Maternal anemia and its effects on obstetrics and neonatal outcomes: A prospective, Cohort study.

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Abstract

Objective(s):

- To assess the frequency of maternal anemia and its association with obstetrics and neonatal adverse outcomes.
- To evaluate the effects of maternal hemoglobin levels during the third trimester on pregnancy outcomes and fetal development.
- To assess the association between anemia severity with pregnancy outcome and newborn mortality and morbidity.

Methodology:

This is a prospective, cohort study, conducted at Lifeline maternity hospital, Karachi. All pregnant females visiting the antenatal clinic during the third trimester were included in the study, blood count was measured from mother during third trimester and from neonates 24 hours after birth. SPSS 23 was used to enter and analyze the data.

Results:

260 pregnant females in their 3rd trimester were included in this study, the mean age was 32.4 ±4.8, The association between maternal anemia with pediatric hemoglobin levels mean values indicated normal mean Hb in neonates born to non-anemic mothers with 15.4 ± 2.7 g/dL, Assessment of fetal outcome was documented at the end of 03 months follow-up, overall results indicated 61(%) Respiratory infection was reported in 29(%), other infections in 37(%), while the prolonged illness was reported in 16(%). NICU stay immediately after birth was reported in 47(%), while excessive hospitalization was documented in 9(%), the excessive need for medication was reported in 17(%) of children, and 6(%) of mortalities were documented from study participants.

Conclusion:

In Pakistan, there is a high frequency of maternal anemia, particularly during the third trimester, which harms the health of both the mother and the fetus. Severe maternal anemia is linked to an increased risk of poor maternal, fetal, and neonatal outcomes. Preventive interventions for severe anemia in pregnant women should be investigated.

Keywords: Maternal anemia, Pregnancy outcomes, maternal mortality, neonatal mortality

Introduction

Anemia remains a significant health problem in pregnant women worldwide with a prevalence of 36.8%. However this percentage is higher in low and middle-income countries.[1,2] In Pakistan, the awareness of maternal health is emerging with beneficial outcomes in urban areas but the rural areas remain under threat of adverse aftermaths. A study conducted in Pakistan shows that the ratio at which we are losing maternal lives is 186 deaths per 100,000 live births [3]. The causes of anemia are multifactorial, which include nutritional deficiencies like folate, B-12, and vitamin-A deficiency, keeping iron deficiency anemia foremost. Other causes comprise parasitic diseases, inflammation, hemoglobinopathies, and G6PD deficiency [4]. According to WHO, in pregnant females, anemia is considered by levels of hemoglobin less than 11.0g/dL and is divided into three levels of severity: mild anemia (Hb levels 9 - 10.9g/dL), moderate anemia (Hb levels 7 - 8.9g/dL), and severe anemia (Hb levels < 7g/dL)[5]. They symptoms of anemia are easy fatigability, general weakness, and decreased levels of cognition/concentration span. The outcomes of anemia in pregnancy can be adverse in females along with deteriorating health conditions in the fetus. The outcomes may include maternal death and perinatal death in severe cases, preterm birth, cesarean delivery, preeclampsia, small-for-gestational-age (SGA) live birth, and low birth weight. [6-12]. In a study conducted in Pakistan and India, women from Pakistan were more plausibly to have severe or moderate anemia and less likely to have mild anemia compared to Indian women [13]. Modifying the hemoglobin levels of mothers, early in pregnancy, of those who are deprived of micronutrients, can alter the adverse outcomes of maternal and neonatal health.

The study aimed to assess the frequency of maternal anemia, obstetrics, and fetal adverse outcomes, and risk factors of anemia among pregnant mothers. It shows the association of anemia with maternal and perinatal morbidity attending the antenatal clinic in Karachi, Pakistan.

Methodology

This is an observational, prospective, cohort study conducted at the Lifeline maternity hospital, Karachi from January 2023 to May 2023. The sample size was calculated with the help of the WHO and RaoSoft Sample Size calculator keeping the confidence interval at 95% and margin of error 5%. The total population size was determined by adding the total number of deliveries registered in our institute in the last 6 months, the number was 800. Then the obtained minimum sample size was 250.

An informed consent in the language of understanding was provided to all pregnant females visiting consultant clinics during the third trimester and requested to accept the study, after signing the informed consent complete demographic details were obtained and a complete blood count test was performed to evaluate the hemoglobin levels of study participants. After documentation of maternal hemoglobin values and other relevant details, PI waited till delivery to get further details. The mode of delivery was noted, and afterward, a neonatal blood count test was performed to evaluate the

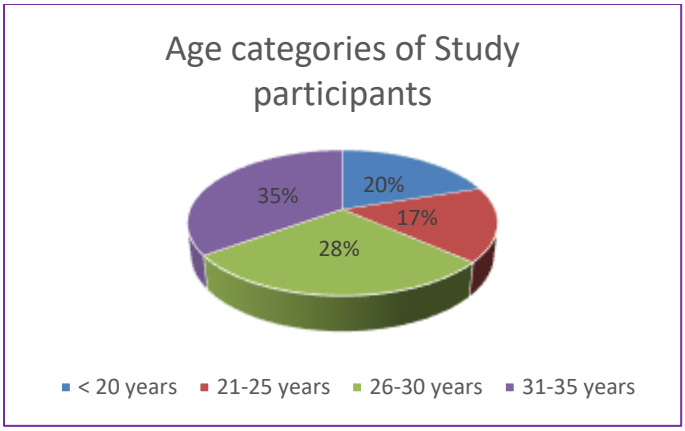
hemoglobin levels. Children born to study participants were followed for 3 months, and all details related to milestones, infections, medicines, hospitalizations, and problems with the health of newborns were documented.

Data was entered and analyzed by using the Statistical Package of Social Sciences (SPSS version 22). The normality of data was analyzed by simple data stratification. Dependent variables were analyzed with the help of frequency, percentages, mean values, and standard deviation tests. Independent variables were analyzed with the same test, however, data significance was analyzed using the Chi-Square test keeping a p-value ≤ 0.05 as significant. Association between two variables was assessed by using paired sample T-Test and/or Cross-Tabulation.

Results

260 pregnant females in their 3rd trimester were included in this study, the mean age was 32.4 ±4.8 years, and age categorization frequency of 91 (35%) in 31-35 years age category, 07 (20%) from < 20 years age category, 73 (28%) in 26-30 years age category, 44 (17%) were from age group of 21-25 years, the results indicated maximum frequency form 31-35 years of females. p-value was significant at 0.03. (Fig 01)

Fig 01: Age category distribution of study participants.

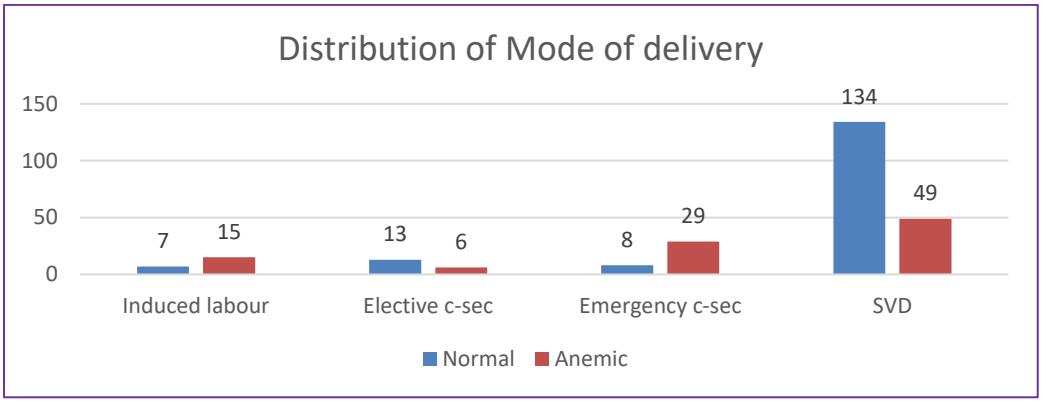


Employment status of participants reported 132(50.7%) were housewives, 73 (28%) were working at home and 55(21.1%) were employed formally.

Parity was categorized as nulliparous with 107 (41.1%) females, 1-3 children in 59 (22.6%), 4-6 children in 67(25.7%), and more than 6 children in 22 (8.4%), with a p-value of 0.81. Medical history reported a mean value of 2.1 ± 0.7 miscarriages in study participants, the assessment of blood count reported 92 (35.3%) females with normal hemoglobin values while 168(64.6%) had lower hemoglobin, categorization of low hemoglobin levels was as mild in 103(39.6%) females, moderate in 38 (14.6%) females and severe in 27 (10.3%) females. The mean value of hemoglobin was 11.7 ± 2.1 g/dL, 11.2 ± 0.7 g/dL, 9.1 ± 2.4 g/dL, and 7.9 ± 1.7 g/dL in Normal, Mild, Moderate, and severe anemia respectively. The mode of delivery was identified as 183(70.3%) Spontaneous vaginal deliveries, 37(14.2%) emergency caesarian, 19(7.3%) elective caesarian, and 21(8%) induced labor, with a p-value of 0.49. The distribution within non-anemic and anemic mothers indicated a higher number of induced labor in anemic mothers as compared to non-anemic mothers with

7(2.6%) versus 15(5.7%) frequency, the p-value was 0.87. elective caesarian was higher in non-anemic mothers with 13(5%) cases out of 21, with a p-value of 0.93, along with spontaneous vaginal delivery of 134(51.5%) out of 183 and a p-value of 0.01. Emergency caesarian was reportedly higher in anemic mothers 29(11.1%) as compared to non-anemic mothers 8(3%) with a p-value of 0.003. (Fig 02)

Fig 02: Mode of delivery within non-anemic and anemic mothers of study.



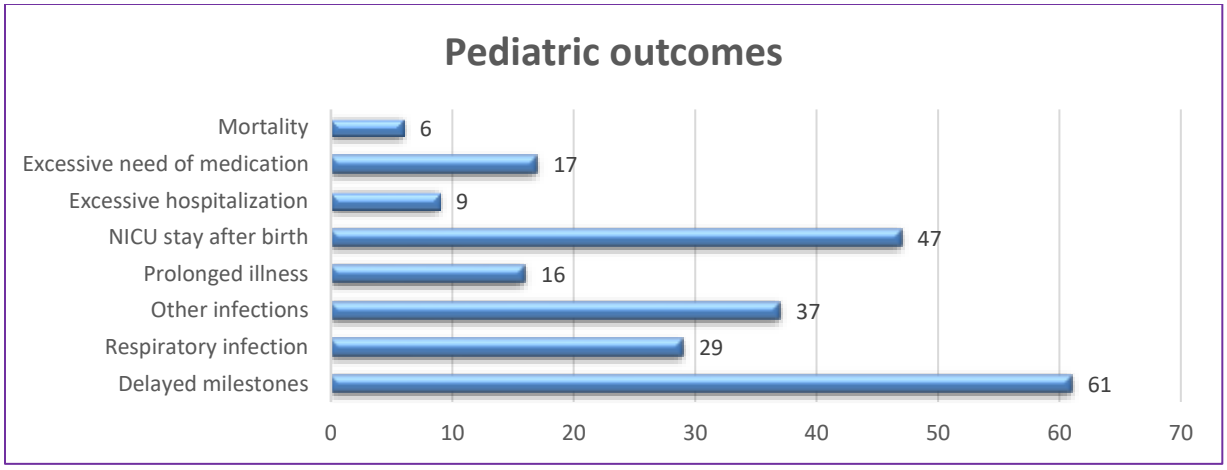
In the association between maternal anemia with pediatric hemoglobin levels, mean values indicated normal mean Hb in neonates born to non-anemic mothers with 15.4 ± 2.7 g/dL, while these values were gradually declining in anemic mothers of mild, moderate, and severe anemia as 14.1 ± 2.8 g/dL, 13.7 ± 1.9 g/dL and 12.7 ± 1.4 g/dL was measured in neonates respectively. The p-values indicated a significant difference between the mean values of mild anemic mothers and their newborns and severely anemic mothers and their newborns as 0.04 and 0.05 respectively. (Table 01)

Table 01: Association of maternal HB levels with neonatal HB levels.

Maternal Hemoglobin levels	Frequency	Mean Maternal HB	Mean Neonatal HB	P-Value
HB> =11g/dl (Normal)	92 (35.3%)	11.7 ± 2.1 g/dL	15.4 ± 2.7 g/dL	0.18
HB =10-10.9g/dl (Mild)	103 (39.6%)	11.2 ± 0.7 g/dL	14.1 ± 2.8 g/dL	0.04
HB =9.-8.9g/dl	38 (14.6%)	9.1 ± 2.4 g/dL	13.7 ± 1.9 g/dL	0.27
HB <7g/dl (severe)	27 (10.3%)	6.9 ± 1.7 g/dL	12.7 ± 1.4 g/dL	0.05

Assessment of fetal outcome was documented at the end of 03-month follow-up, overall results indicated 61(23.4%) children with delayed milestones such as being unable to support their head well and don't reach or grasp at objects, haven't begun to babble, and crossing eyes most of the time. Respiratory infection was reported in 29(11.1%), other infections in 37(14.2%), and prolonged illness was reported in 16(6.1%). NICU stay immediately after birth was reported in 47(18%), while excessive hospitalization was documented in 9(3.4%), excessive need for medication was reported in 17(6.5%) of children, and 6(2.3%) of mortalities were documented from study participants. (Fig 03)

Fig 03: Fetal outcomes on the last follow-up after 3 months of birth.



The association between maternal hemoglobin and fetal outcomes identified that children born to non-anemic mothers had no history of prolonged illness, excessive hospitalization, and other infections. While children born to mildly anemic mothers had a higher frequency of respiratory infections 6(2.3%), other infections 8(3%), 1(0.3%) newborns had reported prolonged illness, and 11 had NICU stay after birth, with a p-value of 0.02. moderately anemic mothers had a slightly higher incident rate of adverse fetal outcomes than mild anemic mothers with 18 NICU stays, the p-value was 0.81. Mothers with severe anemia had the worst frequency of adverse outcomes reporting the highest number of mortalities, NICU stays, delayed milestones, and respiratory infections. The p-values of moderate anemia and severe anemia were reportedly insignificant with 0.81 and 0.24 respectively. (Table 02)

Table 02: Association between maternal HB levels with adverse fetal outcomes.

Maternal Hemoglobin levels	Delayed milestones	Respiratory Infection	Other infections	Prolonged illness	NICU stay after birth	Excessive hospitalization	Excessive need for medication	Mortality	P-Value
HB> 11g/dL (92)	3 (1.1%)	5 (1.9%)	0 (0%)	0 (0%)	2 (0.7%)	0 (0%)	2 (0.7%)	0 (0%)	0.005
HB 10-10.9g/dL (103)	18 (6.9%)	6 (2.3%)	8 (3.0%)	1 (0.3%)	11 (4.2%)	1 (0.3%)	1 (0.3%)	1 (0.3%)	0.02
HB 9.-8.9g/dL (38)	18 (6.9%)	8 (3.0%)	12 (4.6%)	7 (2.6%)	18 (6.9%)	2 (0.7%)	5 (1.9%)	2 (0.7%)	0.81
HB <7g/dL (27)	22 (8.4%)	10 (3.8%)	17 (6.5%)	8 (3.0%)	16 (6.1%)	6 (2.3%)	9 (3.4%)	3 (1.1%)	0.24

Other adverse fetal outcomes were small for gestational age 13 (5%) and pre-mature delivery 9(3.4%) reported in children born to anemic mothers.

Discussion

Our study results indicated increased chances of mild, moderate, and severe anemia in neonates born to anemic mothers with 37%, 17%, and 2% respectively. A study conducted by S Parks, and MK Hoffman on the Pakistani and Indian population published in BJOG, has indicated similar results that showed 37.9% had mild anemia, 49.1% had moderate anemia and 0.67% had severe anemia [13]. A study regarding, Maternal and Child Nutrition, states that nutritional diet at the time of pregnancy is important for fetal growth. Newborns with fetal growth limitation, e.g. SGA, are at increased risk of death throughout infancy. They evaluated that 32 million babies were born SGA, 27% of births in Lower and Middle-Income Countries, and about 800 000 neonatal deaths and 400 000 post-neonatal infant deaths could be attributed to the increased risk associated with having fetal growth restriction. And these were closely related to neonatal deaths associated with low birth weight. [2] This association is closely observed in our study with the fact that 16% of the babies born were small for their respective gestational age. A study conducted by Ajibola I. Abioye, and Emily A. McDonald in Leyte, Philippines in 2019 suggested that maternal iron deficiency anemia was concomitant with an increased threat for iron deficiency anemia during the pediatric age of 9-12 years[14]. Concerning it, our study showed that the chances of respiratory infection and prolonged hospital stay in babies born to mild, moderate, and severely anemic mothers with 30.9%, 19.8%and 18.1% respectively. These frequencies suggest that babies of mothers suffering from anemia are more prone to get infections. Prolonged stay in the NICU, excessive hospitalization, and excessive use of medication indicate poor immune systems in newborns. In a cohort study, in 2019, conducted on Swedish children and their mothers, anemia diagnosed earlier in ≤30 weeks of pregnancy was ominously associated with high offspring risk of autism spectrum disorder, intellectual disability, and attention-deficit/hyperactivity disorder. [15].Likewise, in our study out of 92 neonates who showed delayed milestones, 30.4 %(n=28) had mild anemia, and 27.1 % (n=25) had moderate anemia. A similar study, Maternal Anemia and Risk of Small for Gestational Age, conducted in Pakistan in 2022, postulated that there is 1.4% more risk of SGA in anemic mothers as compared to non-anemic mothers and therefore maternal anemia plays a significant role in the fetal well-being. [16]Maternal anemia not only affects the mother but also affects the health of her children at the developmental stages of the fetus and also as neonates. The undernourishment of pregnant women has a great impact on the agility of future generations.

Conclusion:

In Pakistan, there is a high frequency of maternal anemia, particularly during the third trimester, which harms the health of both the mother and the fetus. Severe maternal anemia is linked to an increased risk of poor maternal, fetal, and neonatal outcomes. Preventive interventions for severe anemia in pregnant women should be investigated. Further study into the causes of anemia is needed; in

particular, a focus on less typically researched components may be necessary to create suitable therapies. In the meanwhile, it is advised that all Pakistani women of reproductive age get basic nutrition instruction about iron-rich foods and how food choices impact iron absorption.

Conflict of interest:

Authors declare no conflict of interest.

Ethical Review:

Submitted.

References

1. Karami M, Chaleshgar M, Salari N, Akbari H, Mohammadi M. Global Prevalence of Anemia in Pregnant Women: A Comprehensive Systematic Review and Meta-Analysis. Maternal and child health journal. 2022 Jul;26(7):1473-87.
2. Black RE, Victora CG, Walker SP, Bhutta ZA, Christian P, De Onis M, Ezzati M, Grantham-McGregor S, Katz J, Martorell R, Uauy R. Maternal and child undernutrition and overweight in low-income and middle-income countries. The lancet. 2013 Aug 3;382(9890):427-51.
3. Hanif M, Khalid S, Rasul A, Mahmood K. Maternal mortality in rural areas of Pakistan: challenges and prospects. Rural Heal. 2021 Jun 7;27:1040-7.
4. van den Broek N. Anaemia in pregnancy in developing countries. Br J Obstet Gynaecol 1998;105:385–90.
5. Goonewardene M, Shehata M, Hamad A. Anaemia in pregnancy. Best practice & research Clinical obstetrics & gynaecology. 2012 Feb 1;26(1):3-24.
6. Stoltzfus R, Mullany L, Black RE. Iron deficiency anaemia. In: Ezzati M, Lopez A, Rodgers A, Murray CJL, editors. *Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors*. Geneva (Switzerland): World Health Organization; 2004:163–210.
7. Brabin BJ, Hakimi M, Pelletier D. An analysis of anemia and pregnancy-related maternal mortality. *J Nutr* 2001;131:604–14s.
8. Klebanoff MA, Shiono PH, Selby JV, Trachtenberg AI, Graubard BI. Anemia and spontaneous preterm birth. *Am J Obstet Gynecol* 1991;164:59–63.
9. Ren A, Wang J, Ye RW, Li S, Liu JM, Li Z. Low first trimester hemoglobin and low birth weight, preterm birth and small for gestational age newborns. *Int J Gynaecol Obstet* 2007;98:124–8.
10. Ali AA, Rayis DA, Abdallah TM, Elbashir MI, Adam I. Severe anaemia is associated with a higher risk for preeclampsia and poor perinatal outcomes in Kassala Hospital, eastern Sudan. *BMC Res Notes* 2011;4:311.
11. Murphy JF, O'Riordan J, Newcombe RG, Coles EC, Pearson JF. Relation of haemoglobin levels in first and second trimester to outcomes of pregnancy. *Lancet* 1986;8488:992–5.
12. Vural T, Toz E, Ozcan A, Biler A, Ileri A, Inan A. Can anemia predict perinatal outcomes in different stages of pregnancy? *Pak J Med Sci* 2016;32:1354–9

13. Parks S, Hoffman MK, Goudar SS, Patel A, Saleem S, Ali SA, Goldenberg RL, Hibberd PL, Moore J, Wallace D, McClure EM. Maternal anaemia and maternal, fetal, and neonatal outcomes in a prospective cohort study in India and Pakistan. BJOG: An International Journal of Obstetrics & Gynaecology. 2019 May;126(6):737-43.
14. Abioye AI, McDonald EA, Park S, Ripp K, Bennett B, Wu HW, Pond-Tor S, Sagliba MJ, Amoylen AJ, Baltazar PI, Tallo V. Maternal anemia type during pregnancy is associated with anemia risk among offspring during infancy. Pediatric research. 2019 Sep;86(3):396-402.
15. Wiegersma AM, Dalman C, Lee BK, Karlsson H, Gardner RM. Association of prenatal maternal anemia with neurodevelopmental disorders. JAMA psychiatry. 2019 Dec 1;76(12):1294-304.
16. Tariq S, Isran BZ, Kiani SN, Shabir R. Maternal Anemia and Risk of Small for Gestational Age. Annals of King Edward Medical University. 2022 Aug 4;28(2):200-4.
17. Noronha JA, Al Khasawneh E, Seshan V, Ramasubramaniam S, Raman S. Anemia in pregnancy-consequences and challenges: a review of literature. Journal of South Asian Federation of Obstetrics and Gynecology. 2012 Jan;4(1):64-70.
18. Malhotra M, Sharma JB, Batra S, Sharma S, Murthy NS, Arora R. Maternal and perinatal outcome in varying degrees of anemia. International Journal of Gynecology & Obstetrics. 2002 Nov 1;79(2):93-100.
19. 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, 2. The American journal of clinical nutrition. 2016 Feb 1;103(2):495-504.
20. Chu FC, Shao SS, Lo LM, Hung TH. Association between maternal anemia at admission for delivery and adverse perinatal outcomes. Journal of the Chinese Medical Association. 2020 Apr 1;83(4):402-7.
21. Patra S, Pasrija S, Trivedi SS, Puri M. Maternal and perinatal outcome in patients with severe anemia in pregnancy. International Journal of Gynecology & Obstetrics. 2005 Nov;91(2):164-5.
22. Zhang Q, Ananth CV, Rhoads GG, Li Z. The impact of maternal anemia on perinatal mortality: a population-based, prospective cohort study in China. Annals of epidemiology. 2009 Nov 1;19(11):793-9.