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Risk Factors for Intrapartum Fever in Term Gestations and Associated Maternal and Neonatal Sequelae

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Abstract

Aim—To determine factors associated with intrapartum fever and to examine associated maternal and neonatal outcomes.

Methods—Retrospective study of patients between $36^{0/7}$ and $42^{0/7}$ gestational weeks who entered spontaneous or induced active labor and developed temperature = 38 °C; a similar group that did not develop fever were controls. Univariate and multivariate analyses were performed with $p < 0.05$ as significant.

Results—Fifty-four febrile patients and 306 nonfebrile controls met inclusion criteria. Nulligravidity (45.8 vs. 77.8%, $p < 0.001$), length of first stage ≥720 min (OR 3.59, 95% CI 1.97–6.55, $p < 0.001$), length of second stage ≥120 min (OR 4.76, 95% CI 2.29–9.89, $p < 0.001$), membrane rupture ≥240 min (46.4 vs. 79.6%, $p < 0.001$), increasing number of vaginal exams (4 vs. 6, $p < 0.001$), oxytocin (44.8 vs. 63.0%, $p = 0.014$), and meperidine (14.7 vs. 35.2%, $p < 0.001$) were all associated with intrapartum fever. Associated morbidity included cesarean delivery (22.5 vs. 44.4%, $p = 0.001$), Apgar score <7 at 5 min (0.7 vs. 5.6%, $p = 0.011$), and neonatal intensive care unit admission (9.5 vs. 51.9%, $p < 0.001$).

Conclusion—We have identified several noninfectious factors that are associated with intrapartum fever. Modification of risk factors may improve both maternal and neonatal outcomes.

Keywords

Maternal fever; Noninfectious etiology; Morbidity; Risk factors; Cesarean section; Acetaminophen

Introduction

The prevalence of intrapartum fever ranges from 1.6 to 14.6% of deliveries [1–3]. Most cases of intrapartum fever are secondary to noninfectious factors [4, 5]. Non-infectious etiologies include epidural analgesia, use of prostaglandins during labor induction,

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dehydration, increased ambient temperature, and the activation of pro-inflammatory cascade during parturition [2, 4]. Both infectious and noninfectious causes of maternal fever have been linked to transient adverse neonatal complications including low Apgar scores, respiratory distress, hypotonia, and neonatal seizures [1]. More importantly, the presence of maternal fever in labor is a strong risk factor for long-term neonatal developmental outcomes, including encephalopathy, cerebral palsy, and neonatal death [3, 6].

The above clinical observations are supported by primate studies that demonstrate maternal hyperthermia, in the absence of infection, is directly associated with the development of neonatal hypoxia and metabolic acidosis [7]. Even a 1–2 °C elevation in brain temperature can potentiate brain damage resulting from an ischemic insult [8]. Maternal oral temperature underestimates the fetal core temperature by as much as 1.6 °C [9]. In the presence of hyperthermia, the observed risk of encephalopathy in term infants increases from 0.12–1.13% [10]. When both maternal fever and acidosis coexist, this observed risk further increases to 12.5%, independent of neonatal sepsis [10]. These findings have led to the hypothesis that intrapartum fever may be associated with increased fetal oxidative stress and depleted intracellular reserves, both of which increase fetal susceptibility to ischemic insults [11].

Although significant morbidity secondary to maternal fever is well documented, the mechanism for the etiology of noninfectious fever in labor is still unclear. It is hypothesized that maternal inflammation, mediated through increased levels of pro-inflammatory cytokines, may be causative in some cases [10, 12, 13]. Other areas that require more study include the development of treatments aimed at reducing maternal hyperthermia as well as proper use of intrapartum antibiotics. Therefore, the objective of this study was to create a comprehensive review of antepartum and intrapartum factors related to the development of intrapartum fever. This study focuses on noninfectious etiologies of intrapartum fever and its effect on short-term neonatal morbidity. We also examine the effects of acetaminophen administration and use of intrapartum antibiotics on maternal and neonatal outcomes.

Methods and Materials

This study was conducted during the time period of November 2014–March 2015 at Richmond University Medical Center, New York, which is a high-risk tertiary care center for obstetrics and neonates. The medical records of patients between $36^{0/7}$ and $42^{0/7}$ gestational weeks who entered active labor (spontaneous or induced) and developed a systemic fever of greater than 38 °C and the records of their respective neonates were retrospectively reviewed. Patients who had incomplete medical records, non-singleton gestations, scheduled cesarean section, infants delivered before $36^{0/7}$ gestational weeks, stillbirths, or congenital fetal anomalies were excluded from analysis. A group of similar patients who did not develop maternal fever (temperature less than 38 °C) during the same time period was used for comparison.

Both groups received similar obstetrical and neonatal care. All mothers had a complete blood count (CBC) recorded at the time of admission to labor and delivery. All patients had one peripheral intravenous (IV) line placed at the time of admission. Those that were

deemed to have a higher risk for hemorrhage had a second prophylactic IV line placed. If patients elected to use epidural, a Foley urinary catheter was placed in the bladder up until the time of delivery. Administration of antibiotics or anti-pyretic therapy in labor was at the discretion of the treating obstetrician. Admission of a neonate to the neonatal intensive care unit was determined by the admitting pediatrician. Neonatal outcomes were followed up for 12 weeks after discharge.

Maternal demographic data collected included age, body mass index (BMI), and race. Antepartum factors included parity, history of preterm births, history of cesarean deliveries, and maternal comorbidities. The intrapartum factors assessed were gestational age at delivery, induction of labor, augmentation of labor with oxytocin or artificial rupture of membranes, number of vaginal exams, admitting diagnoses, pain management (meperidine, epidural), length of stages of labor, length of membrane rupture, mode of delivery, and estimated blood loss. The presence of a nuchal chord, meconium, and fetal heart tracing characteristics was also observed. The diagnosis of clinical chorioamnionitis was made if the mother had maternal fever accompanied by at least 2 of the following signs: fetal tachycardia >160 beats per minute, maternal tachycardia >100 beats per minute, maternal leukocytosis (maternal white blood cell (WBC) >15,000 cells/mm), uterine tenderness, or foul-smelling vaginal discharge [14]. Maternal sepsis was suspected based on the Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012 [15].

Neonatal characteristics that were assessed included fetal weight, gender, and Apgar score, and the incidence of neonatal intensive care admission secondary to respiratory distress, sepsis, hypotonia, and hypoglycemia (glucose <40 mg/dL) was also assessed. The diagnosis of neonatal respiratory syndrome was based on a combination of clinical and radiographic findings including increased respiratory rate (>60 breaths per minute), retractions, nasal flaring, grunting, and cyanosis. In addition to clinical symptoms, typical radiographic findings included reticulogranular pattern or ground glass appearance in both lungs with superimposed air bronchograms [16]. Neonates admitted to the Neonatal Intensive Care Unit Admission (NICU) for suspected sepsis were monitored for the following parameters during the first 72 h of life: tachypnea (>60 breaths per minute), temperature instability (<36 or 37–9 °C), capillary refill more than 3 s, C-reactive protein >10 mg/dL, white blood cell count (<4,000 or > 34,000 × 10^9 mL/L, or interleukin-6 (IL-6), or IL-8 >70 pg/mL [17]. In this study, neonatal sepsis was diagnosed if blood, urine, or cerebral spinal fluid culture was positive for an infectious pathogen.

Statistical analysis was carried out using IBM SPSS 22.0. Univariate analysis for continuous variables was compared using the Student *t* test or Mann–Whitney U test. Categorical data were compared using chi-square test or Fisher's exact tests. A p value of <0.05 was considered statistically significant. Variables that were statistically significant on univariate analysis were tested for interaction of terms. Nonredundant variables were entered into multivariable logistic regression models to test for adjusted associations.

Results

Of the 360 women who were included in this study, 54 had an intrapartum temperature of ≥38 °C and the remaining 306 patients were part of the nonfebrile cohort. The maternal demographic characteristics of both groups are summarized in Table 1. The mean maternal age, gestational week of delivery, and number of previous cesarean deliveries were similar between groups. Other non-significant maternal factors are listed in Table 1.

Factors of past obstetrical history were also assessed. Nulligravidy was shown to be a significant risk factor for developing maternal fever with 42/54 (77.8%) of the febrile patients being nulligravid as compared to 140/306 (45.8%) of the nonfebrile patients being nulligravid (OR 4.15, 95% CI 2.10–8.19, $p < 0.001$). History of preterm birth, history of maternal hypertension or preeclampsia, history of maternal thrombophilic disorder, history of maternal pre-gestational, or history of gestational diabetes were all shown to be nonsignificant (Table 2).

Antepartum Factors

Antepartum risk factors that were examined included maternal obesity (BMI ≥30 kg/m ^{2}), current maternal hypertensive disorder, and pre-gestational or gestational diabetes. None of the above-mentioned antepartum factors were found to be significant (Table 2). Interestingly, the induction of labor with and without the use of prostaglandins analogues was also not a significant factor in the development of intrapartum fever.

Hematological indices from the CBC drawn at admission to labor and delivery were compared between the febrile and nonfebrile cohort. Patients in the febrile cohort had a significantly lower count of hemoglobin and hematocrit, as well as a significantly higher count of WBCs, neutrophils, monocytes, and eosinophils on admission (Table 3).

Intrapartum Factors

The mean length of the first stage of labor was significantly longer in the febrile cohort with a mean of 989.2 min (range 0–2,824) vs. 619.5 min (range 0–5,492; $p < 0.001$; Table 3). A first stage of labor exceeding 720 min was significantly associated with the development of maternal fever (OR 3.59, 95% CI 1.97–6.55, $p < 0.001$; Table 2). Similarly, the mean length of the second stage of labor was significantly longer in the febrile group (87.1 vs. 45.5 min, $p < 0.001$; Table 4). A second stage of labor exceeding 120 min was observed in 15/54 (28.8%) of the febrile patients, and in 24/306 (7.8%) of the nonfebrile patients (OR 4.76, 95% CI 2.29–9.89, $p < 0.001$; Table 2).

The mean duration of membrane rupture was significantly longer in the febrile cohort compared to the non-febrile group, with a mean of 663.1 min (range 0–2,089) vs. 353.8 min (range 0–2869, $p < 0.001$; Table 4). Membrane rupture exceeding 240 min (OR 4.51, 95% CI 2.24–9.09, $p < 0.001$; Table 2) and increasing number of vaginal exams were found to be significantly associated with the development of intrapartum fever ($p < 0.001$; Table 4).

Oxytocin was used to augment labor in 63.0% of febrile patients and 44.8% of nonfebrile patients (OR 2.10, 95% CI 1.15–3.81, $p = 0.014$). Use of epidural for pain management did

not increase the risk of maternal fever; however, meperidine use was significantly associated with the development of maternal fever (OR 3.15, 95% CI 1.66–5.98, $p < 0.001$). Of the 47 patients who had both intrapartum fever and an epidural, 46 (97.9%) developed the fever after epidural placement, while the remaining one patient developed fever before the epidural was placed. Excluding the one patient who had fever prior to epidural placement, the average time from epidural placement to intrapartum fever was 533.95 min (range of 182–1,041 min). The patient who developed the fever before her epidural did so 129 min prior to placement.

Although only 3/54 patients met the clinical criteria for the diagnosis of chorioamnionitis, 26 (48.1%) patients received intrapartum antibiotic therapy. The mean time from the diagnosis of intrapartum fever to antibiotics administration was 63.70 min with a range of 1–353 min. Comparing outcomes of those who received antibiotics to those that did not, there was no difference in terms of the following factors: cesarean delivery (50 vs. 35.7%, $p = 0.250$), presence of meconium (30.8 vs 28.6%, $p = 0.538$), requirement for neonatal bag/mask ventilation (16.7 vs. 10.7%, $p = 0.432$), or requirement for continuous positive pressure ventilation (11. 5 vs. 10.7%, $p = 0.674$). In spite of no differences in neonatal interventions, infants whose mothers received antibiotics in labor were significantly more likely to be admitted to the NICU (84.66 vs. 28.5%, OR 6.46, 95% CI 1.95–18.34, $p = 0.002$).

Acetaminophen (650 mg) was administered to 41/54 (75.9%) patients in the febrile cohort. In 33/41 (61%) patients, the maternal temperature remained at more than 100.4 F 1 h post acetaminophen administration. When comparing outcomes of patients who received acetaminophen to those who did not, no significant differences were found in terms of the following factors: cesarean delivery (39.0 vs. 58.3%, $p = 0.250$), presence of meconium (75.0 vs. 78.4%, $p = 0.524$), requirement for neonatal bag/mask ventilation (15.4 vs. 8.3%, $p = 0.471$), requirement for continuous positive pressure ventilation (12.2 vs. 8.3%, $p = 0.588$), or NICU admission (85.2 vs. 69.2%, $p = 0.145$).

On analysis of our electronic fetal monitoring data, it was found that category II fetal heart tracing occurred in 55.6% of febrile patients vs. 35% of afebrile patients (OR 2.33, 95% CI 1.29–4.18, $p = 0.004$). When the presence of fetal tachycardia was isolated, it was also significantly associated with our febrile cohort (OR 14.29, 95% CI 5.09–40.09, $p < 0.001$). Late decelerations were observed in 31.5% of febrile patients vs. 19% of afebrile patients (OR 1.97, 95% CI 1.03–3.73, $p = 0.037$; Table 2).

Mode of Delivery

While cesarean delivery was found to be significantly associated with intrapartum fever (OR 2.75, 95% CI 1.51–5.01, $p = 0.001$), those who delivered vaginally were less likely to have an intrapartum fever. Of the febrile patients, 57.4% had a vaginal delivery, compared to 76.8% of the nonfebrile patients (OR 0.407, 95% CI 0.22–0.74, $p = 0.003$).

Neonatal Factors and Outcomes

The mean fetal weight in the febrile cohort was significantly larger than that in the nonfebrile group (3,454.8 vs. 3,270.5 g, $p = 0.007$; Table 4). An Apgar score of less than 7 at

1- and 5-min of life was significantly associated with intrapartum fever (Table 2). The presence of meconium was also a significantly associated factor, with 29.6% of the febrile patients being exposed, compared to 9.2% of the nonfebrile patients (OR 10.29, 95% CI 5.33–19.84, $p < 0.001$; Table 2).

Of the patients who had a maternal fever, 44/54 (81.4%) of the neonates were admitted to the NICU, while only 29/306 (9.5%) of the afebrile cohort were admitted to the NICU (OR 10.29, 95% CI 5.33–19.84, $p < 0.001$; Table 2). The most common reason for NICU admission in the febrile cohort was to rule out neonatal sepsis secondary to the presence of maternal fever at the time of delivery in 40/54 (74.1%) of neonates. The most common secondary, nonmutually exclusive, NICU-admitting diagnosis was respiratory distress in 14/54 febrile patients (25.9%).

Infants admitted for suspected sepsis ($n = 40$) were given prophylactic IV antibiotics. The mean number of days spent in NICU was 4.9 for neonates requiring a sepsis work-up and 5.7 for those requiring respiratory support. Only one neonate was found to have a positive bacterial culture. None of the neonates in the febrile cohort were re-admitted to the hospital secondary to febrile complications during the 12 week follow-up period post-discharge.

The variables that retained statistical significance after multiple regression analysis included first stage of labor >720 min (adjusted OR [aOR] 2.024, 95% CI 1.00–4.06, $p = 0.047$), prolonged rupture of membrane >240 min (aOR 3.495, 95% CI 1.50–7.99, $p = 0.004$), use of meperidine for pain management (aOR 2.274, 95% CI 1.07–7.99, $p = 4.834$), fetal tachycardia (aOR 9.761, 95% CI 2.93–32.56, $p < 0.001$), and the presence of meconium (aOR 2.826, 95% CI 1.15–6.95, $p = 0.024$).

Discussion

Many cases of intrapartum fever were not related to systemic or intrauterine infection [4, 5]. Noninfectious etiologies of maternal hyperthermia included epidural use, oxidative stress, normal physiologic change, as well as a secondary response to inflammation [2, 4]. This is consistent with what was previously reported, as only 5.5% of our febrile cohort fit the criteria of clinical chorioamnionitis; no cases of maternal sepsis were identified and only one neonate had positive blood cultures.

Several of the antepartum factors examined, including obesity, disorders of impaired glucose metabolism, and current hypertensive disorders, were not predictive of intrapartum fever. Maternal hemoglobin = 11.0 g/dL was significantly associated with maternal fever. Interestingly, certain hematological indices from the admitting CBC significantly differed among the study cohorts. Although these differences were not clinically significant, several of these cell lines play key roles in mediating immune and inflammatory responses. Therefore, the upregulation of these cells may be involved in the pathogenesis of intrapartum fever. For example, activated monocytes selectively migrate to the sites of inflammation and produce pro-inflammatory cytokines such as tumor necrosis factor (TNF)-α, IL-1, IL-6, and IL-12 that contribute to local and systemic inflammation [18, 19]. Likewise, recruitment of activated eosinophils to tissue sites can cause the release of cytokines, chemokines, lipid

mediators, and cytotoxic granule proteins that can initiate and sustain local inflammatory and remodeling responses [20]. Resting neutrophils are recruited to sites of infection or inflammation by either bacterial products or various cytokines that include TNF-α, GM-CSF, IL-8, and interferon-γ (IFN-γ) [21]. These hematological indices were significantly higher in patients who eventually developed a fever in labor; therefore, it is possible that there was an underlying systemic pro-inflammatory state in these patients with the upregulation of cytokines.

Other evidence also suggests that elevated pro-inflammatory maternal cytokines may have a role in the pathogenesis of intrapartum fever [5, 12, 22, 23]. Romero et al. [23] found that maternal plasma concentration of the pyogenic cytokines IL-1β, IL-2, IL-6, IFN-γ, and TNF-α were elevated in patients with clinical chorioamnionitis at term compare to those in spontaneous labor, even in the absence of intra-amniotic infection or inflammation [22]. Goetzl et al. [12] demonstrated that after epidural placement, maternal plasma IL-6 was significantly higher in the patients who eventually developed intrapartum fever. Likewise, Riley et al. [5] found that admission IL-6 levels greater than 11 pg/mL were associated with an increase in likelihood of developing fever among epidural users (36.4 vs. 15.7% for 11 pg/mL or less; $p = 0.008$). Therefore, it is likely that the upregulation of the pro-inflammatory response within the maternal compartment may contribute to the development of intrapartum fever.

Intrapartum fever may also be the result of dysfunctional labor or increasing length of the first stage of labor, as indicated by our study. A recent study by Abramov et al. [25] illustrated a model in which dysfunctional labor may result in elevated levels of pyrogens such as prostaglandin E2 or prostaglandin F2 alpha, leading to increased levels of inflammatory cytokines, such as interleukin IL-1b, IL-6, IL-8, and high plasma levels of oxytocin [24]. This could also explain the association of oxytocin augmentation with intrapartum fever as related to a possible positive feedback loop [25]. Additionally, oxytocin is often used in the presence of labor dystocia for labor augmentation, which is another potential reason for the association of oxytocin augmentation with intrapartum fever. Although in this study, epidural use was not associated with the development of maternal fever, several other studies have found it to be significant [2, 5, 26]. This study did find the use of meperidine for pain relief to be a significant factor. The association may be attributed to the fact that a majority of the patients who received meperidine did so during the early latent phase of labor. Therefore, the association of meperidine with intrapartum fever may be secondary to a longer first stage of labor, as the two were not mutually exclusive.

The appropriate timing and selection of patients who are to receive intrapartum antibiotic administration still remain uncertain and challenging. Data from randomized trials have shown decreased incidence of neonatal bacteremia when mothers with diagnosed clinical chorioaminionitis receive intrapartum antibiotic therapy [14]. Additionally, in case of suspected maternal sepsis, administration of broad-spectrum antibiotics within the first hour can be life-saving [15]. In our study, the mean time from the onset of first fever to antibiotic administration was 63 min. Although this implies that a number of patients did not receive antibiotic therapy within the first hour of their fever, none were suspected to be septic. It is still unclear how the timing of antibiotic administration affects outcomes that are not

associated with maternal sepsis. However, intrapartum antibiotic administration can also have serious consequences to both the mother and neonate [6]. This can include NICU admission, an unnecessary work-up for sepsis, and antimicrobial treatment of the newborn, as was demonstrated in our study cohort. Exposure to the NICU environment is also associated with increased costs, as well as increased risk of exposure to multi-drug resistant organisms [6]. Infants in NICU were also separated from their mothers, which may have resulted in consequences related to infant–mother bonding and successful breastfeeding [6]. Evidence also suggests that exposure to intrapartum antibiotics may affect the infant gut micro-flora and increase susceptibility to late-onset bacterial infections in infancy [27–29].

In our study, although there were no cases of documented maternal sepsis and only 3 patients met the clinical criteria to diagnosis of chorioamnionitis, almost half the febrile patients received intrapartum antibiotic therapy. There were no differences in neonatal outcomes. As a result, mothers receiving antibiotic therapy except that infants were significantly more likely to be admitted to the NICU and also more likely to receive antibiotic therapy. This is consistent with what was found in other studies [2, 30, 31]. Prediction of which febrile patients would benefit from intrapartum antibiotics is yet another challenging task. Due to the physiological changes that occur during pregnancy, hemodynamic signs of septic shock manifest late in its course, and therefore, its recognition can be elusive [32]. Likewise, a recent retrospective study that included 45 patients with the diagnosis of clinical chorioamnionitis at term found that the clinical signs of chorioaminiotis did not accurately identify patients with microbial-associated intra-amniotic infection or inflammation [33]. For the identification of patients with microbial-associated intra-amniotic inflammation, the study found that maternal tachycardia, leukocytosis, and fetal tachycardia had a low specificity, and foul-smelling vaginal discharge, and also, uterine tenderness had poor sensitivity [33].

Another consequence of maternal fever is its effect on the fetal heart rate. Studies have demonstrated a correlation between maternal fever and the development of fetal tachycardia [34]. However, fetal tachycardia, even in the presence of maternal fever, is poorly correlated with intra-amniotic infection [33–35]. Fetal tachycardia may necessitate a cesarean delivery due to a persistent nonreassuring fetal heart status. In our study, this may have influenced higher cesarean section rates in the febrile cohort, as both outcomes very strongly correlated. Therefore, rapid resolution of maternal fever and fetal tachycardia may have the potential to reduce adverse maternal and neonatal outcomes associated with febrile morbidity.

Reduction in maternal fever is the first step to preventing both short- and long-term neonatal morbidity. Rapid correction of intrapartum fever through early use of acetaminophen may be a means of preventing neonatal sequelae. Although, there were no differences in maternal or neonatal outcomes in patients who received acetaminophen, indications, dose, and route of administration were not standardized. It is possible that there was a selection bias, in that the sicker appearing patients, or those with higher temperature, received treatment with acetaminophen. Therefore, further prospective studies on acetaminophen and its effect on intrapartum fever are needed.

One of the continuing challenges encompassing the management of intrapartum fever is being able to distinguish between microbial-associated and noninfectious etiologies. Our study identified that admission CBC indices significantly differed among patients who eventually developed a noninfectious fever compared to those who did not. Although this may not be clinical useful, data from hematological indices could be incorporated into a risk-prediction model along with other maternal cytokines and chemokines. However, before this is possible, further validation of the data in larger prospective trials would be necessary. Additionally, efforts on determining causal links of noninfectious fever would allow for more specific targeted therapy for fever reduction. This may also help select patients who would benefit from anti-microbial treatment in labor.

The limitations of our study were some of those inherent to any retrospective study, including the possibility that some of the maternal and fetal indications were not well documented by the managing physicians or reporting nurses. Although obstetrical management was within a single institution and was similar among providers, it was not protocol-specific. Therefore, antibiotic and antipyretic administration was left to the discretion of the provider. Finally, the decision for admission to NICU and management of neonatal complications were nonstandardized and at the discretion of neonatologists and pediatricians. This could have led to variation in treatment within the study period.

Conclusion

Due to the multiple etiologies of intrapartum fever, its management continues to be a challenging question. We identified factors that could be a harbinger for maternal and neonatal morbidity. Modifiable maternal factors included length of first stage of labor, length of second stage of labor, duration of membrane rupture, and number of vaginal examinations. Maternal fever was associated with increased risk of cesarean delivery, fetal tachycardia, presence of meconium, low Apgar score, and neonatal intensive care unit admission. The most common reason for NICU admission was for exclusion of sepsis; however, in a majority of the cases, an infectious etiology was not identified. Due to the increased maternal and neonatal morbidity associated with intrapartum fever, further studies are warranted to determine methods for immediate reduction of fever for possible prevention of neonatal sequelae.

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Table 1

Patient demographic continuous variables for intrapartum fever

Factor	Febrile (*n* = 54)	Afebrile (*n* = 306)	*p* value
Maternal age, median (range)	28.57 (18–41)	29.71 (13–43)	0.159
Number of previous term births, median (range)	0 (0–2)	1 (0–10)	<0.001
Number of previous vaginal deliveries, median (range)	0 (0–2)	1 (0–10)	<0.001
Number of previous cesarean deliveries, median (range)	0 (0–1)	1 (0–3)	0.172
Gestational age by weeks, median (range)	40 (35.5–41.5)	39.2 (36–42)	0.074
BMI, kg/m^2, mean (range)	29.37 (17–46.4)	29.69 (18–53.2)	0.76

$p < 0.05$ significant.

Table 2

Categorical risk factors for intrapartum fever

Factor	Febrile (*n* = 54)		Afebrile (*n* = 306)		Univariate analysis	
	exposed, *n* (%)	non-exposed, *n* (%)	exposed, *n* (%)	non-exposed, *n* (%)	OR (95% CI)	*p* value
Maternal history						
Nulligravidy	42 (77.8)	12 (22.2)	140 (45.8)	168 (54.2)	4.15 (2.10–8.19)	<0.001
Previous cesarean section	1 (1.9)	53 (98.1)	20 (6.5)	286 (93.5)		0.462
Maternal history of preterm birth	0 (0.0)	54 (100.0)	294 (96.1)	12 (3.9%)		0.143
Maternal history of HTN/preeclampsia	1 (1.9)	53 (98.1)	10 (3.3)	296 (96.7)		0.577
Maternal history of thrombophilia/PE/DVT	2 (3.7)	52 (96.3)	3 (1.0)	303 (99.0)		0.164
Maternal history of DM/gestational diabetes	0 (0.0)	54 (100.0)	9 (2.9)	297 (97.1)		0.227
Antenatal						
BMI ≥30 kg/m^2 at delivery	25 (46.3)	29 (53.7)	139 (45.4)	167 (54.6)		0.511
Current maternal hypertensive disorder	1 (1.9)	53 (98.1)	9 (2.9)	297 (97.1)		0.653
Antenatal anti-hypertensive medications	1 (1.9)	53 (98.1)	4 (1.3)	302 (98.7)		0.558
Pre-gestational DM	0 (0.0)	54 (100.0)	1 (0.3)	305 (99.7)		0.674
Gestational dibetes, A1	0 (0.0)	54 (100.0)	13 (4.2)	293 (95.8)		0.116
Gestational diabetes, A2	1 (1.9)	53 (98.1)	2 (0.7)	304 (99.3)		0.387
Admitting WBC Count ≥15.0	11 (20.8)	42 (79.2)	49 (16.0)	257 (84.0)		0.251
Admitting hemoglobin ≤11.0	17 (32.1)	36 (67.9)	58 (19.0)	248 (81.0)	2.02 (1.06–3.84)	0.027
Prostaglandin induction	15 (27.8)	39 (72.2)	51 (16.7)	255 (83.3)		0.52
Factors associated with 1st stage of labor						
Admitting diagnosis: active labor	20 (37.0)	34 (63.0)	148 (48.4)	158 (51.6)		0.124
First stage of labor ≥720 min (*n* = 358)	15 (28.8)	37 (71.2)	24 (7.8)	282 (92.2)	3.59 (1.97–6.55)	<0.001
GBS positive	17 (32.1)	36 (67.9)	68 (22.3)	237 (77.7)		0.122
Oxytocin augmentation	34 (63.0)	20 (37.0)	137 (44.8)	169 (55.2)	2.10 (1.15–3.81)	0.014
Meperedine	19 (35.2)	35 (64.8)	45 (14.7)	261 (85.3)	3.15 (1.66–5.98)	<0.001
Epidural	47 (87.0)	7 (13.0)	245 (80.1)	61 (19.9)		0.228
Preeclampsia	0 (0.0)	54 (100.0)	5 (1.6)	301 (98.4)		0.442
Intrapartum IV antihypertensives	5 (9.3)	49 (90.7)	7 (2.3)	299 (97.7)	4.36 (1.33–14.28)	0.022
Magnesium sulfate	0 (0.0)	54 (100.0)	3 (1.0)	303 (99.0)		0.613

Factor	Febrile (*n* = 54)		Afebrile (*n* = 306)		Univariate analysis	
	exposed, *n* (%)	non-exposed, *n* (%)	exposed, *n* (%)	non-exposed, *n* (%)	OR (95% CI)	*p* value
Fetal tachycardia	12 (22.2)	42 (77.8)	6 (2.0)	300 (98.0)	14.29 (5.09–40.09)	<0.001
Category II tracing	30 (55.6)	24 (44.4)	107 (35.0)	199 (65.0)	2.33 (1.29–4.18)	0.004
Category III tracing	1 (1.9)	53 (98.1)	6 (2.0)	300 (98.0)		0.717
Late decelerations	17 (31.5)	37 (68.5)	58 (19.0)	248 (81.0)	1.97 (1.03–3.73)	0.037
Factors associated with rupture of membranes						
Rupture of membranes ≥240 min	43 (79.6)	11 (20.4)	142 (46.4)	164 (53.6)	4.51 (2.24–9.09)	<0.001
Amniotomy	21 (38.9)	33 (61.1)	113 (36.9)	193 (63.1)		0.783
Factors associated with 2nd stage of labor						
Second stage of labor ≥120 min (*n* = 358)	15 (28.8)	37 (71.2)	24 (7.8)	282 (92.2)	4.76 (2.29–9.89)	<0.001
Vaginal delivery	31 (57.4)	23 (42.6)	235 (76.8)	71 (23.2)	0.407 (0.22–0.74)	0.003
Cesarean section	24 (44.4)	30 (55.6)	69 (22.5)	237 (77.5)	2.75 (1.51–5.01)	0.001
Meconium	16 (29.6)	38 (70.4)	28 (9.2)	278 (90.8)	4.18 (2.07–8.43)	<0.001
Neonatal factors						
Gender, male	31 (57.4)	23 (42.6)	152 (49.7)	154 (50.3)		0.295
Nuchal cord	15 (28.8)	37 (71.2)	83 (27.1)	223 (72.9)		0.797
1 min Apgar <7	7 (13.0)	47 (87.0)	8 (2.6)	298 (97.4)	5.55 (1.92–16.01)	0.003
5 min Apgar <7	3 (5.6)	51 (94.4)	1 (0.7)	305 (99.7)	17.94 (1.83–175.85)	0.011
NICU admission	40 (74.1)	14(25.9)	29 (9.5)	277 (90.5)	10.29 (5.33–19.84)	<0.001

* *p* calculated with Fischer's exact test.

$p < 0.05$ significant.

HTN, hypertension; DVT, deep vein thrombosis; PE, pulmonary embolism; DM, diabetes mellitus; WBC, white blood cell; GBS, group B Strep; IV, intravenous; NICU, Neonatal Intensive Care Unit Admission.

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Table 3

Patient admission hematological indices

Factor	Febrile (n = 54), mean (range)	Afebrile (n = 306), mean (range)	p value
WBC count, K/uL	14.34 (7.40–33.10)	11.34 (43.0–28.40)	<0.001
Hemoglobin, g/dL	11.38 (7.70–14.30)	12.06 (8.60–14.80)	<0.001
Hematocrit, %	34.91 (22.90–43.10)	37.24 (26.60–44.00)	<0.001
Granulocytes, K/uL	11.46 (5.00–31.10)	8.62 (2.60–27.60)	<0.001
Lymphocytes, K/uL	1.84 (0.50–3.50)	1.84 (0.60–4.10)	0.96
Monocytes, K/uL	0.68 (0.30–1.50)	0.56 (0.20–1.70)	<0.001
Eosinophils, K/uL	0.12 (0.00–0.90)	0.09 (0.00–1.00)	0.04
Basophils, K/uL	0.12 (0.00–0.10)	0.02 (0.00–0.10)	0.99
Leukocytes, K/uL	0.18 (0.00–0.50)	0.18 (0.10–0.50)	0.86

$p < 0.05$ significant.

WBC, white blood cell.

Table 4

Continuous variables for intrapartum fever

Factor	Febrile, mean (range)	Afebrile, mean (range)	*p* value
Length of first stage of labor, min	989.2 (0–2,824)	619.5 (0–5,492)	<0.001
Length of second stage of labor, min	87.1 (0–400)	45.5 (0–1,450)	0.01
Length of membrane rupture, min	663.1 (0–2,089)	353.8 (0–2,869)	<0.001
Number of vaginal exams	6.2 (3–13)	4.1 (0–11)	<0.001
Fetal weight, g	3,454.8 (2,296–4,394)	3,270.5 (1,843–4,536)	0.007