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Prospective Observational study of Etiological Spectrum of Febrile Illinessess in Pregnancy and Association with Outcomes

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Abstract

Background:- Fever in pregnancy is a common clinical problem worldwide. The risk to the mother and fetus is significantly increased in pregnancy complicated by infection and fever.

Aim and objective:- To determine etiological spectrum of febrile illnesses in pregnancy and its association with maternal & fetal outcomes.

Methodology :- Prospective observational study was conducted in the Department of obstetrics and gynecology in a tertiary care center in western Maharashtra. A total 105 pregnant women reported with fever during the study periods, out of which 37 were followed up longitudinally till delivery and were included in the study analysis.

Results:- In the present study, Fever of unknown origin(32.43%), Dengue(24.32%), COVID-19 (24.32%), Urinary tract infections(16.21%) Malaria(2.7%) were the common cause of febrile illness. Out of 37 pregnant women with febrile illness, 31 (83.8%) had live births, 5 (13.5%) had intrauterine death (IUD) and there was one case of abortion. In 10 (27%) patients, there was a requirement for NICU admission. It was observed that more is the number of febrile episodes higher is the chance of neonatal morbidity and mortality.

Conclusion :- High grade fever with multiple febrile episodes due to any underlying etiology in pregnancy is harmful to the fetal-maternal health.

Keywords: Maternal Fever, Maternal Outcome, Neonatal Outcome

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INTRODUCTION

Environment heat has played a significant role in the evolution of living things like plants and animals. The more successful animal species have evolved the ability to maintain their body temperatures at relatively high levels and with in a relatively narrow range (homeothermy), which improves metabolic processes and increases the

capacity for physical activity under a variety of climatic conditions.[1]

Fever during pregnancy increases the risk of the pregnancy. It is a symptom that must be understood as the mother's body responding to a pathological process. Pyrexia is defined as a temperature above 100-degree Fahrenheit while pregnant. The causes and effects of fever vary depending on when it occurs (pregnancy term, labour or postnatal period). Pregnancy fever is a widespread clinical issue. Pregnancy complications brought by infection and fever significantly increase the risk to the mother and foetus.[2] Pregnancy-related maternal infections have the potential to directly affect the growing foetus and in some cases, even cause foetal death. Some illnesses, including influenza, mastitis, endometritis, wound infections, urinary tract infections, and endometritis, pose a risk primarily to the mother. The risk of foetal or neonatal complications makes other diseases, such as group B streptococci (GBS) infection, herpes simplex virus (HSV) infection, rubella, cytomegalovirus (CMV) infection, and toxoplasmosis, particularly concerning.[3]

WHO had declared COVID-19 pandemic since march-2022. High grade of fever due to illness like COVID-19 could have a significant impact on both the pregnant mother and the fetus.[4,5]

There are restrictions in investigating and treating fever during pregnancy. Investigations like X -Ray, CT scans are to be avoided. On the other hand many powerful antibiotics should be used with caution due to risk of teratogenicity. Therefore, some febrile illnesses may progress more severely during pregnancy, putting the foetus health in danger and resulting in the transmission of infectious agents across the placenta.

Despite the documented absence of neonatal sepsis, the presence of maternal fever exposes the foetus to a variety of inflammatory mediators as measured by umbilical cord blood cytokines. Maternal cytokine polymorphism causing intra-partum fever in mothers is found to be directly correlated with cerebral palsy in term neonates. The threshold for hypoxic injury in neonates is lowered by higher oxygen consumption in the brain.[6]

Miscarriage, premature labour, growth restriction, and still birth are frequently caused by mild exposures during the pre-implantation periods and more severe exposures during embryonic and foetal development. The central nervous system (CNS) is most susceptible to a wide range of structural and functional defects caused by fever in foetuses.[7] Even brief exposure to a mother's body temperature has been shown to cause cellular disruption, vascular disruption, and placental infarcts, all of which increase the likelihood that the unborn child will have a structural or functional defect.[1]

This study aimed to identify the etiological spectrum of febrile illnesses in pregnancy and its association with maternal & fetal outcomes. It was deemed necessary particularly in the era of COVID19 pandemic.

METHODOLOGY

A prospective observational study was conducted in the department of obstetrics and gynecology at tertiary care center in Western Maharashtra, over a period of 2 years in antenatal females coming for delivery. The study was initiated after obtaining approval from the Institutional Ethics Committee. The purpose and rationale of the study as well as their role as participants was explained to all the patients in the study. Written informed consent was obtained from all the patients. The inclusion criteria of study was all ANC patients, irrespective of gestational age, with fever (Temp.- >100 fehrenheit/37.8 0 celsius) are willing to follow up and deliver at our hospital. Exclusion criteria of the study was patients who are not willing for follow up. Detailed history of each case was taken regarding name, age, address, socio-economic status, literacy, obstetric history, menstrual history, any symptoms associated with fever were noted. Investigation sample was sent to the department of pathology and virology laboratory of our hospital. The reports of investigations were collected and prevalence of various pathogen responsible for febrile illness during pregnancy were recorded. Follow up of patients with febrile illness was done and their impact on maternal and perinatal outcome was recorded. Details about COVID-19 cases were collected by residents posted in COVID ward. The sample size was estimated by the formula for calculation of sample size for qualitative data

$n = Z\alpha^2 * p * q / d^2$

n=sample size

Zα – standard normal deviation for α

– 0.05(95%CI) =1.96

p8= proportion under interest =10.5

q= 100-p=89.5

d= allowable error in percentage = 10%

Hence, n = 37

The collected data was coded and entered in Microsoft Excel sheet. The data was analyzed using SPSS (statistical package for social sciences) version 26.0 software.

RESULTS :

A total 105 patients reported with fever during the study period, out of which 37 were followed up longitudinally till delivery and were included in the study analysis. The mean age of the patient was 27.35, SD was 4.16 years ranging between 20 to 36 years. The mean gestational age was 29.38, SD was 8.42 weeks, range in between 6 and 39 weeks. The mean duration of hospitals stay was 6.19 ± 3.96 days. Demographic and clinical parameter including age, gestational age, pulse rate, systolic diastolic blood pressure and temperature are measuring during study. The mean pulse rate was 102.39, SD was 11.48 bpm. The mean systolic blood pressure was 115.68, SD was 9.29 mmHg, ranging between 100 to 140 mmHg. The mean diastolic blood pressure was 73.51, SD was 6.76 mmHg, ranging between 60 to 90 mmHg. The mean temperature was 101.28, SD was 0.61 F, ranging between 100.5 to 103f.

Complete Hematological parameters including Hemoglobin, Total leukocyte count and Platelet count were estimated in ANC patient with fever. The mean hemoglobin level was 10.83, SD was 1.37 g/dL, range in between 7.4 to 14.2 g/dL. The mean TLC count was 10,927.43, SD was 5378.39/cumm, while the mean platelet count was 1,87,165.71, SD was 93,935.82/cumm.

In 37 ANC patients with fever the mean number of febrile episodes reported in the present study was 5.35 ± 2.49, ranged between 2 and 12 episodes. The mean duration of hospitals stay was 6.19 ± 3.96 days.

Table 1: Distribution of Patients According to Number of Febrile Episodes and Etiology

Number of febrile episodes	COVID	Dengue	Fever of Unknown Origin	Malaria	UTI	Total
2	0	0	2(5.40%)	0	0	2(5.40%)
3	2(5.40%)	3(8.10%)	(1)2.70%	0	1(2.70%)	7(18.91%)
4	2(5.40%)	1(2.70%)	4(10.8%)	0	1(2.70%)	8(21.62%)
5	1(2.70%)	1(2.70%)	2(5.40%)	1(2.70%)	1(2.70%)	6(16.21%)
6	1(2.70%)	2(5.40%)	1(2.70%)	0	2(5.40%)	6(16.21%)
7	1(2.70%)	0	0	0	0	1(2.70%)
9	2(5.40%)	0	2(5.40%)	0	0	4(10.81%)
10	0	1(2.70%)	0	0	1(2.70%)	2(5.40%)
12	0	1(2.70%)	0	0	0	1(2.70%)
Grand Total	9(24.32%)	9(24.32%)	12(32.43%)	1(2.70%)	6(16.21%)	37(100%)

Table 2 : Association between fetal outcome and mode of delivery according to cause of fever

Cause of the fever	Mode of delivery					Fetal outcome	
	Abortion	Vaginal		LSCS			
		PTVD	FTVD	PTLSCS	FTLSCS	IUD	Live birth
Dengue	1	2	1	0	5	1	7
COVID-19	0	2	2	1	4	2	7
Malaria	0	1	0	0	0	0	1
UTI	0	2	2	1	1	0	6
Fever of unknown origin	0	3	2	1	6	2	10

Table 3 : Association of number of febrile episodes and fetal outcome

Number of febrile episodes	Total	Outcome			P value
		Abortion	IUD	Live Birth	
2	2	0	0	2	
3	7	0	0	7	
4	8	0	0	8	
5	6	0	0	6	
6	6	0	0	6	0.003
7	1	0	0	1	
9	4	0	4	0	
10	2	0	1	1	
12	1	1	0	0	
Total	37	1	5	31	

It was observed that higher the number of febrile episodes, higher was the neonatal morbidity and mortality (p value:0.003). Among the 5 IUDs reported in the present study, four of them had 9, and one patient had 10 febrile episodes. The number of febrile episodes among mothers of newborns who required NICU admission ranged from 3 to 9, with an average of 5 episodes. While in mothers of newborn which did not require NICU admission, average febrile episodes were 4.5. Thus our study shows that fetal outcomes depend on degree of febrile illness irrespective of the cause of fever.

The requirement of *NICU* admission was there among 10 (27%) of patients, while in 27 (73%) there was no need of *NICU* admission. The mean weight of the baby at birth was 2.56 ± 0.63 kgs, with an *APGAR* score at 1 minute of 6.17 ± 2.32 and at 5 minutes of 7.56 ± 2.77. Three patients had severe oligohydramnios, 1 had anhydraminos and 2 patients had *IUGR*.

DISCUSSION

The present study was done to identify the etiological agents that cause fever in pregnancy as well as the various medical complications that may cause severe morbidity in mother as well as fetus.

A total of 37 ANC patients with evidence of fever were included in the study.

We found that fever of unknown origin was most common cause of febrile illness followed by Dengue, COVID-19, urinary tract infections, malaria in our study population.

The number of febrile episodes in 37 ANC patients with fever ranged from 2 to 12, with a mean of 5.35 2.49. The mean duration of hospitals stay was 6.19 ± 3.96 days and. In the all patients with fever, laboratory parameters such as total leukocyte count and platelet count were estimated. The average hemoglobin level was 10.83 ± 1.37 g/dL, with a range of 7.4 to 14.2 g/dL. The mean *TLC* count was 10,927.43 ± 5378.39/cumm, while the most frequently observed platelet count was 1,84,000/cumm.

Our study finding are comparable to another Indian study done by Brar [9]et al which mentions the average haemoglobin, *TLC*, and platelet count as 10g/dl, 11900/cumm, and 1.7 lacks/cumm, respectively.

In the present study, the rate of caesarean section was 51.4%, out of which 3 were preterm *LSCS* and 16 were full term *LSCS* and 17 (47.6%) were vaginal deliveries, out of which 10 were preterm and 7 were full term deliveries. Most commonly observed indication for *LSCS* was fetal distress.

According to Sultan[10] et al, 46.4 percent of births occurred at full term, 21.6 percent were preterm vaginal births, 27.4 percent were caesarean sections, and 4.6 percent involved abortions. This difference can be because of low threshold for Cesarean sections during COVID -19 pandemic during our study period.

In a study by Sultan[10] et al, among 306 cases, the incidence of pyrexia in pregnancy was 2%, with *UTI* (27.7%) being the most common cause. This was followed by respiratory tract infections (25.1%), enteric fever (15.7%), malaria (14.4%), chicken pox (6.2%), tuberculosis (4.6%), hepatitis (4%) and pyrexia of unknown origin *(PUO)* (1.3 percent)

Dengue, Hepatitis E and *UTI* were the most typical causes of fever in pregnant women, according to Brar[9] et al.

In the present study, out of 37 pregnant women with febrile illness, 31 (83.8%) had live births, 5

(13.5%) had intrauterine death (*IUD*/ still births) and there was one case of abortion(2.7%). In 10 (27%) patients, there was a requirement for NICU admission. The mean weight of the baby at birth was 2.56 ± 0.63 kgs, with an APGAR score at 1 minute of 6.17 ± 2.32 and at 5 minutes of 7.56 ± 2.77.

Our findings are similar to that of Brar[9]et al. In this study, there were 20 (11.9%) still births out of 167, with a miscarriage rate of 4.1 percent. Neonatal *ICU* care was necessary in 31 (22.1%) newborns, while neonatal deaths were reported in 9 (6.4%) cases.

All deliveries were singletons, according to Biswas[11]et al, who also reported that the average birth weight was 2.44 kg (SD = 0.41), this is similar to our study finding.

Sultan[10]et al identified low birth weight (36.6%) as the most common foetal issue associated with pyrexia during pregnancy. Premature delivery was rated at 66. (21.6 percent). 180 babies were admitted to the *NICU* (58.82%), of which 29 (9.5%) were still births and 13 (4.2%) were neonatal deaths.

Amongst 9 pregnant women with dengue fever ,there were 7 live births, 1 abortion, and 1 *IUD*. In this group, one newborn was admitted to the *NICU*. Out of 9 women with dengue, 5 underwent *LSCS*, and 3 had vaginal deliveries including 2 preterm and 1 full term vaginal delivery. In the case of abortion as an outcome, the most, i.e., 12 febrile episodes, were noted.

While all six women with evidence of UTI had live births, three of the newborns were admitted to the *NICU*.

There was only one case of malaria. She had a normal vaginal delivery. She delivered after 1 month of febrile episode with a live birth.

There were 9 cases of COVID-positive pregnant women. As per hospital policy we were doing *RTPCR* test for every patients reporting with fever to the hospital. Diagnosis of COVID-19 disease during antenatal period was a stressful situation in the pandemic times. We had 9 patients who were admitted with fever and turn out to be COVID-19 positive. One patient who was 29 weeks of pregnant had intrauterine death and one full term intrauterine death. Conducting vaginal delivery with all COVID-19 related precautions was an arduous task that for the attending doctors as well as patients. In 3 patients, LSCS was planned 2 weeks from the diagnosis of COVID-19 disease to take care of the isolation period. 2 cases were remote from term , one needed preterm LSCS at 35 weeks , one case could successfully completed term.

Fever of unknown origin is a diagnosis of exclusion. These patients need additional investigations like blood culture or battery of investigations like rickettsial fever, tuberculosis etc. This increases the anxiety in the patients as well as treating doctors. We had 12 cases labelled as fever of unknown origin initially. 4 of these cases were investigated with blood culture. One of them turned out to be staphylococcus haemolytic positive. All these patients received higher antibiotics which adds to the hospital stay and cost and side effects for the patients. These patients also need intensive fetal monitoring and multidisciplinary management. 2 of these cases ended up having intrauterine death. One case was admitted with a diagnosis of IUD at 37 weeks and other case who had fever at 26 weeks , successfully discharged from hospital and reported with *IUD* at 33 weeks.

STRENGTHS AND LIMITATIONS:

We conducted this study while world was facing the COVID 19 pandemic challenge. Studying feto-maternal outcomes because of febrile illnesses during this time frame makes our study special. We could get a very small sample size, that is the limitation of our study.

CONCLUSION:

The present study was done to study etiological spectrum of febrile illnesses in pregnancy and its association with maternal & fetal outcomes. Higher the number of febrile episodes, higher was the neonatal morbidity and mortality. There was significant association between fetal outcomes and number of febrile episodes.

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