proven dengue fever and its effect on maternal and fetal outcome.

II. METHODS:

All antenatal patients who were diagnosed clinically and serologically with dengue fever during a period of 12 months were included in the study irrespective of the gestational age. Patients who presented with features of dengue fever were examined in view of maternal age, parity, gestational age, signs and symptoms and laboratory investigations like complete blood count with hematocrit, liver enzymes, coagulation profile, Dengue NS-1 and Dengue IgM ELISA were done to confirm the diagnosis and were categorized as per WHO classification.

All the patients were closely monitored with temperature charting, pulse, blood pressure, input and output charting, daily fetal movement count charting and ultrasound with Doppler study was done for fetal well being .

Warning signs for capillary leak were looked for vigilantly especially when fever starts subsiding as with capillary leak she can progress to severe Dengue

Warning Signs are: Severe abdominal pain or tenderness, persistent vomiting, mucosal bleed, liver enlargement >2 cm, clinical fluid accumulation, lethargy, restlessness, and increase in hematocrit with rapid decrease in platelet.

Need for ICU admission, blood and blood products transfusion and medical and obstetric complications of dengue fever were also studied.

All the cases were followed till delivery and 6 weeks post partum. Neonates were closely monitored in view thrombocytopenia, vertical transmission and other neonatal complications.

III. RESULTS:

During the study 30 cases of maternal dengue fever were diagnosed and treated, out of which 4 had Dengue Hemorrhagic Fever and 1 was diagnosed with Dengue Shock Syndrome. The mean age of women included in study was 27years with youngest being 20 years and oldest being 34 years.

Table -1 Gestational age and Trimester at diagnosis

Gestational age	Frequency (N)	%	Trimester	N	%
<12 weeks	1	3.33	1st	1	3.33
12-24 weeks	6	20			
24-34 weeks	10	33.33	2nd	8	26.67
34-37 weeks	5	16.67			
>37 weeks	8	26.67	3rd	21	70
Total	30	100		30	100

From the above table it can be seen that 70% cases were infected in 3rd trimester of pregnancy and 26% in 2nd trimester.

Table2 Variation in Platelet count and transfusion received.

Platelet count at diagnosis	N	%	No. of patients receiving transfusion	Platelets Transfused
<20000	1	3.33	1	12 units
21000-50000	6	20	6	8-10 units
51000-1 lakh	12	40	2	8 units
1 -1.5 lakh	6	20	-	-
>1.5 lakhs	5	16.67	-	-

Clinical findings: Most frequent presentation was fever with headache (95%), myalgia or arthralgia(25%)and with acute abdominal pain.10 patients presented with bleeding manifestations of which 6 had bleeding per vaginum. Other clinical signs were breathing discomfort, vomiting and jaundice.

Laboratory findings :Among 30 cases,10(33.3%) were found to have Dengue NS-1 positive,17(56.6%) to have Dengue IgM positive and 3(10%) had Dengue IgM and IgG positive serologically and 6 patients had raised liver enzymes with AST(Aspartate transaminase) and ALT (Alanine transaminase) being 2-5 times above the normal limit.

Obstetric consequences:

Table-3 Mode of delivery

Mode of Delivery	No. of patients
Spontaneous abortion	1
Pre-term vaginal delivery	5
Pre-term caesarean section	3
Term vaginal delivery	13
Caesarean section	8

Before 12 weeks of gestation we had 1 patient with platelet count <1 lakh and she had premature rupture of membranes (PROM) and preterm labour at 35 weeks of gestation.

Between 12-24 weeks we had 6 patients of these 1 had spontaneous abortion at 14 weeks of gestation and had platelet count <20000 .Other 3 patients had platelet count <50000, of which 1 developed preeclampsia with termination of pregnancy at 33 weeks for abruptio placentae,1 patient had Fetal Growth Restriction.1 patient with platelet count<1 lakh had fetal growth restriction and terminated at 38 weeks. Remaining 2 patients had uncomplicated pregnancy and term delivery.

Between 24-34 weeks we had 10 patients out of which 1 patient with platelet count <50000 presented with eclampsia and developed Dengue shock syndrome, 6 patients had platelet count <1 lakh of which 1 presented with bleeding per-vaginum and was diagnosed to have a low lying placenta and was managed conservatively and had a vaginal delivery at 36 weeks of gestation and 1 presented with hematemesis and had preterm delivery at 35 weeks and required platelet transfusion, 2 patients developed oligohydramnios and,2 patients with platelet <1.5 lakh of which 1 had preterm delivery.

Between 34-37 weeks we had 5 patients of which 1 had platelet <50000 and she had a preterm delivery, 2 patients with platelet <1 lakh of which 1 had gestational hypertension and had a preterm delivery.
After 37 weeks we had 8 patients of which 1 had platelet 1 <50000 and she had intrapartum complication of meconium stained liquor, 2 patients had platelet <1lakh of which 1 developed severe oligohydroamios at term, 2 had platelet <1.5 lakh of which 1 patient had postpartum hemorrhage and 1 had uneventful pregnancy,3 patients had platelet >1.5 lakh of which 1 had preeclampsia,1 had intrapartum complication of fetal distress and 1 had uneventful pregnancy.

Maternal complications observed during our study were gestational hypertension, preeclampsia, antepartum and postpartum hemorrhage and dengue shock syndrome and 10 patients (33.3%) required ICU admission.

Neonatal consequences:

Table-4 Fetal Complications

Fetal Growth restriction	**4 (13.37)**
Intrauterine Fetal Death	1 (3.37)
Meconium Stained Liquor	8 (26.67)
Fetal Distress(intrapartum)	5 (16.67)

Table-5 Neonatal consequences

Neonatal outcome	No. of cases (%)
Neonatal ICU admission(NICU)	10 (35.71)
Prematurity	6 (21.43)
Low Birth Weight(LBW)	5 (17.86)
Neonatal thrombocytopenia	1 (3.57)
Vertical transmission	1 (3.57)

Birth weight of 22 of 28 live born neonates were between 2500 g and 3500g, 1 had birth weight of 3620g, 5 neonates had weight<2500g, 6 had features of prematurity and 10 required NICU admission,1 neonate had neonatal thrombocytopenia and was found to have Dengue IgM positive. During our study we did not encounter any fetal and neonatal malformations.

Maternal-fetal transmission:
Rate of transmission came out to be 3.5%.

IV. DISCUSSION:

The outbreak of Dengue fever is common in monsoon and post monsoon season and it creates a state of anxiety among treating obstetrician for the fear of hemorrhagic complications.

Maternal Outcome:

Our study found that 26/30 (86.67%) cases had thrombocytopenia of which 6(20%) had severe thrombocytopenia with platelet <50000 and 1 patient had platelet <20000. There was rapid decline in platelet count initially during the febrile phase. Similar feature was also found in study by S Panicker et al at Coimbatore[3]. Severe thrombocytopenia can also lead to Antepartum hemorrhage and Postpartum hemorrhage
The gestational age at diagnosis of dengue fever has a significant role in prognosis. Early and a late onset has bad prognosis.1 patient diagnosed before 12 weeks had a preterm delivery with PROM at 35 weeks of gestation.1 patient had a spontaneous abortion at 14 weeks. Similar result of abortion were seen in study by carlos et al[4].

Among those infected in near term pregnancy 2 developed oligohydroamnios 8 had meconium stained liquor of which 5 developed fetal distress and required emergency LSCS and 3 had vaginal delivery. Hence the rate of fetal distress in our study was 16.7%, similar to study conducted by Garg R et al[5] at Agra.

Among those presenting with bleeding menifestations, 6 had bleeding per-vaginum with 2 having antepartum hemorrhage,1 with intracranial hemorrhage and 1 with hematemesis. Of these 3 patients had platelet <50000 and required platelet transfusion and this finding is in conjugation with study by Kulkarni et al[6] which suggests hemorrhagic manifestations occurred more in patients with severe thrombocytopenia.

Plasma leakage (rising hematocrit, fluid collection in Third space) and hemorrhagic manifestations are characteristic to DHF. Although 10 patients presented with hemorrhagic manifestations only 4 met the criteria of DHF. Remaining 6 had bleeding without signs of DHF like thrombocytopenia was absent in 3 of them, no hemoconcentration and no clinical signs of plasma leakage were seen . Futhermore hemodilution in normal pregnancy can mask classical hemoconcentration in DHF. Carles G[7] described 22 pregnancies with dengue, 10 with thrombocytopenia without hemorrhagic dengue.

1 patient presented to us at 30 weeks of gestation with fever, eclamptic seizure and raised blood pressure and which was controlled by IV magnesium sulphate and IV labetalol, her platelet count was 35000 and her hemoglobin was 8.5g/dL.her abdominal ultrasound showed intrauterine fetal demise(IUFD), she delivered vaginally and required 4 units platelet and 1 unit of blood transfusion intrapartum, few hours later in postpartum period she continued to be drowsy, and had high grade fever,sudden hypotension,tachypnea and CT brain showed Sub Arachnoid hemorrhage and was disgnosed to have Dengue hemorrhagic fever which progressed to Dengue Shock Syndrome .She was shifted to Neurology ICU where she had recovered. Similar case of DHF complicated by eclampsia was described by Tagore S et al[8]

Patient with DHF with preeclampsia had high blood pressure, protienurea with rising hematocrit and progressive decline in platelet count and normal coagulation profile can often be misdiagnosed as Hemolysis, Elevated liver enzymes,and Low platelet count(HELLP)syndrome like a case studied by Malhotra N et al[9]
In our study 12 patients had an elevated liver enzymes in form of raised ALT and AST which included all the DHF patients,1 DSS patient and 7 with Dengue fever. Liver enzymes returned to normal a few days postpartum when fever subsided. Such results were also seen in the study done by Kariyawasam S et al[10]in Srilanka.

Hemorrhagic complication like Post Partum hemorrhage(PPH) was seen in 2(6.67%) patients, but was managed appropriately with uterotonic agents, platelet and blood transfusion as both the patients had thrombocytopenia. Hence dengue fever as a risk factor of PPH was studied. Basurko C et al[11] also studied cases of PPH in dengue during pregnancy.

With complications like preeclampsia, eclampsia, intracranial hemorrhage, PPH there was no maternal mortality in our study. Ismail et al[12] in a study states maternal mortality of about 2.6 % in patients with dengue during pregnancy.
10(33.3%) patients required platelet transfusion for thrombocytopenia along with intensive hydration therapy.

Neonatal and fetal outcome:

As the rate of preterm labour is significantly increased in dengue during pregnancy. In our study 6(21%) babies were preterm and 4 had Premature Rupture Of Membrane (PROM).Carles G et al[7] and Basurko c et al[11] also had increased risk of preterm labour and prematurity in their study.

5 babies had birth weight <2500gm and lowest being 1860gm. The average birth weight was 2760gm. 4 babies had Intrauterine Growth Restriction (IUGR) secondary to gestational hypertension and preeclampsia.10 babies required NICU admission for low Birth Weight (LBW), neonatal pyrexia with thrombocytopenia and intrapartum complications like meconium stained liquor.

In our study 1 baby(3.5%)was delivered by LSCS for fetal distress in PROM was diagnosed to have dengue fever in NICU on postnatal day-2 with fever, thrombocytopenia and Dengue IgM positive .The baby required platelet transfusion and phototherapy for physiological jaundice and was discharged with complete recovery on postnatal day-13.

V. CONCLUSION:

The clinical features of dengue in pregnancy are similar to those in non-pregnant individuals, but such pregnancies require a very close monitoring for its potential risks and complications to both the mother and fetus. The Dengue Fever in pregnancy increases risk of premature birth and the effect on fetus remains variable with severe neonatal illness and death. Dengue Hemorrhagic Fever can be confused with HELLP syndrome from clinical presentation but serological tests confirms the diagnosis. The gestational age at diagnosis appeared to have a significant role in prognosis.

Dengue fever in pregnancy is most often treated conservatively. Platelet may fall progressively but does not require any intervention unless patient is in labour or has bleeding disorders. Severe thrombocytopenia managed with prompt resuscitation with platelet and blood transfusion before or during labour and in postpartum period had a keyrole in successful outcome. Hence conservative medical and obstetric management remains the treatment of choice.

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Corresponding Author: Dr. Ronak R. Bhankhar
Department of Obstetrics and Gynaecology, Smt. NHL Municipal medical college, SVPIMSR, Ahmedabad