

Maternal Anemia during Pregnancy and Its Association with Preterm Birth

SUMAIYA AZIZ¹, SYEDA NAJMUSAHAR², SOHANI ANWER³, NAZISH BALOCH⁴

¹Clinical Associate Gynae and Obs department, Orthopaedic and Medical Institute Hospital, Karachi

²Consultant Gynae and Obs department, Chiniot General Hospital, Karachi

³Senior Registrar Gynae and Obs department, Jinnah Medical College Hospital Korangi, Karachi

⁴Consultant, Gynae and Obs department, Bolan Medical Complex Hospital, Quetta

Corresponding Author: Dr. Sumaiya Aziz, Email: sumaiya.aziz@aku.edu, Cell No. +923343096134

ABSTRACT

Objective: To determine the association of preterm delivery with maternal anemia in Tertiary Care Hospital, Karachi.

Study Design: Prospective cohort study.

Study Setting: Study was conducted at Department of Obstetrics and Gynecology of Aga Khan University Hospital Karachi, Pakistan.

Duration of Study: Six months from 3rd September, 2018 to 3rd March, 2019.

Subjects and Methods: Data was prospectively collected from 90 patients. 45 patients were in the anemic group and 45 patients were in the non anemic group. Quantitative data was presented as simple descriptive statistics giving mean and standard deviation and qualitative variables were presented as frequency and percentages. Effect modifiers were controlled through stratification. Post stratification chi square was applied and p-value of ≤ 0.05 was considered significant. RR > 1 was considered significant.

Results: In the anemic group, mean age of the patient was 28.82 ± 3.65 years, gestational age at delivery was 36.97 ± 2.58 weeks, booking hemoglobin was 9.79 ± 0.84 g/dl, and delivery hemoglobin was found to be 9.73 ± 1.19 g/dl. In the non-anemic group mean age of the patient was 29.57 ± 5.83 years, gestational age at delivery was 37.08 ± 1.91 weeks, booking hemoglobin was 10.76 ± 0.99 g/dl and delivery hemoglobin was found to be 10.75 ± 1.12 g/dl. Moreover, frequency distribution of preterm status showed that out of 45 patients in anemic and non-anemic group, 35.6% and 46.7% had preterm status respectively. RR was 0.76.

Conclusion: Prematurity is major cause of perinatal mortality. The findings of this study although shows prevalence of preterm delivery in both anemic and non-anemic pregnant women however results were not significant to support our hypothesis. Further research is needed with strategies to address the anemia status of expecting mothers.

Key Words: Maternal anemia, preterm, anemia and non-anemic group.

INTRODUCTION

Pregnancy-related anaemia is a worldwide problem. According to a WHO survey [1], the frequency is 41.8% higher in poor nations like Africa, where the prevalence is 48.1%, as opposed to 24.1% in the United States and 25.1% in Europe. First trimester haemoglobin levels 11g/dl, second and third trimester haemoglobin levels of 10.5g/dl and postnatal haemoglobin levels of 10g/dl, according to UK criteria, define anaemia in pregnancy [2] In a Pakistani study of pregnant women, 90.5% of them were anaemic, with 75.0% having mild anaemia (haemoglobin from 9.0 to 10.9 g/dl) and 14.8% having moderate anaemia (haemoglobin from 7.0 to 8.9 g/dl). Only 0.7 percent of the participants were anaemic (haemoglobin 7.0 g/dl) [3]. Central Asia has the highest frequency, with India reporting an astounding 88% [4].

Maternal anaemia poses a threat since it is linked to poor perinatal outcomes, most notably premature delivery. Preterm delivery (before 37 weeks of pregnancy), which occurs in 5–10% of all deliveries worldwide, leads to long-term physical and neurological morbidity in both developing and industrialised countries. Neonatal fatalities in Pakistan account for 7% of global neonatal deaths. Neonatal infection (36%), premature birth (28%), and birth asphyxia (23%), together account for 87% of neonatal mortality globally [5]. There is a higher risk of cerebral palsy, sensory deficiencies and learning problems in premature babies

than in full-term babies [6]. In 2010, preterm birth rates were compared throughout parts of the world and found to range from 5% in European countries to 18% in some African countries. Preterm birth rates were highest in Asia, with a prevalence of 7.2% in Eastern Asia, a 13.6% in South Eastern Asia, and a 13.3% in Southern Asia. In South Asia and Sub-Saharan Africa, more than 60% of preterm newborns are born [7].

Most women who have a preterm delivery have no identified risk factors, it appears. A previous preterm birth is the most common risk factor. Other risk factors include African-American ethnicity, multiple pregnancies, a short cervical length, and a low BMI before pregnancy [8]. Most preterm births are natural, with the rest caused by a physician's decision to induce labour or break the membranes for maternal or foetal reasons [9]. About 20% of preterm deliveries are iatrogenic. Preterm birth rates were found to be 25% in anaemic women, compared to only 6.3% in non-anemic women, according to a study by Dr. Rahat Qureshi [12].

Given the influence of anaemia in pregnancy on various aspects of maternal and foetal health and the rise in preterm birth rates around the world, an investigation of the association between maternal anaemia in pregnancy and preterm delivery has long been researched [10-11]. However, our population has not yet fully investigated this critical connection. It's impossible to do international

studies on our community because we're genetically, geographically, and socioeconomically unique. As a result of this research, we will learn more about the connection between preterm birth and maternal anaemia, as well as the seriousness of the situation and the need for further interventional research aimed at resolving this troubling but treatable cause of preterm birth in our study population.

MATERIALS AND METHODS

This prospective cohort study was conducted at Obstetrics and Gynecology Department of Aga Khan University Hospital Karachi, Pakistan for six months during from 3rd September, 2018 to 3rd March, 2019. Sample size of the study was 90. 45 cases in each group. Group A (Anemic): 45 cases, Group B (Non-Anemic): 45 cases. Patients with Age between 16-35years, singleton pregnancy as assessed on ultrasound and Pregnancy interval of more than 6 months (with the immediately previous pregnancy) were included in study. Anemic pregnant women less than 10.5 gm/dl (expose group).Non-anemic pregnant women with booking hemoglobin of more than 10.5 gm/dl (unexposed group).Patients with a previous history of preterm delivery multiple preterm birth (having more than one delivery at less than 37 weeks of gestation in the past), patients with hereditary causes of anemia, Any major systemic (type 2 Diabetes mellitus and chronic hypertension) that could hinder the course of pregnancy were excluded from the study. Data was collected after approval from CPSP and Ethical review committee. Patients were divided in 2 groups exposed (anemic pregnant women) and unexposed (non-anemic pregnant women) based on their hemoglobin levels at booking visit at or before 14 weeks of pregnancy. Patients were followed till the end of pregnancy to see the delivery outcomes (in terms of gestational age).Anonymity and confidentiality of the patients was protected by assigning codes to the data set, instead of names and keeping the data password protected. Data was collected after approval from CPSP and Ethical review committee. Patients were divided in 2 groups exposed (anemic pregnant women) and unexposed (non-anemic pregnant women) based on their hemoglobin levels at booking visit at or before 14 weeks of pregnancy. Patients were followed till the end of pregnancy to see the delivery outcomes (in terms of gestational age).Anonymity and confidentiality of the patients was protected by assigning codes to the data set, instead of names and keeping the data password protected.

RESULTS

A total of 90 patients, including 45 anemic and non-anemic pregnant patients visiting Department of Obstetrics and Gynecology of Aga Khan University Hospital Karachi, Pakistan who met the inclusion and exclusion criteria were included in this study. Out of 45 patients in the anemic group, the minimum age of the patient was 23 while the maximum age of the patients was 35 years. Mean age in our study was 28.82 years with the standard deviation of ±3.65. Mean gestational age at delivery was found to be 36.97±2.58 weeks, booking hemoglobin was 9.79±0.84 g/dl, and delivery hemoglobin in our study was 9.73±1.19 g/dl respectively. Similarly, out of 45 patients in a non-anemic group minimum age of the patient was 19 while

maximum age of the patients was 35 years. Mean age in our study was 29.57 years with the standard deviation of ±5.83. Mean gestational age at delivery was 37.08±1.91 weeks, booking hemoglobin was 10.76±0.99 g/dl, and delivery hemoglobin in our study was 10.75±1.91 weeks respectively. As shown in Table 1.

Frequency distribution of age groups showed that out of 45 patients in anemic group, 02 (4.4%), 09 (20%), 21 (46.7%) and 13 (28.9%) were in age group 16-20 years, 21-25 years, 26-30 years and 31-35 years respectively. Similarly, out of 45 patients in non-anemic group, 03 (6.7%), 10 (22.2%), 13 (28.9%) and 19 (42.2%) were in age group 16-20 years, 21-25 years, 26-30 years and 31-35 years respectively As shown in Figure 1.

Frequency distribution of preterm status showed that out of 45 patients in the anemic group, 16 (35.6%) delivered preterm and 29 (64.4%) delivered at term respectively. Similarly, out of 45 patients in the non-anemic group, 21 (46.7%) delivered preterm and 24 (53.3%) delivered at term respectively. P- Value was 0.28. RR was 0.76. As presented in Table 2.

Table-1: Descriptive Statistics
n=90 (45 in Anemia and Non-Anemic Group)

VARIABLE	ANEMIC GROUP MEAN ± SD	NON-ANEMIC GROUP MEAN ± SD	MIN-MAX
AGE (YEARS)	28.82±3.65	29.57±5.83	19-35
GESTATIONAL AGE (WEEKS)	36.97±2.58	37.08±1.91	27-40
BOOKING HEMOGLOBIN	9.79±0.84	10.76±0.99	7.9-12
DELIVERY HEMOGLOBIN	9.73±1.19	10.75±1.21	6.8-14

Figure-1 Age Distribution
n=90 (45 in Anemia and Non-Anemic Group)

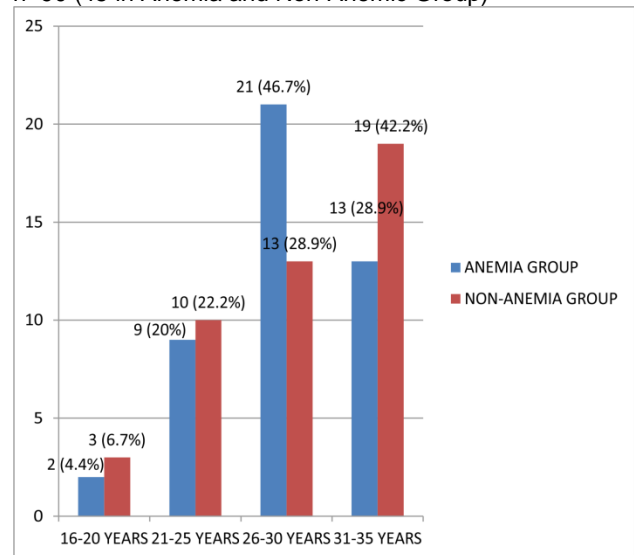


Table-2 :Preterm Status Distribution
n=90 (45 in Anemia and Non-Anemic Group)

GROUPS	PRETERM STATUS		P VALUE	RR
	YES	NO		
ANEMIC GROUP	16 (35.6%)	29 (64.4%)	0.28	0.76
NON-ANEMIC GROUP	21 (46.7%)	24 (53.3%)		

DISCUSSION

Preterm birth is still one of the leading causes of perinatal mortality and morbidity in the world. It's still unclear whether or not maternal anaemia increases the chance of preterm birth, with some research finding it to be true while others don't. According to research, the link between anaemia and preterm delivery can change depending on when it occurs during pregnancy [13]. Very few studies have attempted to evaluate whether associations between anaemia and preterm birth are largely driven by associations with one specific subtype despite the considerable etiological heterogeneity in preterm clinical subtypes, namely preterm PROM, spontaneous preterm labour and medically induced preterm births. It's possible that the link between maternal anaemia and one type of preterm birth will be lessened if it's only connected with one preterm birth subtype [14].

The results of our research showed that 45 anaemic and non-anaemic pregnant women were among the 90 total patients. Our study found that the mean age, gestational age, booking haemoglobin, and delivery haemoglobin were all higher in the anaemic group: 28.82 years old, 36.97 weeks pregnant, 9.79 g/dl, and 9.73 g/dl, respectively. In our study, the mean age, gestational age, booking haemoglobin, and delivery haemoglobin were 29.57 years, 37.08 weeks, 10.76 g/dl, and 10.75 g/dl, respectively, in the non-anaemic group. Additionally, the frequency distribution of preterm status revealed that 35.6% and 46.7% of 45 individuals in the anaemic and non-anaemic groups had preterm status, respectively. The RR came out to be just about one hundred percent.

From October 2001 to October 2002, researchers followed up with a group of 629 expectant mothers. Three hundred and thirteen of them were anaemic (haemoglobin 11 g/dl at labour and on two previous times throughout the current pregnancy). A total of 316 pregnant women had haemoglobin levels more than or equal to 11 g/dl throughout their pregnancies, and they were classified as non-anaemic. Preterm birth occurs more frequently in anaemic women (25.2%) than in non-anaemic ones (6.3%). Preterm birth and low birth weight (LBW) were four and one and a half times more likely in anaemic women. The probability of an APGAR score of 5 at 1 minute was 1.8 times greater in newborns of anaemic moms, while the likelihood of an IUD was 3.7 times higher in anaemic women [15].

Another population-based prospective cohort research in East China's 13 counties found that preterm birth rates were 4.1% for anaemic women and 5% for non-anaemic women (P 0.05). A haemoglobin level of 5 g/dl or below in the first trimester was linked to an increased risk of preterm PROM [hazard ratio (HR) 3.3, 95 percent confidence interval (CI) 1.4–7.7], but a low haemoglobin

level in the third trimester was linked to a lower risk of spontaneous preterm labour. Hemodilution was linked to a lower incidence of premature delivery. Anaemia in early pregnancy has been linked to an increased risk of preterm PROM, whereas exposure in late pregnancy has been linked to a decreased risk of spontaneous preterm labour [16].

In a study evaluating risk variables for preterm birth in a healthy cohort, Adams et al. looked at whether risk factors differed among subgroups of preterm deliveries and found that anaemia and preterm delivery had no connection. As a result, they came to the same conclusion as other researchers, who found that most causes of preterm birth are still unknown.

In a control-cases study, Klebanoff et al. found that anaemia during the second trimester was related with premature birth; however, the huge racial disparity in preterm was not explained by this finding. In another study, the same researchers discovered a weak link between preterm and maternal anaemia in the early third trimester, but no link was detected after 30 weeks of gestation [18-19].

The researchers found that a high Hematocrit (Ht) was linked to foetal retardation and preterm delivery in a uni and multivariable analysis, particularly when Ht was equal to or greater than 43 percent between 31 and 34 weeks of gestation (Odds Ratio -OR- 1.5 - 2.5). Most of the 17,149 pregnant women who participated in the study took iron and folate supplements and had regular prenatal checks [20].

Low birthweight and preterm have been linked to Ht above 38% reporting ORs ranging from 2.4 to 4.2, according to Knottnerus et al. High blood viscosity, according to them, is a risk factor for good placental perfusion. In 54,832 singleton births, Murphy et al. found that elevated Ht was associated with an increased risk of perinatal death, low birth weight, and preterm [21].

All research on this subject, whether or not they found a link between preterm and maternal anaemia, were carried out in industrialised countries. In a poor country, Mart et al studied pregnant women in a city (Valencia) with a frequency of 34.44 percent anaemia. Hb less than 11g/dL is considered anaemia by the World Health Organization (WHO). The data were analysed using logistic regression, and the likelihood ratio test was employed to compare the two models. It was revealed that after correcting for Placental Abruption, PROM, previous premature labour, prenatal care visits, and uterine bleeding in more than one trimester, maternal anaemia was substantially linked to prematurity (Odds Ratio: 1.70; 95 percent CI = 1.18 to 2.57 P <.001). A higher risk of preterm was seen in women who had maternal anaemia during the third trimester of pregnancy and during childbirth [22-23].

CONCLUSIONS

In the first trimester, maternal anaemia is linked to a higher risk of preterm PROM, while anaemia in the second trimester is linked to a lower chance of spontaneous preterm labour. A lower risk of preterm birth may be linked to adequate physiological hemo-dilution during the middle to late stages of pregnancy. Prematurity is a leading cause of perinatal death. Despite the fact that our study found a

high rate of preterm birth in both anaemic and non-anaemic pregnant women, the results were insufficient to prove our hypothesis.

REFERENCES

1. Emegoakor CF, Iyoke CA, Ezegwui HU, Umeora OU, Lawani LO, Madu AJ. Rates and determinants of peripartum and puerperal anemia in Enugu, Nigeria. *Niger J Clin Pract* 2016;19(6):709-14.
2. Rukuni R, Bhattacharya S, Murphy MF, Roberts D, Stanworth SJ, Knight M. Maternal and neonatal outcomes of antenatal anemia in a Scottish population: a retrospective cohort study. *Acta Obstet et Gynecol Scandinavica*. 2016;95(5):555-64.
3. Baig-Ansari N, Badruddin SH, Karmaliani R, Harris H, Jehan I, Pasha O, Moss N et al. Anemia prevalence and risk factors in pregnant women in an urban area of Pakistan. *Food and nutrition bulletin*. 2008 Jun;29(2):132-9.
4. Jaleel RI, Khan A. Severe anaemia and adverse pregnancy outcome. *J Surg Pak (Int)*. 2008 Oct;13(4):147-50.
5. Jehan I, Harris H, Salat S, Zeb A, Mobeen N, Pasha O et al. Neonatal mortality, risk factors and causes: a prospective population-based cohort study in urban Pakistan. *Bulletin of the world Health Organization*. 2009 Feb;87(2):130-8.
6. Beck S, Wojdyla D, Say L, Betran AP, Merialdi M, Requejo JH et al. The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. *Bulletin of the World Health Organization*. 2010 Jan;88(1):31-8.
7. Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. *The Lancet*. 2012 Jun 15;379(9832):2162-72.
8. Stagnaro-Green A. Maternal thyroid disease and preterm delivery. *J Clin Endocrinol Metab*. 2009 Jan;94(1):21-5.
9. Vovsha I, Salleb-Aouissi A, Raja A, Koch T, Rybchuk A, Radeva A et al. Using Kernel Methods and Model Selection for Prediction of Preterm Birth. In *Machine Learning for Healthcare Conference 2016 Dec 10* (pp. 55-72).
10. World Health Organization. (2018). Anaemia. [online] Available at: <http://www.who.int/topics/anaemia/en/> [Accessed 10 Mar. 2018].
11. World Health Organization. (2018). Anaemia. [online] Available at: <http://www.who.int/topics/anaemia/en/> [Accessed 10 Mar. 2018].
12. Lone FW, Qureshi RN, Emanuel F. Maternal anaemia and its impact on perinatal outcome. *Trop. Med. Int. Health*. 2004 Apr 1;9(4):486-90.
13. Rahman MM, Abe SK, Rahman MS, Kanda M, Narita S, Bilano V, Ota E, Gilmour S, Shibuya K. Maternal anemia and risk of adverse birth and health outcomes in low- and middle-income countries: systematic review and meta-analysis. *Am J Clin Nutr*. 2016;103(2):495-504.
14. Padhi BK, Baker KK, Dutta A, Cumming O, Freeman MC, Satpathy R, Das BS, Panigrahi P. Risk of Adverse Pregnancy Outcomes among Women Practicing Poor Sanitation in Rural India: A Population-Based Prospective Cohort Study. *PLoS Med*. 2015;12(7):e1001851.
15. Zhang Q, Ananth CV, Li Z, Smulian JC. Maternal anaemia and preterm birth: a prospective cohort study. *Int J Epidemiol*. 2009 Oct;38(5):1380-9.
16. Lone FW, Qureshi RN, Emanuel F. Maternal anaemia and its impact on perinatal outcome. *Trop. Med. Int. Health*. 2004 Apr 1;9(4):486-90.
17. Adams MM, Sarno AP, Harlass FE, Rawlings JS, Read JA. Risk factors for preterm delivery in a healthy cohort. *Epidemiology* 1995;5:525-32.
18. Klebanoff MA, Shiono PH, Selby JV, Trachtenberg AI, Graubard BI. Anemia and spontaneous preterm birth. *Am J Obstet Gynecol* 1991;164:59-63.
19. Klebanoff MA, Shiono PH, Berendes HW, Rhoads GG. Facts and artifacts about preterm delivery. *JAMA* 1989;262:511-515.
20. Lu ZM, Goldenberg RL, Cliver SP, Cutter G, Blankson M. The relationship between maternal hematocrit and pregnancy outcome. *Obstet Gynecol* 1991;77:190-194.
21. Knottnerus JA, Delgado LR, Knipschild PG, Essed GGM, Smits F. Haematologic parameters and pregnancy outcome. *J Clin Epidemiol* 1990;43:461-466.
22. Murphy JF, O'Riordan J, Newcombe RG, Coles EC, Pearson JF. Relation of haemoglobin levels in first and second trimester to outcome of pregnancy. *Lancet* 1986;992-995.
23. Martí A, Peña-Martí G, Muñoz S, Lanás F, Comunian G. Association between prematurity and maternal anemia in Venezuelan pregnant women during third trimester at labor. *Arch Latinoam Nutr*. 2001 Mar;51(1):44-8.