

# Pyrexia in Pregnancy and its Maternal and Fetal Outcome

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## ABSTRACT

### Background

Contemporary obstetrics has witnessed improved maternal and fetal outcomes, owing to several advances. Any source of maternal hyperthermia that results in significant core temperature increase (> 38°C), could potentially affect the fetus. Fetus being an integral part of the feto-maternal unit and pregnancy involving numerous physiological changes and adaptations, pyrexia during the pregnancy affects both the mother and her fetus adversely.

### Objective

To find the etiology and prevalence of fever in pregnancy and to know the effect of fever on maternal and fetal outcome.

### Method

Pregnant ladies with fever > 38°C, presenting to Obstetrics and Gynecology, Department of Dhulikhel Hospital were enrolled in the study. A detailed clinical history, thorough general and physical examinations were done. All risk factors were asked and recorded including all baseline investigations and cases were followed up till delivery. Maternal and fetal outcomes were recorded. Data were recorded in Excel and calculated using SPSS 26.

### Result

Eighty patients presented with complaints of fever were included in this study. The mean age of the patient was 25.49± 4.50 years. Out of 80 patients, 46 (57.50%) presented with fever in the third trimester. The most common etiology of fever being urinary tract infection in 21 (26%) cases followed by respiratory tract infection in 20 (25.1%) cases. Twenty two newborns had low birth weight among which 12 (15%) neonates had IUGR. About 14 (17.5%) neonates were admitted in NICU due to various complications and perinatal mortality was in 9 (11.25%) cases. The most common antepartum complication was preterm labor in 16 (20%) cases.

### Conclusion

Fever in pregnancy is still a challenge to obstetrician and the society at large due to its problems related to its prevention, diagnosis, management and its feto-maternal outcome. Hence, an evaluation of the effect and outcomes of fever in pregnancy, provides definite knowledge of clinical epidemiology, and facilitates optimum prioritization of efforts and resources.

## KEY WORDS

*Fever, Feto-maternal outcome, Pregnancy, Preterm labour*

## INTRODUCTION

Fever in pregnancy is a common clinical problem worldwide. The febrile parturient presents a unique diagnostic dilemma and therapeutic challenge to an obstetrician involved in her care. Fever can result from a variety of infectious microorganisms, tissue trauma, malignancy, drug administration, endocrine and immunological disorders. However, infection is by far the most common cause of fever in the parturient. The risk to the mother and fetus is significantly increased in pregnancy complicated by infection and fever.<sup>1,2</sup> Maternal immune function decreases in pregnancy. Therefore, some febrile diseases may take a more severe course in pregnancy leading to transplacental transmission of infectious agent and causing foetal jeopardy. The effect of fever during pregnancy depends on the level of temperature rise, duration and the stage of fetal development. Pyrexia during pre-implantation, embryonic and fetal development period may result in miscarriage, growth restriction, preterm labour and stillbirth.<sup>2-4</sup> Identification of source of fever and possible fetal implications is of utmost importance.

Hyperthermia interferes with protein synthesis via heat-shock proteins, inducing S-phase cell death and delay in mitotic activity in the M phase. Vascular disruption and placental infarction hence, occur ultimately leading to lethal malformations and fetal death. Furthermore, maternal pyrexia increases uterine contractility, which can lead to expulsion of the fetus at a non-viable stage of gestation.<sup>5</sup> UTI is the commonest cause of fever in pregnancy worldwide.<sup>6</sup> Other causes of fever varies according to geographical area. The infectious causes of febrile illness remains poorly characterized in Nepal, largely due to limited diagnostic and microbiological facility.<sup>7</sup> So, the purpose of this study is to assess the maternal and fetal complications due to fever in pregnancy and to find out the various aetiology of fever during pregnancy.

## METHODS

This is the cross sectional study involves all antenatal patients presenting with fever to the Obstetrics and Gynecology outpatient department, labour room and emergency department of Dhulikhel from 15<sup>th</sup> January 2019 to 15<sup>th</sup> January 2020. Patients, meeting the criteria and willing to give consent were enrolled for the study.

Sample size calculation

Number of patients (N) =  $Z^2 \times P \times Q / e^2$

Z = 1.96 for Confidence Interval of 95%

Prevalence (P) = 0.05 (5%) in Dhulikhel hospital according to last three years data

Q = 1 - P (1 - 0.05)

Allowable error = 5%

Calculation:

$$N = 1.96 \times 1.96 \times 0.05 \times (1-0.05);$$

Hence, N=73

$$5/100 \times 5/10$$

All patients included in the study were informed about the modalities of the study. Informed and written consent were obtained for inclusion in the study. Approval from the institutional review committee of the hospital for the conduction of the study were obtained.

A detailed clinical history, thorough general and physical examinations including Demographic profile, Last menstrual period, Menstrual history and regularity of the cycle, Significant past medical history, Significant family history and Personal history like Drug abuse, Smoking, Alcohol intake, Socioeconomic status etc. Gestational age determination was based on the best estimate from a reliable menstrual history, and confirmed by a Fetal dating scan done early in the first trimester. Vital signs of patients were monitored and all ANC visit investigations along with CBC (Complete Blood Count), Urine Culture and Sensitivity, C-Reactive Protein, Blood culture and sensitivity and Serology to detect Malarial parasites, Scrub typhus, Dengue and Leptospira (in case of unknown etiology) and Abdominal shield chest X-ray were done. Obstetric Ultrasound examination were done with emphasis on the fetus gestational age, fetus weight, and congenital anomaly. The findings were recorded in the predesigned pro forma.

After correlating the clinical findings and investigations, and the response to empirical therapy, diagnosis was established. Patient who are treated with empirical therapy were discharged if asymptomatic and afebrile for 48 hours, with advice on regular ANC follow up.

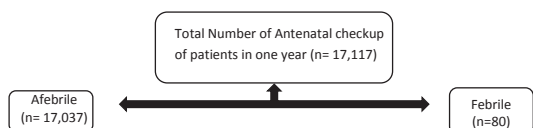
Effort was made to continue pregnancy till 37 completed weeks. However in the event, if cases went into preterm labor, they were managed with tocolytics, sedation, and dexamethasone administration to enhance pulmonary maturity. All cases received intensive intra partum monitoring including recording of partograph and the presence of pediatrician at the time of delivery. Otherwise, at term the cases were scheduled either for vaginal delivery or caesarean section depending upon their obstetric profile and bishop's score and same were recorded with reasons in the prescribed pro forma.

Following delivery APGAR score was recorded by attending pediatrician. The placenta was looked for any morphological abnormalities and if found sent for histopathological examination. All neonates who required NICU care were strictly followed up till date of their discharge.

All data were recorded in predesigned proforma and entered in Microsoft EXCEL software. Data were analyzed in SPSS 26.0 software.

**RESULTS**

A total of 17,117 patients had attained antenatal checkup in Obstetrics and Gynecology OPD and Emergency Department of Dhulikhel hospital during one year study period. Out of which 80 patients presented with complaints of fever and were admitted, evaluated, treated and discharged as needed and then followed up till delivery, and were included in this study as shown in figure 1. A total of 3980 patients had given birth in the study period, out of which 2525 were booked cases and remaining 1455 were unbooked. 2535 had normal vaginal delivery, 1372 had caesarean section and 73 had instrumental delivery.



**Figure 1. The consort flow chart of our study**

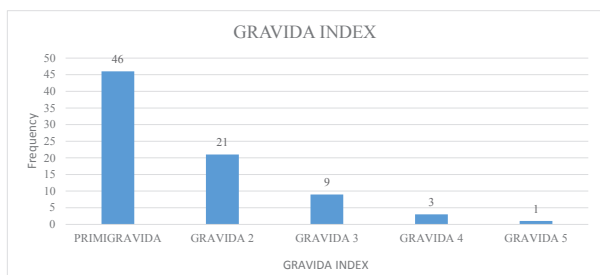
The mean age of the patient was 25.49±4.50years. Youngest pregnant lady was 17 years and the oldest was 40 years, amongst pregnant women included in the study. Majority of women were between 20-34 years and as shown in table 1.

**Table 1. Analysis of age distribution (n=80)**

Age Group	Frequency (n)	Percentage (%)
< 20 years	7	8.75
20-34 years	69	86.25
≥ 35 years	4	5
Total	80	100

We studied 80 pregnant women with fever. Different etiologies of fever were urinary tract infection (UTI) in 21 (26%) cases, respiratory tract infections (RTIs) in 20 (25.10%) cases which included upper respiratory tract infection in 17 (21.30%) cases and lower respiratory tract infection in 3 (3.80%) cases, scrub typhus in 9 (11.30%) cases, fever associated with vaginitis in 8 (10.20%) cases, enteric fever in 6 (7.5%) cases, dengue in 4 (5%) cases, chicken pox in 4 (5%) cases, acute gastroenteritis (AGE) in 3 (3.80%) cases, viral hepatitis (Hepatitis E) in 2 (2.50%) cases, tuberculosis in 2 (2.5%) cases and lung abscess in 1 (1.3%) case. The most common etiology being UTI followed by RTIs.

Regarding the gravida index, Out of 80 patients, 46 cases were primigravida, and 1 was fifth gravida respectively as shown in figure 2.



**Figure 2. Analysis of gravida index (n=80)**

Regarding the period of gestation at presentation amongst 80 patients, the different trimester presentation is as shown in table 2. The different mode of delivery is as shown in table 3. Perinatal outcome were analyzed in our study with respect to following parameters.

**Table 2. Analysis of period of gestation at presentation (n=80)**

Trimester at presentation	No of Patients (n)	Percentage (%)
First Trimester (1-13 weeks of gestation)	10	12.5
Second Trimester (14-26 weeks of gestation)	24	30
Third Trimester (27-40 weeks of gestation)	46	57.5
Total	80	100

**Table 3. Analysis of mode of delivery (n=80)**

Mode of delivery	No of patients (n)	Percentage (%)
Vaginal delivery	47	58.75
Caesarean Section	29	36.25
Abortion	4	5
Total	80	100

About APGAR score in our study, 4 newborns delivered before period of viability and hence, allocation of APGAR score was not applicable. Amongst the remaining 76 newborns, the analysis is as shown in table 4. Regarding the birth weight in our study, most of the new born i.e. 72.5% were > 2.5 kg as shown in table 5. The mean birth weight was 2.86 Kg.

**Table 4. Analysis of APGAR score at 1 minute and 5 minutes (n=80)**

APGAR score	No. of baby (n)	Percentage (%)	
1 minute	Normal (7-10)	52	65
	Minor depression (4-6)	18	22.5
	Severe depression (0-3)	6	7.5
	Not applicable	4	5
5 minutes	Normal (7-10)	59	73.75
	Minor depression (4-6)	14	17.5
	Severe depression (0-3)	3	3.75
	Not applicable	4	5
<b>Total</b>	<b>80</b>	<b>100</b>	

**Table 5. Analysis of Birth Weight (n=80)**

Birth weight	No. of baby (n)	Percentage (%)
< 1 Kg	4	5
1 Kg - <1.5 Kg (Very Low Birth Weight)	3	3.75
1.5 Kg - 2.5 Kg (Low Birth Weight)	15	18.75
> 2.5 Kg	58	72.5
Total	80	100

Regarding the intrauterine growth retardation (IUGR), 12 neonates (15%) had IUGR whereas 68 neonates were not IUGR.

For NICU admission, 14 neonates (17.5%) were admitted in NICU due to various complications. Amongst the remaining 66, 1 case was stillbirth, 2 cases were IUFDs, 4 cases were abortions and 59 were healthy newborns.

Out of 14 newborns shifted to NICU, 8 newborns were shifted to neonatal ward and later discharged. Six newborns (i.e.3 suffering from congenital pneumonia, 1 from neonatal sepsis, 1 from meconium aspiration syndrome (MAS) and 1 from perinatal asphyxia) had neonatal deaths.

In our study, perinatal mortality was in 9 (11.25%) cases, amongst which 6 were neonatal deaths, 2 were IUFDs and 1 was stillbirth.

Maternal complications in our study was analyzed in respect to following parameters. In antepartum complications, the most common complication was preterm labor seen in 16 (20%) patients out of 80, whereas 15 (18.75%) patients were free of any complications in antenatal period as shown in table 6.

**Table 6. Analysis of antepartum complications (n=80)**

Antepartum Complications	Number of patients (n)	Percentage (%)
Preterm	16	20
Thrombocytopenia	6	7.5
Anemia	6	7.5
Postdated	6	7.5
IUFD	2	2.5
Hyperemesis gravidarum	5	6.25
Oligohydramnios	5	6.25
APH	2	2.50
Preeclampsia	4	5
Abortion	4	5
Cholestasis of pregnancy	1	1.25
Prelabour rupture of membranes	8	10
None	15	18.75
Total	80	100

In intrapartum complications, the most common complications was fetal distress in 10 (12.5%) patients. The detail analysis is as shown in table 7.

In postpartum complications, the most commonly seen complications were puerperial sepsis and wound infection seen in 6 (7.5%) patients each which are shown in table 8.

## DISCUSSION

The present study performed in a tertiary-care center in provides insights into the contemporary epidemiology of fever during pregnancy. In our study, total 80 cases of pregnancy with fever were admitted during the study

**Table 7. Analysis of intrapartum complications (n=80)**

Intrapartum Complications	Number of patients (n)	Percentage (%)
Fetal distress	10	12.5
Chorioamnionitis	4	5
Meconium stained amniotic fluid	8	10
APH	2	2.5
Stillbirth	1	1.25
None	55	68.75
Total	80	100

**Table 8. Analysis of Postpartum Complications (n=80)**

Postpartum Complications	Number of patient (n)	Percentage (%)
Retained Placenta	2	2.5
Atonic PPH	4	5
Puerperial Sepsis	6	7.5
Wound Infection	6	7.5
None	62	77.5
Total	80	100

period which accounted for 2% of the total pregnancy related admission which is higher in comparison to the study conducted by Shrestha et al.<sup>7</sup>

A study conducted by Poovathi et al. in a tertiary care centre in Tamil Nadu, India, reported incidence of fever to be 6% and by More et al. in a tertiary care centre in Mumbai, India, reported incidence of fever to be 10.5% which was higher than our study.<sup>8,9</sup>

The reason for higher rate of fever as compare to other study of Nepal is, our hospital is the tertiary care hospital which caters the most of population in the eastern part of Kathmandu and partly Nepal also. But lesser than study in India because the volume of patients in India in much more than that of ours.

UTI was the most common cause of fever, which was similar to the study conducted by Shrestha et al.<sup>7</sup> The table 9 shows the comparison of etiological factors of fever in different studies with ours.

**Table 9. Etiology of fever in different studies.**

Study	Year	Country	Most common etiology
Poovathi et al. <sup>8</sup>	2018	India	Dengue
More <sup>9</sup>	2017	India	Malaria
Biswas et al. <sup>10</sup>	2015	India	Malaria
Nath et al. <sup>11</sup>	2013	India	Malaria
Chansamouthet et al. <sup>15</sup>	2010	Laos	Dengue
Shrestha et al. <sup>7</sup>	2010	Nepal	UTI
Chambers et al. <sup>12</sup>	1998	USA	Viral infections
Our study	2020	Nepal	UTI and RTI

In our study the mean age of the pregnant lady with fever was 25.49 years which was similar with study conducted by Biswas et al.<sup>10</sup> Majority of women were between 20-34 years and, 8.75 percent were less than 20 years and 5 percent were more than 35 years. A study by More et al. observed that majority of pregnant lady were between 21 to 25 years.<sup>9</sup> Majority of cases in our study were primigravida which is comparable with different other studies.<sup>9-12</sup> The major reason of pregnant ladies in the concerned age group in our study is the marital age which is around 20 years.

Regarding the period of gestation at presentation, majority of cases in our study presented in the third trimester which is comparable with different other studies.<sup>9,11</sup> This contrasts with the observation by Dick Lyn, who observed 79% of cases of fever in the first trimester and Biswas et al., who observed 56.2% of cases in second trimester respectively.<sup>10,12</sup> Likewise, the most common cause of fever was UTI. The reason behind UTI as a cause of fever and presentation at third trimester in our study is because of the gravid uterus which causes pressure on the bladder leading to retention of urine and UTI.

In our study, rate of caesarean section was 36.25 % which is higher in comparison with different other studies.<sup>8,9</sup> The most common indication for caesarean section was fetal distress due to meconium stained amniotic fluid. The incidence of abortion was 5% which was lower than that observed by Chambers CD (10%) and Jennie-Kline (18%).<sup>9,12</sup>

A study conducted by Lieberman et al. showed a strong association between intrapartum fever and low Apgar score, increased requirement of resuscitation and neonatal seizures in the first 24 hours following birth.<sup>13</sup> In our study, low APGAR score (< 7 at 5 minutes) were observed in 21.25% of neonates which is higher to the study conducted by Nath et al. and lower compared to study by Biswas et al.<sup>10,11</sup> We could not find the any definitive reason for this.

In our study, the mean birth weight was 2.86 Kg which is higher in comparison to different studies and about 27.5% neonates had low birth weight (< 2.5 Kg) which is less when compared with different studies.<sup>8,10,11</sup> Such a variation in result could be due to variation in the utero-placental insufficiency due to fever in different cases.

Low birth weight was the most common fetal complications with higher rates among pregnant ladies with UTI and URTI. In the study conducted by Iqbal et al. 24.5% of neonates born to pregnant ladies with UTI had low birth weight.<sup>14</sup> The rate of IUGR babies in our study was 15% which is less in comparison to study conducted by Nath et al. which observed IUGR in 20.3% of neonates.<sup>10</sup> The known reason is pyrexia leading to preterm labour which leads to low birth weight baby.

Our study showed that 17.5% i.e. 14 neonates were admitted in NICU. Among these 14 neonates, 50% had congenital pneumonia, 28.57% had neonatal sepsis, 14.28% had meconium aspiration syndrome and 7.15% had perinatal asphyxia. Out of 14 newborns shifted to NICU, 8 newborns were shifted to neonatal ward and later discharged. Six newborns (i.e. 3 suffering from congenital pneumonia, 1 from neonatal sepsis, 1 from meconium aspiration syndrome and 1 from perinatal asphyxia) had neonatal deaths.

Our study showed that the perinatal mortality was in 11.25% i.e. 9 newborns amongst which 6 were neonatal deaths, 2 were IUFDs and 1 was stillbirth. One stillbirth was observed in a pregnant lady suffering from Scrub typhus. Two cases of IUFD were observed in pregnant ladies suffering from dengue and scrub typhus. In a study, conducted by Biswas et al. perinatal mortality was 2.1% with malaria being the most prominent cause.<sup>10</sup> The reason for six neonatal death in our study is because of early onset neonatal sepsis.

The most common antepartum complication was preterm labour commonly observed in pregnant ladies with UTI and URTI. The reason behind is pyrexia leading to preterm labour. Among 6 pregnant ladies with thrombocytopenia, 3 suffered from dengue and 3 from scrub typhus. Two ladies with dengue fever had preeclampsia and 1 had antepartum hemorrhage.

The most common complication was fetal distress in about 12.5% with the most common cause being meconium stained amniotic fluid. Among the 4 cases of chorioamnionitis, 2 were intrauterine fetal death, born to mothers with dengue and scrub typhus respectively; whereas other 2 newborns were born to mothers with fever with vaginitis and were admitted to NICU with neonatal sepsis. Both mothers had E.coli isolated on high vaginal swab (HVS) culture.

The most commonly seen postpartum complications were puerperial sepsis and wound infection seen in 6 patients (7.5%) each. Three patients with puerperial sepsis had UTI in the antenatal period.

Two cases of retained placenta was observed in pregnant ladies with preterm labour who were suffering from UTI. Atonic postpartum hemorrhage (PPH) was observed in 2 patients with dengue fever. The reason is dengue fever leads to low platelets count which ultimately leads to atonic PPH.

The main limitations of our study is the sample size is very small. Further studies can be done with larger sample size. Time limitation; because of which we were able to follow up the cases only till the time of discharge, hence, late maternal complications and fetal outcomes remained unidentified and loss of follow up.

## CONCLUSION

Fever in pregnancy is still a challenge to obstetrician and the society at large due its problems related to its prevention, diagnosis, management and its feto-maternal outcome.

Different causes of fever had different impact on maternal and fetal outcome. Hence, it is suggested that an evaluation of the effect and outcomes of fever in pregnancy, provides definite knowledge of clinical epidemiology, and facilitates optimum prioritization of efforts and resources.

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