ORIGINAL RESEARCH PAPER
Volume - 13 | Issue - 10 | October - 2024 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

PREDICTION OF PRETERM BIRTH ON THE BASIS OF COMPLETE MATERNAL HEMOGRAM-A PROSPECTIVE OBSERVATIONAL STUDY

Obstetrics & Gynaecology

Dr. Inchara S* Postgraduate, Dept of Obstetrics and Gynaecology, Vijayanagar Institute Of Medical Sciences Ballari. *Corresponding Author

Dr. Chandrashekhar T Professor, Dept of Obstetrics and Gynaecology, Vijayanagar Institute Of Medical Sciences Ballari.

Dr. Shamili Kantamneni Assistant Professor, Dept of Obstetrics and Gynaecology, Vijayanagar Institute Of Medical Sciences Ballari.

Dr. Nikhitha CU Postgraduate, Dept of Obstetrics and Gynaecology, Vijayanagar Institute Of Medical Sciences Ballari.

ABSTRACT

Prematurity is defined as a birth that occurs before 37 completed weeks (less than 259 days) of gestation. It is associated considerable risk of morbidity and mortality, particularly among extremely preterm infants. It complicates 5-8% of pregnancies in most developed and developing countries and incidence is still increasing worldwide. This study was aimed to estimate the importance of complete blood count parameters like neutrophils, neutrophil to lymphocyte parameters, platelet to lymphocyte parameters for predicting the timing of birth in threatened preterm labour cases. This prospective observational study was conducted in Department of OBG, Vijayanagar Institute of Medical Sciences, Ballari, between 01st August 2023 to 31 st January 2024. Gestational week at delivery showed weak negative correlations with LMR (Lymphocyte- to-Monocyte Ratio) ($r^* = -0.211$, $p = 0.03^*$) and CRP (C-Reactive Protein) ($r^* = -0.06$, $p = 0.56$), indicating that higher LMR and lower CRP levels may be associated with longer gestational periods. The correlations for WBC (White Blood Cell count) and NLR (Neutrophil-to- Lymphocyte Ratio) were not significant (NS). As a result, only WBC was found to be a valuable parameter in predicting preterm labor and PPROM, as the CBC test is a cheap and routinely applied test. Although increased LMR levels were demonstrated to be associated with preterm birth and threatened preterm labor, respectively, to be able to extrapolate these findings into clinical daily practice, further studies are needed.

KEYWORDS

INTRODUCTION

Preterm birth may be defined as birth between the age of viability and before 37 completed weeks of gestation and complicates 5-8% of pregnancies in most developed and developing countries and incidence is still increasing worldwide.[1] The term "premature rupture of membranes" (PROM) refers to the amniotic fluid leaking before the onset of labour. Preterm premature rupture of the membranes is what is meant if this happens before 37 weeks of pregnancy (PPROM).The association between maternal anemia and preterm delivery is controversial. Several studies have showed that maternal anemia was associated with preterm labor,[2] whereas some studies found no correlation between maternal anemia and poor pregnancy outcomes including preterm delivery.[3]

Prediction of preterm birth is important for saving time for health workers and pregnant women to perform the necessary interventions. Many markers have been used to predict preterm labour. These include the patient's history, evaluation of maternal signs and symptoms, a clinical examination, biochemical markers, and cervical length. Cervical evaluation by transvaginal sonography, and foetal fibronectin and interleukin-6 levels appear to be the best method for predicting preterm birth.[3,4] Although preterm labour is the most common cause of perinatal morbidity and mortality, its aetiology is still unclear.

The signs of clinical inflammation have been described as fever, pain, redness, and swelling. These manifestations can be because of the release of inflammatory mediators which affect the blood vessels and tissues. On the contrary, we have known about subclinical inflammation in which there can be infiltration of the tissues with neutrophils, lymphocytes, and macrophages but they will not lead to the signs of the classical clinical inflammation. Various theories have been proposed which impart the role of both clinical and subclinical infection in the causation of Preterm labor .

Various methods can evaluate intrauterine infection – the systemic immune response to intrauterine infection results in the release of neutrophils and lymphocytes. An increase in these cells is indicative of subclinical infection [12]. Various scoring systems such as platelet-lymphocyte ratio (PLR) and neutrophil-lymphocyte ratio (NLR) are used to predict the prognosis of inflammatory diseases In Threatened PTL patients, due to inflammation and possible ongoing ischemia process, platelet activation indices like MPV and PDW should be altered than the controls. Previous studies suggested that in inflammation via some cytokines, the platelets size and volume alter differently: in low grade inflammatory disorders, by the involvement of the large platelets in thrombi, MPV values may increase.[6]

On the other hand, in high grade inflammatory conditions, the consumption of the large platelets at the inflammation site cause a decrease in MPV levels. It is well known that pregnancy itself and also labor causes platelet activation. Platelet indices also vary depending on the gestational week. In general, dilutional thrombocytopenia exists with an compensatory increase in MPV and PDWlevels during the pregnancy.[6] Cardiovascular risk factors like smoking status, hypertension, dyslipidemia, diabetes also affect the size of platelets.[7,8]

This study was aimed to estimate the importance of complete blood count parameters like neutrophils, neutrophil to lymphocyte parameters, platelet to lymphocyte parameters for predicting the timing of birth in threatened preterm labour cases.

METHODOLOGY

This prospective observational study was conducted in Department of OBG, Vijayanagar Institute of Medical Sciences, Ballari, between 01st August 2023 to 31 st January 2024.The local Institutional Board of Ethics approved the study and signed informed consent was obtained from participants. All patients with diagnosis of threatened preterm labour (>28 weeks and <36 weeks 6 days of gestation) and controls who are ≥ 37 weeks of gestation were included in the study. A minimum of 35 pregnant women with threatened pre term, 35 not in labour pregnant women who are of ≥ 37 weeks of gestation(controls)were included in the study. After taking an informed written consent and after fulfilling the inclusion criteria patients were enrolled for the study.

Inclusion Criteria

All cases who fulfill the diagnostic criteria of Threatened preterm(cases) and pregnant women who were ≥37 weeks of gestation and not in labour (controls) were included in the study

Exclusion Criteria

1. Patients with chronic inflammatory diseases(i.e. connective tissue disorders, rheumatoid arthritis,renal or hepatic insufficiency, hemoglobinopathies)

2. Diabetes mellitus
3. Hypertensive disorders
4. Previous myocardial infarction
5. Previous thrombosis history
6. Patients with urinary tract infection
7. Chronic anemia
8. Uterine anomalies
9. PPROM

Detailed history including socio demographic history, history of pre term labour, h/o pregnancy loss, history of fever, history of local infection, obstetric history and past medical history were elicited. General and systemic examination ,systemic examination including per speculum and per vaginal examination were done and investigation such as complete haemogram, CRP, Urine routine , urine culture sensitivity, vaginal swab and culture sensitivity will be done. All patients were treated with antibiotics and antenatal steroid prophylaxis according to institutional protocol. Cases were followed up until delivery and complete haemogram done during admission will be correlated to the timing of delivery. Maternal outcome like mode of delivery, maternal morbidity and perinatal morbidity & mortality were studied.

RESULTS

Table 1 presents a comparison of demographic and obstetric characteristics between Group 1 (Control) and Group 2 (Cases). Both groups showed no significant differences in maternal age, gravidity, parity, maternal weight, height, body temperature, and educational status distribution. Maternal age was similar between Group 1 (24.1 ± 2.5 years) and Group 2 (23.3 ± 3.2 years), as were gravidity (median 2 for both) and parity (median 1 for both), indicating comparable pregnancy histories between the groups. Likewise, there were no significant differences in maternal weight (Group 1: 60.8 ± 07.3 kg; Group 2: 57.2 ± 06.4 kg), height (Group 1: 153.5 ± 4.9 cm; Group 2: 152.8 ± 5.3 cm), or body temperature (Group 1: 36.7 ± 0.6°C; Group 2: 36.8 ± 0.7°C). Educational attainment also showed no significant disparity between the groups, with similar proportions in primary (54.2% vs. 60%), secondary 34.2% vs. 31.4%), and post-secondary (11.4% vs. 8.57%) education categories. However, significant differences were noted in gestational week at delivery and birth weight. Group 1 pregnancies lasted statistically longer on average (39.3± 1.4 weeks) compared to Group 2 (37.4 ± 1.5 weeks) ($p < 0.05$), and infants in Group 1 had significantly higher birth weights (3050 ± 190 g) compared to Group 2 (2880 ± 210 g) ($p < 0.01$). These findings suggest that while both groups share similar demographic and maternal characteristics, Group 1 experienced longer gestational periods and delivered infants with higher birth weights compared to Group 2. (table 1)There were no significant differences (NS) between Group 1 and Group 2 in most serum levels of inflammatory markers and blood parameters, except for NLR (Neutrophil-to-Lymphocyte Ratio) and CRP (C-Reactive Protein). Group 2 had significantly higher NLR and CRP levels compared to Group 1.(Table 2). Gestational week at delivery showed weak negative correlations with LMR (Lymphocyte-to-Monocyte Ratio) ($r^* = - 0.211$, $p = 0.03^*$) and CRP (C-Reactive Protein) ($r^* = -0.06$, $p = 0.56$), indicating that higher LMR and lower CRP levels may be associated with longer gestational periods. The correlations for WBC (White Blood Cell count) and NLR (Neutrophil-to-Lymphocyte Ratio) were not significant (NS) (table 3)

Table 1: Demographic And Obstetric Characteristics Of The Control (group 1) And Cases (Group 2)

Variable	Group 1	Group 2	P Value
Maternal age, yrs	24.1 ± 2.5	23.3 ± 3.2	NS
Gravidity, range	2 (1-3)	2 (0-3)	NS
Weight, kg	60.8 ± 7.3	57.2 ± 6.4	NS
Height, cm	153.5 ± 4.9	152.8 ± 5.3	NS
Body temperature, °C	36.7 ± 0.6	36.8 ± 0.7	NS
Educational status, n (%)			
- Primary	19 (54.2%)	21 (60.0%)	NS
- Secondary	12 (34.2%)	11 (31.4%)	NS
- Post secondary	4 (11..4%)	3 (8.57%)	NS
Gestational week at assessment	38.2 ± 1.1	33.4 ± 2.3	NS
Gestational week at delivery	39.3 ± 1.4	37.4 ± 1.5	< 0.05
Birth weight	3050 ± 190	2880 ± 210	< 0.01

Table 2: Comparison of serum levels of inflammatory markers and the other blood parameters among the Control (Group 1), and cases (Group 2)

Parameters	Group 1 (n = 35)	Group 2 (n = 35)	p-value
WBC count, ×10^3/mm³	8.98 ± 4.3	10.77 ± 3.4	NS
Hemoglobin, g/dL	10.9 ± 0.2	10.4 ± 0.3	NS
Hematocrit	36.9 ± 4.1	33.8 ± 2.7	NS
Platelet count, ×10^3/mm³	219.8 ± 56	238.7 ± 76	NS
NLR	4.57 ± 3.18a,b	4.91 ± 2.77c	< 0.01
PLR	135.8 ± 88	138.7 ± 56	NS
LMR	2.42 ± 2.4	2.88 ± 1.75	0.02
CRP, mg/dL	0.39 ± 1.7	1.1 ± 2.5	0.01

Table 3: Correlations Of Gestational Week At Delivery With Hematological Markers

Hematological Marker	r*	p
WBC	-0.04	0.98
NLR	-0.005	0.57
LMR	-0.211	0.03*
CRP	-0.06	0.56

DISCUSSION

Although various factors are involved in the pathogenesis of preterm labor and PPROM, infection and inflammation play an important role in the onset of preterm labor. The most accurate detection of infection occurs with amniocentesis, which is an invasive procedure.[9] Thus, there is a need to research easier diagnostic methods. Many studies have revealed that maternal and fetal inflammation triggers preterm labor and affects birth weight.[10-12] Various inflammatory markers, including CBC parameters, have been identified as predictive factors in various diseases.[13] Since labor is also an inflammatory response, the role of inflammatory markers such as CRP or CBC parameters has been implicated in term and preterm labor.[14] Analysis of inflammatory markers in addition to CBC parameters may prove to be more informative. NLR is characterized by increased neutrophils and decreased lymphocyte count as a physiological immune response in various stress situations. Based on this informa tion, some researchers have suggested using NLR as an additional infection marker.[15]

Normal human parturition is a multi- factorial physiologic event involving an integrated set of changes within the maternal tissues and fetal membranes. There is mounting evidence that labor is an inflammatory process that is accompanied by increased expression of cell adhesion molecules, chemotactic agents such as interleukin (IL)-8, and proinflammatory cytokines and WBC activation. Despite its significance as a marker of infection, WBC count is normally increased during pregnancy and is strongly affected by factors like stress or physical activity[16,17].Yuan et al[17] conclude that WBC in peripheral blood is primed in preparation for activation dur- ing term and preterm labor. They suggested that this might contribute to the pathophysiological events of parturition. Furthermore, it has been shown that inflammatory cells mainly neutrophils and macrophages massively infiltrate myometrium and cervix during parturition[18]. Although WBC count was suggested to predict upcoming preterm birth, mean WBC count was comparable within the groups, in the present study.

Kim et al.[19] stated that the success of NLR in predicting preterm labor is second only to cervical length. Gezer et al.[20] reported that a high NLR value at the time of admission is an independent risk factor for preterm labor in women with TPL between 34 and 37 weeks of gestation. In a similar study, Ozel et al.[21] found high NLR values in PPROM cases in preterm pregnancies. In our study, although NLR values were higher in the PPROM and TPL groups, there was no statistically sig- nificant difference.

Lymphopenia, which indicates a decrease in cell mediated immunity, has been indicated in many studies. Redistribution and apoptosis of lymphocytes are responsible for lymphopenia incidence.[22,23] But, in our study, lymphocyte values were not statistically significantly different.

Although high leukocyte and CRP values have been used as a marker of intrauterine infection for years,[24] research has shown that the diagnostic sensitivity and specificity of these values is low compared to amniotic cultures.

Platelet activation is mentioned in cases of infection and malignancy.

Ekin et al.[24] reported an increase in platelet counts with a decrease in MPV levels in patients with PPROM compared to control patients. A relationship between PLR values and PPROM and adverse maternal and newborn outcomes were observed in a study.[25] In the present study, no difference was found between the groups in terms of MPV and platelet and PLR values, and no correlation was found with TPL and PPROM.

CONCLUSION

As a result, only WBC was found to be a valuable parameter in predicting preterm labor and PPROM, as the CBC test is a cheap and routinely applied test. Although increased LMR levels were demonstrated to be associated with preterm birth and threatened preterm labor, respectively, to be able to extrapolate these findings into clinical daily practice, further studies are needed.

REFERENCES

1. Arias A. Pratical guide to high-risk pregnancy and delivery: A south Indian perspective. Mol Hum Reprod. 2015;4:135.
2. A.Levy, D.Fraser, M.Katz. Maternal anemia during pregnancy is an independent risk factor for lowbirthweight and preterm delivery. Eur J Obstet Gynecol Reprod Biol, Vol. 122, PP.182–186, 2005.
3. MacDorman MF. Race and ethnic dispar- ities in fetal mortality, preterm birth, and infant mortality in the United States: an overview. Semin Perinatol 2011; 35: 200–208. DOI: 10.1053/j. semperi.2011.02.017.
4. Russell RB, Green NS, Steiner CA, et al. Cost of hospitalization for preterm and low birth weight infants in the United States. Pediatrics 2007; 120: e1–e9. DOI: 10.1542/ peds.2006- 2386
5. Z.M.Lu, R.L.Goldenberg, S.P.Cliver. The relationship between maternal hematocrit and pregnancy outcome. Obstet Gynecol, Vol.71, PP.190–194,1991.
6. A.Turgut, M.E.Sak, A.Ozler. Alterations of peripheral blood cells in tubal ectopic pregnancy. Ginekologica Polsaka J., Vol. 84, PP.193–196, 2013.
7. Q.Zhang, C.V.Ananth, Z.Li. Maternal anaemia and preterm birth: A prospective cohort study. International Journal of Epidemiology, Vol. 38(5), PP.1380-1389,2009.
8. T.T.Lao, T.C.Pun. Anaemia in pregnancy—is the current definition meaningful? Eur J Obstet Gynecol Reprod Biol, Vol. 68, PP.53–58, 1996.
9. Kozlowski P, Knippel A, Stressig R. Individu- al risk of fetal loss following routine second trimester amniocentesis: a controlled study of 20,460 cases. Ultraschall Med. 2008;29(2): 165–72.
10. Stout MJ, Cao B, Landeau M, French J, Ma- cones GA, Mysorekar IU. Increased human leukocyte antigen-G expression at the mater- nal-fetal interface is associated with preterm birth. J Matern Fetal Neonatal Med. 2015; 28(4):454–9.
11. Oaks B, Stewart C, Laugero K, Adu-Afarwuah S, Lartey A, Baldiviez L, et al. Associations of maternal cortisol, inflammation, hemoglo- bin, iron status, and BMI with birth outcomes in pregnant women in Ghana. FASEB J. 2015; 29:579–1.
12. Akgun N, Namli Kalem M, Yuce E, Kalem Z, Aktas H. Correlations of maternal neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) with birth weight. J Matern Fetal Neonatal Med. 2017;30(17): 2086–91.
13. Yasar Z, Buyuksirin M, Ucsular F, Kargi A, Erdem F, Talay F, et al. Is an elevated neutro- phil-to-lymphocyte ratio a predictor of meta- bolic syndrome in patients with chronic ob- structive pulmonary disease. Eur Rev Med Pharmacol Sci. 2015;19(6):956–62.
14. Qiu Y, Wen Y, Li G, Tao Z, Yan X, Zang N, et al. Maternal neutrophil-to-lymphocyte ratio as a prognostic biomarker for placental inflammatory response in late pregnancy. Nan Fang Yi Ke Da Xue Xue Bao. 2018;38(9): 1131–4.
15. De Jager CP, Wever PC, Gemen EF, Kusters R, van Gageldonk-Lafeber AB, van der Poll T, et al. The neutrophil-lymphocyte count ratio in patients with community-acquired pneumo- nia. PLoS One. 2012;7(10):e46561.
16. THOMSON AJ, TELFER JF, YOUNG A, CAMPBELL S, STEW- ART CJ, CAMERON IT, GREER IA, NORMAN JE. Leuko- cytes infiltrate the myometrium during human par- turition: further evidence that labour is an inflam- matory process. Hum Reprod 1999; 14: 229-236.
17. YUAN M, JORDAN F, MCINNES IB, HARNETT MM, NOR- MAN JE. Leukocytes are primed in peripheral blood for activation during term and preterm labour. Mol Hum Reprod 2009; 15: 713-724.
18. OSMAN I, YOUNG A, LEDINGHAM MA, THOMSON AJ, JORDAN F, GREER IA, NORMAN JE. Leukocyte density and pro-inflammatory cytokine expression in hu- man fetal membranes, decidua, cervix and my- ometrium before and during labour at term. Mol Hum Reprod 2003; 9: 41-45.
19. Kim MA, Lee BS, Park YW, Seo K. Serum markers for prediction of spontaneous pre- term delivery in preterm labour. Eur J Clin Invest. 2011;41(7):773–80.
20. Gezer C, Ekin A, Solmaz U, Sahingoz Yildirim AG, Dogan A, Ozeren M. Identification of preterm birth in women with threatened pre- term labour between 34 and 37 weeks of gesta- tion. J Obstet Gynaecol. 2018;38(5):652–7.
21. Ozel A, Alici Davutoglu E, Yurtkal A, Madazli R. How do platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio change in women with preterm premature rupture of membranes, and threaten preterm labour? J Obstet Gynaecol. 2020;40(2):195–9.
22. Obstet Gynaecol. 2020;40(2):195–9. Zahorec R. Ratio of neutrophil to lymphocyte counts: rapid and simple parameter of sys- temic inflammation and stress in critically ill. Bratisl Lek Listy. 2001;102(1):5–14.
23. Hotchkiss RS, Swanson PE, Freeman BD, Tinsley KW, Cobb JP, Matuschak GM, et al. Apoptotic cell death in patients with sepsis, shock, and multiple organ dysfunction. Crit Care Med. 1999;27(7):1230–51.
24. Ekin A, Gezer C, Taner CE, Ozeren M, Uyar I, Gulhan I. Risk factors and perinatal out- comes associated with latency in preterm pre- mature rupture of membranes between 24 and 34 weeks of gestation. Arch Gynecol Ob- stet. 2014;290(3):449–55.
25. Toprak E, Bozkurt M, Dinçgez Çakmak BD, O zçimen EE, Silahlı M, Ender Yumru AE, et al. Platelet-to-lymphocyte ratio: a new in- flammatory marker for the diagnosis of pre- termpremature rupture of membranes. J Turk Ger Gynecol Assoc. 2017;18(3):122–6.