International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Mamatha K et al. Int J Reprod Contracept Obstet Gynecol. 2023 Oct;12(10):3069-3075
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20232949

Original Research Article

Maternal and fetal outcome of febrile morbidity in pregnancy at tertiary care level

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Received: 05 August 2023
Revised: 03 September 2023
Accepted: 04 September 2023

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ABSTRACT

Background: Fever in pregnancy is a common clinical problem worldwide. Effects of hyperthermia depends on the extent and duration of temperature elevation, timing of exposure in pregnancy and possibly on maternal nutritional status, comorbidities, medications, socio-economic background and several other factors. The exposure of maternal temperature has been reported to lead to cell disruptions, vascular disturbance and placental infarction which can lead to the risk of structural and functional defects in progeny. The underlying maternal cytokine polymorphism is strongly associated with both intrapartum fever and neonatal outcome. Hence there is a need to detect the various life-threatening medical complications of febrile morbidity leading to severe maternal morbidity and its impact on fetal outcome. Aim of study were to study the etiology of fever in pregnancy during the study period and to know the effect of fever on both the mother and the fetus.
Methods: A prospective observational study.
Results: Out of the 60 cases of fever in pregnancy, most common cause of fever was urinary tract infection (30%), followed by dengue fever (25%) and upper respiratory tract infection (23.3%). Fever was associated with complications as such PROM, PPROM, preterm labour, PPH, thrombocytopenia, anemia and abortions. Fetal outcome were preterm birth (25%), low birth weight (36%), neonatal sepsis (20%) and perinatal death (13.8%).
Conclusions: Febrile morbidity in pregnancy leads to numerous maternal and fetal complications can occur due to fever in pregnancy from various causes. The most common cause of fever was UTI followed by dengue fever. The maternal and fetal complications can be avoidable if the cause for the fever is diagnosed and treated early.

Keywords: Fever, Preterm, Temperature, Urinary tract infection

INTRODUCTION

Febrile morbidity can be an intriguing entity in the maternal period. Fever during pregnancy causes significant maternal and fetal complications. Any acute or chronic infectious diseases may be aggravated during the period of pregnancy.[1] The febrile mother presents a unique diagnostic dilemma and therapeutic challenge to an obstetrician involved in her care.[2] Fever can result from a variety of infectious microorganisms, tissue trauma, malignancy, drug administration, endocrine and immunological disorders. The infectious etiology of fever in a parturient may be pregnancy specific, such as chorioamnionitis, or not specific to pregnancy, such as altered or compromised functions of immune system may predispose to several infections. Restrictions of antibiotics due to teratogenicity preclude the infection control. Anatomical and physiological changes occurring during pregnancy may predispose certain infections, for example, the urinary tract infections.[3-4]

Some infections affecting the mother may also be transmitted to the fetus in utero. The effect of fever during pregnancy depends on the level of temperature rise,

duration and the stage of fetal development. Some febrile diseases will lead to more severe and life-threatening course in pregnancy and transplacental transmission leading to adverse fetal outcome. Pyrexia during pre-implantation, embryonic and fetal development period, may result in miscarriage, growth restriction, preterm labour and still birth. Protein synthesis gets interfered by hyperthermia via heat-shock proteins, S-phase cell death is induced and cause delay in mitotic activity during M phase. Vascular disruption and placental infarction also can happen. Ultimately it will lead to lethal malformations and fetal death.[5,6] Furthermore, uterine contractility will be increased by pyrexia leading to expulsion of the fetus at a non-viable stage of gestation. The hyperthermia induced feto-maternal outcome will differ according to the gestational time of exposure.[7-8] During intrauterine life, the temperature of fetus is maintained by utero-placental circulation and heat- exchange at the amniotic fluid interface. Pyrexia effect on pregnancy depends on the extent of the rise in the temperature.[4]

Because of maternal pyrexia, various inflammatory mediators as evidenced by umbilical cord blood cytokines are documented in the absence of neonatal sepsis. The underlying maternal cytokine polymorphism is strongly associated with both intra partum fever and cerebral palsy at term.[5] Some infectious diseases are more severe in pregnancy (e.g., malaria, listeriosis, hepatitis E virus (HEV), herpes simplex virus and influenza). Increased brain temperature increases oxygen consumption and also lowering the threshold for hypoxic injury. Hypoxic brain injury is increased by hyperthermia in term neonates.[9]

According to studies of healthy individuals of 18-40 years of age, the mean oral temperature is 36^0C±0.4ºC (98.2ºF±0.7ºF) with low levels at 6 A.M and higher levels at 4-6 P.M. An A.M temperature of >37.2ºC or a P.M temperature of >37.7 ºC would define a fever. The normal daily temperature variation is typically 0.5ºC.[10]

Physiologic changes of pregnancy include an increase in the maternal basal metabolic rate. The notion that pregnant women become globally immunosuppressed during pregnancy is inconsistent with evolution and the overall favourable survival of the human fetus.[11] The alterations that occur in maternal innate and cellular immunity during pregnancy are decreased T-cell function and decreased NK-cell function. Maternal body temperature in labour is also significantly affected by the degree of physical activity and intensity of uterine contractions. Pain associated with uterine contractions causes the parturient to hyperventilate, which along with accompanying perspiration, leads to compensatory heat dissipation. The maternal-fetal temperature gradient closely correlates with utero-placental blood flow and fetal oxygen delivery.[11] Perinatal morbidity is significantly increased in pregnancies complicated by the presence of peripartum maternal infection and fever.[12,2]

The anatomic changes associated with pregnancy may predispose women to certain infections. Urinary tract dilation is one of the most significant alterations induced by pregnancy. These changes are mediated by hormonal (progesterone) and mechanical factors, resulting in urinary stasis and predilection to urinary tract infections. The incidence of pyelonephritis in pregnancy is approximately 1%. The possibility of peripartum transmission of infectious microorganisms will affect the obstetric and subsequent anaesthetic management of these patients. The overall incidence of maternal infection in labour has been estimated as 3.1%.[4]

Proliferation of somatic cells is adapted to the normal body temperature range of the species. Increase in basal body temperature adversely affects the mitotic and meiotic proliferation of cells. In the same way embryonic death, abortion, growth retardation, and defects of development are the consequences of hyperthermic episodes during pregnancy. In term infants, intrapartum fever has been associated with a risk of cerebral palsy, neonatal hypoxic encephalopathy, and seizures. Studies have examined limiting the effects of inflammation and fever on the neonatal brain by giving acetaminophen, steroids and antibiotics, and other neuroprotective agents during planned vaginal deliveries.[12,13,15,16]

There are several ways in which maternal infection might lead to inflammation with in the fetal tissue. Bacterial products crosses the placenta and binds with cell-membrane receptors like CD-14 and toll-like receptors. They initiate a cascade of intracellular events in inflammatory cells. They further activate nuclear factor κ-B and production of pro inflammatory cytokines. These pro inflammatory cytokines are granulocyte colony-stimulating factor, tumour necrosis factor-α, interleukin-1β, C-reactive protein and Interferon γ. It causes increase in metabolic rate and demand for oxygen in fetal brain.[17-19]

The common infections during pregnancy urinary tract infection, respiratory tract infection, vaginal infections, typhoid and paratyphoid fever, malaria, dengue, tuberculosis, chicken pox.

METHODS

A prospective observational study with source of data from OPD/IPD of Dept of Obstetrics and Gynaecology, Cheluvamba Hospital, MMCRI. Study period was 1.5 years [January, 2020 to June, 2021].

Inclusion criteria

Inclusion criteria was all prenatal mothers above 18 yrs. admitted with fever, willing to give informed consent and diagnosis as per CDC criteria where the patient has fever with a temperature of 100.4 F (38 C) or greater, or feels warm to the touch, or gives a history of feeling feverish.

Exclusion criteria

Exclusion criteria was patient not willing to give informed consent, fever due to septic abortion, blood transfusion reaction, hypertension, diabetes mellitus, renal diseases, cardiovascular diseases.

A written informed consent was taken from the selected patients attending the OPD a detailed clinical history with age, parity and the trimester of pregnancy at diagnosis of fever was recorded and a physical examination will be performed. Patients were admitted and was subjected to blood investigations such as complete blood count, urine routine and microscopy, blood and urine culture and sensitivity, fever profile including dengue serology, thin and thick peripheral smear for malaria, widal test, throat swab, high vaginal swab for culture and sensitivity. The causes of fever were identified and treated with follow up of maternal and fetal outcome. Discharged patients were followed up during their regular ANC visits. At the time of delivery birth weight of the baby, gestational age at birth, APGAR score was studied. Fetal outcome will be studied by taking variables-low birth weight, intrauterine growth retardation, preterm delivery, neonatal sepsis and perinatal death. Maternal complications post-operative wound infection, post-partum haemorrhage, pneumonia, septicaemia, jaundice, hypoglycaemia and other complications of specific fever were treated. Approval from the ethical committee was obtained.

Statistical analysis

SPSS (Statistical Package For Social Sciences) version 20. [IBM SPASS statistics (IBM corp. Armonk, NY, USA released 2011)] will be used to perform the statistical analysis. Data was be entered in the excel spread sheet. Descriptive statistics of the explanatory and outcome variables will be calculated by mean, standard deviation for quantitative variables, frequency and proportions for qualitative variables. Inferential statistics like Chi-square test will be applied for categorical variables. The level of significance is set at 5%.

RESULTS

Most of the mothers presenting with fever belonged to 21-25 years and 26-30 years age group. Maternal age did not play a part in mothers with febrile morbidity (Table 1).

Majority of the study participants were primigravida (60%) who presented with antenatal fever. Among the multigravidae, 3 of them were had previous caesarean section and the rest underwent vaginal delivery (Table 2).

Among them, 60% presented with fever at term and were in latent phase of labour, 34% presented between 29-36 weeks and had preterm labour or PPROM as a complication. Hence it is seen that febrile morbidity has a part to play in the onset of labour (Table 3).

Table 1: Age distribution of study participants.

Age group	Frequency	Percentage
≤20 years	13	21.7
21-25 years	23	38.3
26-30 years	18	30.0
31-35 years	5	8.3
≥36 years	1	1.7
Total	60	100.0

Table 2: Distribution of study participants as per their parity.

Parity	Frequency	Percentage
1	36	60.0
2	15	25.0
3	9	15.0
Total	60	100.0

Table 3: Distribution of study participants as per gestational age at the time of fever onset.

GA when fever occurred	Frequency	Percentage
≤ 13 weeks	2	3.3
14 to 28 weeks	2	3.3
29 to 32 weeks	4	6.7
33 to 36 weeks	16	26.7
37 to 40 weeks	36	60.0
Total	60	100.0

After thoroughly evaluating the mothers who presented with fever, the most common cause of fever among them was urinary tract infections (30%), followed by dengue fever (25%) and upper respiratory tract infection (23%). There was one case malarial fever caused by *Plasmodium falciparum* and one case of pulmonary tuberculosis. All the 60 mothers recovered without any significant morbidity (Figure 1).

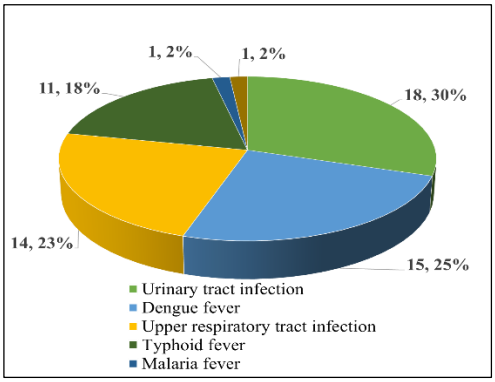

Figure 1: Etiology of fever among study participants.

Maternal complications like acute gastroenteritis were seen in patients tested positive for typhoid fever. Those with anemia were seen associated with urinary tract infections. All of these cases had moderate anemia (Hb-7-

9g/dl). Among these cases, 2 of them needed blood transfusion. Among the 15 cases of dengue fever, 9 of them had mild thrombocytopenia but did not require platelet transfusion. Other complications such as PPROM, PROM and PPH were seen associated with fever (Figure 2).

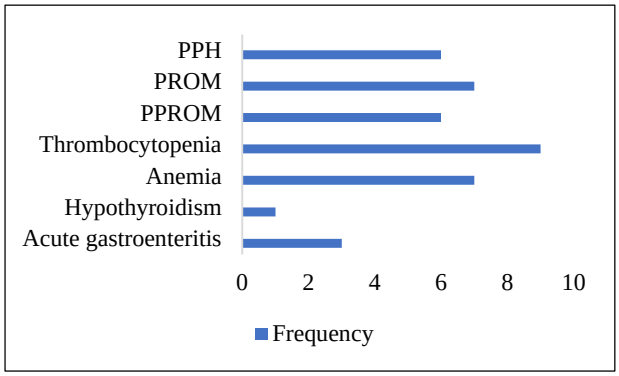

Figure 2: Maternal complications.

Among the mothers who presented with fever, 70% had spontaneous delivery at term, 25 % had preterm delivery, 3% had first trimester spontaneous abortion and 1 among them required instrumental evacuation with the coverage of antibiotics and 2% had second trimester abortion. Intrapartum fever was seen in 20% of the term deliveries. They were also covered with intravenous antibiotics. Among the 60 antenatal mothers with fever, 2 of them who presented in the first trimester underwent spontaneous abortion. Among the two cases who presented with fever in the second trimester, 1 had spontaneous abortion at 20 weeks and the other continued pregnancy from 26 weeks to 28 weeks and delivered spontaneously at 28 weeks. The baby had very low birth weight and did not survive. Those mothers who presented from 29 to 32 weeks had preterm delivery. Among the 10 patients from 33 to 36 weeks, one presented with intrauterine fetal demise at 34 weeks and she had typhoid fever with sepsis. Also 6 of them continued pregnancy till term. Out of these 2 of them underwent caesarean section (Table 4).

Table 4: Association between GA when fever occurred and GA at the time of delivery.

GA at fever (weeks)	GA at the time of delivery (weeks)				
	≤ 13 (%)	14 to 28 (%)	29 to 32 (%)	33 to 36 (%)	37 to 40 (%)
≤ 13	2 (100.0)	0	0	0	0
14 to 28	0	1 (50.0)	1 (50.0)	0	0
29 to 32	0	0	4 (100.0)	0	0
33 to 36	0	0	0	10 (62.5)	6 (37.5)
37 to 40	0	0	0	0	36 (100.0)
Chi – square test: χ^2: 176.143; df: 16; p value: < 0.001*					

*p value significant at < 0.05

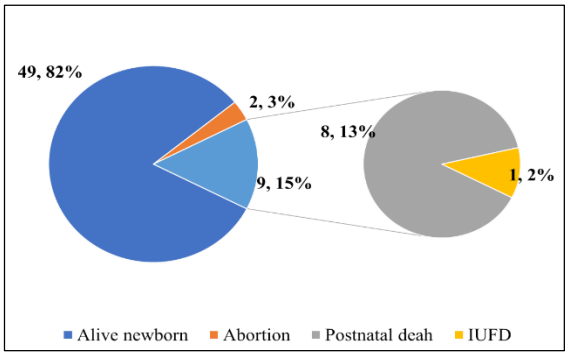

Figure 3: Fetal/newborn mortality of study participants.

One was a primigravida with cephalopelvic disproportion and the other was previous C-section with scar tenderness. The remaining 4 delivered vaginally and among them 2 babies required NICU admission in view of low APGAR score and low birth weight. Those who came with fever at term were in latent labour, 12 of them underwent caesarean section, 1 underwent VBAC and the rest 23 had vaginal delivery. Applying Chi-square test showed a p value <0.001 which was significant. Postnatal deaths were 8 in number out of which one baby had meconium aspiration syndrome, 6 babies were preterm with very low birth weight and all 6 babies had sepsis (Figure 3).

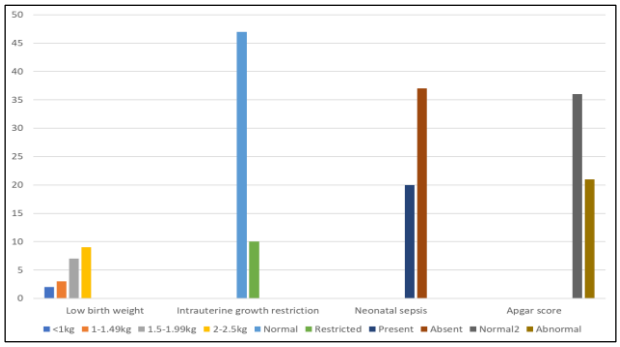

Figure 4: Neonatal complications of study participants.

Among the babies delivered, 82% had normal growth whereas 18% had intrauterine growth retardation with fever in pregnancy. Out of the 10, all of them had neonatal sepsis and 6 of them had perinatal deaths. The remaining 4 babies survived with appropriate antibiotics and neonatal care. Among the newborn, 35% had neonatal sepsis out which, 50% had early onset sepsis. They were treated with

appropriate sensitive antibiotics. Among those with neonatal sepsis, there were 6 perinatal deaths. The remaining 14 babies survived (Figure 4).

DISCUSSION

We studied 60 pregnant women with fever during the study period. The maternal and fetal outcome of febrile morbidity in pregnancy was studied. The etiology of fever in the study group was made out. Urinary tract infection was the most common cause of fever in the study group.

Suri et al in 2017 at PGI, Chandigarh studied the fetomaternal outcome of fever in pregnancy. They studied 180 pregnant women with fever. In their study dengue was the most common cause of fever. In my study urinary tract infection was the most common cause of fever. In their study most of the patients are in the age group of 20-30 years and most of them were primigravida. In my study also the most of the patients are in the age group of 20-30 years. Low birth weight was the most common fetal outcome followed by preterm labour.[20]

In our study low birth weight, preterm labor, IUGR were more common. Maternal complications are thrombocytopenia, anemia, PPROM, PROM and even PPH were seen associated with fever. The most common etiology was UTI (18 cases) in which 4 of them had moderate anemia and 2 of them needed blood transfusion and 1 of them had PPH, 4 of them had preterm labour, 4 low birth weight babies, 4 babies had Apgar less than 7 at 5 minutes and needed NICU admission. There were 2 cases of first trimester abortion. This suggests the need for promotion of screening urine cultures during pregnancy to detect asymptomatic bacteriuria and use of bacterial sensitivity guided antibiotic use in pregnant women with UTI.

The second most common cause of fever was dengue. There were 15 cases of dengue fever. Of these 7 patients had thrombocytopenia but did not require platelet transfusion. 2 patients had hypotension and were managed with intravenous fluids during labour. Five of them had preterm labour and low birth weight and 6 patients had low APGAR score. Seasonal preventive measures should be instituted and standard management protocols should be optimized. There was one case of malarial fever and one case of tuberculosis. Both were associated with maternal anemia and neonatal low birth weight.

In our study 15 cases underwent C-section. Most common indication was fetal distress (9 cases). All 9 of them had meconium-stained liquor. Neonatal complications include perinatal mortality, neonatal seizures, poor APGAR score at birth, need for resuscitation after delivery, neonatal sepsis. Intrapartum antibiotics reduces the risk of neonatal morbidity. There was one IUFD were the mother had typhoid fever with sepsis.

A prospective observational study by Rekha Rao and Sheshadri Sahaja done at GMC, Kadapa, Andhra Pradesh, 2019-20, causes of fever were found to be malaria (35%), typhoid (14%), URTI (12%), UTI (9%), viral (11.4%), dengue (8%), viral (6%) LRTI (2%). Out of 100 antenatal cases admitted with fever, 55 delivered vaginally (55%), 35 delivered by LSCS (35%) and 10 were abortions (10%). Among vaginal deliveries 10 babies had fetal distress. Among 100 deliveries, 25 babies admitted to NICU, 15 were due to preterm and its complications (60%) and 10 were due to fetal distress (40%). There were no fetal and maternal deaths. In this study, it is observed that malaria is the most common cause of fever followed by typhoid. Preterm and PROM were observed as the most common complications followed by abortions. NICU admissions were most commonly due to preterm and its complications and there were no fetal deaths[21] (Table 5, 6).

Table 5: Comparison of etiology of fever with reference studies.

Etiology of fever	Present study (%)	Brar et al (2017) (%)	Rao et al (2019) (%)
Urinary tract infection	30	12.2	9
Respiratory infection	23	9	14
Dengue fever	25	24.3	8
Typhoid fever	18.3	2.7	14
Malaria	1.7	6.1	35
Tuberculosis	1.7	6.1	0
Influenza	0	1.7	20

Table 6: Comparison of fetal outcome with reference studies.

Fetal outcome	Present study (%)	Brar et al (2017) (%)	Rao et al (2019) (%)
Preterm	25	4.1	67
LBW	36	46.9	40
APGAR<7	21	22.1	25
Neonatal Sepsis	20	20	-
IUGR	10	20	15
Perinatal death	13.8	9	0
IUFD	1.7	11.9	0

A prospective study done by Prasanna et al at KAPV Government Medical College, Trichy, 2018 showed that the incidence of fever was 6%. Out of which the most common cause of fever was viral. Many preterm labour (24%) were noted in this study which needed NICU admission of the babies. Maternal mortality was 25%, most of it were associated with DIC, IUD and one or two combined risk factors.[22]

A prospective observational study done by Biswas et al at Eden hospital, Kolkata, 2010-11 showed both maternal and feta complications were highest when malaria was the cause of fever. Low birth weight was the most common adverse pregnancy outcome and there were 4 perinatal deaths. No statistical association was present between age, parity or period of gestation and frequency of occurrence of maternal complications in antepartum febrile illness.[23]

The sample size of this study was small. More studies can be done with larger groups. Maternal and fetal outcome of each etiology can also be studied. These are some limitations of this study.

CONCLUSION

Febrile morbidity in pregnancy is an important entity to be dealt by an obstetrician. Numerous maternal and fetal complications can occur due to fever in pregnancy from various causes. The most common cause of fever was UTI followed by dengue fever. The complications associated with these can be preventable if the patient present to the health care center at the appropriate time and antenatal screening. The maternal and fetal complications can be avoidable if the cause for the fever is diagnosed and treated accordingly. They should be treated with antipyretics and antibiotic according to their etiology and sensitivity to prevent the adverse maternal and fetal mortality and morbidity. Maternal and fetal outcome for specific etiology can be studied. Hence standard methods for infection control in homes, communities and health care settings and prompt identification of symptoms and early approach to the health care center should be emphasized.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Mamatha K, Antony A, Nagaveni S, Anusha BC. Maternal and fetal outcome of febrile morbidity in pregnancy at tertiary care level. Int J Reprod Contracept Obstet Gynecol 2023;12:3069-75.