RESEARCH ARTICLE

Prediction of Preterm Birth on the Basis of Complete Blood Count Parameters

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Abstract

Objective: Preterm labor (PL) is the onset of labor pains before 37 weeks and it eventually leads to preterm birth. Preterm birth accounts for 75% of perinatal mortality and more than half the long-term morbidity.[1] Various studies have been done on the ratios of blood cell subtypes like neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), and platelet-to-lymphocyte ratio (PLR) to find out if they can be used as a predictor for diseases in which chronic low-grade inflammation is involved. Inflammation is one of the components in the initiation of PL, so markers of inflammation can be used as a potential predictor of PL. We aimed to study if any association exists between PL and the various blood cell subtypes like NLR, LMR, and PLR in a group of women who were hospitalized with the diagnosis of PL.

Materials and methods: A total of 80 pregnant women were enrolled in the study. Forty cases who were admitted in the maternity ward with the diagnosis of PL and 40 gestational age-matched controls who came for routine antenatal care. The cases were further followed and divided into two groups according to gestational age at which they delivered, i.e., pregnant with PL who delivered <37 weeks and pregnant with PL who delivered at ≥37 weeks. The sociodemographic profile and the biochemical parameters of all the groups were compared.

Results: The study showed that the neutrophils were significantly elevated in pregnant women with PL and lymphocytes reduced. However, the ratios like NLR, LMR, and PLR were not found to be significantly raised in pregnant women with PL when compared with control.

Conclusion: Although we found a significant elevation of neutrophils and a significant reduction of lymphocytes in our study but to use these blood count parameters as a predictor of PL needs more validation. Further measurement of the ratio of subtypes of blood cells like NLR, LMR, and PLR was comparable in both cases and controls.

Keywords: Lymphocytes, Neutrophils, Preterm labor.

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Introduction

Preterm birth is a major clinical problem in the developing country because they have limited resources to handle the problems of a premature baby. The majority of the preterm births occur in South Asia and Africa but it had been a global problem. The survival rate of premature babies born in resource-limited countries lags far behind those of resource-rich countries. Complications of prematurity can be poor feeding, difficulty in respiration, inability to maintain adequate body temperature, and infections. These all can contribute to inflating the neonatal mortality rate. Nearly 75% of perinatal deaths occur in infants born prematurely.[2]

Labor has been traditionally defined as the occurrence of regular uterine contractions which are gradually increasing in intensity, frequency, and duration and it is also associated with cervical dilatation and effacement. Inflammation has been found to play a major role in the pathophysiology of the onset of labor. So, it can be said that inflammation can be responsible for the initiation of preterm labor (PL) as well.[2,3]

Seventy-five percent of women who present with PL will eventually remain undelivered after the initial courses of tocolysis of 48 hours; however, the chances of them delivering prematurely is increased; 65% will eventually deliver before 37 weeks.[3,4]

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.[4]

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Various theories have been proposed which impart the role of both clinical and subclinical infection in the causation of PL.[4,5] Many cases have been reported which time and again have emphasized that histopathological inflammation and chorioamnionitis, both term and preterm delivery, are found to be subclinical in the majority of the cases.[4]

Since a long-time effort is being made to find out specific tests and evaluation modalities like measurement of cervical length, fetal fibronectin testing, and bacterial vaginosis testing to predict the occurrence of PL so we can reduce this global problem of preterm birth, but none of these modalities have been found to improve the perinatal outcome.[1,5]

Recent studies have been done which have shown that inflammation can be measured using various hematological

and biochemical markers. Even the measurement of the ratio of subtypes of blood cells like lymphocyte-to-monocyte ratio (LMR), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) have shown promising results in the prediction of PL.

It has been said that these blood cell subtypes are also increased in infections probably causing inflammation, so they might have a prognostic significance in the prediction of diseases where inflammation is involved.[6,7]

So in our study, we aimed to see if any association exists between the ratios of subtypes of blood cells like LMR, NLR, PLR, and PL.

Materials and Methods

This was a case-control study done in the obstetrics and gynecology department of Era's Lucknow Medical College and Hospital from July 2017 to June 2018. Pregnant females with gestational age between 24 and 37 weeks with intact membranes who were diagnosed with PL were taken as a study group. They were further followed up till delivery. Gestational age-matched controls were taken. Exclusion criteria included all the pregnant women with fever, urinary tract infection, chorioamnionitis, severe anemia, cervical incompetence, preterm premature rupture of membranes, and uterine anomalies. Routine blood tests were done at the time of admission. All the pregnant women were examined for infection, routine urine microscopy and cultures were done, and body temperature was measured. The clinical data including the age, body mass index (BMI), gravidity, parity, the clinical findings of antenatal follow-up, and gestational age at delivery, also the laboratory data and vital findings (body temperature, blood pressure) were recorded for each patient. All pregnant women were followed till delivery. The study was approved by the institutional ethical committee.

Results

Eighty women (40 cases and 40 controls) were enrolled in the study. Based on the time of delivery, the cases were further divided into two groups, i.e., group I who had PL pains and delivered before 37 weeks, group II who had labor pains but they delivered after 37 weeks, and group III was the control group. In Table 1, a comparison of different demographic parameters was done. The age, gravidity, and educational status were found to be similar among all the groups. The mean BMI in group I, group II, and group III were 24.08 $\pm$ 3.18, 25.86 $\pm$ 3.14, and 22.88 $\pm$ 2.04, respectively. The *p* value was 0.002. The mean birth weight in group I, group II, and group III were 2.05 $\pm$ 0.55, 2.55 $\pm$ 0.41, and 2.34 $\pm$ 0.47, respectively. The *p* value was 0.006. So, the study showed that BMI may be one of the factors which are also affecting preterm birth and there was a significant difference in birth weight in the group who are delivering <37 weeks in comparison who are delivering beyond the gestational age of 37 weeks.

In Table 2, various blood parameters and inflammatory marker levels were studied. It was seen that the admission levels of hemoglobin, WBC count, LMR, NLR, and PLR were found to be statistically insignificant between the three groups. The mean C-reactive protein was found to be elevated in groups who delivered prematurely; however, the result was not statistically significant. The neutrophil count was significantly found to be elevated in those who presented with PL and more in those who delivered prematurely. The lymphocyte count was also significantly lower in those who had PL. Eosinophils and monocytes were comparable among the groups.

Discussion

In a study by Daglar et al., LMR was found to be significantly elevated in women who had PL and delivered prematurely.[5] In another study by Melissa et al. again NLR was found to be elevated in PL patients.[6] However, the ratios like LMR, NLR, and PLR were not significant in our study which is a qualitative check to see whether we would be getting any benefit from these studies to predict or withhold the process of PL by implicating any kinds of intervention.

The mechanism involved in the process of labor and delivery in humans has been identified to be an inflammatory process. During pregnancy, the inflammatory responses to a large extent remain inhibited. So, the hypothesis of our study was to find the relationships of different leukocytes with each other and their correlation with PL as these would be the cases where stimulation of different blood cell types in the peripheral blood takes place early and might be responsible for PL.[7]

Yuan et al.[7] in their study found that the number of monocytes and neutrophils was found to be increased in those who were in labor when compared with those who were not. Certain studies have found that it is the neutrophils and monocytes which have increased during the labor and they have been found in higher concentrations in uterine tissues. However, they must rise whenever the women are in labor but there is no difference between patients with PL and those coming in labor at term. Hence in our study, the increase in the neutrophils might be because of the very physiology of labor which is initiated early.[7]

A study done by Pawelczyk et al. found that neutrophil count does not increase in patients with PL when compared with controls but the toll receptors TLR4 on the monocytes increased.[8] This study again supports the fact found in our study that if the receptors are

Table 1: Comparison of different demographic parameters among the three groups of patients

Parameter	*Group I (n = 26)*	*Group II (n = 14)*	*Group III (n = 40)*	*p value*
Maternal age (years)	26.38 $\pm$ 5.32	26.57 $\pm$ 4.89	26.68 $\pm$ 4.12	0.979
Median gravidity (range)	2 (0–8)	2.5 (0–7)	1 (0–5)	0.320
BMI (kg/m^2)	24.08 $\pm$ 3.18	25.86 $\pm$ 3.14	22.88 $\pm$ 2.04	0.002
S-E status				
Lower	0	0	2 (5%)	0.255
Middle	26 (100%)	14 (100%)	35 (87.5%)	
Upper	0	0	3 (7.5%)	
GA (weeks) at assessment	33.15 $\pm$ 2.16	34.89 $\pm$ 1.63	33.10 $\pm$ 2.16	0.019
B. weight (kg)	2.05 $\pm$ 0.55	2.55 $\pm$ 0.41	2.34 $\pm$ 0.47	0.006

Table 2: Comparison of serum levels of inflammatory markers and other blood parameters among patient delivered prematurely (group I), patient who reached term (group II), and control (group III)

Parameter	*Group I (n = 26)*	*Group II (n = 14)*	*Group III (n = 40)*	*p value*
WBC count × 10^3/mm^3	10.16 ± 4.04	10.14 ± 2.31	8.84 ± 2.16	0.140
Hb (g%)	10.45 ± 1.53	11.03 ± 1.34	10.60 ± 1.15	0.418
Hematocrit	28.15 ± 3.20	26.64 ± 3.90	33.18 ± 5.82	<0.001
CRP	8.56 ± 4.86	6.66 ± 1.77	7.40 ± 1.88	0.159
DLC				
Neutrophils	77.23 ± 7.04	74.57 ± 7.65	68.18 ± 10.58	0.001
Lymphocytes	20.15 ± 6.53	20.50 ± 5.46	25.08 ± 5.39	0.002
Eosinophils	2.15 ± 1.38	2.79 ± 2.36	1.98 ± 1.19	0.228
Monocytes	2.00 ± 1.58	3.14 ± 3.33	1.80 ± 1.07	0.059
LMR	8.98 ± 8.81	9.88 ± 7.25	13.71 ± 13.15	0.239
NLR	4.30 ± 1.68	4.06 ± 1.54	4.29 ± 6.04	0.984
PLR	132.32 ± 75.09	119.91 ± 32.75	154.14 ± 216.20	0.746

increasing then the proportion of cells expressing toll receptors must be studied in a large population to get the real picture.

Melissa et al. found in their study that NLR was significantly elevated in preterm births which were similar to the findings by Akkar et al. The rationale behind these studies was the inflammatory response which was stated by Kim et al. as placental inflammatory response and concluded that NLR may be used as a predictor of preterm birth.[6] Raised NLR also indirectly implicates that neutrophils must be increased for such high ratios and need a large sample to study.

In our study, the neutrophil counts were found to be significantly elevated and lymphocytes significantly reduced in women who presented with PL. These findings were in collaboration with the findings of a study done by Gazer et al.[9] Moreover, Gazer et al. found NLR to be significantly higher in PL (coinciding with Melissa et al.).[6,9]

Strength of the Study

To the best of my knowledge, this will be the pioneer Indian study to be done to see the association between inflammatory markers and preterm delivery prediction which will give a better idea about the leukocytic changes in the tropical area as well as Asian races which are more prone for preterm deliveries.

Weakness of the Study

The large sample size for the study is required to get the real picture of leukocytic changes and we should have included the comparison between laboring and non-laboring women at term to know whether this neutrophil rise is a normal phenomenon during labor or it has led to PL.

Conclusion

Although WBC counts are a significant marker of infection they can also be increased in other conditions like stress, physical activity, etc. So to use these ratios (LMR, NLR, and PLR) as predictors of preterm delivery would be too early. Furthermore, studies are required to see if alone neutrophils or lymphocytes can be used as a predictor of preterm delivery.

References

1. Goldenberg RL, Culhane JF, Iams JD, et al. Epidemiology and causes of preterm birth. Lancet 2008;371(9606):75–84. DOI: 10.1016/S0140-6736(08)60074-4.
2. Romero R, Espinoza J, Goncalves LF, et al. Inflammation in preterm and term labor and delivery. Semin Fetal Neonatal Med 2006;11(5):317–326. DOI: 10.1016/j.siny.2006.05.001.
3. Henderson JJ, Mcwilliam OA, Newnham JP, et al. Preterm birth aetiology 2004-2008. Maternal factors associated with three phenotypes: spontaneous preterm labour, preterm pre-labour rupture of membranes and medically indicated preterm birth. J Matern Fetal Neonatal Med 2012;25(6):642–647. DOI: 10.3109/14767058.2011.597899.
4. Fergusan KK, Mcelrath TF, Chen YH, et al. Repeated measures of urinary oxidative stress biomarkers during pregnancy and preterm birth. Am J Obstet Gynecol 2015;212(2):e1–e8. DOI: 10.1016/j.ajog.2014.08.007.
5. Daglar HK, Kirbas A, Kaya B, et al. The value of complete blood count parameters in predicting preterm delivery. Eur Rev Med Pharmacol Sci 2016;20(5):801–805.
6. Melissa CL, Aaron HG, Jonathan HBS, et al. Neutrophil to lymphocyte ratio and red cell distribution width levelsin preterm vs term births. J Mol Genet Med 2018;12(1):317. DOI: 10.4172/1747-0862.1000317.
7. Yuan M, Jordan F, Mcinnes IB, et al. Leukocytes are primed in peripheral blood for activation during term and preterm labour. Mol Hum Reprod 2009;15(11):713–724. DOI: 10.1093/molehr/gap054.
8. Pawelczyk E, Nowicki BJ, Izban MG, et al. Spontaneous preterm labor is associated with an increase in the proinflammatory signal transducer TLR4 receptor on maternal blood monocytes. BMC Pregnancy Childbirth 2010;10:66. DOI: 10.1186/1471-2393-10-66.
9. Gazer C, Ekin A, Solmaz U, et al. Identification of preterm birth in women with threatened preterm labour between 34 and 37 weeks of gestation. J Obstet Gynaecol 2018;38(5):652–657. DOI: 10.1080/01443615.2017.1399990.