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ORIGINAL ARTICLE

Comparative Study of Anemia of Inflammation in Pregnant and Non-Pregnant Women

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ABSTRACT

Aim: To compare the prevalence of Anemia of Inflammation (AI) in pregnant and Non-pregnant women.
Study design: A Cross sectional study.
Place and duration of study: Indus Medical College, Tando Muhammad Khan, between the duration of January 2021 to November 2021
Methodology: A total of 300 participants were enrolled for this study which comprises of 133 pregnant and 167 non-pregnant women. Pregnant women between 7th to 13th weeks of gestation were selected with hemoglobin and serum ferritin level less than 10 g/dL. Different hematological parameters were analyzed to assess the prevalence of AI in anemic pregnant and non-pregnant women which include Hemoglobin (Hb), Red Blood Cells (RBCs), hematocrit (HCT), Mean Corpuscular Volume (MCV), Hepcidin, Total Serum Iron (TSI), Transferrin, Serum Ferritin (sFtn) and Soluble transferrin receptor (sTfR).
Results: Our data indicates that, AI was most prevalent in women with child bearing age, about 17% pregnant and 23% non-pregnant women were associated with β-thalassemia which could be a reason of anemia of inflammation. High level of Hepcidin, transferrin saturation and serum ferritin were observed in our participants that indicates the presence of AI in our study population.
Conclusions: In our study, the prevalence of AI were high in women with chronic inflammation in comparison to women without subsequent infection. The proper diagnosis is necessary for the management and better treatment of AI in pregnant women.
Keywords: anaemia, pregnant women, non pregnant women, inflammation

INTRODUCTION

Anemia of inflammation (AI) usually known as Anemia of chronic disease (ACD). It is the most frequent type of anemia in hospitalized and elderly patient. It also prevalent in chronically ill, immunocompromised and patient with autoimmune disease. Recently, it is also reported in chronic disease like cancer, kidney failure, obesity, chronic inflammation, chronic pulmonary diseases and congestive heart failure. According to a report it is estimated that 40% of all anemia's globally is due to AI[1].Iron plays a vital role for the production of hemoglobin and it halts the production of HB if not supplied adequately. This condition is termed as Anemia. AI is the result of inflammatory action rather than the deficiencies of micronutrients like Vitamin B12 or folate[2].

In third world and developing countries, children and pregnant women are at highest risk to anemia and have minimum access to services and interventions for the cure of anemia[3,4]. According to a World Bank Report, the prevalence of Anemia decreases with income all over the country[5].

Anemia of inflammation is basically a condition which is diagnosed by increased serum Hepcidin level, low total Serum Iron Concentration (TSI) with low Hemoglobin Hb level (100µg/L), High Concentration of C-Reactive Protein (CRP),serum transferrin receptor (sTfR), and Serum ferritin. It is reported that the high level of Hepcidin in serum is dangerous for fetus because it can cause unavailability of Iron to placenta and fetus[6].

Hepcidin is an important marker in the diagnosis of AI. It produced in response to inflammatory action by the liver when iron is excess in the body. It is also involve in the degradation of iron export protein called ferroportin, which prevents absorption of iron from small intestine thus play an important role in the release of iron from macrophages, in this way hepcidin controls iron homeostasis.Increase serum hepcidin level with low inflammation in normal pregnancy has no such side effects but hepcidin considerably increases due to impaired inflammation in complex pregnancy. In this way it may disturb body iron metabolism and affects the intestinal iron absorption from food. Moreover, it also decreases the efficiency of parental iron therapy[8,9].

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Coexisting of AI with IDA is remarkably dangerous in pregnancy. Poor delivery of iron from food to the body is responsible for Iron deficiency Anemia which ultimately leads to simultaneously inflammation and results in functional deficiency AI. Women with AI and IDA during their pregnancy are at high risk because they require high level of additional iron. AI and IDA characterize risk factors for pregnancy and they may cause preterm delivery, neonate's deaths and postnatal child growth[6,7,8].
AI is considered to be developed as an effect of efficient defense mechanism against any microbial infection. As majority of microbes are dependent on availability of sufficient iron supply to progress its pathogenicity and multiplication. The growths of proliferating malignant cells are negatively affected by iron limitation and IDA. For this reason, the cause of AI is multifactorial. It includes inflammatory mediators that affects iron homeostasis results in iron limitation and ultimately develop[10,11].

The goal of this study was to check the occurrence, cause and hematological parameters of Anemia of inflammation (AI) in pregnant and non-pregnant women in the premises of Al-Tibri Medical College, Isra University, Karachi.

METHODOLOGY

Study design: After approval from Ethical Review Committee, this study was carried out over a period of 11 months from January 2021 to November 2021 at Indus Medical College, Tando Muhammad Khan. Women were recruited in this study who were reported the outpatient department OPD for their maternal care. Non-Pregnant Women were recruited from healthy population of Indus Medical College Hospital, Tando Muhammad Khan. All pregnant and non-pregnant women included in this study were diagnosed with moderate to severe anemia and a concern form was filled out by the participants before the study. A total of 300 participants were enrolled for the study which comprises of 133 pregnant and 167 non-pregnant women. Pregnant women between 7th to 13th weeks of gestation were selected with hemoglobin level less than 10g/dL.
Exclusion criteria: Exclusion criteria include non-anemic women, or having and taking any type oral contraception medicine and breast-feeding mothers. Non- pregnant women with a habit of smoking were also excluded.

Collection of Sample: Blood was drawn from all participants including pregnant and non-pregnant women for the analysis of hematological parameters including Hemoglobin (Hb), Red Blood Cells (RBCs), hematocrit (HCT), Mean Corpuscular Volume (MCV), Hepcidin, Total Serum Iron (TSI), Transferrin, Serum Ferritin (sFtn) and Soluble transferrin receptor (sTfR). All tests were carried out on fully automated blood cell counter SYSMEX XE-200 & SYSMEX XE-100.Serum ferritin was tested by using chemiluminescent microparticle immunoassay, soluble transferrin receptor was determined by Immunoturbidometric method.

Data analysis: Statistical data were analyzed by using SPSS version 20.00. Mean and standard deviation between the groups and intra groups were determined by Paired T-test and ANOVA.

RESULTS

Our selection criteria were based on hematological parameters of the participant. As we have chosen only anemic participants suffering from any infectious disease as the reason for their low hemoglobin level. After the selection, the elected participants were further tested for CBC, level of Hepcidin, Total Serum Iron (TSI), Transferrin, and Serum Ferritin (sFtn), and Transferrin saturation to ensure the cause of Anemia. All participants were 28.46±8.54 (22-37) years old. The pregnant women enrolled during gestational age of 28.7 ± 17.4 weeks (Table 1).

Table 2 summarizes the distribution of related disorders in pregnant women which include 23 (17%) β-thalassemia, 26 (19%) Type2 Diabetes, 21 (15%) High blood pressure, 9 (6%) Epilepsy, and 7 (5%) suffering from Inflammatory bowel disease sometimes called Crohn's disease. Similarly, women of child bearing age have more or less same distribution except the frequency of Type 2 diabetes and high blood pressure which were found to be 6(3%) and 4(2%) respectively. A high percentage (35-47%) of participants was free from any prior infection but suffering from anemia. It has been noted that β-thalassemia, IBD and Epilepsy were slightly prevalent in non-pregnant women as comparison to pregnant women.

Table 1: Demographic Data of Pregnant Women (n=133)

Variables	Mean Value
Maternal Age	27.42 ± 5 Years
Gestational age	28.7 ± 17.4 Week
Gravidity*	2 ± 1

**Gravidity= no of times a women conceives*

Table 2. Distribution of supplementary diseases in Pregnant and Non-pregnant women (n=300)

Name of disease	Frequency & Percentage	
	Pregnant Women (n=133)	Non-Pregnant Women (n=167)
β-thalassemia	17.29323% (23)	23.35329% (39)
Type 2 diabetes	19.54887% (26)	3.592814% (6)
High Blood Pressure	15.78947% (21)	2.39521% (4)
Epilepsy	6.766917% (9)	10.77844% (18)
Inflammatory bowel disease (IBD)	5.263158% (7)	12.57485% (21)
Without any prior infection	35.33835% (47)	47.30539% (79)

Table 3. Hematological parameters, Mean ± SD of pregnant and Non-pregnant Women suffering from any infection or disease (Group 1)

Parameters	Unit	Pregnant Women (n=86)	Non-Pregnant Women (n=88)	p-value
Hemoglobin	g/dl	8.2 ± 0.9	10.2 ± 0.8	0.045
Red Blood Corpuscles	$X10^{12}$/L	3.2 ± 1.4	4.0± 0.7	0.80
Hematocrit	%	28.3± 0.23	31.5 ± 0.21	0.089
MCV	fL	75.2 ± 0.45	82.2± 0.03	<0.05
MCHC	g/L	22.1± 0.16	30.1 ± 0.11	<0.05
Total Serum Iron	µg/dL	33 **±**13	42 ± 9	<0.05
Serum ferritin	µg/L	21**±** 7	28 ± 8	<0.05
Serum transferrin receptor	mg/L	13 **±** 9	11**±** 7	0.078
Transferrin saturation	%	19.4 ± 12.5	23.2 ± 10.4	0.256
Hepcidin	ng/ml	110 ± 21	99 ± 12	0.671

Table 4 Hematological parameters, Mean ± SD of pregnant and Non-pregnant Women without any infection or disease (Group 2)

Parameters	Unit	Pregnant Women (n=86)	Non-Pregnant Women (n=88)	p-value
Hemoglobin	g/dl	9.8 ± 1.4	10.7 ± 1.2	0.068
Red Blood Corpuscles	$X10^{12}$/L	4.2 ± 0.11	4.41± 0.3	0.768
Hematocrit	%	29.3± 0.3	33.8± 1.2	<0.05
MCV	fL	78.2 ± 0.7	90.2± 0.6	<0.05
MCHC	g/L	29.1± 1.3	31.1 ± 1.7	0.045
Total Serum Iron	µg/dL	31**±**9	45 ± 6.2	<0.05
Serum ferritin	µg/L	14**±** 5	13 ± 4.1	<0.05
Serum transferrin receptor	mg/L	28 **±** 9	32**±** 4	<0.05
Transferrin saturation	%	9.4 ± 7.5	8.2 ± 11.2	0.256
Hepcidin	ng/ml	10 ± 9.7	17 ± 6.4	0.057

DISCUSSION

Anemia of inflammation is somehow reported to be associated with Iron Deficiency Anemia. The diagnostic challenge is the identification of women with parallel iron deficiency as it is necessary to evaluate specific blood loss in those women and to treat them accordingly.

A lot of studies have been carried out to determine the prevalence of anemia and its influence on pregnant women but there are limited studies on the etiology of anemia. According to a study carried out by Abioye et. al 9% of pregnant women were suffering from Non-iron deficiency anemia NIDA and represents high probability of Anemia of inflammation (AI) in respective population mostly suffering from infectious diseases like helminthiasis. They also worked to distinguish the etiologies of anemia in anemic women and found out that the hepcidin and Soluble transferrin receptor (sTfR) both can distinguish between IDA and IA[12,13,14].

It has been reported several times that the blood staining of AI represents mild to moderate normochromic or normocytic anemia which differs it from hypochromic and microcytic anemia which commonly found in iron deficiency anemia[15,16]. Previously it was difficult to differentiate anemia from IA to IDA due to their same hematological profile including low iron concentration and transferrin saturation as well as reduced count of reticulocytes. According to WHO report on Anemia, IDA could easily be distinguished from IA by knowing the concentration of serum ferritin, Transferrin saturation, and hepcidin[17,18,19].

According to our data, AI was most prevalent on women with child bearing age, about 17% pregnant and 23% non-pregnant women were associated with β-thalassemia which could be a reason of anemia of inflammation. As we are familiar that β-thalassemia is a genetic disorder in which the body do not have enough capability to make normal hemoglobin an important constituent of red blood cells, that's why the patient with this disease have low hemoglobin level as compared to normal individuals and they suffer from anemia.

Hematological parameters of all participants were analyzed that shows a significant difference between pregnant women with prior infection and without infection. As summarized in Table 3 and 4. Our data demonstrate that the hemoglobin level is independent tonature of anemia as it concentration was below 10 g/dL in both circumstances. The concentration of Total Serum Iron (TSI) was considerably low (between 33 to 42 µg/dl) with p value less than 0.05 in pregnant and non-pregnant women with prior infection. Similar concentration (31 to 45 µg/dl) was observed in pregnant and non-pregnant women without any prior infection. According to WHO guideline, the normal iron concentration in serum ranges between 50 to120 µg/dl and iron deficiency lies if this concentration is below >50 µg/dl[17].

Serum ferritin concentration has been reported to be elevated in chronic inflammation conditions. Serum ferritin is the most useful parameter to distinguish between AI and IDA as it is primarily secreted by macrophages and hepatocytes[21]. In the present research we found elevated concentration of serum ferritin (i.e. 21 **±** 7 and 28 ± 8) in prior infected pregnant and non-pregnant women respectively, and 14 **±** 5 and 13 ± 4.1 in non-infected pregnant and non- pregnant womenwith statistically significant outcomes (i.e. P <0.05) which means that both the groups have the contrasting difference.

Serum transferrin Receptor (sTfR) concentration comparatively decline in AI whereas in IDA it remains in the upper limit of normal values. Several studies reported the normal concentration of serum transferrin in iron deficiency anemia which lies in the range of 20-30 mg/L [20]. In our study women with infectious disease were found to have low sTfR concentration (i.e. 13**±** 9 and **11±**7) in comparison to women without any infection (i.e. 28 **±** 9 and 32± 4) that confirms AI in our group 1 and ADA in group 2 with statistically significant difference between groups. Similarly, Transferrin saturation was previously reported to be elevated >10 in patient with Anemia of Inflammation and lower percentage indicates Iron Deficiency Anemia [21]. In our findings, group 1 was observed to have high Transferrin saturation (i.e. 19.4 ± 12.5 and 23.2 ± 10.4) that characterizes AI in our participants and low Transferrin saturation (i.e. 9.4 ± 7.5 and 8.2 ± 11.2) that represent IDA in our group 2 participants respectively.

The concentration of serum hepcidin raised in chronic inflammation condition as reported by D'Angelo. The normal values of hepcidin is >55 ng/ml. In our findings its value were fund to be high (i.e. > 100) in women with prior infection (Group 1) and < 20 ng/ml in group 2. This high and low concentration clearly indicates the prevalence of AI in our study population[22,23].

CONCLUSION

Hepcidin, serum ferritin and transferrin are important biomarkers in the diagnosis of Anemia of inflammation. The prevalence of AI were high in women with chronic inflammation or any prior infection. Other women without any subsequent infection or chronic disease were found to be suffer with Iron deficiency Anemia. It is essential to determine the etiology of anemia before starting the treatment of anemic women and pregnant women specially. It is because mediation to decrease the pathogenicity of IA is quite differ from IDA.

Conflict of interest: Nil

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