International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2017; 1(1): 14-16
Received: 03-05-2017
Accepted: 04-06-2017

Dr. Khushboo
Senior Resident, Department of Gynecology and Obstetrics, AIIMS Patna, Bihar, India

Dr. Mriganka Mauli Saha
Assistant Professor, Department of Obstetrics and Gynaecology, Kalyani medical college, Kolkata, West Bengal, India

Dr. SC Biswas
Professor, Department of Obstetrics and Gynaecology IPGME & R, Kolkata, West Bengal, India

GS Kamilya
Professor, Department of Obstetrics and Gynaecology IPGME & R Kolkata, West Bengal, India

Correspondence
Dr Khushboo
Senior Resident, Department of Gynecology and Obstetrics, AIIMS Patna, Bihar, India

Role of novel biomarker IL-6 in the prediction of pre-term labor

Dr. Khushboo, Dr. Mriganka Mauli Saha, Dr. SC Biswas and GS Kamilya

Abstract
Objective: To evaluate the diagnostic value of maternal serum interleukin 6 (IL-6), for the prediction of preterm labor. Association of few major maternal high risk factors and occurrence of preterm labor was also studied.
Material and methods: Maternal serum IL-6 were prospectively determined in thirty patients in threatened preterm labor and thirty controls. Data was analyzed in study and control groups. Risk factors studied were - maternal age, socioeconomic status, parity, antenatal checkup, history of preterm labor in previous pregnancy, history of 2 or more spontaneous or induced abortion, vaginal infection.
Results: The strongest risk factor for preterm birth in our study is a previous preterm birth. In this study 60% mothers with history of preterm birth delivered preterm (p value - 0.05). Maternal serum IL-6 levels were significantly higher in the study group than controls. The IL-6 value associated with the highest percent of true positives and true negatives for the prediction of preterm labor was 5 pg/ml.
Conclusions: Maternal serum IL-6 is a reliable marker in the prediction and management of preterm labor and delivery.

Keywords: Preterm labour, Interleukin-6, High risk factors

1. Introduction
With its high morbidity and mortality, preterm delivery is major obstetric problem. Spontaneous preterm birth complicates 3-11% of pregnancies [1] and is a major cause of neonatal mortality and morbidity worldwide [1]. The incidence of preterm birth is increasing.
Its complications can be reduced by timely diagnosis and interventions to delay delivery, administration of corticosteroids and of neonatal care.
Currently there is no routine screening test for spontaneous preterm birth apart from obtaining history of previous pregnancies. The prediction of spontaneous preterm birth is important because it could allow for the identification of women at high risk of preterm birth, in whom a specific intervention could be tested. Being able to predict which women are likely to have a preterm birth is a prerequisite for the effective use of most interventions aimed at preventing preterm birth.
Several biologic and biochemical markers have been recently studied that may allow early identification of patients at risk of preterm delivery. Research is ongoing to identify a chemical or physical marker that predicts whether and when premature delivery will occur.
Based on the known risk factors and pathways of preterm birth [2, 3], several biomarkers have been tested to see if they predict spontaneous preterm birth. Several biologic and biochemical markers have been recently studied that may allow early identification of patients at risk of preterm delivery.
Interleukin 6 (IL6) is a protein compound produced in response to presence of inflammation usually in response to presence of an infection. It can be found in amniotic fluid, cervical secretion and in maternal blood serum. Their presence or increasing values have been purported to predict spontaneous preterm birth in symptomatic women who presented with threatened preterm labor. In this study we aim to assess whether Interleukin 6 concentration in maternal serum is associated with onset of preterm labor.

2. Materials and methods
This parallel group observational study was conducted in department of obstetrics and gynaecology, IPGME&R Kolkata, in collaboration with the Biochemistry department in year 2012-2013.

The study population consisted with of 60 pregnant women with Singleton pregnancy with gestational age 28-37 weeks with no associated medical or surgical illness. These 60 women contained two groups, Group I- Threatened preterm labor cases having regular uterine contraction (at least once every 10 min), spontaneous in onset with no evidence of cervical change (n=30). Group II- Gestational age matched controls not in labor (n=30) were taken from OPD.

All the women in the study were asked for risk factors. Risk factor noted in the study were– Age, Parity, Socioeconomic status, history of regular antenatal checkup during pregnancy – booked (at least two antenatal visits) or unbooked (no antenatal checkup), previous h/o preterm labor, therapeutic abortion (bleeding in first trimester) or spontaneous abortion.

Serum interlukin-6 was measured by sensitive ELISA in biochemistry department. Any medication received by the patient noted.

Finally all patients followed up closely throughout pregnancy and pregnancy outcome noted. Admission delivery interval noted in threatened preterm labor cases who delivered preterm. Mode of delivery & delivery events were noted.

Annova f test was used for calculation.

3. Results

There was no significant difference in demographic profile of study population. Mean age in both groups were comparable; 27.33±4.428 years for cases versus 26.07±4.299 years for controls (*p*=0.266). Mean BMI in both the groups did not show any significant difference. Maximum incidence of preterm labor is in the age group of 25-29 years.

Mean GA at diagnosis in both the groups was 227 days ranging from 196 days to 252 days.

Among 30 cases with threatened preterm labour 12 (40 %) delivered preterm and rest were continued till term, while among 30 controls 20% delivered preterm(table1). Among all risk factor studied, history of preterm labor in previous pregnancy was most strongly associated with its recurrence.

Table 1: Relationship of history of preterm birth with preterm labor

	NO H/O PTB	H/O PTB
Term delivery	38(90.48%)	4(9.52%)
Delivered preterm	12(66.67%)	6(33.33%)

p value 0.05

6 out of 10 mothers with h/o preterm labor delivered preterm which is a significant data (p value 0.05). Out of 18 cases, who delivered preterm, 12 (66.6%) were multigravida (44.4% 3rd gravida and 22.22% 4th gravida or more).This shows high incidence of preterm labor in multigravida.

Among 18 preterm deliveries, 11 (61.11%) mothers had history of 2 or more spontaneous or induced abortion.

All the mothers were examined for evidence of abnormal genital tract colonization, and no statistically significant association was found between the presence of pathogens in vaginal swab culture and preterm labor.

No statistically significant association was found between, antenatal check-up, socioeconomic status and preterm labor (p value > 0.05)

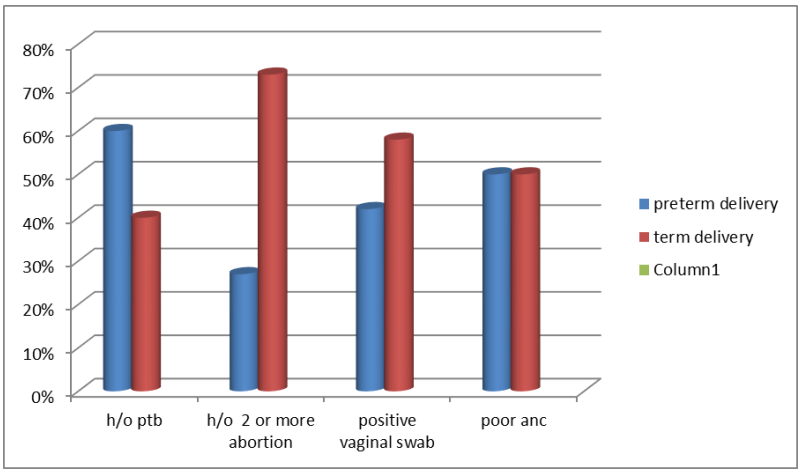

Table 2: Relationship of high risk factors with pre-term labour

In our study there was a significant difference in mean serum interleukin-6 in mothers who delivered preterm (6.12 pm/ml) compared to those who delivered at term (3.11pgm/ml) (p value 0.003).

Mean admission to delivery interval in those who delivered preterm was 3.69 days.

Taking a cut off value of serum IL-6> 5pg/ml; out of 13 mothers with raised serum IL-6 level, preterm delivery occurred in nine mothers (table 3). Sensitivity of raised serum IL-6 for predicting preterm labor is poor- 50% in the study which means only 50% of preterm antenatal cases screened by the test with serum IL-6> 5 pg/ml will deliver preterm (true positive), but decreased serum IL-6 < 5 pg/ml is found to be very specific for ruling out the possibility of preterm labor with specificity of 90% i.e. the mothers with serum IL-6<5pg/ml 90% did not deliver preterm. Positive predictive value is found to be low 69.2% but Negative predictive value of 80.8% is found in the study.

Table 3: Relationship of in interleukin and delivery

Test result	Preterm delivery	Term delivery	Total
S. IL-6 >5 pg/ml	9 (a)	4 (b)	13
S IL-6 <5 pg/ml	9 (c)	38 (d)	47
TOTAL	18	42	60

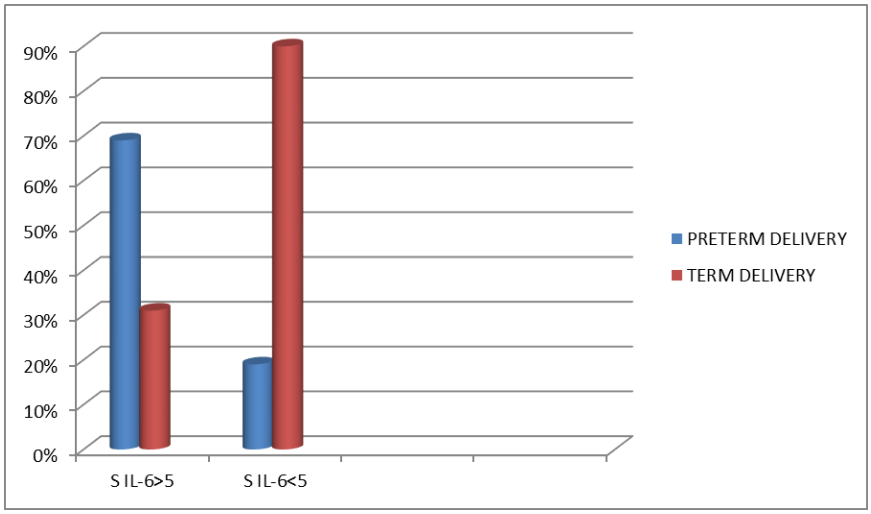

Table 4: Sensitivity of IL-6 as a diagnostic tool.

4. Discussion

The strongest risk factor for preterm birth in our study is a previous preterm birth. In this study 60% mothers with history of preterm birth delivered preterm (p value - 0.05). Similar results were shown by Goldenberg *et al.* [2] study of Epidemiology and causes of preterm birth, in which the recurrence risk in women with a previous preterm delivery ranges from 15% to more than 50%, depending on the number and gestational age of previous deliveries.

The present study shows that maximum number of preterm labor occurred among multigravida, out of 18 cases who delivered preterm, 12 (66.6%) were multigravida (44.4% 3rd gravida and 22.22% 4th gravida or more).

Pratt *et al.* suggested that the highest incidence of prematurity is found in the primigravida and multigravida having 5 or more pregnancies. In Goldenberg RL *et al.* [3] study Bacterial vaginosis has been linked to preterm birth raising the risk by a factor of 1.5 – 3.

In our study there was a significant difference in mean serum interleukin-6 in mothers who delivered preterm (6.12 pgm/ml) compared to those who delivered at term (3.11pgm/ml) (p value0.003). In our study sensitivity of predicting preterm labor is poor- 50%, raised serum IL-6> 5 pgm/ml is found to be very specific for the prediction of preterm labor with specificity of 90%. Positive predictive value is found to be low 69.2% but Negative predictive value of 80.8% is found in the study.

Our results were similar to a study done by Turhan *et al.* [4] ,maternal serum IL-6 levels were significantly higher ,which were pospectively determined in eighty-two patients in preterm labor and 21 controls. The IL-6 value associated with the highest percent of true positives and true negatives for the prediction of preterm labor was 5 pg/ml.

Von Minckwitz G, *et al.* [5] found significantly increased serum levels of interleukin-6 and -8 in patients with preterm labor or preterm rupture of the membranes when compared to the control group (p<0.001 and p<0.005, respectively).

In contrast Sozmen S, *et al.* [6] found no significant relationships between maternal serum concentrations of IL-6 and preterm delivery. Vaginal IL-6 levels were significantly higher in the study group as compared with the control group (P<.001).

5. Conclusion

With its associated morbidity and mortality preterm delivery still represents one of the major unsolved problems in Obstetrics.

The rate of fetal morbidity can be reduced with, the identification of risk factors for preterm labor, early and accurate diagnosis, intervention to delay preterm delivery, administration of corticosteroids and provision of neonatal care.

Research into biochemical markers such as serum IL-6, prolactin and the use of more selective tocolytic therapy offers hope that new therapeutic approaches may increase rates of fetal survival.

So from this small study it is at least evident that on continuing this study over a longer period, and including a large number of subjects, the etiology of preterm labor would become clearer and definite preventive measures can be taken to reduce the incidence of preterm labor and its associated adverse effects.

6. References

1. Maternal and child health consortium.6th annual report: confidential enquiries into stillbirths and deaths in infancy. London: CESDI, 1999.
2. Goldenberg RL *et al.* Epidemiology and causes of preterm birth. Lancet. 2008; 371:75.
3. Goldenberg RL *et al.* Epidemiology and causes of preterm birth. The Lancet. 2008; 371(9606):75-84. doi:10.1016/S0140-6736(08)60074-4.
4. Turhan NO *et al.* Maternal serum interleukin 6 levels in preterm labor: prediction of admission-to-delivery interval. J Perinat Med. 2000; 28:133-9.
5. Von Minckwitz G *et al.* Predictive value of serum interleukin-6 and -8 levels in preterm labor or rupture of the membranes. Acta Obstet Gynecol Scand. 2000; 79:667-72.
6. Sozmen S *et al.* Predictive value of maternal serum and vaginal interleukin-6 levels in preterm labor. J Soc Gynecol Investig. 2005; 12(4):e1-6.