

Association of Iron Deficiency

Anemia with Preterm Labor

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ABSTRACT

Objective: To investigate the association of iron deficiency anemia as a cause of preterm labour.

Study Design: Descriptive/cross sectional study

Place and Duration of Study: This study was conducted at the Department of Obstetrics and Gynaecology, Nishtar Hospital Multan from July 2016 to December 2016

Materials and Methods: After approval from ethical committee of hospital, informed consent was taken from patients and data was entered and analyzed with computer software SPSS version 20. All numerical data was presented as mean and Standard Deviation and categorical data was presented as frequency and percentages. P Value of 0.05 was considered as significant.

Results: Total patients included in this study were 196 (100%), all were females, in which 138 (70.4%) were house wives and 58 (29.6%) were working ladies. Mean Hb of the patients was 8.06 ± 1.42 , mean of serum Ferritin was 12.90 ± 2.62 , mean of delivery time was 34.78 ± 2.35 , mean of BMI was 29.85 ± 1.67 , mean of parity was 3.24 ± 1.37 , mean of gravidity was 3.15 ± 1.23 . Out of 196 (100%) it was observed that 128 (65.3%) were facing the condition of pre-term labor and 68 (37.7%) delivered normally.

Conclusion: Anaemia in pregnancy was found to be associated with increased risk for preterm labour.

Key Words: Haemoglobin, anemia, preterm birth, Hemoglobin, Parity

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INTRODUCTION

Out of the numerous causes of perinatal mortality and morbidity, preterm birth is one of the most frequent underlying factor worldwide¹. Maternal anemia and preterm birth goes hand in hand with each other in various studies done for the purpose of documenting their association². Chinese studies done for documenting the association between anemia and preterm birth are erratic, inconsistent and variable. Studies have given a notion and are now pointing to the fact that the strength of association of anemia and preterm birth may fluctuate vary based primarily on the time of gestation at the onset of anemia and duration of gestation till the persistence of anemia³. Spontaneous preterm labour, preterm premature rupture of membranes (PROM) and medically indicated preterm birth are subtypes of preterm birth, in spite of knowing

this fact rarely a study is performed for judging the relation of anemia and specific subtype of preterm birth to determine individual burden of each subtype on the association of preterm birth and anemia⁴. Any study for this purpose might blow the whole concept of any association between anemia and preterm labour, if only an individual subtype show increased risk contrary to other subtypes⁵. This type of study embody the potential of throwing light on hidden etiologies and underlying mechanisms for preterm labour which are still waiting to be discovered⁵.

Multiple pathways including maternal infection, hypoxia and aerophilous stress are the suspected culprits for preterm labour being quoted over and over as major underlying biological pathways⁶. There is possibility of increase susceptibility of mother toward infections and also increase stress on both fetus and mother due to chronic hypoxia caused by iron deficiency anemia. Activation of maternal or fetal hypothalamic-pituitary-adrenal axis resulting from cascade following active immune response to combat infection leads to initiation of preterm labour⁷. Oxidative stress harming erythrocytes and fetoplacental unit add the final stone to the adverse possibilities of iron deficiency anemia⁸.

Our hypothesis is based on the possibility of increased risk of preterm labour due to maternal anemia which may lead to the discovery of the hidden mechanism and causes of preterm labour.

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MATERIALS AND METHODS

After approval from ethical committee of hospital, informed consent was taken from patients before including patient’s data in research and they were ensured about their confidentiality. Patient’s telephonic contacts and addresses were taken. Blood was collected with all septic precaution in CBC vial for hemoglobin count. Gestational age, in completed weeks, was estimated based on the last menstrual period. Preterm birth was defined as live births delivered before 37 completed weeks. Pregnant women with preterm labor of age 25 to 35 years were included in the study. Any other cause which can induce preterm labor (twins or infections diagnosed radiologically and complete urine examination respectively) were excluded from the study. All the data entered and analyzed using computer software SPSS version 10. Mean and standard deviation was calculated for quantitative variables like age, hemoglobin count and gestational age. Frequency and percentage were calculated for qualitative variables like preterm birth and outcome (iron deficiency anemia) Yes/No. Effect modifier like age, gravidity and parity was controlled by stratification of data. Post stratification multiple regression test was applied. A p value 0.05 was considered statistically significant.

RESULTS

Total subjects included in this study were one hundred and ninety six 196 (100%), all were females, in which 138 (70.4%) were house wives and 58 (29.6%) were working ladies. Mean of Hb of the subjects was 8.06 ± 1.42, mean of serum Ferritin was 12.90 ± 2.62, mean of delivery time was 34.78 ± 2.35, mean of BMI was 29.85 ± 1.67, mean of parity 3.24 ± 1.37, mean of gravidity was 3.15 ± 1.23. It was observed that out of these 196 subjects, 128 (65.3%) were facing the condition of pre-term labor and 68 (37.7%) delivered normally (Table-1-2).

Table No.1: Demographic Variables

Characteristics	Mean	Std. Deviation
Hb	8.061	1.416
Serum Ferritin	12.903	2.626
Time of delivery	34.785	2.350
BMI	29.852	1.674
Parity	3.244	1.377
Gravidity	3.158	1.232

In this study, the outcome variable was pre-term labor. We applied the logistic regression to find the predictors for preterm labor, it was noted that serum Ferritin and gravidity were significant with pre-term labor and time of delivery, Hb, BMI, Parity and occupation of women were not. Odds ratios also described this trend. Others measures of association such as Concordant Discordant

showed the association but Goodman-Kruskal Gamma not showed the association (Table-3-4).

The logistic regression equation was as;

$$\text{Pre-term labor} = 3.587 - 0.1693, \text{Hb} + 0.1732, \text{Serum Ferritin} - 0.07691, \text{Time of delivery} - 0.06083, \text{BMI} + 0.03033, \text{Parity} + 0.2822 \text{Gravidity}$$

Table No.2: Women Occupation and Preterm Birth

Women occupation.		
Characteristics	Frequency	Percent (%)
House wife	138	70.4 %
Working Lady	58	29.6 %
Preterm Birth		
Yes	128	65.3 %
No	68	34.7 %

Table No.3: Multiple Regressions for association

Term	Coef	SE Coef	P-value
Constant	3.23	3.90	0.019
Hb	-0.169	0.113	0.130
Serum Ferritin	0.1732	0.0636	0.005
Time of Delivery	-0.0769	0.0669	0.250
BMI	-0.0608	0.0934	0.514
Parity	0.030	0.115	0.791
Gravidity	0.282	0.138	0.035
Occupation	0.361	0.368	0.322

Table No.4: Odds Ratios for Continuous Predictors

	Odds Ratio	95% CI
Hb	0.8443	(0.6770, 1.0528)
Serum Ferritin	1.1891	(1.0497, 1.3470)
Time of Delivery	0.9260	(0.8122, 1.0557)
BMI	0.9410	(0.7835, 1.1301)
Parity	1.0308	(0.8231, 1.2909)
Gravidity	1.3261	(1.0127, 1.7365)

Pairs	Number	Percent
Concordant	5843	67.1
Discordant	2813	32.3
P-value of Goodman-Kruskal Gamma		0.35

DISCUSSION

Erratic results of multiple studies done to find out the correlation between maternal anemia and pterm birth could be explained by analyzing anemia as an adverse and cumulative exposure. Like any other adverse agent, resulting adverse effect response could vary with the

time of exposure and also extent of exposure. This explanation paves the way for the certain possibility of different correlation of anemia to the outcome of pregnancy and preterm birth depending upon the time of gestation at the time of anemia i.e showing strong co-relation at early gestation compared to late gestational age. Also, Heterogeneous subtypes of preterm birth are not usually observed and considered in each study done on preterm labour,⁹ leading to difficulty in finding out any co-relation among etiologically distinct endpoints¹⁰. Even in previous Chinese studies, only minute level of attention has been paid to study anemia as a risk factor for preterm birth clinical subtypes¹¹. Only spontaneous preterm births are usually focused in most studies. In our study, meticulous study design was used to overpower these limitations and to explore any existing relation between physiological haemo-dilution and preterm birth.

In our study, early trimester anemia was related to moderately increased risk of preterm birth. This association could not be attributed to any random happening. Though mainly restricted to spontaneous preterm labour, anemia in third trimester gestation was related to decrease incidences of preterm birth in all of its subtypes. There is no relation between anemia and medically indicated preterm birth. Our findings make a valid point by addressing the effect of exposure window of anemia and different risk profile for various different preterm birth subtypes.

Results of our study coincide with a meta-analysis showing increased risk of preterm birth in patient who develop anemia in early gestation. It also shows that there is an inverse relation between anemia developing at late gestation to preterm birth. Preterm birth clinical subtypes were neglected in all four Chinese studies emphasizing only on association and relation of anemia with preterm births giving superior and confused results¹¹. Some researchers narrated association of high risk of preterm birth to anemia in the early trimester, while others show no relation among them¹². Only severe anemia (Hb<7 g/dl) in the third trimester was related to a slightly high risk for preterm birth in last study observation.¹³ Antecedently, Associations between maternal anemia and preterm birth clinical subtypes was only reported by five studies¹³. Dichotomized of pregnant women into two groups of anemic or non-anemic was done in most studies using single cut-off point, remaining categorized them with several cut-off points using different values of Hb.¹³ Reliability of spline analysis is more than continuous exposure data.¹⁴ In our study, non-linear effects were taken in to account by flexible spline transformation using Hb concentrations as a continuous variable. Association of anemia varies with every subtype of preterm birth, showing the divergent nature of this relation. Increase risk of spontaneous preterm labour was seen to be related with early gestation anemia and

also with anemia present throughout the gestation in contrast to reduced risk of preterm labour with mid or late pregnancy anemia. Iron deficiency leads to anemia emergence in the form of pre-existing or early onset anemia which could reveal just the early period of pregnancy or throughout the pregnancy. Hypoxia, aerophilous stress, maternal infection and triggering of the spontaneous onset of preterm labour are the potential consequences of iron deficiency anemia.

Physiological haemo-dilution during pregnancy on reaching its rock bottom (lowest value) might be able to hide the true association between anemia and preterm birth, was the cause of apprehension for researchers of previous studies¹⁵. Till now, no study is done to find out the association between physiological anemia occurring secondary to haemodilution and preterm birth. We used 1st trimester hemoglobin level as the baseline and Hb reduction across trimesters to mimic haemo-dilution in our study. Our study shows that haemo-dilution was related with reduced risk for preterm birth. That fact my friend might be the justification for the reciprocal relationship of the late trimester anemia and preterm birth.

Chinese cohort had a fairly low (4.7%) overall preterm birth rate with the main contribution from its spontaneous preterm labour (77%) subtype. Consistency of this rate is observed in various cohort done in this region. However, the obstetrical interventions rate at preterm and term gestations was 11.6 and 16.7% in our study. Most industrialised societies have much higher rate of intervention than our population due to impending fetal compromise. Probably, these inconsistencies in threshold for intervention in practice of both culture could have played a significant role in our study findings. In our setting, we used 1st day of last menstrual period to calculate the gestational age. So, patient ability to remember her last menstrual date and other errors associated with menstrual geological dating might have altered a little bit of our clinical findings. The association of preterm birth and anemia in 1st trimester was likely related to iron deficiency, with little or no effect of iron supplementation because iron supplements were prescribed after the diagnosis of anemia. Nevertheless, women in their late gestation were more susceptible to take iron supplement as treatment advice and a lot of medical attention for anemia. The reciprocal association between late gestation anemia and spontaneous preterm labour, in addition to the effects of conventional physiological haemo-dilution,¹⁶ might be representing an artifact because of advantageous medical interventions. The effect of prevention, early diagnosis and prompt treatment of maternal anemia on trimming the rates of spontaneous preterm labour and preterm promenade needs further investigation and research.

CONCLUSION

Maternal anemia in pregnancy is in strong relation with increased risk of preterm labour in contrast to adequate physiological haemo-dilution during pregnancy which is associated with reduced risk of preterm birth. Prevention, early diagnosis and aggressive treatment of maternal anemia may be a broadway for intervention, and a topic worthy of further investigation.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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