European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 10, Issue 1, Winter 2023

ORIGINAL RESEARCH

Pre & Postpartum Leukocyte Difference: A Predictor of postpartum maternal infectious morbidity and neonatal outcome

[1]Dr. Rashmi Bajpai, [2]Dr. Priyanka Verma, [3]Dr. Nishi Mitra, [4]Dr. Shweta Chaurasia

[1,2]Assistant Professor, [3]Associate Professor, [4]PG 3year, (Dept of Obstetrics & Gynecology), L N Medical College & Research Center, J K Hospital, Bhopal, Madhya Pradesh, India

Corresponding Author
Dr. Shweta Chaurasia
PG 3year, (Dept of Obstetrics & Gynecology), L N Medical College & Research Center, J K Hospital, Bhopal, Madhya Pradesh, India
Email: Shubhshweta0@gmail.com

Received: 10 November, 2022 Accepted: 13 December, 2022

ABSTRACT

Background: Clinically, an increase in the White Blood Cells (WBC) count is regarded as an active sign of an infection. However, the WBC count also increases throughout pregnancy and declines only during the late postpartum period.

Aim and objectives:To determine the association between the change in the maternal leukocyte count (between admission and post-partum) and the incidence of Postpartum Infectious Maternal morbidity (PPIM) among afebrile women with term pregnancy.

Material and Methods: This was a single centre, hospital-based, prospective observational study involving 185 pregnant women coming for delivery. We collected data on obstetric details, total WBC count (at admission and within 24 hours after delivery), and maternal and neonatal outcomes.

Results: Overall, among the 185 study participants, only 12 women were diagnosed with PPIM (6.5%). The mean WBC count before (10,200) and after (15,200) delivery among women who developed PPIM was statistically highly significant ($p<0.0001$). The difference in the mean delta counts for women having puerperal fever was highly significant ($p<0.0001$). However, the delta WBC count was not significant for women having abnormal lochia ($p=0.067$). Among neonatal outcomes, the delta WBC count was statistically significant for low APGAR score @ five minutes and developing neonatal sepsis. The delta WBC count was statistically insignificant for admission to NICU ($p=0.072$).

Conclusion: A higher delta leukocyte count between admission for labour and the postpartum period was a significant risk predictor of PPIM.

Key words: Leukocyte count; Maternal infectious morbidity; Neonatal infectious morbidity; Postpartum.

INTRODUCTION

Puerperal sepsis is an infective condition following the birth of the child i.e., during the postpartum period(1). Puerperal sepsis is defined as an "infection of the genital tract occurring anytime between the onset of rupture of membrane or labour and 42 days day postpartum"(1).As per World Health Organization's report, puerperal sepsis is the third most common cause of maternal death worldwide after postpartum haemorrhage and unsafe

abortion(2,3). Postpartum infections also present a significant social burden: they increase maternal anxiety and the risk of postpartum depression, interfere with bonding, and negatively impact breastfeeding(4,5). The medical burden of these infections is compounded by the alarmingly rapid increase in bacterial resistance to commonly used antibiotics(3,6,7). Neutrophilicleucocytosis commonly presents in conjunction with infection,stress, smoking, pregnancy and following exercise, andis attributed to the movement of neutrophils from themarginated pool into the circulating pool(8–10). Pregnancy is associated withleucocytosis,the leukocyte count begins to rise during thefirst trimester of pregnancy andcontinues to increase in the second and thirdtrimesters(9,10). However, data are limited regarding White Blood Cell (WBC) count during labour and puerperium(11,13). Due to the unique physiologic state of theparturient, diagnosing a puerperal infection poses a clinical challenge(12,14). The rise in the leukocytes count during pregnancy and labour raises questions about a possible correlation with maternal or neonatal infection, especially among afebrile pregnant women at admission for labour(13–15).The difference between admission and post-partum (24 hrs) leukocyte count (Δ Leukocyte)was calculated and its association with post-partum maternal infectious morbidity and neonatal outcome was seen.

MATERIAL AND METHODS

This was a single-centre hospital based, prospective, observational studyconducted at the Department of Obstetrics & Gynaecology, LN Medical College, Bhopal. The data collection for the present study was initiated after the research protocol approval by the Institute's Ethical Committee. The total duration of the study was 12 months. Primary Outcome studied :The incidence of postpartum maternal infectious morbidity which included: (a) puerperal fever (oral temperature >38ºC on any two of the first five days postpartum), (b) Any wound infection, (c) abnormal lochia, and (d) extended hospitalization (>5 days for normal delivery &>8 days for caesarean section)(1) . Secondary Outcomes included : early neonatal sepsis, APGAR score <8 @five minutes, and admission to NICU. A total of 185 women at term (>37 weeks)with uncomplicated pregnancy admitted for labour and delivery /Caesarean section were included. (16) All pregnant women of more than 37 weeks of gestation,with Singleton, uncomplicated, live pregnancy,who delivered within 48 hours of admission ,giving written informed consent to participate were included in the study.Pregnant women with less than 37 weeks of gestation,with PPROM, with History of PROM > 6 hours,Chorio-amnionitis, Urinary Tract Infection, Pneumonia, any febrile illness at the time of admission, and ongoing antibiotic therapy at the time of admission also who refused to give written informed consent to participate in the study were excluded from the study.The study protocol required two records of routine Complete Blood Count (CBC), first at admission and second within 24 hours after delivery/ caesarean section. Blood samples were collected as per standard institutional procedure and transported to the laboratory, analysedina single laboratory, using automated computerized analysers.Pre/Postpartum difference of leukocytes in numbers was calculated. Continuous variables in the two comparison groups were analysed using a student's t-test and categorical variables were analysed using chi-square (χ^2) tests. A *P*-value < 0.05 was considered statistically significant.

RESULTS

Overall, among the 185 study participants, only 12 women were diagnosed with PPIM (6.5%). The characteristics of the study participants are described in Table 1. The percent of women who gave birth to a child through caesarean section and who did and did not havePPIM was 10.5% and 89.5%, respectively. The percent of women who had a normal vaginal delivery with and without PPIM was 1.2% and 98.8%, respectively. The Chi-square

test for the distribution between the type of delivery and the incidence of PPIM was statistically significant (0.012).

Table 1: Descriptive Characteristics of the participants (n=185)

Variable	No PPIMn (%)	PPIMn (%)	P value
Agein years			
<=25	71 (41.)	5 (41.7)	
26-35	87 (50.3)	6 (50.0)	
36 or more	15 (8.7)	1 (8.3)	
Mean	24.3	26.2	0.395
Type of Delivery			
Vaginal	79 (98.8)	1 (1.2)	0.012
C-Section	94 (89.5)	11 (10.5)	

Table 2 shows the details about the WBC counts among the women who did and did not have PPIM in the present study. The mean WBC count among women who did not have PPIM at the time of admission and after delivery was 10,200 and 9300. Further, the difference in the mean WBC count before and after the delivery was statistically non-significant (p=0.325). The mean WBC count before and after delivery among women who developed PPIM was 10,200 and 15,200. Moreover, the difference in WBC count before and after the delivery was statistically highly significant (p<0.0001).

Table 2: White Blood Cell count before and after the birth (n=185)

WBC count	Before Childbirth	After Childbirth	P- Value
Mean	10100 (±2928)	10600 (±3190)	0.169
Median	9800	10400	
Range	4800-23,200	5100-22200	
No PPIM			
Mean	10200	9300	0.325
Median	9900	9500	
Range	5600-23,200	4600-16100	
PPIM			
Mean	10200	15200	<0.0001
WBC count	Before Childbirth	After Childbirth	P- Value
Mean	10100 (±2928)	10600 (±3190)	0.169

Table 3 illustrates the delta WBC count (Post-delivery minus Pre-delivery) . The difference in the mean delta counts for women having puerperal fever was highly significant (p<0.0001). Furthermore, the difference in the mean delta WBC counts was also statistically significant for women developing wound infection and prolonged hospital stay (p<0.05). However, the delta WBC count was not significant for women having abnormal lochia (p=0.067). Among neonatal outcomes, the delta WBC count was statistically significant for low APGAR score @ five minutes and developing neonatal sepsis. The delta WBC count was statistically insignificant for admission to NICU (p=0.072). The adjusted odds ratio for developing PPIM (dependent variable) and the delta leukocytes count (independent variable) was 2.9 (AOR= 2.9; 95% CI 1.7-4.2, p= 0.039).

Table 3: Various study outcomes and Delta Leucocyte count among the participants (n=185)			
Outcome	**Delta-WBC count (mean)**		**P-value**
	Yes	**No**	
Maternal Outcome			
Puerperalfever (n=12)	5800	400	<0.0001
AbnormalLochia(n=31)	2900	1100	0.067
WoundInfection (n=17)	4400	700	0.002
Extended Hospitalization (n=33)	3100	1200	0.019
Neonatal Outcomes			
Admission to NICU (n=56)	1100	200	0.072
APGAR score @5 minutes <8 (n=29)	2200	700	0.027
Early Neonatal Sepsis (n= 18)	4400	600	0.032

DISCUSSION

The problem possessed by maternal sepsis is exacerbated by widespread bacterial resistance to routinely prescribed antibiotics. Other than maternal death, postpartum sepsis has several adverse consequences (short & long-term) both for the mother and her newborn(3,7). Towards this end, it will be very useful if 'at risk' women for puerperal sepsis could be identified at the earliest. Moreover, it will be even better, if any such method employed to identify such women is cost-effective and routinely available at all levels of healthcare facilities.

Several studies have earlier reported the leukocyte count and differential count in healthy pregnant women(8,9,13,17). The mechanism at the basis of this phenomenon has not been elucidated yet and suggested mechanisms include the high levels of estrogen and cortisol in late pregnancy(11,18,19). This physiological increase in WBCs count during labour and immediate postpartum raises the challenges of the utility of maternal leukocyte level in the prediction and management of peripartum infectious complications(20–22).

In the present study, among the women who did not have PPIM, the difference in the WBCs count before (10,200) and after (9300) delivery was statistically insignificant (p=0.325). The mean WBC count before (10,200) and after (15,200) delivery among women who developed PPIM was statistically significant (p<0.0001). For other maternal outcomes, the difference in the mean delta counts for women having puerperal fever was highly significant (p<0.0001). Furthermore, the difference in the mean delta WBC counts was also statistically significant for women developing wound infection and prolonged hospital stay (p<0.05). However, the delta WBC count was not significant for women having abnormal lochia (p=0.067).Similar to our findings, Srebnik N et al. (2020) also reported that the maternal leukocyte counts at admission for labour, and the delta leukocyte count were significant predictive indicators for early maternal postpartum infectious morbidity(23). In addition, Dior UP et al. (2013) also reported a positive association between the postpartum maternal leukocyte level and infectious morbidity (defined as postpartum fever)(24). However, Dior UP et al. did not find any association between high leukocyte and neutrophil counts and positive bacterial culture(24).We also observed that the delta leukocyte count of more than 3500/ml was highly associated with PPIM. Similarly, Srebnik N et al. (2020) also reported that a delta leukocyte count of 3700/ml was highly predictive of early PPIM(23). It is hypothesized that the change

in leukocyte count of women at admission for labour and the first 24 h postpartum, augmented by a labour-related stress reaction, may facilitate the women's susceptibility to infection(11,25–27).

Among neonatal outcomes, the delta WBC count was statistically significant for low APGAR score @ five minutes and developing neonatal sepsis. The delta WBC count was statistically insignificant for admission to NICU (p=0.072).Similar to our findings, Srebnik N et al. (2020) also reported that the maternal leukocyte counts at admission for labour, and the delta leukocyte count are significant predictive indicators for adverse neonatal outcome risks(23). In the present study, we observed that the delta leukocyte count of more than 4100/ml was highly associated with early neonatal sepsis. Similarly, Srebnik N et al. (2020) also reported that a delta leukocyte count of 3700/ml was highly predictive ofadverse neonatal outcomes(23). The potential explanation for the association between high delta leukocyte count and the neonatal adverse outcome may be secondary to maternal complications

CONCLUSION

The present study illustrated the potential role of the total leukocyte and neutrophil counts in early labour and the immediate postpartum period. The preliminary findings from our study suggest that delta leukocyte count in early puerperium appears to be a reliable tool for diagnosing a puerperal bacterial infection. We propose that the delta leukocyte count of healthy women in labour should be regarded as a subtle and significant risk predictor of early PPIM. We suggest that the leukocyte level, an easily measurable and reproducible tool, can be used in the labour room algorithmsto determine maternal and neonatal management.These findings should encourage physicians to combine their clinical judgment and laboratory tests to make a diagnosis of puerperal sepsis/PIM. However, we need routinely collected empirical data from more than one hospital/site involving a much larger population before a definite conclusion could be reached about the potential role of WBCs count in the prediction of PPIM.

CONFLICTS OF INTEREST

None

SOURCE OF FUNDING

NA

REFERENCES

1. Bonet M, Pileggi VN, Rijken M, al. et. Towards a consensus definition of maternal sepsis: results of a systematic review and expert consultation. Reprod Heal. 2017;14:67.
2. Say L, Chou D, Gemmill A, al. et. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Heal. 2014;2:e323–33.
3. Group GM and NSIW. The Global Maternal and Neonatal Sepsis Initiative: a call for collaboration and action by 2030. Lancet Glob Heal. 2017;5:e390–1.
4. Bonet M, Souza J, Abalos E, al. et. The global maternal sepsis study and awareness campaign (GLOSS): study protocol. Reprod Heal. 2018;15:16.
5. Rudd K, Johnson S, Agesa K, al. et. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. Lancet. 2020;395:200–11.
6. Cornelissen L, Woodd S, Shakur-Still H, al. et. Secondary analysis of the WOMAN trial to explore the risk of sepsis after invasive treatments for postpartum hemorrhage. Int J Gynaecol Obs. 2019;146:231–7.
7. Bonet M, Brizuela V, Abalos E, Cuesta C, Baguiya A, Chamillard M, et al. Frequency

and management of maternal infection in health facilities in 52 countries (GLOSS): a 1-week inception cohort study. Lancet Glob Heal [Internet]. 2020 May 1 [cited 2022 Aug 5];8(5):e661–71. Available from: http://www.thelancet.com/article/S2214109X20301091/fulltext

8. Chen H, Zhang Z, Zhou Y, Liu Y, Lin X, Wei Y, et al. Maternal leucocyte trajectory across pregnancy associated with offspring's growth. Pediatr Res [Internet]. 2021 Nov 8 [cited 2022 Aug 5]; Available from: http://www.ncbi.nlm.nih.gov/pubmed/34750526
9. Pitkin RM, Witte DL. Platelet and Leukocyte Counts in Pregnancy. JAMA J Am Med Assoc. 1979 Dec 14;242(24):2696–8.
10. Lurie S, Weiner E, Golan A, Sadan O. Total and Differential Leukocyte Count Percentiles in Healthy Singleton Term Women during the First Stage of Labor. Gynecol Obstet Invest [Internet]. 2014 Apr 18 [cited 2022 Aug 5];78(4):251–4. Available from: https://www.karger.com/Article/FullText/365084
11. Acker DB, Johnson MP, Sachs BP, Friedman EA. The leukocyte count in labor. Am J Obstet Gynecol [Internet]. 1985 Dec 1 [cited 2022 Aug 5];153(7):737–9. Available from: https://pubmed.ncbi.nlm.nih.gov/4073137/
12. Churgay CA, Smith MA, Blok B. Maternal fever during labor--what does it mean? J Am Board Fam Pract. 1994 Jan;7(1):14–24.
13. Molberg P, Johnson C, Brown TS. Leukocytosis in labor: what are its implications? Fam Pract Res J. 1994;14(3):229–36.
14. Shapiro MF, Greenfield S. The complete blood count and leukocyte differential count. An approach to their rational application. Ann Intern Med. 1987;106(1):65–74.
15. Wu PL. Significance of total leukocytes and differential counts. Zhonghua Hu Li Za Zhi. 1993 Jul;28(7):423–4.
16. Charan J, Biswas T. How to Calculate Sample Size for Different Study Designs in Medical Research? Indian J Psychol Med [Internet]. 2013 Apr [cited 2022 Jan 30];35(2):121. Available from: /pmc/articles/PMC3775042/
17. Fleming AF, Harrison KA. Leucocyte counts during pregnancy and the puerperium and at birth in Nigerians. East Afr Med J. 1985;62(3):175–84.
18. Dhabhar FS, Malarkey WB, Neri E, McEwen BS. Stress-induced redistribution of immune cells—From barracks to boulevards to battlefields: A tale of three hormones – Curt Richter Award Winner. Psychoneuroendocrinology. 2012 Sep 1;37(9):1345–68.
19. Efrati P, Presentey B, Margalith M, Rozenszain L. Luekocytes of normal pregnant women. Obs Gynecol. 1964;23:429–32.
20. Edelstam G, Lowbeer C, Kral G, Gustafsson SA, Venge P. New reference values for routine blood samples and human neutrophilic lipocalin during third-trimester pregnancy. Scand J Clin Lab Invest. 2001;61:583–92.
21. Tysoe FW, Lowenstein L. Blood volume and hematologic studies in pregnancy and the puerperium. Am J Obs Gynecol. 1950;60:1187–205.
22. Andrews WC, Bonsnes RW. The leucocytosis during pregnancy. Am J Obs Gynecol. 1951;61:1129–35.
23. Srebnik N, Michaeli J, Shalev L, Ruchlemer R, Farkash R, Grisaru-Granovsky S. The maternal leukocyte count at admission for labor is indicative of early maternal postpartum infectious morbidity and adverse neonatal outcome. Eur J Obstet Gynecol Reprod Biol [Internet]. 2021;258:9–15. Available from: https://doi.org/10.1016/j.ejogrb.2020.12.032
24. Dior UP, Kogan L, Elchalal U, Goldschmidt N, Burger A, Nir-paz R, et al. Leukocyte blood count during early puerperium and its relation to puerperal infection y. 2013 Jan [cited 2022 Aug 5];7058(1):1–6. Available from: https://www.tandfonline.com/doi/abs/10.3109/14767058.2013.799653
25. Schoenfeld Y, Schindel D, Nery A. Leukocytosis during labor and delivery. Harefuah.

1983 Jan 16;104(2):69–70.

26. Arbib N, Aviram A, Gabbay Ben-Ziv R, Sneh O, Yogev Y, Hadar E. The effect of labor and delivery on white blood cell count. Sep [cited 2022 Aug 5];29(18):2904–8. Available from: https://www.tandfonline.com/doi/abs/10.3109/14767058.2015.1110572
27. Sivasankar R, Kumar RA, Baraz R, Collis RE. The white cell count in pregnancy and labour: a reference range. https://doi.org/103109/147670582014932765 [Internet]. 2015 May 1 [cited 2022 Aug 5];28(7):790–2. Available from: https://www.tandfonline.com/doi/abs/10.3109/14767058.2014.932765