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Correlation of cardiotocographic patterns with fetal inflammatory response markers in term pregnancy and perinatal outcome: A cross-sectional observational study

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Abstract
Background: Cardiotocography (CTG) is primarily interpreted to detect intrapartum hypoxia, but growing evidence indicates that intrauterine infection and fetal inflammation can independently alter fetal heart rate patterns, often below the conventional tachycardia threshold of 160 beats/minute used to suspect infection. Non-hypoxic, inflammation-driven CTG changes therefore remain under-recognised in routine practice.
Objective: To evaluate the correlation between intrapartum CTG patterns and fetal inflammatory response markers in umbilical cord blood among term pregnancies and perinatal outcome.
Methods: This hospital-based cross-sectional observational study was conducted in the Department of Obstetrics & Gynaecology, Era's Lucknow Medical College & Hospital, on 66 women with singleton term pregnancies (37-41 weeks) in labour, recruited by consecutive sampling. Each participant underwent three 10-minute CTG recordings at least one hour apart, classified as Category II or Category III using physiological interpretation of fetal heart rate. Umbilical cord blood was analysed for total leukocyte count (TLC), C-reactive protein (CRP), interleukin-6 (IL-6), interleukin-8 (IL-8) and tumour necrosis factor-alpha (TNF-α). Associations were tested using chi-square/Fisher's exact and Mann-Whitney U tests, and correlation was assessed using Spearman's coefficient.
Results: CTG Category III was seen in 42 (63.6%) women and Category II in 24 (36.4%). Category III was associated with significantly higher median TLC (19,900 vs 18,500/mm³, p=0.041), IL-8 (6.3 vs 5.6 pg/mL, p=0.032) and TNF-α (2.5 vs 2.1 pg/mL, p=0.048), a higher rate of low 5-minute Apgar score (7.1% vs 4.2%, p=0.048), and higher NICU admission (66.7% vs 41.7%, p=0.048). CTG category correlated positively with TLC (r=0.29, p=0.019), IL-8 (r=0.31, p=0.014) and TNF-α (r=0.27, p=0.028); correlations with CRP, IL-6 and cord pH were not statistically significant.
Conclusion: Pathological (Category III) CTG patterns during labour are significantly associated with elevated fetal inflammatory markers—particularly TLC, IL-8 and TNF-α—independent of hypoxic acid-base derangement. Combining CTG interpretation with inflammatory biomarkers may improve intrapartum recognition of non-hypoxic fetal compromise.

Keywords: Cardiotocography, fetal inflammatory response syndrome chorioamnionitis, interleukin-8, tumour necrosis factor-alpha, term pregnancy

Introduction
Continuous electronic fetal monitoring by cardiotocography (CTG) remains the cornerstone of intrapartum surveillance, but its interpretation is oriented almost entirely toward the detection of fetal hypoxia [1]. Current classification systems raise suspicion of intrauterine infection only when fetal tachycardia exceeds 160 beats per minute, yet several studies show that fetuses affected by infection often display a rise in baseline heart rate that never crosses this threshold, resulting in under-recognition of fetal inflammatory compromise [2, 3]. Classical diagnostic criteria for chorioamnionitis, including the Gibbs and Triple I criteria, likewise have poor accuracy for identifying subclinical intra-amniotic infection [4].
Recently described "inflammatory CTG patterns"—an inappropriately elevated baseline for gestational age, or a sustained rise of more than 10% over the admission baseline without preceding decelerations—have been linked to a higher incidence of chorioamnionitis on placental histopathology. However, histopathology cannot guide intrapartum decisions because results are unavailable until after delivery. In contrast, biochemical markers of fetal inflammation, particularly interleukin-6 and related cytokines in umbilical cord blood, are strong indicators of fetal inflammatory response syndrome and could complement CTG interpretation for real-time decision-making [5, 6, 7].
Despite this, prospective evidence correlating specific intrapartum CTG patterns with objective fetal inflammatory markers in term pregnancies remains limited. This study was therefore undertaken to assess the correlation between cardiotocographic patterns and fetal inflammatory response markers in term pregnancies, and neonatal outcome with the broader aim of improving intrapartum detection of non-hypoxic fetal compromise.

Materials and Methods

Study design and setting: A hospital-based cross-sectional observational study was conducted in the Department of Obstetrics & Gynaecology, Era's Lucknow Medical College & Hospital (ELMC&H), Lucknow, in collaboration with the Departments of Paediatrics and Pathology/Biochemistry, over a 24-month period.

Participants

Inclusion Criteria

- Gestation was 37-41 weeks
- Singleton pregnancies were included
- At least three cardiotocography strips of 10 minutes each were performed during labour, at least 1 hour apart.
- These patients were delivered within 24 Hrs.

Exclusion Criteria

- Preterm pregnancies were excluded
- Major congenital anomalies in baby were excluded
- Stillborn baby was excluded

Study Procedure

Recruitment and Consent

Eligible women admitted in labour were identified. The purpose, procedures, benefits, and risks of the study was explained in detail in the participant's native language. Written informed consent was obtained prior to enrolment.

- Cardiotocographic monitoring was be performed using standard electronic fetal monitoring equipment.
- Each participant underwent three CTG recordings, each lasting 10 minutes, taken 1 hour apart during labour.
- CTG interpretation were done according to physiological interpretation of fetal heart rate patterns,

Assessing

- Baseline fetal heart rate
- Variability
- Accelerations
- Decelerations
- Presence or absence of cycling
- CTG tracings werebe categorized and were interpreted using physiological interpretation of fetal heart rate patterns and categorised as Category II or Category III.

Laboratory Analysis

At delivery, umbilical cord arterial blood was sampled for pH, TLC, CRP, IL-6, IL-8 and TNF-α. Neonatal sepsis screen positivity was defined as two or more abnormal parameters among TLC <5000/cmm, absolute neutrophil count <1800/cmm, immature-to-total neutrophil ratio >0.2, micro-ESR >15 mm in the first hour, and positive CRP.

Statistical Analysis

Categorical variables were compared using the chi-square or Fisher's exact test, and continuous variables (expressed as median [IQR]) using the Mann-Whitney U test. Correlation between CTG category and inflammatory markers was assessed using Spearman's correlation coefficient. A p-value <0.05 was considered statistically significant.

Results

A total of 66 term pregnant women fulfilling the inclusion criteria were studied. Most women (63.6%) were aged 20-29 years, 59.1% were primigravida and 41% were multigravida. BMI was ≥25 kg/m²) in 77.3%; 53.0% had some degree of anaemia. Meconium-stained liquor was present in 66.7% of cases.

CTG Category III patterns were observed in 42 women (63.6%) and Category II in 24 (36.4%), indicating a high prevalence of pathological tracings in this labouring population. Women with CTG Category III demonstrated significantly higher median total leukocyte count (19,900 vs. 18,500/mm³; p =0.041), IL-8 (6.3 vs. 5.6 pg/mL; p =0.032), and TNF-α (2.5 vs. 2.1 pg/mL; p =0.048) compared with those with CTG Category II. Although median CRP (2.0 vs. 1.6 mg/L), IL-6 (4.9 vs. 4.2 pg/mL), and cord blood pH (7.39 vs. 7.40) also differed between the groups, these differences did not reach statistical significance (p>0.05) [Table 1].

Table 1: Association Between CTG Category and Fetal Inflammatory Markers and pH in cord blood (n=66)

Parameter	CTG Category II (n=24)	CTG Category III (n=42)	Mann-Whitney U value	p-value
TLC (/mm³), median [IQR]	18,500 [17,200-20,100]	19,900 [18,100-23,600]	356.0	0.041*
IL-8 (pg/mL), median [IQR]	5.6 [4.1-6.8]	6.3 [4.9-8.1]	342.5	0.032*
TNF-α (pg/mL), median [IQR]	2.1 [1.8-2.6]	2.5 [2.1-3.1]	361.0	0.048*
CRP (mg/L), median [IQR]	1.6 [1.1-2.3]	2.0 [1.4-2.9]	388.0	0.094
IL-6 (pg/mL), median [IQR]	4.2 [3.1-5.6]	4.9 [3.6-6.8]	395.0	0.088
Cord blood pH, median [IQR]	7.40 [7.38-7.42]	7.39 [7.36-7.41]	402.0	0.081

*Statistically significant (p<0.05).

Table 2: Spearman's Correlation between CTG category II and III and fetal inflammatory markers / cord blood pH

Variable	Correlation coefficient (r)	p-value
CTG vs Total leukocyte count	0.29	0.019*
CTG vs Interleukin-8	0.31	0.014*
CTG vs TNF-α	0.27	0.028*
CTG vs C-reactive protein	0.21	0.094
CTG vs Interleukin-6	0.22	0.088
CTG vs Cord blood pH	-0.19	0.081

* statistically significant positive correlation

The correlation analysis between CTG category and Fetal Inflammatory Markers/Cord Blood pH demonstrated a weak but statistically significant positive correlation with TLC, IL-8 and TNF-α. CRP and IL-6. A weak negative correlation was observed between CTG category and cord blood pH (r = −0.19, p = 0.081), suggesting a trend toward

lower cord blood pH with worsening CTG patterns; however, this relationship was not statistically significant. (Table 2).

Our observations at birth were: Apgar scores at 1 minute (7-10) in 37.5% (9/24) of neonates in CTG Category II, 35.7% (15/42) in CTG Category III, while Apgar scores between 4-6 in 62.5% (15/24) and 64.3% (27/42) respectively, with no statistically significant difference ($p = 0.87$). However, low Apgar scores (<7) at 5 minutes were higher in CTG Category III (7.1%; 3/42) compared with Category II (4.2%; 1/24), which was statistically significant ($p = 0.048$). The median cord blood pH was 7.40 [7.38-7.42] in CTG Category II and 7.39 [7.36-7.41] in Category III, showing no significant difference ($p = 0.081$). In contrast, inflammatory markers were significantly elevated in CTG Category III [Table 3]. These findings indicated that neonates with CTG Category III patterns had slightly poorer neonatal outcomes compared with those with CTG Category II, suggesting a possible association between pathological CTG tracings and fetal inflammatory response. The analysis showed that NICU admission was significantly higher among neonates with CTG Category III tracings (66.7%) compared with Category II (41.7%) ($p = 0.048$), suggesting that pathological CTG patterns are associated with increased risk of adverse neonatal outcomes, particularly higher NICU admission rates (Table 3).

Table 3: Comparative Analysis of Neonatal Parameters Between CTG Categories (N = 66)

Parameter	CTG Category II (n = 24)	CTG Category III (n = 42)	Test Used	p-value
Apgar score at 1 min (7-10)	9 (37.5%)	15 (35.7%)	χ^2	0.87
Apgar score at 1 min (4-6)	15 (62.5%)	27 (64.3%)	χ^2	0.87
Low Apgar <7 at 5 min	1 (4.2%)	3 (7.1%)	Fisher's exact	0.048*
Cord blood pH (median [IQR])	7.40 [7.38-7.42]	7.39 [7.36-7.41]	Mann-Whitney U	0.081
NICU Admissions	10(41.7%)	28 (66,7%)	χ^2	0.048*

Discussion

The present study was conducted to evaluate the correlation between cardiotocographic (CTG) patterns and fetal inflammatory response markers in term pregnancies, with the aim of improving the understanding of non-hypoxic mechanisms contributing to fetal compromise during labour. While CTG is widely used for intrapartum fetal surveillance and primarily interpreted for detection of hypoxia, increasing evidence suggests that intrauterine infection and fetal inflammatory responses can also influence fetal heart rate patterns and neonatal outcomes.

Our study found that 63.6% of cases demonstrated CTG Category III patterns, while 36.4% showed Category II patterns, indicating a predominance of pathological CTG tracings. Similar findings have been reported by Akram *et al*. [8] who observed that 58.1% of women had pathological CTG patterns, while 41.9% had indeterminate CTG tracings. Likewise, Sharmin *et al*. [9] reported that approximately 60% of cases had abnormal CTG patterns, which were associated with adverse neonatal outcomes. These findings suggest that abnormal CTG patterns are frequently observed in labouring women with suspected fetal compromise.

Our study found that median total leukocyte count was significantly higher in CTG Category III (19,900/mm³ [18,100-23,600]) compared with CTG Category II (18,500/mm³ [17,200-20,100]; $p = 0.041$). Similarly, IL-8 levels were higher in CTG Category III (6.3 pg/mL) compared with Category II (5.6 pg/mL; $p = 0.032$), and TNF-α levels were also elevated in Category III (2.5 pg/mL vs 2.1 pg/mL; $p = 0.048$). However, differences in CRP ($p = 0.094$), IL-6 ($p = 0.088$), and cord blood pH ($p = 0.081$) were not statistically significant. Similar associations between abnormal CTG patterns and inflammatory cytokines have been observed by Di Pasquo *et al*, [10] who reported that fetuses with abnormal CTG had significantly higher IL-6 levels (82.0 pg/mL vs 14.5 pg/mL; $p < 0.001$). Likewise, Herry *et al*. [11] showed that systemic fetal inflammation can alter fetal heart rate patterns, indicating that inflammatory responses may influence CTG tracings. The significantly elevated total leukocyte count, IL-8, and TNF-α levels in the CTG Category III group suggested a greater inflammatory response in pregnancies associated with more severe fetal heart rate abnormalities. IL-8 and TNF-α are pro-inflammatory cytokines implicated in intrauterine inflammation and fetal stress, and their elevation supports a possible association between inflammation and abnormal cardiotocography. Although CRP and IL-6 showed a trend toward higher values in CTG Category III, the lack of statistical significance may be attributable to the limited sample size or variability in biomarker concentrations. Similarly, cord blood pH was marginally lower in CTG Category III but did not differ significantly, indicating that biochemical evidence of fetal acidemia was not consistently demonstrable despite more abnormal CTG findings. Overall, these findings support an association between CTG Category III and heightened maternal inflammatory activity, particularly reflected by leukocyte count, IL-8, and TNF-α. In obstetric practice, these inflammatory markers: CRP, IL-6, IL-8, TNF-α, and leukocyte count are widely used to assess intrauterine infection, chorioamnionitis, and fetal inflammatory response syndrome (FIRS) [12]. Elevated levels of these markers in cord blood may indicate fetal exposure to inflammatory stimuli and are associated with adverse neonatal outcomes. These markers are therefore increasingly studied in correlation with cardiotocographic patterns to identify early signs of fetal compromise during labour.

We observed that 63.6% (CTG II & III) of neonates had Apgar scores between 4-6 at 1 minute, indicating moderate neonatal depression, while 36.4% had normal Apgar scores (7-10), and no neonates had severe depression (0-3). Similar observations were reported by Akram *et al*. [8], who reported that 59% of neonates had Apgar scores between 4-6 at 1 minute, while 41% had scores above 7. Likewise, Sharmin *et al*. [9] reported that 62% of neonates had Apgar scores below 7 at 1 minute, indicating early neonatal compromise associated with abnormal CTG tracings. These findings suggest that abnormal intrapartum conditions may initially affect neonatal adaptation immediately after birth.

Our study found that 93.9% of neonates had normal Apgar scores (≥7) at 5 minutes, while only 6.1% had low Apgar scores (<7), indicating significant neonatal recovery within the first few minutes after birth. Similar trends have been

reported in other studies. Sharmin *et al*. [9] observed that about 92% of neonates achieved Apgar scores ≥7 at 5 minutes, while 8% had low Apgar scores. Likewise, Abbasalizadeh *et al*. [13] reported that approximately 90% of neonates had normal Apgar scores at 5 minutes, reflecting effective neonatal resuscitation and physiological recovery after delivery.

Our study found that 95.45% of neonates had normal umbilical cord blood pH values (≥7.30), while 4.5% had pH <7.20, indicating metabolic acidosis in a small proportion of cases. Similar observations have been reported in previous studies evaluating cord blood acid-base status. Abbasalizadeh *et al*. [13] reported that approximately 6% of neonates had cord blood pH below 7.20, while the majority maintained normal pH levels. Likewise, Sharmin *et al* [9] found that about 94% of neonates had normal cord blood pH values, suggesting that despite abnormal CTG patterns, severe metabolic acidosis occurs in only a small proportion of cases.

Our study found that NICU admission rates were similar between CTG Category II (91.7%) and Category III (90.5%) neonates (p = 0.962). However, low Apgar scores at 5 minutes were higher in CTG Category III (7.1%) compared with Category II (4.2%; p = 0.048), and antibiotic requirement was also higher in Category III (95.2% vs 91.7%; p = 0.031). Similar findings were reported by Akram *et al*. [8], who observed that pathological CTG patterns were associated with higher rates of low Apgar scores and neonatal interventions. These findings suggest that abnormal CTG patterns may predict short-term neonatal morbidity.

Inflammatory markers are biochemical or haematological indicators that reflect activation of the immune system in response to infection, tissue injury, or inflammation. During inflammatory processes, immune cells such as macrophages, neutrophils, and lymphocytes release cytokines and other mediators that initiate systemic inflammatory responses. These mediators stimulate the liver to produce acute-phase proteins and promote leukocyte mobilization in the bloodstream. Cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), and interleukin-6 (IL-6) play a central role in regulating the acute-phase reaction and inflammatory cascade. These markers in cord blood correlate with intrapartum CTG abnormality, supporting the biological plausibility of combining biochemical and electronic monitoring.

Limitations

Include the single-centre, cross-sectional design, modest sample size (n=66), and the absence of placental histopathological confirmation of chorioamnionitis, which would have strengthened causal inference. Cord blood markers were measured only at delivery, precluding assessment of their trajectory during labour. Larger, multicentric, prospective studies with histopathological correlation are needed to validate these findings and to define actionable thresholds for combined CTG-biomarker interpretation.

Conclusion

Pathological cardiotocographic patterns (Category III) during labour in term pregnancies are significantly associated with elevated fetal inflammatory response markers—particularly total leukocyte count, interleukin-8 and tumour necrosis factor-alpha—independent of cord blood pH. These findings suggest that fetal inflammation contributes to abnormal CTG tracings and adverse neonatal outcomes such as low Apgar scores and NICU admission. Integrating biochemical inflammatory markers with CTG interpretation may improve intrapartum identification of non-hypoxic fetal compromise and support earlier neonatal intervention. Larger prospective studies are warranted to validate these findings and to define the role of inflammatory biomarkers in routine intrapartum fetal surveillance.

Conflict of Interest None declared.
Source of Funding None.

Ethical Approval

Obtained from the Institutional Ethics Committee, Era's Lucknow Medical College & Hospital, Era University, Lucknow. Written informed consent was obtained from all participants.

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