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*Original*

Intrapartum fetal heart rate between 150 and 160 bpm at or after 40 weeks and labor outcome / Ghi, Tullio; Di Pasquo, Elvira; Dall'Asta, Andrea; Commare, Arianna; Melandri, Elena; Casciaro, Alessia; Fieni, Stefania; Frusca, Tiziana. - In: ACTA OBSTETRICIA ET GYNECOLOGICA SCANDINAVICA. - ISSN 0001-6349. - (2020). [10.1111/aogs.14024]

*Availability:*

This version is available at: 11381/2881601 since: 2022-01-18T16:47:49Z

*Publisher:*

John Wiley and Sons Inc

*Published*

DOI:10.1111/aogs.14024

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Article type : Original Research Article

## **Intrapartum fetal heart rate between 150 and 160 bpm at or after 40 weeks and labor outcome**

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### **Conflicts of interest**

None

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/aogs.14024](https://doi.org/10.1111/aogs.14024)

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## ABSTRACT

**Introduction:** A baseline fetal heart rate between 110 and 160 bpm is considered normal. However among normal fetuses the average baseline heart rate has been shown to diminish progressively and the 90th centile of the fetal heart rate at 40 weeks of gestation has been consistently found at around 150 bpm. The aim of our study was to assess the labor and neonatal outcome of fetuses at 40 gestational weeks or beyond, whose intrapartum baseline fetal heart rate was between 150 and 160 bpm.

**Material and methods:** Retrospective cohort study including singleton pregnancies with spontaneous onset of labor, gestational age between 40<sup>+0</sup> and 42<sup>+0</sup>, category I CTG trace according to the FIGO guidelines 2015 with baseline fetal heart rate between 110-160 bpm during the first 60 minutes of the active labor. Exclusion criteria were maternal hyperpyrexia at admission, fetal arrhythmias, maternal tachycardia (>110 bpm) and uterine tachysystole (>5 contractions/10 minutes). The following outcomes were compared between fetuses with a baseline ranging between 110-149 bpm and those with a baseline ranging between 150-160 bpm: incidence of meconium-stained amniotic fluid, intrapartum hyperpyrexia, mode of delivery, Apgar at 5th minute<7, arterial pH<7.1 and Neonatal Intensive Care Unit admission, incidence of a composite adverse neonatal outcome.

**Results:** One-thousand and four CTG traces were included in the analysis, 860 in Group 110-149 bpm and 144 in Group 150-160. Group 150-160 bpm had a significantly higher incidence of meconium-stained amniotic fluid (OR 2.6; 95%CI 1.8-3.8), maternal intrapartum hyperpyrexia (OR 4.7; 95%CI 1.1-14.6), urgent/emergent cesarean section for suspected fetal distress (OR 13.4; 95% CI 3.3-54.3), Apgar <7 at 5<sup>th</sup> min (OR 9.13; 95%CI 1.5-55.1) and neonatal acidemia (OR 3.5; 95%CI 1.5-55.1). Logistic regression including adjusted for potential confounders showed that fetal heart rate between 150-160 bpm is an independent predictor of meconium-stained amniotic fluid (aOR 2.2; 95% CI 1.5-3.3), cesarean section during labor for fetal distress (aOR 10.7; 95%CI 2.9-44.6), neonatal acidemia (aOR 2.6; 95%CI 1.1-6.7) and adverse composite neonatal outcome (aOR 2.6; 95% CI 1.2-5.6).

**Conclusions:** In fetuses at 40 weeks or beyond, an intrapartum fetal heart rate baseline ranging between 150 and 160 bpm seems associated with a higher incidence of labor complications.

## **Keywords**

Fetal heart rate, cardiotocography, chorioamnionitis, chronic hypoxia, neonatal acidosis

## **Abbreviations**

aOR adjusted odds ratio

CI confidence interval

CS: cesarean section

CTG: cardiotocography

FHR: fetal heart rate

FIGO International Federation of Gynecology and Obstetrics

OR odds ratio

## **Key-message**

Although normal, a fetal heart rate between 150-160 bpm at or after 40 weeks should be considered above the upper limits for the gestational age and, even as isolated finding, seems to warrant strict fetal surveillance due to association with adverse labor outcome.

## INTRODUCTION

The use of cardiotocography (CTG) for continuous fetal heart rate (FHR) monitoring during labor is the most widely adopted method to identify the occurrence of intrapartum hypoxia<sup>1</sup>. A baseline FHR between 110 and 160 bpm irrespective of gestational age is considered in the normal range, and appears associated to low probability of fetal acidosis and good neonatal outcome. On the contrary, baseline FHR recordings above (or below) the normal range have been shown to herald the presence of fetal compromise. Based on this premise, according to most guidelines on fetal intrapartum surveillance produced by the main scientific societies, an expectant management is recommended whenever the FHR is within this normal band while an obstetric intervention is warranted due to a suspicious or abnormal trace in case of fetal tachycardia or bradycardia, respectively defined as  $> 160$  or  $< 110$  bpm<sup>2-4</sup>. The baseline FHR is finely tuned by the parasympathetic and sympathetic components of the autonomic nervous system, which are known to exert oppositely a depressive and an excitatory effect on the cardiac frequency. Since the maturation of the parasympathetic component is physiologically delayed in fetal life, the inhibitory effect of the vagal tone on fetal heart is expected to become increasingly stronger at term of gestation<sup>5,6</sup>. In accordance with this hypothesis, among normal fetuses the average baseline heart rate has been shown to diminish progressively from 145 bpm at around 36 weeks to 135 bpm at 41 weeks of gestation<sup>7,8</sup>. In a few large studies conducted by means of antepartum computerized CTG the 90<sup>th</sup> centile of the FHR at 40 weeks of gestation has been consistently found at around 150 bpm<sup>9,10</sup>.

One may raise the hypothesis that an intrapartum baseline FHR between 150 and 160 bpm at 40 weeks or beyond, despite being within the range indicate by the guidelines on CTG interpretation, might be considered as an abnormal finding for the given, individual fetus. Using a physiologic approach, even as isolated finding, a higher than expected

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intrapartum baseline FHR may be judged as a clue to an underlying fetal disorder such as subclinical inflammation or chronic hypoxia, leading respectively to a dysregulated autonomic response or to an abnormally increased sympathetic activity<sup>7,8,11,12</sup>.

The aim of our study was to assess the labor and neonatal outcome of fetuses at 40 gestational weeks or beyond, whose intrapartum baseline FHR during the first 60 minutes of active labor was between 150 and 160 bpm.

## MATERIAL AND METHODS

### Study design and study population

This is a retrospective cohort study conducted at the tertiary referral Hospital of Parma, between May 2018 and January 2020, and included a consecutive series of unselected pregnant women at term gestation or beyond in the active phase of the 1<sup>st</sup> stage of labor.

Inclusion criteria were singleton pregnancy, cephalic presentation, spontaneous onset of labor, gestational age between 40<sup>+0</sup> and 41<sup>+3</sup>, normal CTG trace (Category I or ‘normal’ according to the International Federation of Gynecology and Obstetrics (FIGO) guidelines 2015<sup>4</sup>) with a baseline FHR ranging between 110-160 bpm during the first 60 minutes of the active phase of 1<sup>st</sup> stage. Active labor was defined by a fully effaced, >6 cm dilated cervix coupled with >3 contractions in 10 minutes recorded at tocography<sup>13</sup>.

Maternal hyperpyrexia was defined as temperature (oral or auricular) >39.0 °C (102.2 °F) on any one occasion or a temperature between 38.0 °C (100.4 °F) and 39.0 °C (102.0 °F), confirmed by 2 measurements within 30 minutes<sup>14</sup>

Exclusion criteria were: gestational age <39+6 weeks, rupture of membranes > 12hours or >6 hours when associated with documented Group B Streptococcus (GBS) infection, maternal hyperpyrexia at admission, suspicious or pathological CTG trace during the first hour of active labor monitoring (category II or III or ‘suspicious’ or ‘pathological’ according to FIGO guidelines 2015<sup>4</sup>), uterine tachysystole (>5 contractions/10 minutes), suspected or documented fetal arrhythmias, qualitatively poor CTG signal, admission in the 2<sup>nd</sup> stage of labor, maternal tachycardia (>110 bpm), use of antibiotics or drugs which can interfere with maternal or FHR (beta blockers, thyroid blockers) at labor onset, postnatal evidence of congenital anomalies.

Gestational age was calculated from crown-rump length measure at 11+0-13+6 weeks' gestation<sup>15</sup>.

In the eligible cases a continuous CTG trace had been obtained by a Doppler ultrasound system (Philips AVALON) from the beginning of active labor to delivery. Maternal temperature, blood pressure and heart rate had been recorded at labor admission and after 60 minutes of fetal monitoring. Lack of these latter data or of a continuous CTG recording was also considered an exclusion criterion.

All CTG traces were retrospectively evaluated by three investigators with a specific training on CTG interpretation and on each of them the baseline heart rate of the 1<sup>st</sup> hour of active labor was determined.

Baseline FHR was defined as the approximate mean FHR during at least ten minutes of stable segments, excluding accelerations and decelerations<sup>4</sup>. Cases were excluded if in the 1<sup>st</sup> hour of active labor the baseline appeared unstable and could not clearly determined or if the CTG trace was characterized by one of the following aspects: baseline above 160 or below 110 bpm; reduced (<5bpm) or increased (>25 bpm) variability, sinusoid pattern, presence of one or more decelerations, absence of accelerations, lack of cycling or if they received epidural analgesia during the 1<sup>st</sup> hour of active labor<sup>16,17</sup>.

For all the included cases labor characteristics and clinical outcomes were retrospectively collected from a dedicated electronic database.

## **Outcome**

The following labor and clinical characteristics between cases with a baseline FHR of 110-149 vs. 150-160 bpm during the 1<sup>st</sup> hour of active labor were compared: meconium-stained amniotic fluid, intrapartum hyperpyrexia (>38°C), mode of delivery, Apgar at 5<sup>th</sup> min <7, arterial umbilical cord pH<7.1 and Neonatal Intensive Care Unit admission. Cesarean section (CS) performed during labor where further categorized into 1) CS for suspected fetal compromise; 2) CS for labor arrest. The incidence of an adverse composite neonatal outcome defined as the presence of at least one of the following was also compared between the two groups: arterial pH<7.1, Apgar at 5<sup>th</sup> minute <7, Neonatal Intensive Care Unit admission, Neonatal resuscitation.

## **Statistical analyses**

Statistical analysis was performed by using the Statistical Package for Social Science (SPSS), release 21.0 (IBM Corp., Armonk, USA). The Kolmogorov–Smirnov test was used to assess the normality of the distribution of the data. Categorical variables were compared using the Chi-square or Fisher exact test, while comparison of continuous variables included T test for independent sample and 2-tailed t-tests. A binary logistic regression analysis was performed to assess the independent predictors of outcomes using all the variables that resulted significantly different between the two FHR groups at the univariate analysis. Data were expressed as odds ratio (OR)  $\pm$ 95% confidence interval (CI). Multiple regression including significant variables was used to examine the adjusted OR (aOR) for each predictor.

### **Ethical approval**

The study project was approved by the local ethics committee on 05-04-2019 (number 14976).

### **RESULTS**

Overall, 4623 deliveries occurred during the study period; 2770 (59.9%) were excluded for gestational age <40 weeks; among the remaining 1853, 556 (30.0%) underwent induction of labor and 37 (2.0%) underwent elective CS. A total of 1260 deliveries were assessed for eligibility and 1004 CTG traces fulfilled the inclusion criteria; 860 (85.6%) of them presented a baseline between 110-149 bpm and 144 (14.4%) presented a baseline between 150-160 bpm (Figure 1).

On Table 1 maternal, labor and neonatal characteristics of the two FHR groups are presented. At univariate analysis a significantly higher rate of nulliparous (59.0% vs. 47.8%;  $P=0.01$ ) was noted in the group 150-160 bpm as well as a higher incidence of epidural analgesia (43.8% vs. 27.8%;  $p<0.001$ ), augmentation with oxytocin (39.6% vs. 18.1%;  $p<0.001$ ). Furthermore, the group with 150-160 bpm FHR had a longer length of active labor ( $370.8\pm 229.6$  vs.  $253.6\pm 182.9$ ;  $p<0.001$ ).

The primary outcome of the study is reported on Table 2. Compared to the group 110-149 bpm, the group 150-160 bpm had a higher incidence of meconium-stained amniotic fluid (OR 2.6; 95%CI 1.8-3.8), intrapartum maternal pyrexia (OR 4.7; 95%CI 1.1-14.6), CS



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during labor (OR 4.5; 95% CI .2-9.0), neonatal acidemia (OR 3.5; 95%CI 1.5-55.1) and adverse Composite Neonatal Outcome (OR 3.5; 95%CI 1.7-7.3). The risk of low Apgar was also increased (OR 9.13 95%CI 1.55-55.1) although this was registered only in 5 cases. No case of stillbirth or neonatal death have been reported.

The logistic regression including all the variables which appeared significantly different between the two FHR groups at univariate analysis is shown on Table 3. FHR between 150-160 bpm remained the only independent predictor of CS for suspected fetal distress (aOR 10.7; 95%CI 2.9-44.6), neonatal acidemia (aOR 2.6; 95%CI 1.1-6.7) and adverse Composite Neonatal Outcome (aOR 2.6; 95% CI 1.2-5.6) while both FHR (aOR 2.2; 95% CI 1.5-3.3). and epidural (aOR 1.8; 95% CI 1.2-2.6) appeared significantly associated with meconium stained amniotic fluid.

## DISCUSSION

Our study demonstrated that a baseline FHR between 150 and 160 bpm at or after 40 weeks during the first 60 minutes of spontaneous active labor is an independent risk factor for an adverse labor and neonatal outcome being associated with a higher incidence of meconium-stained amniotic fluid, intrapartum maternal pyrexia, emergency CS for suspected fetal compromise and neonatal acidemia.

Our findings are novel, but difficult to explain. An intrapartum fetal baseline between 150 and 160 bpm at 40 weeks or beyond despite being within the normal range proposed by most CTG guidelines may indicate the effects on the fetal heart of a dysregulated autonomic system or of an unexpected prevalence of the sympathetic nervous system over the vagal tone. A dysregulated autonomic response may be triggered by the early steps of an inflammatory process<sup>18,19</sup> arising in the fetus or in the adnexa whereas the abnormally exaggerated activity of the sympathetic nervous system may be due to an increased release of the catecholamines by the fetal adrenal glands, which may reflect an underlying condition of chronic hypoxia<sup>20-22</sup>. Both inflammation/infection or hypoxic pathways can act independently or synergically during labor and are known to promote the occurrence of adverse outcomes including acidemia, passage of meconium/meconium aspiration syndrome and/or fetal compromise<sup>23,24</sup>.

In case of subtle chronic hypoxia, the mechanism leading to a greater release of catecholamines is a subclinical placental insufficiency which can primarily manifest during labor due to presence of uterine contractions and under these conditions may precipitate fetal acidemia<sup>20-22</sup>.

On the other hand, in the presence of fetoplacental infection or inflammation, the production of cytokines and other inflammatory mediators lead to an increase of the FHR baseline secondary to a dysregulation of the thermoregulatory center and to the increased metabolic rate<sup>10, 28</sup>.

This may explain why in our series a baseline FHR in early active labor between 150 and 160 bpm was associated with the later occurrence of maternal fever, meconium staining of amniotic fluid and fetal acidemia. Indeed, independently from the concomitance of chronic hypoxia, in presence of intrauterine inflammation/infection there is an increased metabolic demand leading to a higher oxygen consumption and to an accelerated fall in the fetal pH<sup>30-32</sup>.

To the best of our knowledge, this is the first study in which the clinical significance of a higher than expected baseline FHR for the given gestational age (but <160 bpm) has been investigated as isolated finding. Previous studies have demonstrated that FHR patterns change throughout the pregnancy due to the progressive maturation of parasympathetic system. In normal fetuses a progressive decline of the baseline FHR throughout the last weeks of pregnancy has been consistently described by a large number of studies<sup>10-12</sup>.

To date, no difference has been reported in the baseline heart rate values at term according to parity although in our large series, the incidence of 150-160 bpm was more likely among nulliparous women. This finding remains of uncertain significance and may explain as to why in the higher FHR group at univariate analysis, the rate of epidural, the use of oxytocin and the duration of labor were also significantly higher.

However, after adjustment for all variables at logistic regression the baseline FHR and not the parity or the other baseline characteristics of the two FHR groups turned out to be significantly associated with labor outcome.

Based on our study, a higher than expected baseline FHR during active labor, even as isolated finding, seems to warrant a strict fetal surveillance due to its association with adverse labor outcome. More specifically, continuous CTG since the early stages of labor

and the assessment of inflammatory markers (eg maternal temperature, CPR, WBC count) are to be considered in these cases.

While the intrapartum CTG findings associated with established chronic hypoxia or chorioamnionitis have been inconsistently described and include mostly tachycardia, reduced variability, no accelerations and lack of cycling, it seems likely that these two conditions may be anticipated by an isolated rise of the baseline towards the upper limits<sup>33</sup>.

If suspecting subtle fetal hypoxia or inflammation at their subclinical early stages based on the observation of a higher than expected baseline FHR on the CTG trace may positively impact on labor management and ultimately on clinical outcome remains to be proven. However, it seems likely that under these circumstances some obstetrics interventions including early antibiotic or antipyretic administration, exercising caution in the use of oxytocin may be beneficial for both the mother and the fetus slowing the progression of the process and reducing the occurrence of severe intrapartum complications<sup>12,34</sup>

The main strengths of our study are represented by its original design, by the large study population and by its consecutive enrollment.

Additionally, given that all the CTG traces have been evaluated in consensus by three experts and that the baseline is considered the most reproducible parameter, such evaluation is expected to be reliable.

The main limitations of our study include its retrospective design, and the lack of clinical and laboratory data related to a possible neonatal or maternal infection. Moreover, since the evaluation of placental histopathology has not been systematically performed, the association between the higher than expected baseline FHR and the pathology findings suggestive of chorioamnionitis or chronic hypoxia has not been assessed.

## **CONCLUSION**

Our study has shown that as isolated finding a higher than expected baseline FHR for the given gestational age, even if it is within the normal stipulated range (110-160 bpm) appears to be associated with adverse labor and neonatal outcomes. Further larger prospective studies are needed to confirm our novel observation, and to assess if a tailored strategy of labor management may improve the clinical outcome of these cases.

## Acknowledgment

We would like to acknowledge the contribution of dr. Edwin Chandraharan whose novel approach in the interpretation of intrapartum CTG has represented the milestone of this research work

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## Legend

Figure 1. Flow chart of included cases.

	<b>Group 110-149bpm (n=860)</b>	<b>Group 150-160 bpm (n=144)</b>	<b>p-value</b>
Maternal age	32.0 [28.0-35.0]	32.0 [29.0-36.0]	0.12
Caucasian	699(81.3)	114(79.1)	0.55
Pre-pregnant BMI	22.0 [20.0-25.0]	22.0 [20.0-25.0]	0.73
Gestational weight gain (Kg)	12.0 [10.0-14.0]	12.0 [10.0-14.0]	0.33
Artificial Reproductive Techniques	17(1.9)	2(1.4)	0.63
Nulliparous	411(47.8)	85(59.0)	0.01
Baseline FHR at examination (bpm)	135.0 [130.0-140.0]	153.0 [151.0-155.0]	<.001
Gestational Age at delivery (weeks)	40.6[40.3-41.0]	40.6[40.3-41.0]	0.50
Birthweight (g)	3490.0 [3240.0-3751.0]	3530.0 [3255.0-3823.0]	0.70
Birthweight percentile	54.0[28.0-77.0]	56.0[35.0-82.5]	0.16
Birthweight <10 percentile	49(5.7)	5(3.4)	0.27
ROM at admission	235(27.3)	41(28.4)	0.77
Interval time from ROM to active labor (min)	318.0±480.0	309.0±391.0	0.89
Genito-urinary infections <ul style="list-style-type: none"> <li>• No infections</li> <li>• GBS</li> <li>• Others</li> </ul>	620(72.1) 17(19.9) 69(8.0)	107(74.3) 31(21.5) 6(4.2)	0.26
Epidural Analgesia	238(27.8)	63(43.8)	<.001

**Table 1.** Maternal and neonatal characteristics



Augmentation with oxytocin	156(18.1)	57(39.6)	<.001
Total length of active labor (min)	253.6±182.9	370.8±229.6	<.001

Data have been expressed as n (N%), mean±SD or median [IQR]

BMI, body Mass Index; FHR, fetal Heart Rate; ROM, rupture of membranes; GBS, group B Streptococcus

**Table 2.** Comparison of labor and neonatal outcome between women with baseline Fetal Heart Rate (FHR) between 110-149 bpm and women with baseline FHR between 150-160 bpm during the first 60 minutes of active labor

	<b>Group 110-149bpm (n=860)</b>	<b>Group 150-160 bpm (n=144)</b>	<b>p-value</b>	<b>Odds Ratio</b>	<b>95% CI</b>
Meconium-stained Amniotic fluid	180(20.9)	59(40.9)	<.001	2.6	1.8-3.8
Intrapartum hyperpyrexia	6(0.7)	4(2.8)	0.02	4.7	1.1-14.6
Spontaneous vaginal delivery	777(90.3)	116(80.6)	<.001	<i>Reference</i>	<i>Reference</i>
Operative vaginal delivery					
Overall CS	62(7.2)	14(9.7)		1.5	0.8-2.8
CS for fetal distress	21(2.5)	14(9.7)		4.5	2.2-9.0
	3(0.4)	6(4.1)		13.4	3.3-54.3
Apgar <7 at 5 <sup>th</sup> min	2 (0.2)	3 (2.1)	0.004	9.1	1.51-55.1
Arterial pH<7.10	14/696 (2.0)	8/118 (6.8)	0.003	3.5	1.5-8.6
NICU admission	8(0.9)	3(2.1)	0.21	2.3	0.5-8.6
Composite Neonatal Outcome	22/696	12/117	<0.001	3.5	1.7-7.3

	(3.2)	(10.3)			
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Data are expressed as n (%).

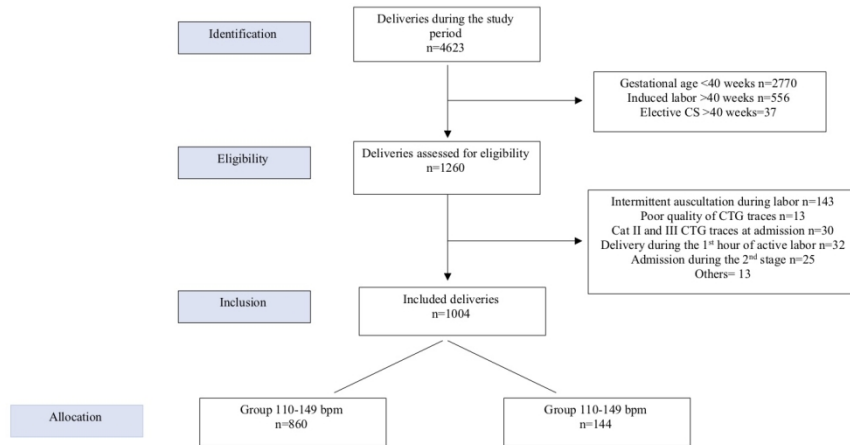
CS, cesarean Section; NICU, Neonatal Intensive Care Unit

**Table 3.** Multivariate analysis of factors influencing labor and neonatal outcome

	<b>FHR 150-160 bpm</b> <b>aOR</b> <b>(95%CI)</b>	<b>Nulliparous</b> <b>aOR</b> <b>(95%CI)</b>	<b>Analgesia</b> <b>aOR</b> <b>(95%CI)</b>	<b>Augmentation</b> <b>aOR</b> <b>(95%CI)</b>	<b>Labor length</b> <b>aOR</b> <b>(95%CI)</b>
<b>Meconium-stained amniotic fluid</b>	2.2 (1.5-3.3)	1.3 (0.9-1.8)	1.8 (1.2-2.6)	1.3 (0.8-1.9)	1.0 (0.99-1.01)
<b>Intrapartum hyperpyrexia</b>	2.0 (0.5-7.6)	3.1 (0.3-26.7)	7.43 (0.8-66.9)	3.68 (0.5-20.7)	1.0 (0.9-1.01)
<b>Overall Caesarean Section</b>	2.5 (1.2-5.2)	1.5 (0.6-3.6)	1.3 (0.6-2.9)	2.4 (0.9-6.0)	1.0 (0.99-1.1)
<b>Caesarean Section for fetal distress</b>	10.7 (2.9-44.6)	1.20 (0.2-5.8)	0.9 (0.2-3.8)	3.1 (0.5-17.8)	0.99 (0.99-1.01)

<b>Apgar&lt;7 at 5<sup>th</sup> min</b>	5.03 (0.7-32.9)	1.40 (0.1-15.8)	0.9 (0.1-6.7)	8.2 (0.5-128.8)	1.0 (0.9-1.01)
<b>Ph&lt;7.10</b>	2.6 (1.1-6.7)	1.3 (0.5-3.7)	0.90 (0.3-2.6)	1.6 (0.5-5.0)	1.0 (0.99-1.01)
<b>Composite Neonatal Outcome</b>	2.6 (1.2-5.6)	0.8 (0.5-1.1)	1.3 (0.60-3.0)	1.1 (0.4-2.7)	1.0 (0.99-1.01)

Figure 1. Flow-chart of included cases



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