Original Article

Association of Gestational Anemia with Pregnancy-Induced Hypertension in a Private Hospital Maternity Care

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ABSTRACT

Anemia, a prevalent global health concern affecting a quarter of the world's population, notably impacts pregnant women, with approximately 56 million affected globally. Its repercussions on maternal and neonatal health are extreme, leading to increased risks of low birth weight, fetal complications, and maternal morbidity and mortality. Concurrently, pregnancy-induced hypertension (PIH) poses significant risks to maternal and fetal well-being, yet the link between anemia and PIH remains an understudied area, particularly in Pakistan. **Objective:** To investigate the association between anemia and the heightened risk of PIH, offering critical insights into perinatal outcomes. **Methods:** A retrospective study was designed and the data was collected from Hijaz Hospital Gulberg III Lahore, Pakistan. Total 120 pregnant women were selected for the study and split into two groups. Group A consisted of 65 pregnant women with hypertension, whereas group B included 55 non-hypertensive pregnant women. Hemoglobin levels and Complete Blood Count were evaluated using standard protocols. The association of hemoglobin levels and PIH was investigated using independent-students test and one-way ANOVA by utilizing SPSS version-25. **Results:** Our findings showed that the hemoglobin levels were lowest (9.953846±1.924584 g/dl) in hypertensive women as compared to no-hypertensive women (11.52±1.584172) in their 3rd trimester. It coincided with the lowest number of red blood cells (4.1067±0.57816 million/mm3) in women with hypertension. **Conclusions:** Our finding demonstrated that the lower the levels of hemoglobin, the higher the risk of PIH.

INTRODUCTION

Anemia, characterized as a diminished convergence of blood hemoglobin, is a standout amongst the most well-known dietary inadequacy infections watched universally and influences more than a fourth of the total populace [1]. Universally, iron deficiency influences 1.62 billion individuals (25%), among which 56 million are pregnant women [2]. Anemia, in pregnant women, has serious outcomes on wellbeing, social, and monetary improvement [3]. Weak pregnant women will be in danger of low physical action, expanded maternal dreariness and mortality, particularly those with serious anemia. What's more, pregnant women and their neonates experience negative outcome including low birth weight (LBW), fetal anemia, intrauterine development confinement, perinatal mortality and preterm conveyance [4]. The reason for gestational anemia is multi-factorial. Iron, folate, nutrient B12 and nutrient and insufficiencies just as intestinal parasitic diseases, jungle fever, and perpetual sickness have all been demonstrated to be the primary driver of anemia among pregnant women [5]. Pregnancy-induced hypertension (PIH) is the systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or both and occurs after 20 weeks of gestational period in women without the history of hypertension. It can be classified into gestational hypertension, eclampsia and preeclampsia. Severe pre-eclampsia in pregnancy is a systolic blood pressure ≥160

mmHg or diastolic blood pressure ≥110 mmHg or both. Eclampsia is a severe form of PIH that develops near the end of pregnancy in one in every 1,600 pregnancies. Protein in the urine, high blood pressure, and pathologic edema are the three basic features of PIH disorders [6]. Anemia in pregnant women is common in Pakistan. Women make up 30-50% of the population. Prevalence of anemia among pregnant women is in the range of 30-50% depending upon different sociodemographic factors. There are contradictory studies regarding the relation between anemia and perinatal outcomes. Some previous reports have depicted a strong association between anemia and adverse perinatal outcomes such as LBW and preterm delivery, while other studies found no significant relationship. A meta-analysis depicted that anemia during early pregnancy, but not during late pregnancy, is associated with slightly increased risk of adverse perinatal outcomes [7]. As a result, there is little evidence to assess the effect of maternal anemia on maternal and perinatal outcomes, particularly PIH. The literature depicting the correlation between anemia and PIH is scarce and almost non-existent in Pakistan. The present study was designed to investigate the relation of anemia with the increased risk of PIH in pregnant women and contribute in further understanding of the anemia and associated perinatal outcomes.

METHODS

A retrospective study was designed and was conducted at Institute of Molecular Biology and Biotechnology at The University of Lahore and the data was collected from Hijaz Hospital Gulberg III Lahore, Pakistan from July 2018 to June 2019. Total 120 pregnant women were selected for the study and split into two groups. Group A consisted of 65 pregnant women with hypertension, whereas group B included 55 non-hypertensive pregnant women. The subjects were provided with questionnaire to collect necessary socio-demographic information during sampling. People suffering from viral hepatitis, cardiac diseases, cancer and any genetic disorders were excluded from the study. For blood sampling, 5ml whole blood was drawn from antecubital vein by aseptic technique then shifted in a properly labelled vacutainer (EDTA). Samples were then transported in ice box to lab and were stored and preserved at 4℃ for future use. For the estimation hemoglobin levels in blood, the Drabkin's method was followed with a few modifications [8]. The vacutainers were rolled on the test tube roller for homogenization and mixing of EDTA and blood. 4ml of the Drabkin's reagent was mixed well with 20ul of blood sample and incubated at room temperature away from sunlight for 5 minutes. The absorbance of the solution was then measured using UV-visible spectrophotometer at 546 nm. To estimate the value of hemoglobin, following formula was used:

Hb (g/dl) = (abs. of the sample/abs. of the standard) x standard conc.

For the evaluation of complete blood count (CBC), all tests were performed in Swelab Alfa Plus hematology analyzer based on CLSI Standard H26-A2. The independent student's test was used to determine the significance of the difference between quantitative variables. The correlation between variables of interest was calculated by using One-Way ANOVA. p-value < 0.05 was considered statistically significant. All calculations were carried out with the SPSS version-25. Frequency distribution charts were constructed for better demonstration of data.

RESULTS

Table 1 shows clear-cut distribution of data in based upon different sociodemographic variables. The data reflected that most of the pregnant women belongs to age group of 26-35. Abortion history of patients was also noted which shows that 37% of the pregnant women had the history of abortion. The data showed that group A had a higher number of women with an abortion history. Nutritional status of pregnant women was studied as well as shown in table 1.

Table 1: Socio-demographic variables of study population of pregnant women.

Variables	Range	Group A	Group B	%
Variables	18-25	21	20	34%
	26-35	35	28	52%
	36- onward	9	7	14%
Abortion History	Yes	26	19	37%
	No	39	36	63%
Nutritional status	Good	15	7	18%
	Moderate	28	30	48%
	Poor	22	18	34%

Out of 120 pregnant women, 27 were in their 1st trimester of pregnancy out of which 26 women belongs to group A and remaining 20 belongs to group B. 55 were included in 2nd trimester which means that 27 were hypertensive and 28 were non-hypertensive. In 3rd semester 19 women were recorded with classification of 12 and 7 in group A and group B respectively. So, the current study reflected that number of hypertensive women recorded was greater in 2nd trimester as compared to 1st and 3rd trimester as shown in table 2. Out of 120 pregnant women, 27 were in their 1st trimester of pregnancy out of which 26 women belongs to group A and remaining 20 belongs to group B. 55 were included in 2nd trimester which means that 27 were hypertensive and 28 were non-hypertensive. In 3rd semester 19 women were recorded with classification of 12 and 7 in group A and group B respectively. So, the current

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study reflected that number of hypertensive women recorded was greater in 2nd trimester as compared to 1st and 3rd trimester as shown in table 2.

Table 2: Trimester-wise data distribution of pregnant women

Pregnancy Status	Group A	Group B	%
1st trimester	26	20	24%
2nd trimester	27	28	45%
3rd trimester	12	7	31%
Total Participants	**65**	**55**	**100%**

Mean ± SD of Hb levels were estimated as 11.66667±1.182746, 10.05±1.47902, 9.953846±1.924584 in the group A according to first second and third trimester respectively. Similarly, in group B values were 11.06071±1.53816, 10.80714±1.804939 and 11.52±1.584172 according to the trimesters. The significant difference of Hb levels were observed in third trimester as illustrated in table 3.

Table 3: Descriptive statistics of hemoglobin (Hb) in pregnant women

Trimesters	Hemoglobin (Hb) g/dl (Mean ± SD)		Comparison of Anemic status
	Group A	Group B	
1st trimester	11.66667±1.182746	11.06071±1.538167	Non-significant difference
2nd trimester	10.05±1.47902	10.80714±1.804939	Non-significant difference
3rd trimester	9.953846±1.924584	11.52±1.584172	Significant difference

Amount of red blood cells levels were estimated as 4.1067±0.57816 and 5.5973±10.73055in the group A and group B respectively. The significant difference of red blood cells was observed in these groups. Similarly, WBCs were calculated 10.908±2.7353 million/mm3 and 9.806±2.0800 million/mm3 in the group A and group B respectively. The significant difference of WBC levels was observed in these groups.

Platelets levels were recorded as 296.73±76.003 million/mm3 and 269.89±52.530 million/mm3 in the group A and group B respectively. The non-significant difference of platelets was observed in these groups. These results were in the terms of mean±SD and depicted in table 4.

Table 4: Descriptive statistics of red blood cells (RBC), white blood cells (WBC) and platelets (PLT) in pregnant women

Parameters	(Mean ± SD)		p-value
	Group A	Group B	
RBC	4.1067±0.57816	5.5973±10.73055	0.652
WBC	10.908±2.7353	9.806±2.0800	0.030
PLT	296.73±76.003	269.89±52.530	0.009

DISCUSSION

From our study, we found that there exists a relationship between anemia and pregnancy-induced hypertension, significantly among women in their 3rd trimester of pregnancy. It coincided with our results of the complete blood count (CBC) in which hypertensive women had the least number of RBCs. In addition, we found that there was no significant association in anemia and PIH in 1st and 2nd trimesters, where hypertension may be due other factors, such as nutritional status, as PIH is multifactorial [9]. Overall, much smaller number of studies have investigated the correlation between anemia and PIH globally. Our positive results might be owed a variety of factors. Anemia effects the ability of blood to carry oxygen, which in turn increases stress on cardiovascular system as hear tries to compensate the decreased oxygen-carrying capacity by pumping more blood [10]. As oxygen delivery is already compromised, anemia can lead to exacerbation of the existing chronic diseases in the affected individuals [11]. In addition, anemia can lead to the weakening of immune system, and the individuals can become susceptible to the infections due decreased oxygen [12, 13]. In our study, it can be seen that hypertensive women had an increased number of WBCs and Platelets as compared to non-hypertensive women, which harmonizes with the study performed by Carey et al [14]. Another reason of hypertension in pregnant women with anemia is the dysfunction of trophoblast cells [15]. These cells are specialized cells that play a significant part in the early stages of pregnancy They are derived from the outer layer of the blastocyst, and are primarily responsible for implantation into the uterine wall and the subsequent formation of the placenta [16]. Anemia-induced hypoxia (deficiency of oxygen) can severely impact the function of these cells by altering the normal differentiation and proper vascularization of the uterine arteries, consequently increasing the risk of hypertension [17]. Our studies support the previous reports present in the literature. Lewandowska et al., reported the association of low iron in serum with the increased risk of pregnancy-induced hypertension [18]. Iron levels were measured using mass spectroscopy with inductively coupled plasma (ICP-MS). According to this study, the women in the lowest quartile (with the lowest iron levels) demonstrated 2.19-fold increased risk of PIH. Johnson et al., reported the association of anemia and PIH and studied the perinatal outcomes related to them. 51.3 % of the study population had anemia with PIH [19]. Similarly, Ali et al., studied the correlation between severe anemia and preeclampsia in the pregnant women at Kassala Hospital, Sudan [5]. The results of this study are in harmony with our study and state that severity of anemia is directly linked with the risk of preeclampsia and preterm delivery complications along with LBW and stillbirth. Conversely, there are studies, which provided opposite results as compared to our findings. According to Asres et al., pregnant women having high hemoglobin levels had greater risk of PIH as compared to those who did not [20]. Our study is one of the first studies in Pakistan that focus on analyzing the risk of PIH and anemia in pregnant women. This study not only

provides a starting point for further research in Pakistan, but also paves the way to investigate other factors contributing to PIH as not enough literature is present on the current topic.

CONCLUSIONS

In conclusion, this study highlights the substantial link between anemia and the risk of PIH. Our findings consequently demonstrate that lower levels of hemoglobin correspond to the greater risk of developing high blood pressure during pregnancy. These results underscore the importance of early identification and management of anemia in prenatal care in order to mitigate the risk of PIH. Our research emphasizes on the necessity of proactive strategies to address anemia in pregnant women, ultimately contributing to improved maternal and neonatal health outcomes.

Authors Contribution

Conceptualization: KZ
Methodology: HS, KZ
Formal analysis: KZ, SA
Writing-review and editing: AS
All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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REFERENCES

[1]   Zekarias B, Meleko A, Hayder A, Nigatu A, Yetagessu T. Prevalence of anemia and its associated factors among pregnant women attending antenatal care (ANC) in Mizan Tepi University Teaching Hospital, South West Ethiopia. Health Science Journal. 2017 Oct; 11(5): 1-8. doi: 10.21767/1791-809X.1000529.

[2]   Juárez-Cedillo T, Basurto-Acevedo L, Vega-García S, Manuel-Apolinar L, Cruz-Tesoro E, Rodríguez-Pérez JM, et al. Prevalence of anemia and its impact on the state of frailty in elderly people living in the community: SADEM study. Annals of Hematology. 2014 Dec; 93: 2057-62. doi: 10.1007/s00277-014-2155-4.

[3]   Abdulwahid RG and Ahmed HM. Nutritional characteristics of pregnant women and its relation with anemia during pregnancy in a sample of Kurdish women/Iraq. Cihan University-Erbil Scientific Journal. 2020 Jan; 4(1): 37-44. doi: 10.24086/cuesj.v4n1y2020.pp37-44.

[4]   De-Regil LM, Harding KB, Roche ML. Preconceptional nutrition interventions for adolescent girls and adult women: global guidelines and gaps in evidence and policy with emphasis on micronutrients. The Journal of Nutrition. 2016 Jul; 146(7): 1461S-70S. doi: 10.3945/jn.115.223487.

[5]   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 Research Notes. 2011 Dec; 4(1): 1-5. doi: 10.1186/1756-0500-4-311.

[6]   Karegoudar DJ. Evaluation of Prevalence of Pregnancy Induced Hypertension and Its Associated Factors Among Women at a Tertiary Care Centre. International Journal of Life Sciences Biotechnology and Pharma Research. 2020 Feb; 9(1): 5-7.

[7]   Bergen NE, Schalekamp-Timmermans S, Roos-Hesselink J, Roeters van Lennep JE, Jaddoe VV, Steegers EA. Hypertensive disorders of pregnancy and subsequent maternal cardiovascular health. European Journal of Epidemiology. 2018 Aug; 33: 763-71. doi: 10.1007/s10654-018-0400-1.

[8]   Srivastava T, Negandhi H, Neogi SB, Sharma J, Saxena R. Methods for hemoglobin estimation: A review of" what works. Journal of Hematology & Transfusion. 2014 Nov; 2(3): 1028.

[9]   Abid F, Ali R, Tahir MM, Siddique K. A Cross-Sectional Study to Assess the Dietary Intake and Habits of Expecting Women with Anemia. Annals of Punjab Medical College (APMC). 2019 Sep; 13(2): 160-3.

[10]   Mozos I. Mechanisms linking red blood cell disorders and cardiovascular diseases. BioMed Research International. 2015 Oct; 2015; 682054. doi: 10.1155/2015/682054

[11]   Weiss G. Anemia of chronic disorders: new diagnostic tools and new treatment strategies. Seminars in Hematology. 2015 Oct; 52(4): 313-20. doi: 10.1053/j.seminhematol.2015.07.004.

[12]   Zohora F, Bidad K, Pourpak Z, Moin M. Biological and immunological aspects of iron deficiency anemia in cancer development: a narrative review. Nutrition and Cancer. 2018 May; 70(4): 546-56. doi: 10.1080/01635581.2018.1460685.

[13]   He GL, Sun X, Tan J, He J, Chen X, Liu CX, et al. Survey of prevalence of iron deficiency and iron deficiency anemia in pregnant women in urban areas of China. Zhonghua fu Chan ke za zhi. 2018 Nov; 53(11): 761-7.

[14]   Tang YM, Chen XZ, Li GR, Zhou RH, Ning H, Yan H. Effects of iron deficiency anemia on immunity and infectious disease in pregnant women. Wei sheng yan jiu= Journal of Hygiene Research. 2006 Jan; 35(1): 79-

81.

[15] Chakraborty D, Cui W, Rosario GX, Scott RL, Dhakal P, Renaud SJ, et al. HIF-KDM3A-MMP12 regulatory circuit ensures trophoblast plasticity and placental adaptations to hypoxia. Proceedings of the National Academy of Sciences. 2016 Nov; 113(46): E7212-21. doi: 10.1073/pnas.1612626113.

[16] Awad O, Ochieng SJ, Malek A, Ogeng'o J. Chronic anaemia causes degenerative changes in trophoblast cells of the rat placenta. Anatomy. 2017 Aug; 11(2): 72-8. doi: 10.2399/ana.17.013.

[17] Labarrere CA, DiCarlo HL, Bammerlin E, Hardin JW, Kim YM, Chaemsaithong P, et al. Failure of physiologic transformation of spiral arteries, endothelial and trophoblast cell activation, and acute atherosis in the basal plate of the placenta. American Journal of Obstetrics and Gynecology. 2017 Mar; 216(3): 287-e1. doi: 10.1016/j.ajog.2016.12.029.

[18] Lewandowska M, Sajdak S, Lubiński J. Can serum iron concentrations in early healthy pregnancy be risk marker of pregnancy-induced hypertension? Nutrients. 2019 May; 11(5): 1086. doi: 10.3390/nu11051086.

[19] Johnson A, Vaithilingan S, Avudaiappan SL, Vaithilingan Sr S. The Interplay of Hypertension and Anemia on Pregnancy Outcomes. Cureus. 2023 Oct; 15(10). doi: 10.7759/cureus.46390.

[20] Asres AW, Samuel S, Daga WB, Tena A, Alemu A, Workie SB, et al. Association between iron-folic acid supplementation and pregnancy-induced hypertension among pregnant women in public hospitals, Wolaita Sodo, Ethiopia 2021: a case-control study. BMC Public Health. 2023 Dec; 23(1): 1-1. doi: 10.1186/s12889-023-15794-6.