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Research Article

FREQUENCY OF PRETERM LABOUR AND HYPERTENSIVE DISORDERS IN ANEMIC PATIENTS

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Abstract:

Background: Anemia is one of the high burden morbidities found in the developing countries and it can further be fatal when it is found in pregnant females as the morbidity and mortality can occur both in mother as well as fetus due to various complications. Hypertensive disorders like pre eclampsia, eclampsia and pre term labor are well reported in pregnant females.

Objectives: To determine the frequency of pre-term labor and hypertensive disorders (pre-eclampsia and eclampsia) in anemic pregnant women. **Study design:** Descriptive case series study. **Setting:** Department of Gynaecology, Shaikh Zayed Hospital, Rahim Yar Khan.

Duration of Study: 15 March 2017 to 15 March 2018. **Methodology:** The patients with age 20-40 years with single pregnancy of 20 weeks gestation or more (assessed by history and USG) irrespective of the number of parity with hemoglobin level less than 10 mg/dl will be included. **Results:** In the present study there were total 188 anemic pregnant women. The mean age was 28.59 ± 4.52 years and mean BMI was 28.65 ± 4.12 . Mean parity was 2.06 ± 0.95 while mean duration of gestation at presentation was 28.86 ± 4.52 weeks. There were 90 (47.87%) of cases that had previous history of C section and 141 (75%) of the females belonged rural family. Regarding different outcomes pre eclampsia was seen in 33 (17.55%) of cases, eclampsia in 9 (4.79%) of cases and pre term labor in 48 (25.53%) of cases. On stratification of data with respect to pre eclampsia which was more seen in young age and those with single gravida n para; but none of the variable was found statistically significant. Eclampsia was seen significantly high in cases that had BMI more than 30 where it was seen in 8 (9.52%) of cases as compared to only 1 (0.96%) cases in their respective groups with p value of 0.01. In contrast to pre eclampsia, eclampsia was more seen in multiparous women and those with previous history of C section; although this difference was also not statistically significant. There was no significant difference in terms of pre term labor and the effect modifiers. However, it was relatively higher in cases that were multiparous and had gravida more than one with p values of 0.16 and 0.15.

Conclusion: Complications are not uncommon in pregnant females suffering from anaemia and pre term labor is the most commonly observed. Moreover eclampsia is significantly associated with cases that had BMI more than 30 kg/m².

Key words: Anemia, Pre term labor, Eclampsia, Pre eclampsia.

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INTRODUCTION:**OBJECTIVE:**

To determine the frequency of pre-term labor and hypertensive disorders (pre-eclampsia and eclampsia) in anemic pregnant women.

OPERATIONAL DEFINITIONS:**Anemia;**

It was labeled yes when the hemoglobin concentration is less than 10 mg/dl.

Pre-term labor;

It was labeled yes when the fetus is delivered (spontaneously via vaginal delivery or C section) before 37 weeks of gestation (assessed by history and medical record).

Pre eclampsia;

It was labeled yes when there is new onset HTN (previously normal assessed by history and medical record) i.e. BP more than 140/90 mm Hg (both systolic and diastolic were high) taken 4 hours apart and 24 hour urinary protein more than 300 mg/dl (both should be present) after 20 weeks of gestation.

Eclampsia;

It was labeled yes when all of these are present after 20 weeks of gestation.

- New onset HTN (previously normal assessed by history and medical record) i.e. BP more than 140/90 mm Hg (both systolic and diastolic should be high) taken 4 hours apart
- 24 hour urinary protein more than 300 mg/dl
- History of fits (one or more episode of jerky movement of one or more parts of the body lasting at least 30 seconds with or without loss of consciousness or coma labeled as loss of consciousness for at least 1 hour assessed by history and medical record).

Hypothesis: There are significant number of cases with pre-term labor, pre-eclampsia and eclampsia in anemic patients.

MATERIALS AND METHODS:

Study Design: It was a descriptive study.

Setting: Department of Gynecology, Sheikh Zayed Hospital, Rahim Yar Khan.

Duration: 15 March 2017 to 15 March 2018

Sample Size: The sample was calculated as 188 by keeping the confidence equal to 95%, and margin of error equal to 3% and prevalence of Eclampsia in 4.6%, with anemia in previous studies.⁸

Sampling Technique: Non probability consecutive sampling

SAMPLE SELECTION:

Inclusion Criteria: The patients with age 20-40 years with single pregnancy of 20 weeks gestation or more (assessed by history and USG) irrespective of the number of parity with hemoglobin level less than 10 mg/dl were included.

Exclusion Criteria:

1. Patients with history of HTN, DM (assessed on history and medical record).
2. Patients with more than one pregnancy assessed on USG.
3. Patients undergoing iatrogenic delivery (delivery done due to condition like premature rupture of membranes, antepartum haemorrhage assessed by medical record)
4. Patients having UTI (assessed by having pus cells at least 5/HPF on urine examination).
5. Patients with history of trauma within last 3 days (assessed on history and medical record).

DATA COLLECTION PROCEDURE:

After the acceptance from ethical review committee of Sheikh Zayed hospital, RYK, an informed consent was taken from each subject for inclusion in this study. Socio demographic and clinical data like age, weight, height, BMI, age of gestation, history of gravidity, and previous C section was taken from all the subjects with gestation more than 20 weeks presenting to Department of Gynecology SZH, RYK and recorded on a proforma. Then all the cases with Hemoglobin less than 10 gm% were included in this study. These cases then were followed on every 2 weeks to look for hypertensive disorder (pre-eclampsia and eclampsia) and preterm labor as per operational definition. The results were noted and recorded on the same proforma.

DATA ANALYSIS:

Data was analyzed with the help of SPSS version 17. Quantitative variables like age, gestational age at presentation, parity, gravida, blood pressure, amount of 24 hour urinary protein, hemoglobin and time of gestation at delivery (weeks) were presented in terms of mean \pm SD (Standard Deviation). Frequency & percentages were calculated for gender, pre-eclampsia, eclampsia, pre-term labor (yes/no), residence (rural/urban) and previous C section. Effect modifiers were controlled through stratification of age, BMI, gestational age at presentation, gravida, parity, h/o C section and residence to see the effect on outcome variable. Post stratification chi square test was applied. P-value ≤ 0.05 was taken as significant.

1.1. RESULTS:

In the present study there were total 188 anemic pregnant women. The mean age was 28.59 ± 4.52 years and mean BMI was 28.65 ± 4.12 as shown in table 1. Mean parity was 2.06 ± 0.95 as in table 2 while mean duration of gestation at presentation was 28.86 ± 4.52 weeks as shown in table 03. There were 90 (47.87%) of cases that had previous history of C

section (figure 3) and 141 (75%) of the females belonged rural family as in figure 04. Regarding different outcomes pre eclampsia was seen in 33 (17.55%) of cases, eclampsia in 9 (4.79%) of cases and pre term labor in 48 (25.53%) of cases as displayed in figures 05-07 respectively. Table 04 and 05 reveal stratification of data with respect to pre eclampsia which was more seen in young age and those with single gravida n para; but none of the variable was found statistically significant. Eclampsia was seen significantly high in cases that had BMI more than 30 where it was seen in 8 (9.52%) of cases

as compared to only 1 (0.96%) cases in their respective groups with p value of 0.01 as shown in table 06. In contrast to pre eclampsia, eclampsia was more seen in multiparous women and those with previous history of C section; although this difference was also not statistically significant as shown in table 07. There was no significant difference in terms of pre term labor and the effect modifiers (table 8-9). However, it was relatively higher in cases that were multiparous and had gravida more than one with p values of 0.16 and 0.15 as shown in table 09.

1.2. TABLES & FIGURES:

TABLE NO. 01: STUDY VARIABLES (age, BMI n hemoglobin n= 188

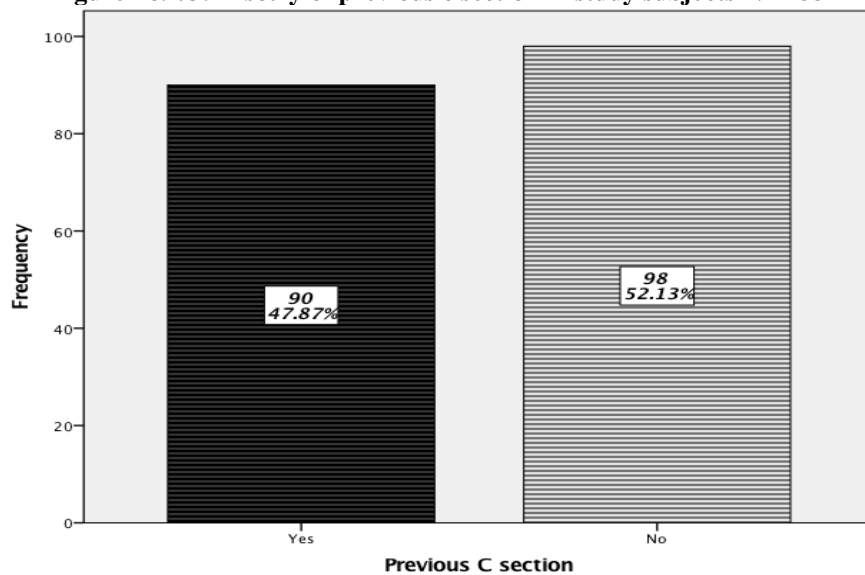
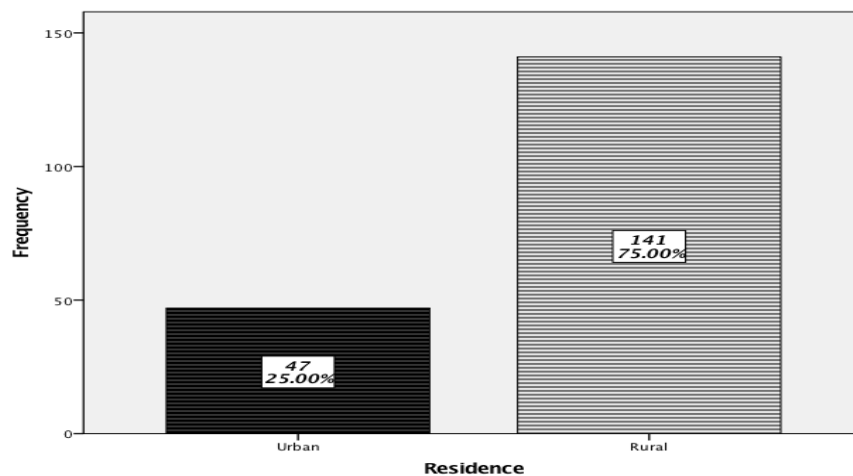
		VARIABLES		
		AGE	BMI	Hb
Mean		28.59	28.65	7.92
95% Confidence Interval for Mean	Lower bound	27.94	28.06	7.76
	Upper bound	29.24	29.25	8.08
Median		29.00	27.50	8.00
Std. Deviation		4.52	4.12	1.14

TABLE NO. 02: STUDY VARIABLES (Gravida, parity, urinary protein) n= 188

		VARIABLES		
		Gravida	Parity	Urinary protein (mg/dl)
Mean		2.16	2.06	479.26
95% Confidence Interval for Mean	Lower bound	2.00	1.93	412.02
	Upper bound	2.33	2.20	546.49
Median		2.00	2	180
Std. Deviation		1.14	0.95	467.28

TABLE NO. 03: STUDY VARIABLES (duration of gestation at presentation, delivery and systolic BP) n= 188

		VARIABLES		
		Duration of Gestation at Presentation	Duration of Gestation at Delivery	Systolic BP
Mean		28.86	35.07	126.01
95% Confidence Interval for Mean	Lower bound	28.30	34.71	121.84
	Upper bound	29.41	35.43	130.18
Median		28.00	36.00	120.00
Std. Deviation		4.52	2.52	28.98

Figure no. 03: Hisotry of previous c section in study subjects N= 188**FIGURE NO. 04: RESIDENCE OF STUDY SUBJECTS n= 188****FIGURE NO 05: PRE ECLAMPSIA IN STUDY SUBJECTS n= 188**

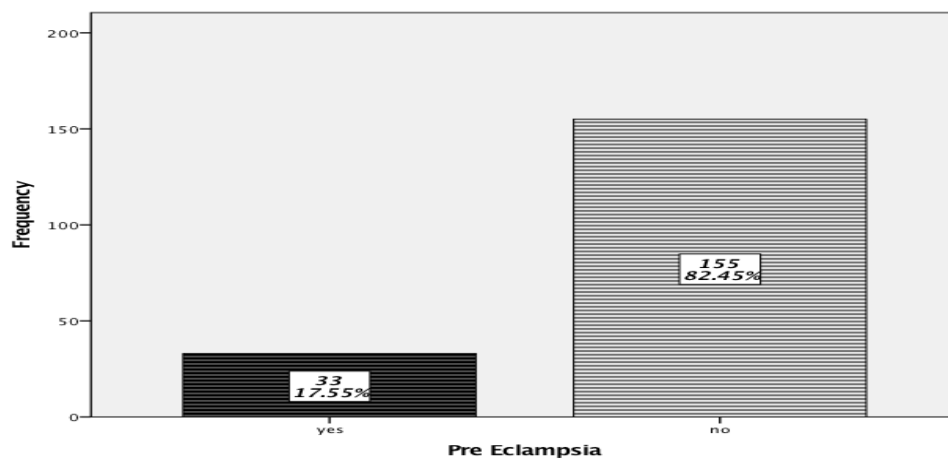
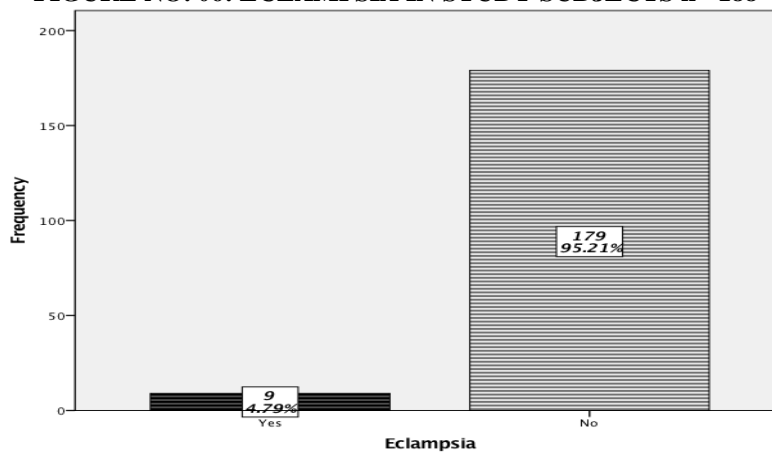
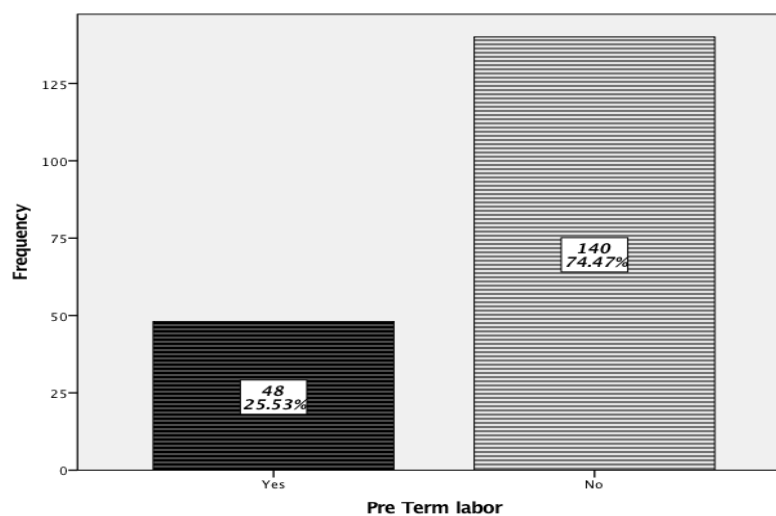
**FIGURE NO. 06: ECLAMPSIA IN STUDY SUBJECTS n= 188****FIGURE NO. 07: PRE TERM LABOR IN STUDY SUBJECTS n= 188**

TABLE NO. 04: PRE-ECLAMPSIA WITH RESPECT TO AGE, BMI, GESTATIONAL AGE AND RESIDENCE n= 188

VARIABLES		PRE ECLAMPSIA		p value
		Yes	No	
Age	20-29	20 (20.8%)	76 (79.2%)	0.22
	30-40	13 (14.1%)	79 (85.9%)	
BMI	30 or less	19 (18.3%)	85 (81.7%)	0.77
		14 (16.7%)	70 (83.3%)	
Gestational age at presentation	20-29	21 (16.4%)	107 (83.6%)	0.54
	30 or more	12 (20%)	48 (80%)	
Residence	Urban	12 (25.5%)	35 (74.5%)	0.12
	Rural	21 (14.9%)	120 (85.1%)	

TABLE NO. 05: PRE ECLAMPSIA WITH RESPECT TO GRAVIDA, PARITY AND H/O C SECTION n= 188

VARIABLES		PRE ECLAMPSIA		p value
		Yes	No	
Gravida	Single	12 (20%)	48 (80%)	0.54
	Multiple	21 (16.4%)	107 (83.6%)	
Parity	Single	11 (18.3%)	49 (81.7%)	0.84
	Multiple	22 (17.2%)	106 (82.8%)	
H/O C section	Yes	13 (11.1%)	77 (88.9%)	0.34
	No	20 (20.4%)	78 (79.6%)	

TABLE NO. 06: ECLAMPSIA WITH RESPECT TO AGE, BMI, GESTATIONAL AGE AND RESIDENCE n= 188

VARIABLES		ECLAMPSIA		p value
		Yes	No	
Age	20-29	6 (6.25%)	90 (93.75%)	0.49
	30-40	3 (3.26%)	89 (96.74%)	
BMI	30 or less	1 (0.96%)	103 (99.04%)	0.01
		8 (9.52%)	76 (90.48%)	
Gestational age at presentation	20-29	6 (4.68%)	122 (94.32%)	1.0
	30 or more	3 (5%)	57 (95%)	
Residence	Urban	2 (4.25%)	45 (95.75%)	1.0
	Rural	7 (4.96%)	134 (95.04%)	

TABLE NO. 07: ECLAMPSIA WITH RESPECT TO GRAVIDA, PARITY AND H/O C SECTION n= 188

VARIABLES		ECLAMPSIA		p value
		Yes	No	
Gravida	Single	1 (1.67%)	59 (98.33%)	0.27
	Multiple	8 (6.25%)	120 (93.75%)	
Parity	Single	2 (3.33%)	58 (96.67%)	0.28
	Multiple	7 (5.55%)	119 (94.45%)	
H/O C section	Yes	3 (3.33%)	87 (94.67%)	0.50
	No	6 (6.12%)	92 (93.88%)	

TABLE NO. 08: PRE TERM LABOR WITH RESPECT TO AGE, BMI, GESTATIONAL AGE AND RESIDENCE n= 188

VARIABLES		PRE TERM LABOR		p value
		Yes	No	
Age	20-29	28 (29.2%)	68 (70.8%)	0.31
	30-40	20 (21.7%)	72 (78.3%)	
BMI	30 or less	27 (25.9%)	77 (74.1%)	1.0
		21 (25%)	63 (75%)	
Gestational age at presentation	20-29	34 (26.6%)	94 (73.4%)	0.72
	30 or more	14 (23.3%)	46 (76.7%)	
Residence	Urban	13 (27.7%)	34 (72.3%)	0.70
	Rural	35 (24.8%)	106 (75.2%)	

TABLE NO. 09: PRE TERM LABOR WITH RESPECT TO GRAVIDA, PARITY AND H/O C SECTION n= 188

VARIABLES		PRE TERM LABOR		p value
		Yes	No	
Gravida	Single	11 (18.3%)	49 (81.7%)	0.15
	Multiple	37 (28.9%)	91 (71.1%)	
Parity	Single	10 (16.7%)	50 (83.3%)	0.16
	Multiple	38 (29.7%)	90 (70.3%)	
H/O C section	Yes	20 (22.2%)	70 (77.7%)	0.40
	No	28 (28.6%)	70 (71.4%)	

1.3. DISCUSSION:

The various studies on maternal anaemia and adverse reproductive outcomes have produced inconsistent findings. This is largely mitigated by the fact that maternal anaemia has been analysed as an aggregated exposure such as 'any anaemia during pregnancy'. It is likely that anaemia diagnosed early in pregnancy

may exert stronger associations on pregnancy outcomes than anaemia diagnosed later in gestation. Equally, studies on preterm birth have paid little attention to its heterogeneous underpinnings, thereby combining aetiologically distinct endpoints as being homogeneous, and perhaps leading to attenuated association measures. Finally, little attention has been

devoted as to how anaemia affects the risk for preterm birth clinical subtypes, including previous Chinese studies. Most studies have exclusively focused on spontaneous preterm births. Our study was designed to see not only the pre term birth but also the other hypertensive disorders of pregnancy like pre eclampsia and eclampsia.

In the present study regarding the hypertensive disorders, pre eclampsia was seen in 33 (17.55%) of cases while eclampsia was observed in 9 (4.79%) of cases only. According to a study done by Ali AA et al, they evaluated the association of anemia with risk of pre eclampsia and it was seen that in women with severe anaemia had a 3.6 times higher risk of preeclampsia than women with no anaemia.¹ It was recently observed that 17 (17.7%) of 97 women with severe anaemia had gestational hypertension or preeclampsia and 2 (2.1%) had eclampsia.² However, it might be difficult to reach a firm conclusion from this report since the authors did not mention the incidence of these events in women with mild/moderate anaemia or with no anaemia. The susceptibility of women with severe anaemia to preeclampsia could be explained by a deficiency of micronutrients and antioxidants. Recent results indicate that reduction in serum levels of calcium, magnesium and zinc during pregnancy might be possible contributors to the development of preeclampsia. [3]

According to another study it was observed that the cases having anemia have a high prevalence of micronutrient deficiency as well.⁴ In such scenario it might be difficult to determine if severe anaemia was the cause or effect of preeclampsia/eclampsia in this study as the anaemia was diagnosed at admission and may have been a consequence of the disease process (haemolysis in HELLP syndrome). A longitudinal study with a large sample size is needed to explore whether severe anaemia is a cause or effect of preeclampsia. There may, however, be ethical issues with such a study as severe anaemia is a medical emergency which should be prevented and treated immediately. Poor maternal and perinatal outcomes in cases of anaemia associated with malaria have recently been documented in some regions. [5] It appears probable that the severe anaemia caused by malaria is a major factor in those outcomes. Previous studies have indicated that malaria increases the risk of hypertensive disorder during pregnancy⁶ Placental histology is the gold standard for the diagnosis of malaria during pregnancy, and is preferred over the peripheral blood film, which has many abnormalities in this setting. [7]

Interestingly, earlier studies have reported controversial results and have shown higher incidence of preeclampsia and an increased incidence of hypertensive disorders in women with high Hb levels (13.3 g/dl and 12.5 g/dl) than in those with normal levels.⁸⁻⁹ Murphy et al. (1986) reported that, in primiparas, the frequency of hypertension ranged from 7% with Hb < 10.5 g/dl to 42% with Hb > 14.5 g/dl.¹⁰ The increased incidence of preeclampsia in pregnant women with high Hb levels could be explained by the toxic effects of methaemoglobin-derived haeme deposition on the vascular endothelium and consequent atherosclerosis. Atherosclerotic blood vessels were commonly seen in the placental beds of preeclamptic pregnancies¹¹⁻¹² None of the aforementioned studies found significant association with any of the confounding variables like age, duration of gestation, parity etc as was also not seen in the present study and all the parameter revealed the p value of more than 0.05.

Eclampsia was seen significantly high in cases that had BMI more than 30 where it was seen in 8 (9.52%) of cases as compared to only 1 (0.96%) cases in their respective groups with p value of 0.01. There were no studies that used such cut off values to confabulate the effect of BMI in eclampsia in cases of anemia. But this can be explained by the fact that the higher BMI serves as another entity along with anemia to lead to hypertensive disorders due to atherosclerosis and narrowing of vessels.

In this study pre term labor was the most common finding observed as it was seen in 48 (25.53%) out of 188 cases with anemia. This was also supported by the data of the previous studies where they also revealed that the risk of preterm birth, LBW and stillbirth was higher in anaemic women, and increased with the severity of anaemia. This supports previous observations from Sudan as well as from other African countries. LBW is one of the major causes of the 4 million neonatal deaths per year in developing countries. Neonatal deaths account for 38% of child deaths under the age of 5 years.[13, 14]

Our findings on all preterm birth were consistent with a meta-analysis which concluded that early pregnancy anaemia was associated with slightly increased risk for preterm birth and late pregnancy anaemia was inversely associated with preterm birth.¹⁵ Previous Chinese studies conducted in the same or nearby regions, examined the association between anaemia and preterm birth without consideration of associations by preterm birth clinical subtypes.¹⁶⁻¹⁷ Whereas some reported anaemia in the first trimester to be associated with increased

risk¹⁸ of preterm birth, others did not.⁸⁷ The last study reported that only the third trimester haemoglobin.

Anaemia in early pregnancy or throughout pregnancy may represent pre-existing, or early onset and persistent iron deficiency. Iron deficiency anaemia, in turn, could induce maternal infection, hypoxia and oxidative stress, and trigger the spontaneous onset of preterm labour.^[19, 20]

There were many strengthening points of the present study, as it elaborated in detail, the different confounding factors as were not studies in the past in that detail. Moreover, it also look for non only pre term labor but also different hypertensive disorders.

However, there were few limitations as well, as this study did not categorize the different degrees or severity of anemia and also did not look for the time to develop anemia as the data has shown that this has the impact on different outcomes.

1.4. CONCLUSION:

Complications are not uncommon in pregnant females suffering from anaemia and pre term labor is the most commonly observed. Moreover eclampsia is significantly associated with cases that had BMI more than 30 kg/m².

REFERENCES:

1. Levine RJ, Hauth JC, Curet LB, Sibai BM, Catalano PM, Morris CD, et al. Trial of calcium to prevent preeclampsia. *N Engl J Med*. 1997 Jul 10; 337(2):69-76. [\[Medline\]](#).
2. Ali AA, Rayis DA. 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.
3. Rohilla M, Raveendran A, Dhaliwal LK, Chopra S. Severe anaemia in pregnancy: a tertiary hospital experience from northern India. *J Obstet Gynaecol*. 2010;30(7):694-6.
4. Jain S, Sharma P, Kulshreshtha S, Mohan G, Singh S. The role of calcium, magnesium, and zinc in pre-eclampsia. *Biol Trace Elem Res*. 2010;133(2):162-70. doi: 10.1007/s12011-009-8423-9.
5. Mohamed AA, Ali AA, Ali NI, Abusalama EH, Elbashir MI, Adam I. Zinc, parity, Huisman A, Aarnoudse JG. Increased 2nd trimester hemoglobin concentration in pregnancies later complicated by hypertension and growth retardation. Early evidence of a reduced plasma volume. *Acta Obstet Gynecol Scand*. 1986;65:605-8. doi: 10.3109/00016348609158396. [\[PubMed\]](#) [\[Cross Ref\]](#)
6. Phaloprakarn C, Tangjitgamol S. Impact of high maternal hemoglobin at first antenatal visit on pregnancy outcomes: a cohort study. *J Perinat Med*. 2008;36(2):115-9. doi: 10.1515/JPM.2008.018. [\[PubMed\]](#) [\[Cross Ref\]](#)
7. Murphy JF, O'Riordan J, Newcombe RG, Coles EC, Pearson JF. Relation haemoglobin levels in first and second trimesters to outcome of pregnancy. *Lancet*. 1986;3;1(8488):992-5. [\[PubMed\]](#)
8. Balla G, Vercellotti GM, Muller-Eberhard U, Eaton J, Jacob HS. Exposure of endothelial cells to free heme potentiates damage mediated by granulocyte and toxic oxygen species. *Lab Invest*. 1991. pp. 648-55. [\[PubMed\]](#)
9. Balla J, Nath K, Balla G, Juckett MB, Jacob HS, Vercellotti GM. Endothelial cell heme oxygenase and ferritin induction in rat lung by hemoglobin in vivo. *Am J Physiol*. 1995. pp. 321-7.
10. infection and severe anaemia among pregnant women in Kassala, eastern Sudan. *Biol Trace Elem Res*. 2010;137(3):225-230.
11. Adam I, Elhassan EM, Haggaz AD, Ali AA, Adam GK. Apprespective of the pidemiology of malaria and anemia and their impact on maternal and perinatal outcomes in different regions of Sudan. *J Infec Dev Ctries*. 2011;5(2):83-7. [\[PubMed\]](#)
12. Ndao CT, Dumont A, Fievet N, Doucoure S, Gaye A, Lehesran JY. Placental malarial infection as a risk factor for hypertensive disorders during pregnancy in Africa: a case-control study in an urban area of Senegal, West Africa. *Am J Epidemiol*. 2009;170(7):847-5.
13. Elhassan EM, Haggaz AD, Magzoub MM, Adam I. Non-malarial fever among pregnant women in Medani Hospital, Sudan: Diagnostic uncertainty and overtreatment with quinine. *Asian Pac J Trop Med*. 2010;5:395-398.
14. Haggaz AD, Radi EA, Adam I. Anaemia and low birth weight in Western Sudan. *Trans R Soc Trop Med Hyg*. 2010;104:234-236. doi: 10.1016/j.trstmh.2009.07.013. [\[PubMed\]](#) [\[Cross Ref\]](#)
15. Kidanto HL, Mogren I, Lindmark G, Massawe S, Nystrom L. Risks for preterm delivery and low birth weight are independently increased by severity of maternal anaemia. *S Afr Med J*. 2009;99(2):98-102.
16. Xiong X, Buekens P, Alexander S, Demianczuk N, Wollast E. Anemia during pregnancy and birth outcome: a meta-analysis. *Am J Perinatol*. 2000;17:137-46. 29 Adams MM, Sarno AP,

- Harlass FE, Rawlings JS, R
17. Zhou L, Yang W, Hua J, Deng C, Tao X, Stoltzfus R. Relation of hemoglobin measured at different times in pregnancy to preterm birth and low birth weight in Shanghai, China. *Am J Epidemiol* 1998;148: 998–1006.
 18. Xiong X, Buekens P, Fraser WD, Guo Z. Anemia during pregnancy in a Chinese population. *Int J Gynecol Obstet* 2003;83:159–64.
 19. Ren A, Wang J, Ye R, Li S, Liu J, Li Z. Low first-trimester hemoglobin and low birth weight, preterm birth and small for gestational age newborns. *Int J Gynecol Obstet* 2007;98:124–28.
 20. Allen LH. Biological mechanisms that might underlie iron's effects on fetal growth and preterm birth. *J Nutr* 2001;131:581s–89s.