An evaluation into the use of procalcitonin levels as a biomarker of bacterial sepsis to aid the management of intrapartum pyrexia and chorioamnionitis

Sarah Walker, MRCOG; Irasha Harding, FRCPath; Kamran Soomro, Dr; Andrew R. Bamber, MD(Res); Sophie Carrick, MBBS; Abdul H. Waheed, MBBS; Rachel E. Liebling, MRCOG

BACKGROUND: Procalcitonin is an established biomarker for bacterial sepsis in the nonpregnant population with better diagnostic and prognostic value for bacterial infections.

OBJECTIVE: This study aimed to evaluate whether procalcitonin levels could be used in the diagnosis and management of intrapartum sepsis in women and their neonates suspected of intrapartum bacterial sepsis.

STUDY DESIGN: A prospective observational cohort study was conducted at the University Hospitals of Bristol and Weston NHS Foundation Trust. Overall, 117 women and their neonates managed for suspected intrapartum sepsis from June 2020 to October 2020 were included. Procalcitonin levels were measured in addition to routine biomarkers white cell count and C-reactive protein in women and their neonates during the initial septic screen and follow-up blood samples. The placentas underwent detailed histopathology. Maternal and neonatal parameters were used to categorize cases into "high-suspicion bacterial sepsis," "equivocal bacterial sepsis," and "low-suspicion bacterial sepsis." The Kruskal-Wallis test was used to compare categories with biomarker values and placental histology scores.

RESULTS: Procalcitonin level was increased in 6 women in the initial septic screen sample, compared with 100 women with an increased C-reactive protein level. There was a significant difference in maternal postnatal procalcitonin results between "high-suspicion bacterial sepsis" and "low-suspicion bacterial sepsis" categories (P=.004). Moreover, 71.2% of placentas showed varying degrees of chorioamnionitis.

CONCLUSION: In our cohort of women, 94.6% had normal procalcitonin levels while in labor at the time of the septic screen, consistent with the low number of confirmed bacteremia. The result provided a basis that procalcitonin may complement clinical judgment and interpretation of already used prognostic and diagnostic tests, improving patient care in the management of intrapartum sepsis.

Key words: chorioamnionitis, intrapartum sepsis, procalcitonin, sepsis biomarkers

Introduction

Sepsis biomarkers have been the subject of several research studies, aiming to identify patients with bacterial sepsis (BS), differentiate sepsis from other noninfectious inflammatory pathologies, predict clinical severity, and guide antibiotic stewardship. The biomarkers predominantly used in the pregnant population include white cell count (WCC), C-reactive protein (CRP), and lactate, all known to be nonspecific for inflammation vs infection.[1]

Procalcitonin (PCT) is an established marker for sepsis in the nonpregnant population, with better diagnostic and prognostic value for bacterial infections.[2,3] PCT, a precursor of calcitonin produced by C cells of the thyroid gland, is involved in maintaining calcium levels in the blood and released into the circulation in response to endotoxins and proinflammatory stimuli, specifically those originating from

From the Department of Obstetrics and Gynaecology, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, United Kingdom (Dr Walker, Dr Carrick, Dr Waheed, and Dr Liebling); UK Health Security Agency, Bristol, United Kingdom (Dr Harding); Department of Computer Science Research Centre, University of the West of England, Bristol, United Kingdom (Dr Soomro); Department of Cellular Pathology, North Bristol NHS Trust, Bristol, United Kingdom (Dr Bamber)

The authors report no conflict of interest.

The hospital research ethics committee approved the study protocol (date of approval: June 9, 2020).

This pilot project was supported by a grant from the local obstetrical department. The funders played no role in the data analysis, interpretation of findings, or decision to submit the manuscript for publication.

Cite this article as: Walker S, Harding I, Soomro K, et al. An evaluation into the use of procalcitonin levels as a biomarker of bacterial sepsis to aid the management of intrapartum pyrexia and chorioamnionitis. Am J Obstet Gynecol Glob Rep 2022;2:100064.

Corresponding author: Sarah Walker, s.walker31@nhs.net

2666-5778/$36.00

http://dx.doi.org/10.1016/j.xagr.2022.100064

AJOG Global Reports at a Glance

Why was this study conducted?

This study aimed to evaluate whether procalcitonin (PCT) levels could be used in the diagnosis and management of intrapartum sepsis in women and their neonates suspected of intrapartum bacterial sepsis.

Key findings

Compared with 86% of women with an increased C-reactive protein level and 96% of women with an increased white cell count, the PCT level was increased in 5.4% of women in the initial septic screen (SS) sample.

What does this add to what is known?

Compared with the normal adult population, 94.6% of women had normal PCT levels at the time of the SS, supporting the evidence that PCT as a biomarker is not influenced by pregnancy or labor. Moreover, 58.5% of women had normal serial PCT levels, consistent with the low number of confirmed bacteremia in this population.

bacteria. Levels are usually low in healthy people and people with viral infections, chronic inflammatory disorders, or autoimmune processes. PCT level increases significantly within the first hours in severe bacterial infections (latent period, 2−4 hours) and has a short half-life, helping guide and monitor response to antibiotic therapy.[3,4] PCT used in diagnosing pregnancy-associated sepsis is relatively unexplored, and reference values for PCT in pregnancy have not been established.[5,6]

Chorioamnionitis is reported to complicate 1% to 4% of births worldwide and is associated with significant maternal and perinatal adverse outcomes.[7,8] Consequently, a low threshold to commence empirical broad−spectrum antibiotics in women developing intrapartum pyrexia is advised.[1,9,10] The reported incidence of intrapartum pyrexia is high, ranging from 3% to 7%.[11,12] The risk of neonatal sepsis in newborns delivered from mothers with intrapartum pyrexia is low at 0.24% (rate of <1 in 400 cases).[11]

Diagnosing chorioamnionitis and managing intrapartum sepsis present unique diagnostic difficulties and are ongoing clinical challenges. Although intrapartum pyrexia may be an indicator of chorioamnionitis, most cases are secondary to noninfectious factors, including epidural analgesia, prolonged labor, increased ambient temperature, use of prostaglandins, and activation of the proinflammatory cascade during parturition.[1,12] Furthermore, pregnancy causes physiological adaptations, which mimic those of early infection, including increased heart rate and reduced blood pressure. These challenges lead to overdiagnosis and treatment of sepsis in labor.[1]

There is growing evidence suggesting that exposure to intrapartum antibiotics is associated with alterations in infant intestinal microbiome, influencing early immune development and increasing the risk of immune-mediated diseases, such as asthma, allergy, and atopy.[13,14]

This study aimed to evaluate whether PCT levels could be used in the diagnosis and management of intrapartum sepsis in women and their neonates suspected of intrapartum BS.

Materials and Methods

A prospective observational cohort study was conducted at St. Michael's Hospital, University Hospitals of Bristol and Weston (UHBW) NHS Foundation Trust, Bristol, United Kingdom, averaging 5000 deliveries a year. The hospital research ethics committee approved the study protocol, and funding was provided by the department.

Over a 4-month period (June 2020 to October 2020), all women who developed intrapartum pyrexia and were started on the sepsis pathway, according to local and national guidance, were included in the study. The recommendations were for 1 temperature of >38°C on 1 occasion or >37.5°C on 2 consecutive occasions at least an hour apart to administer paracetamol. Blood cultures were performed and intravenous (IV) antibiotics were started in women with persistent pyrexia an hour after paracetamol administration.[9,10] To determine the severity of infection and a possible source, these women routinely had samples taken for blood cultures, full blood count, urea and electrolytes, liver function, lactate, and CRP. PCT levels were added to this initial sample (denoted by the term "septic screen [SS]" blood sample) together with subsequent CRP samples ("postnatal [PN]" blood sample) to avoid additional sampling. The PCT results were concealed from clinicians to avoid influencing the management of intrapartum sepsis.

At the UHBW NHS Foundation Trust, all neonates born to women treated for intrapartum pyrexia routinely have blood collected for blood cultures, full blood count, and CRP and are started on IV antibiotics for at least 36 hours. Treatments are stopped according to repeat inflammatory marker results and clinical appearance. For this study, initial samples were also tested for PCT levels ("time 0" blood sample) together with subsequent CRP samples ("day 1" blood sample). The PCT results were concealed from the clinicians.

The PCT was measured with the Elecsys BRAHMS PCT assay, with a value of <0.25 ng/mL considered normal for patients not in the intensive care unit (ICU) and a cutoff value of <0.5 ng/mL considered normal for patients in the ICU.[15,16]

Women treated for intrapartum pyrexia routinely have a urine sample, low vaginal swab (LVS), and throat swab sent for microbiology, and all women in this cohort were tested for COVID-19. The placentas were sent for histopathologic assessment and examined by a consultant perinatal pathologist who scored any inflammation present using published criteria.[17] The staging and grading of chorioamnionitis were scored using the following criteria:

umbilical cord inflammation stage (maximum 3), umbilical cord inflammation grade (maximum 2), membranes inflammation stage (maximum 3), membranes inflammation grade (maximum 2), chorionic vasculitis stage (maximum 3), chorionic vasculitis grade (maximum 3), chorionic plate inflammation stage (maximum 3), chorionic plate inflammation grade (maximum 3), villitis (maximum 1), and intervillositis score (maximum 1)—giving a maximum possible score of 24.[17,18]

Maternal antepartum and intrapartum records were reviewed for vital signs on admission, uterine tenderness, foul-smelling amniotic fluid, urine output, and maximum maternal temperature before delivery. Additional variables were recorded, such as duration of rupture of membranes, epidural, induction of labor, route and location of delivery, group B streptococcus (GBS) status, and postpartum maternal length of hospital stay. Clinical markers of neonatal infection were identified by reviewing neonatal records. Specific neonatal markers included fetal tachycardia, temperature, respiratory distress, and poor feeding. Additional neonatal variables reviewed were birthweight, neonatal course of antibiotics, and length of stay. All information was recorded and stored in a dedicated database.

Maternal cases were divided into 3 categories of "high-suspicion BS," "equivocal BS," and "low-suspicion BS," using a composite of clinical features, investigation results, and Sepsis in Obstetrics Score, an obstetrical-focused scoring system, incorporating recognized physiological changes of pregnancy.[19] Moreover, the neonates were divided into 3 categories of "high-suspicion BS," "equivocal BS," and "low-suspicion BS," using a composite of clinical features, neonatal early-onset sepsis calculator,[20,21] and investigation results. To provide triangulation, the categorization was performed by 3 clinicians blinded to each other and the PCT results. The histopathology of the placenta was analyzed separately with the pathologist blinded to the clinical findings.

Correlations were performed between each biomarker value and placental score from initial and follow-up samples (0 = no correlation and 1 = complete correlation). The Kruskal-Wallis test was performed to correlate each clinical category with the individual biomarker values and placental histology scores. A P value of $<.05$ was considered significant.

Results

A total of 117 women along with their neonates were included in the study (7% of our delivered population in the study period). Table 1 A previous audit performed in the department demonstrated the rate of intrapartum pyrexia at 13.5%, and therefore, we estimated that we included approximately 53% of the cases. The exclusion criteria included incomplete data and factors that may skew sepsis biomarkers, gestational age of <37 weeks, women with immunocompromising conditions, and known chronic infection.

Blood cultures were performed in 98.3% of women, and all blood cultures were taken before the start of antibiotics. Of note, 2 blood cultures were positive with clinically significant organisms (1.7%). Moreover, 1 blood culture grew *Proteus mirabilis*, which correlated to an increased PN maternal PCT level of 2.6, but normal PCT level in the neonate. The other blood cultures grew GBS (as did microbiology for the LVS and placental swab), which correlated to an increased PCT level of 3.6 in the neonate.

Compared with an increased CRP level of ≥10 mg/L in 100 women (86%) and an increased WCC of $>11 \times 10^9$/L in 112 women (96%), an increased PCT level of ≥0.25 ug/L in "SS" blood samples was found in 6 women (5.4%). Compared with an increased CRP level of ≥10 mg/L in all women (100%; range, 13−304 mg/L), an increased PCT level in "PN" blood samples was found in 39 women (41.5%; range, 0.3−38.5 ug/L).

An increased PCT level of ≥0.25 ug/L was found in 47 neonates (55.3%; range, 0.3−4.6) in the "time 0" blood samples and 95 neonates (98.9%; range, 0.3−58.5 ug/L) in the "day 1" blood samples. Moreover, an increased CRP level of ≥10 mg/L was found in 7 neonates (5.98%; range, 10−58 mg/L) in the "time 0" blood samples and 41 neonates (35.04%; range 10−88 mg/L) in the "day 1" blood samples (Table 2).

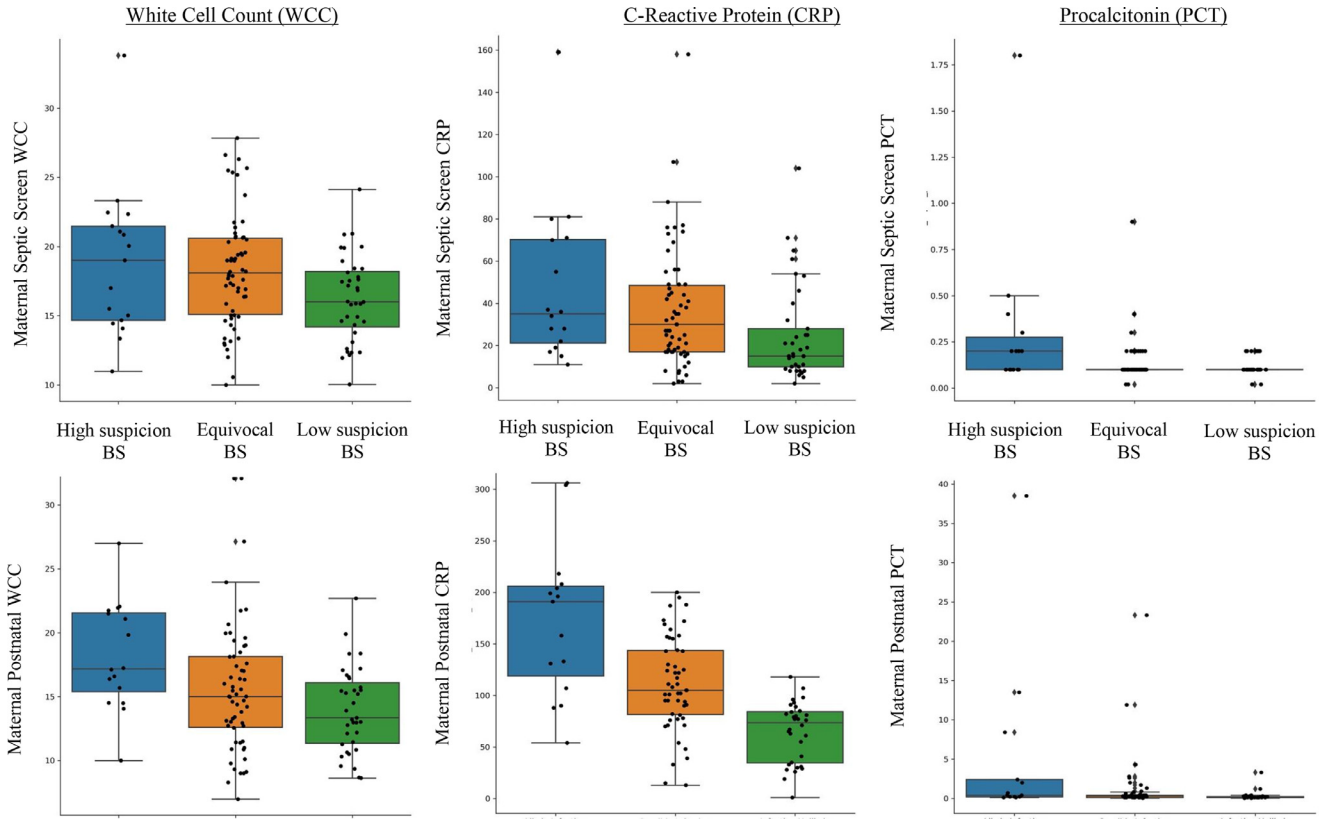
Statistics

The correlations were performed to compare the values of maternal and neonatal biomarkers from initial and follow-up blood samples. When the CRP level was increased for the mother and neonate on initial sampling, it was likely to be increased on the second sample. Moreover, there was a positive correlation between both "time 0" and "day 1" PCT levels with the CRP results for the neonate, +0.509 and +0.409, respectively. There was a positive correlation between maternal "SS" PCT level and neonatal "time 0" PCT level (+0.305) and neonatal "day 1" PCT level (+0.404). This was a higher correlation compared with maternal "SS" CRP level and neonatal "time 0" CRP level (+0.098) or neonatal "day 1" CRP level (+0.141).

Table 3 shows the number of maternal and neonatal participants that were divided into the 3 determined categories. The spread of biomarker results for the maternal "SS" and "PN" blood samples according to the 3 categories are illustrated in Figure 1.

Figure 2 shows the mean PCT results for the 3 categories for both maternal and neonatal blood tests taken during their initial and follow-up blood samples. When performing the Kruskal-Wallis test among the categories, there was no significant difference in maternal "SS" PCT results among the 3 categories, which would be expected as the "SS" PCT levels were only increased in 6 women (PCT level of ≥0.25 ug/L). However, for the "PN" PCT results, there was a significant difference between the "high-suspicion BS" and "low-suspicion BS" categories (P=.004). For neonates, there was a significant difference between the "high-suspicion BS" and "low-suspicion BS" categories for both "time 0" (P=.0349) and "day 1" (P=.008) PCT results.

FIGURE 1
Boxplots showing the spread of biomarkers (WCC, CRP, and PCT)



The graphs show the spread of biomarker results (WCC, CRP, and PCT) with quartiles represented by the *lines* across the 3 determined categories of "high-suspicion BS," "equivocal BS," and "low-suspicion BS." The top 3 graphs represent the septic screen blood results, and the bottom 3 graphs represent the postnatal blood results.

BS, bacterial sepsis; *CRP*, C-reactive protein; *PCT*, procalcitonin; *WCC*, white cell count.

Walker. Procalcitonin levels in intrapartum pyrexia and suspected chorioamnionitis. Am J Obstet Gynecol Glob Rep 2022.

There was no significant difference between the CRP and WCC results in the 3 categories for maternal results and no significant difference between the CRP and WCC results in the 3 categories for neonatal results. However, there was a significant difference in CRP results between "high-suspicion BS" and "equivocal BS" for the neonatal "time 0" (P=.022) and "day 1" (P=.0002) CRP results.

A total of 80 women (68.3%) had completed placental histopathology and were scored a total of 24 for their grading and staging of chorioamnionitis. A high proportion of women (57 of 80 [71.2%]) showed varying degrees of chorioamnionitis (range, 5−18; mean score, 10.6). Figure 3 shows the placental histopathology scores for the 3 maternal categories. In the maternal categories, there was a significant difference between "high-suspicion BS" and both "equivocal BS" (P=.02) and "low-suspicion BS" (P=.00018). There was a weak correlation between maternal "PN" PCT level and placental score (+0.17) and neonatal "day 1" PCT level and placental score (+0.234).

Comment

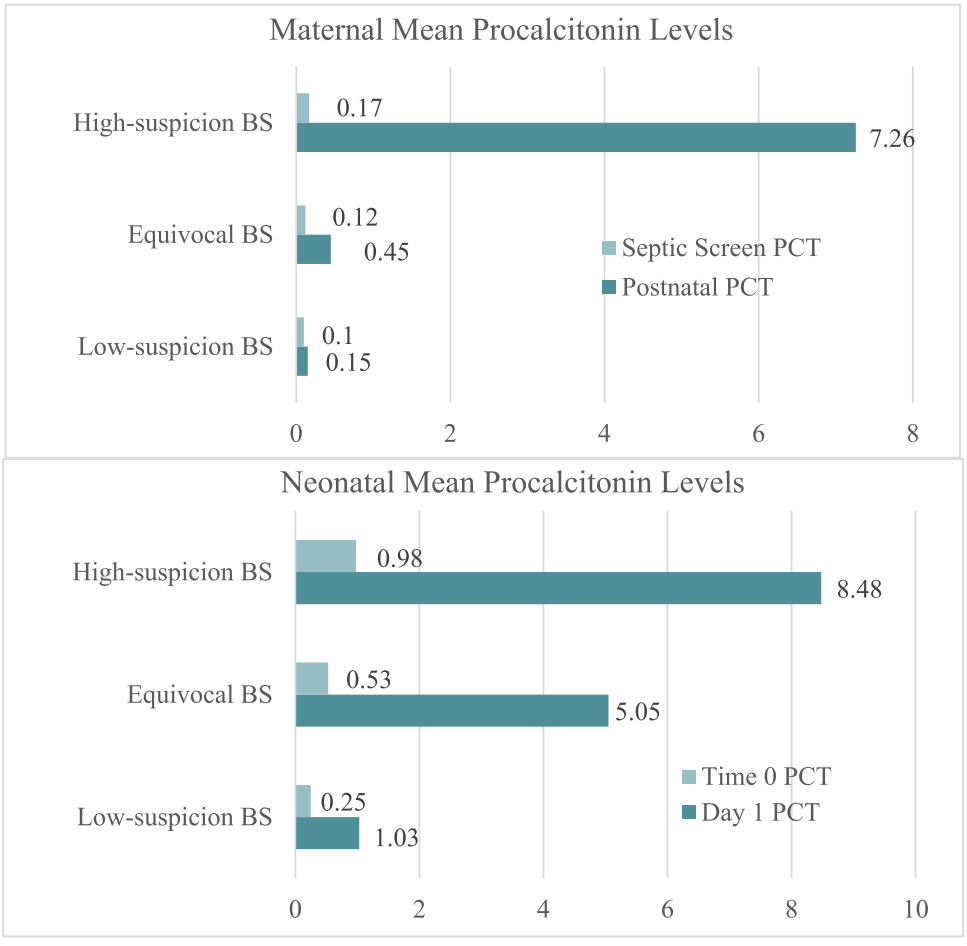
Principal findings

We sought to analyze PCT levels in a cohort of women who presented with possible intrapartum sepsis. We hypothesized that a small number of women would have a proven bacteremia but that a proportion of women would display features highly suggestive of BS. We set out to determine if there was a relationship between PCT and BS. The results showed a significant difference in PCT results between the "low-suspicion BS" and "high-suspicion BS" categories for maternal and neonatal follow-up PCT results. In addition, there seems to be a linear correlation between maternal and neonatal PCT levels with maternal and neonatal clinical conditions (Figure 1). This suggests that PCT could be of diagnostic and prognostic values for bacterial infections in the management of intrapartum pyrexia.

Results: clinical implications

Clinical utilization of the host response, blood infection biomarker PCT has gained attention and has already been approved for the guidance of antimicrobial therapies and antimicrobial stewardship in patients with respiratory infection and sepsis.[22,23] More recently,

FIGURE 2
Mean PCT levels for the 3 determined categories



The graphs show the mean PCT levels for the 3 determined categories of "high-suspicion BS," "equivocal BS," and "low-suspicion BS" for both maternal and neonatal results taken during their initial and follow-up blood tests.

BS, bacterial sepsis; *PCT*, procalcitonin.

Walker. Procalcitonin levels in intrapartum pyrexia and suspected chorioamnionitis. Am J Obstet Gynecol Glob Rep 2022.

it has been shown as an indicator of superimposed bacterial infection in COVID-19 and guided reduced antibiotic use in COVID-19.[24,25] Clinical application in maternity and neonates is relatively unexplored and remains unvalidated.

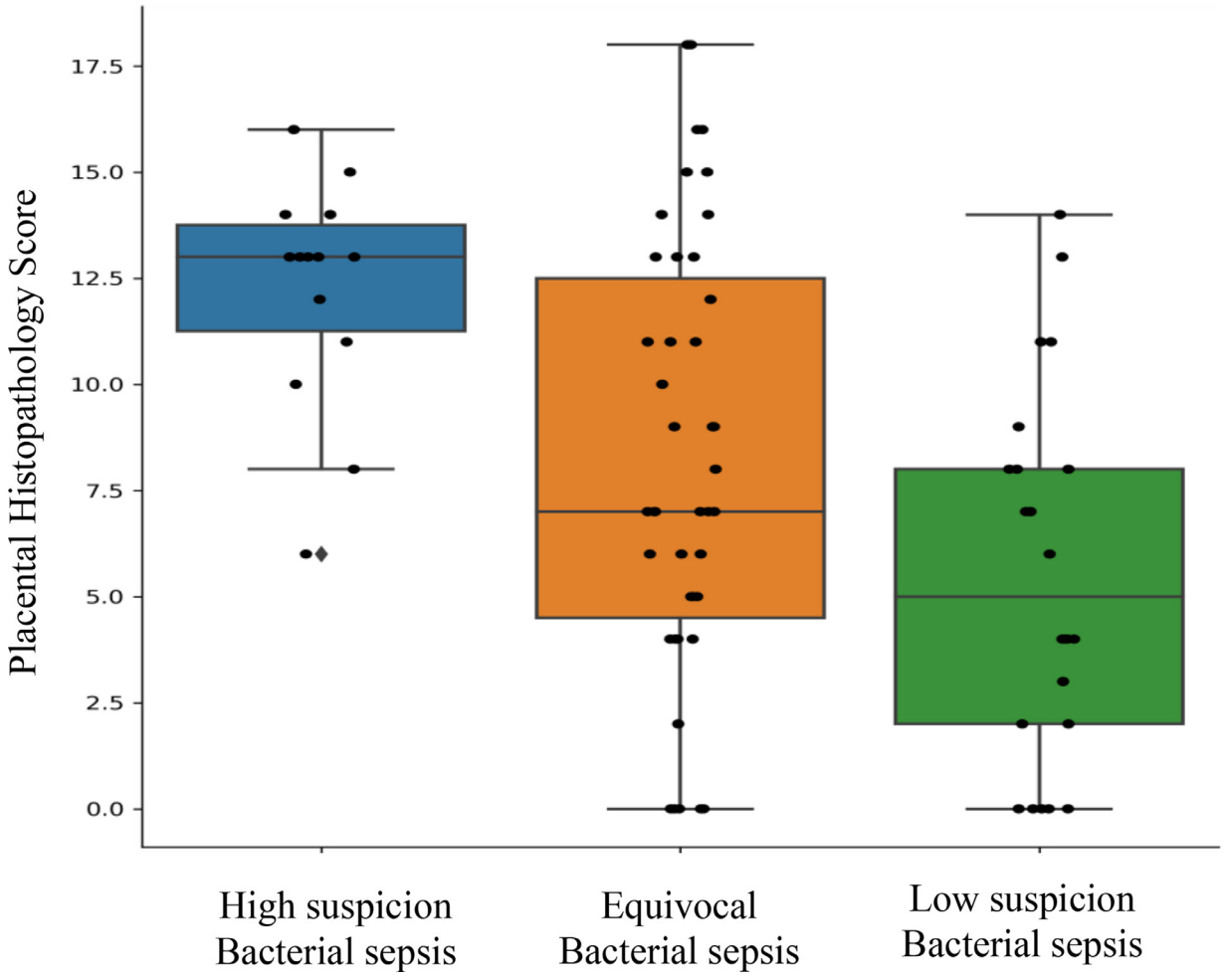
All women had an SS PCT level of <0.25 ug/L except 6 women (5.4%). This result supported other studies, which showed that PCT as a biomarker is not influenced by pregnancy or labor.[26–28] Our results showed that CRP and WCC were increased in a significant proportion of women in labor, in stark contrast to the small number of women with an increased PCT level (86%, 96%, and 5%, respectively). Although our numbers were small, this study suggested that PCT may identify BS in the obstetrical population with greater specificity. Moreover, PCT could be used as an antibiotic stewardship tool, aiding cessation of antibiotics in women with a low likelihood of infection and 2 negative serial PCT measurements.

Results: research implications

Here, the neonates had an increased PCT level of ≥0.25 ug/L in 55.3% in "time 0" blood samples and 98.9% in "day 1" blood samples. However, an increased CRP level of ≥10 mg/L was found in 5.98% in "time 0" blood samples and in 35.04% in "day 1" blood samples. This study supported recent evidence suggesting a physiological rise in PCT in a well neonate.[29]

Blood cultures are used to diagnose bacteremia and identify pathogens, to provide information about the type of microorganism and antimicrobial susceptibility. Here, only 2 blood cultures (1.7%) were positive with clinically significant organisms. Furthermore, when looking at the total number of blood cultures received from our obstetrical population in 2020, of 723 blood cultures, only 13 (1.8%) were positive. The result supported the theories of low yield or low levels of bacteremia in this population.[1]

FIGURE 3
Boxplots showing the spread of placental histopathology scores



The graph shows the spread of placental histopathology scores with the quartiles for the 3 determined categories of women for "high-suspicion BS," "equivocal BS," and "low-suspicion BS."

BS, bacterial sepsis.

Walker. Procalcitonin levels in intrapartum pyrexia and suspected chorioamnionitis. Am J Obstet Gynecol Glob Rep 2022.

Other studies have sought to address this issue with <10% of cultures showing growth of bacteria.[30] Moreover, contamination limits their specificity, as was the case for 1 woman in this study.[31] A study by Laukemann et al[32] analyzed 1083 patients with suspected infection who had blood culture sampling on admission to the emergency department. Only 9.6% of patients had positive blood cultures, and PCT proved to be the most reliable predictor of blood culture positivity, being 8.5-fold higher in positive blood cultures. The study suggested a cutoff for their PCT assay level of <0.1 Ug/L to identify patients with a low risk of bacteremia; consequently, unnecessary blood culture sampling could be avoided in these patients.

Here, detailed placental histopathology found that most placentas (71.2%) have varying degrees of inflammation. Placental histopathology has long been the "gold standard" for the diagnosis of chorioamnionitis. Evidence is emerging that challenges the correlation between clinical chorioamnionitis and histologic chorioamnionitis.[33–35] A study by Smulian et al[34] focused on clinical chorioamnionitis and histologic placental inflammation in 139 pregnancies. They concluded that clinical chorioamnionitis and possible neonatal infection were not supported by histologic evidence of infection in 38.1% and 26.8% of cases, respectively, suggesting other noninflammatory causes of signs and symptoms. Another study by Roberts et al[36] concluded that 96% of histologic chorioamnionitis cases occurred without infection, suggesting that there may be alternative causes among low-risk women at term.

Here, the presence of inflammation in a substantial proportion of the "low-suspicion BS" group could be supportive of the assertion that not all placental

TABLE 1
Maternal and neonatal demographics of results

Maternal demographics	n (%)
N	117
Multiparous	26 (17.7)
Primiparous	91 (82.3)
Mean age (y)	29.8
Mean gestation (wk)	39 6/7
Mean BMI (kg/m^2)	26.1
Maternal comorbidities	
Preeclampsia, n	5
Fatty liver disease, n	1
Gestational diabetes mellitus, n	6
Inflammatory bowel disease, n	2
Known vaginally colonized GBS, n	7
Risk factors for intrapartum pyrexia	
Epidurals	95 (81.2)
Fetal blood samples	11 (9.4)
Induction of labor	76 (64.9)
Mean time from ruptured membranes and delivery (h)	23.8
Augmentation of labor with oxytocin infusion, n/N (%)	20/41 (48.8)
Location of delivery	
Obstetrical theater	58 (49.6)
Obstetrical-led delivery suite	56 (47.8)
Midwifery-led unit	3 (2.6)
Mode of delivery	
Normal vaginal delivery	26 (22.2)
Ventouse-assisted delivery	10 (8.5)
Forcep-assisted delivery	41 (35.1)
Emergency cesarean delivery	40 (34.2)
Maternal intravenous antibiotic length of course	
24 h	86 (73.5)
48 h	25 (21.4)
72 h	6 (5.1)
Completed a 5- to 7-day course of oral antibiotics during discharge from the hospital	117 (100)
Neonatal demographics	
N	117
Female	62 (52.9)
Male	55 (47.1)
Mean birthweight (g)	3458
Other features	
Meconium	29 (24.8)
Fetal tachycardia before delivery	47 (40.2)
Admission to the NICU	15 (12.8)
Neonates requiring assisted ventilation	11 (9.4)
Average day of discharge (d), median (interquartile range)	6.6 (2–13)
Neonatal intravenous antibiotic length of course	
36 h	46 (39.3)
48 h	29 (24.8)
72 h	10 (8.5)
5 d	29 (24.8)
7 d	3 (2.6)

Data are presented as number (percentage), unless otherwise specified.

BMI, body mass index; *GBS*, group B *Streptococcus*; *NICU*, neonatal intensive care unit.

Walker. Procalcitonin levels in intrapartum pyrexia and suspected chorioamnionitis. Am J Obstet Gynecol Glob Rep 2022.

inflammations are the result of an infection. An alternative, and perhaps more likely, explanation of the findings is that although inflammation in the placenta is caused by local infection, this may be limited to the placenta, cord, and membranes and does not always lead to significant infection in the mother or baby. When inflammation in both maternal and fetal aspects of the placenta was graded, there was a correlation between clinical condition and scores for placental inflammation, with mean scores of 5.5 for "low-suspicion BS," 8.186 for "equivocal BS," and 12.214 for "high-suspicion BS'" (Figure 3). This suggests that the more severe the placental inflammation, the more likely it is to represent a clinically significant infection. However, the spread of the scores in each group limits the use of this scoring system in individual cases.

Strengths and limitations

This study analyzed PCT together with the routine SS investigations in both maternal and neonatal patients, thus reflecting a "real-world" clinical context. We collected a detailed dataset for each patient, ensuring accurate interrogation of each clinical episode.

We did not anticipate such a low number of increased PCT levels in this cohort of women, necessitating a larger cohort to adequately power a study investigating clinical outcomes with PCT levels. However, this finding was important, demonstrating that PCT does not seem to be altered by the physiology of labor, unlike other inflammatory markers in clinical use.

We chose to categorize our cases into "low-suspicion BS," "equivocal BS," and "high-suspicion BS." This approach has been adopted in other studies.[26] We were careful to include validated methods of categorization, such as "Sepsis in Obstetrics Score" and the "Kaiser" scoring for neonates.[19,21] Moreover, we acknowledge that the routine investigation results formed part of this categorization and so any effect may have been artificially strengthened. However, as in the case of CRP, this would have led to an enhanced correlation, where if high

TABLE 2
Total number of maternal and neonatal biomarker and microbiology samples performed and whether the biomarkers were increased or microbiology had positive culture growth

Maternal septic screen blood sample Biomarker	n (%)	Number increased
WCC	115 (98.3)	112 (96.0)
CRP	115 (98.3)	100 (86.0)
PCT	111 (94.9)	6 (5.4)
Lactate	103 (88.1)	—
Maternal postnatal blood sample		
Biomarker	n (%)	Number increased
WCC	100 (85.5)	90 (82.6)
CRP	98 (83.8)	117 (100.0)
PCT	94 (80.4)	39 (41.5)
Maternal microbiology results		
Microbiology sample	n (%)	Positive culture growth
Bloods cultures	115 (98.3)	2 (1.7)
Urine culture	107 (91.5)	2 (1.9)
Low vaginal swabs	100 (85.5)	15 (15.0)
Throat swabs	86 (73.5)	2 (2.3)
Placental swabs	21 (17.9)	6 (28.6)
COVID-19	107 (91.5)	2 (1.9)
Neonatal time 0 blood sample		
Biomarker	n (%)	Number increased
WCC	108 (92.30)	102 (94.40)
CRP	117 (100.00)	7 (5.98)
PCT	85 (72.70)	47 (55.40)
Neonatal day 1 blood sample		
Biomarker	n (%)	Number increased
CRP	117 (100.0)	41 (35.04)
PCT	96 (82.1)	95 (98.9)
Neonatal microbiology results		
Microbiology sample	n (%)	Positive culture growth
Blood cultures	117 (100.0)	0 (0)
Lumbar puncture CSF	26 (22.2)	0 (0)

Data are presented as number (percentage), unless otherwise specified. Increase PCT level=≥0.25 ug/L; increased CRP level = ≥10 mg/L; and increased WCC = >11 × 10^9/L.

CRP, C-reactive protein; *CSF*, cerebrospinal fluid; *PCT*, procalcitonin; *WCC*, white cell count.

Walker. Procalcitonin levels in intrapartum pyrexia and suspected chorioamnionitis. Am J Obstet Gynecol Glob Rep 2022.

TABLE 3
The number of maternal and neonatal participants (N=117) in the 3 determined categories for "low-suspicion BS," "equivocal BS," and "high-suspicion BS

Categorization Variable	Low-suspicion BS	Equivocal BS	High-suspicion BS
Maternal	37 (32)	63 (54)	17 (15)
Neonatal	20 (17)	55 (47)	42 (36)

Data are presented as number (percentage), unless otherwise specified.

BS, bacterial sepsis.

Walker. Procalcitonin levels in intrapartum pyrexia and suspected chorioamnionitis. Am J Obstet Gynecol Glob Rep 2022.

CRP was used to denote "high-suspicion BS," one would anticipate a higher correlation coefficient for CRP.

Conclusion

In a cohort of women managed for intrapartum sepsis during labor, 94.6% had normal PCT levels at the time of the SS, compared with the normal adult population, supporting the evidence that PCT as a biomarker is not influenced by pregnancy or labor. Moreover, 58.5% of women had normal serial PCT levels, consistent with the low number of confirmed bacteremia in this population. The result provided a basis that PCT may complement clinical judgment and interpretation of already used prognostic and diagnostic tests, improving patient care in the management of intrapartum sepsis. Serial PCT measurements may be useful in antibiotic stewardship, predicting the prognosis, monitoring patients, and tailoring therapy to the individual needs of the patients. ■

REFERENCES

1. Greer O, Shah NM, Johnson MR. Maternal sepsis update: current management and controversies. Obstet Gynecol 2020;22:45–55.

2. Tujula B, Kokki H, Räsänen J, Kokki M. Procalcitonin; a feasible biomarker for severe bacterial infections in obstetrics and gynecology? Acta Obstet Gynecol Scand 2018;97:505–6.

3. National Institute for Health and Care Excellence. Procalcitonin testing for diagnosing and monitoring sepsis (ADVIA Centaur BRAHMS PCT assay, BRAHMS PCT Sensitive Kryptor assay, Elecsys BRAHMS PCT assay, LIAISON BRAHMS PCT assay and VIDAS BRAHMS PCT assay). 2015. Available at: http://www.nice.org.uk/guidance/dg18. Accessed March 28, 2022.

4. Agarwal R, Priyadarshini P, Mehndiratta M. Serum procalcitonin in pregnancy-associated sepsis: a case control study. S Afr J Obstet Gynaecol 2019;25:15–9.

5. Velasquez JESUS, Zuleta J, Portilla P, Caicedo K, Portilla L, Patiño J. 864: Usefulness of measuring procalcitonin (PTC) in pregnancy for the initial diagnosis of bacterial infection with systemic features. Am J Obstet Gynecol 2018;218:S514–5.

6. Roche Diagnostics. Electrochemiluminescence immunoassay "ECLIA" for the in vitro quantitative determination of PCT (procalcitonin) in human serum and plasma. 2022. Available at: https://diagnostics.roche.com/global/en/products/params/elecsys-brahms-procalcitonin-pct.html. Accessed March 28, 2022.

7. Woodd SL, Montoya A, Barreix M, et al. Incidence of maternal peripartum infection: a systematic review and meta-analysis. PLoS Med 2019;16:e1002984.

8. Tita AT, Andrews WW. Diagnosis and management of clinical chorioamnionitis. Clin Perinatol 2010;37:339–54.

9. Royal College of Obstetricians and Gynaecologists. Sepsis in pregnancy, Bacterial (Green-top Guideline No. 64a). 2012. Available at: https://www.rcog.org.uk/guidance/browse-all-guidance/green-top-guidelines/sepsis-in-pregnancy-bacterial-green-top-guideline-no-64a/. Accessed March 28, 2022.

10. National Institute for Health and Care Excellence. Intrapartum care for women with existing medical conditions or obstetric complications and their babies. 2019. Available at: https://www.nice.org.uk/guidance/ng121. Accessed March 28, 2022.

11. Towers CV, Yates A, Zite N, Smith C, Chernicky L, Howard B. Incidence of fever in labor and risk of neonatal sepsis. Am J Obstet Gynecol 2017;216: 596.e1–5.

12. Burgess APH, Katz JE, Moretti M, Lakhi N. Risk factors for intrapartum fever in term gestations and associated maternal and neonatal sequelae. Gynecol Obstet Invest 2017;82:508–16.

13. Coker MO, Hoen AG, Dade E, et al. Specific class of intrapartum antibiotics relates to maturation of the infant gut microbiota: a prospective cohort study. BJOG 2020;127:217–27.

14. Tapiainen T, Koivusaari P, Brinkac L, et al. Impact of intrapartum and postnatal antibiotics on the gut microbiome and emergence of antimicrobial resistance in infants. Sci Rep 2019;9:10635.

15. Vijayan AL, Vanimaya Ravindran S, et al. Procalcitonin: a promising diagnostic marker for sepsis and antibiotic therapy. J Intensive Care 2017;5:51.

16. Schuetz P, Beishuizen A, Broyles M, et al. Procalcitonin (PCT)-guided antibiotic stewardship: an international experts consensus on optimized clinical use. Clin Chem Lab Med 2019;57:1308–18.

17. Redline RW, Faye-Petersen O, Heller D, et al. Amniotic infection syndrome: nosology and reproducibility of placental reaction patterns. Pediatr Dev Pathol 2003;6:435–48.

18. Khong TY, Mooney EE, Ariel I, et al. Sampling and definitions of placental lesions: Amsterdam placental workshop group consensus statement. Arch Pathol Lab Med 2016;140:698–713.

19. Albright CM, Ali TN, Lopes V, Rouse DJ, Anderson BL. The Sepsis in Obstetrics Score: a model to identify risk of morbidity from sepsis in pregnancy. Am J Obstet Gynecol 2014;211: 39.e1–8.

20. Kuzniewicz MW, Walsh EM, Li S, Fischer A, Escobar GJ. Development and implementation of an early-onset sepsis calculator to guide antibiotic management in late preterm and term Neonates. Jt Comm J Qual Patient Saf 2016;42:232–9.

21. Kaiser Permanente Division of Research. Neonatal early-onset sepsis calculator. 2022. Available at: https://neonatalsepsiscalculator.kaiserpermanente.org. Accessed March 28, 2022.

22. Gregoriano C, Heilmann E, Molitor A, Schuetz P. Role of procalcitonin use in the management of sepsis. J Thorac Dis 2020;12 (Suppl1):S5–15.

23. Rhee C. Using procalcitonin to guide antibiotic therapy. Open Forum Infect Dis 2016;4: ofw249.

24. Hu R, Han C, Pei S, Yin M, Chen X. Procalcitonin levels in COVID-19 patients. Int J Antimicrob Agents 2020;56:10651.

25. Peters C, Williams K, Un EA, et al. Use of procalcitonin for antibiotic stewardship in patients with COVID-19: a quality improvement project in a district general hospital. Clin Med (Lond) 2021;21:e71–6.

26. Do SC, Miller H, Leonard SA, et al. Lactate and procalcitonin levels in peripartum women with intraamniotic infection. Am J Obstet Gynecol MFM 2021;3:100367.

27. Dockree S, Brook J, James T, Shine B, Vatish M. A pregnancy-specific reference interval for procalcitonin. Clin Chim Acta 2021;513:13–6.

28. Joyce CM, Deasy S, Abu H, Lim YY, O'Shea PM, O'Donoghue K. Reference values for C-reactive protein and procalcitonin at term pregnancy and in the early postnatal period. Ann Clin Biochem 2021;58:452–60.

29. Lee J, Bang YH, Lee EH, Choi BM, Hong YS. The influencing factors on procalcitonin values in newborns with noninfectious conditions during the first week of life. Korean J Pediatr 2017;60:10–6.

30. Coburn B, Morris AM, Tomlinson G, Detsky AS. Does this adult patient with suspected bacteremia require blood cultures? JAMA 2012;308:502–11.

31. Schuetz P, Mueller B, Trampuz A. Serum procalcitonin for discrimination of blood contamination from bloodstream infection due to coagulase-negative staphylococci. Infection 2007;35:352–5.

32. Laukemann S, Kasper N, Kulkarni P, et al. Can we reduce negative blood cultures with clinical scores and blood markers? Results from an observational cohort study. Medicine (Baltimore) 2015;94:e2264.

33. Jessop F, Sebire NJ. Histological chorioamnionitis: current concepts of diagnosis, classification and clinical significance. Fetal Matern Med Rev 2011;22:25–44.

34. Smulian JC, Shen-Schwarz S, Vintzileos AM, Lake MF, Ananth CV. Clinical chorioamnionitis and histologic placental inflammation. Obstet Gynecol 1999;94:1000–5.

35. Goldstein JA, Gallagher K, Beck C, Kumar R, Gernand AD. Maternal-fetal inflammation in the placenta and the developmental origins of health and disease. Front Immunol 2020;11:531543.

36. Roberts DJ, Celi AC, Riley LE, et al. Acute histologic chorioamnionitis at term: nearly always noninfectious. PLoS One 2012;7: e31819.