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Original Article

Association of Iron Deficiency Anemia with Maternal Psychological Distress During Pregnancy

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ABSTRACT

Objective: To establish an association between iron deficiency anemia and maternal psychological distress during pregnancy.
Study Design: Cross-sectional study.
Place and Duration of Study: Chemical Pathology & Endocrinology department of Armed Forces Institute of Pathology (AFIP), Rawalpindi Pakistan, from July to December 2022.
Methodology: A total of 131 individuals were categorized into iron deficiency anemia (IDA) Group (n = 51) and non-IDA Group with normal pregnant females or those having anemias of etiology other than iron deficiency (n = 80) using a non-probability convenient sampling technique. The risk of psychological distress was measured by a scale adopted from Depression Anxiety Stress Scale 21.
Results: Antenatal depression, anxiety and stress in IDA as compared to non-IDA Group (86.3 % vs 43.8 %, 84.3 % vs 51.2 %, and 91.1 % vs 66.3 %) showed significant difference (< 0.001) respectively. There was a significant negative correlation (r) of depression (r = -0.32), anxiety (r = -0.40), and stress (r = -0.37) with the serum ferritin levels (p= <0.001). Women having IDA were eight times more likely to develop depression (OR=8.08, CI 95% [3.25, 20.11]), five times more likely to develop anxiety (OR=5.11, CI 95% [2.14, 12.24]) and eight times more likely to develop stress (OR=8.15, CI 95% [2.32, 28.59]) than those without IDA during pregnancy.
Conclusion: Iron deficiency anemia plays a significant role in increasing the risk of antenatal psychological distress when compared with non-IDA Group which should be addressed timely for better pregnancy outcomes.

Keywords: Ferritin, Iron deficiency anemia, Pregnancy, Psychological distress

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INTRODUCTION

Pregnancy involves numerous somatic and psychological changes and therefore requires adequate intake of nutrients for a healthy outcome. Iron is one of the most important nutrient required during pregnancy, which is essential for the transportation of oxygen, immune function, cellular respiration, neurotransmitter metabolism, and synthesis of DNA. A total of 360 milligrams (mg) of iron is needed for the development of the placenta and fetus, and an additional 450 mg is required to increase the mass of the mother's red blood cells (RBCs) throughout pregnancy. In order to maintain the mother's iron balance and assist feto-placental growth, 1 gram of iron must be consumed during pregnancy.[1]

Iron insufficiency has various forms varying from iron depletion to iron deficiency anemia (IDA). Although serum ferritin levels are reduced in cases of iron depletion, the transport and functional levels of iron may not be impacted. People who are iron depleted have no iron reserves to draw upon if their bodies require more iron. Hemoglobin (Hb), serum ferritin, erythrocyte proto-porphyrin concentration, and transferrin saturation are all reduced in IDA due to a lack of iron storage, transport, and functional iron in the body.

Brain iron deficiency affects the balance of neurotransmitters including glutamate and -aminobutyric acid (GABA) and dopamine, which results in memory, behavior, and learning problems as well as emotional and psychological issues.[2] Dopamine is one of the neurotransmitters in the brain that influences our mood, feelings of reward and motivation for which iron is required for the conversion of tyrosine to dopamine. Impaired emotional behavior patterns are linked to iron deficiency via dysregulated dopamine metabolism.[3] Dopamine functions are negatively affected by iron deficiency. These functions are specific to the brain region and the phases of neural development.[4]

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IDA correlates with psychological distress and psychosocial consequences that include adverse psychomotor function and psychiatric morbidity including anxiety disorders, sleep disorders, bipolar disorders, and depression.[5,6] Stress, anxiety, and depression are symptoms of psychological distress and are risk factors for unfavorable pregnancy outcomes. Pregnancy anxiety is linked to shorter gestation, negative effects on fetal neurodevelopment, and adverse outcomes for children, whereas depression symptoms are linked to low birth weight and negative consequences for infant development.[7] Given that no prior study had been conducted in Pakistan, the study was geared toward finding a link between IDA and maternal psychological distress during pregnancy.

METHODOLOGY

This was an observational cross-sectional study conducted at Chemical Pathology & Endocrinology department of the Armed Forces Institute of Pathology (AFIP) Rawalpindi from July to December 2022 after approval from the Institutional Review Board (IRB certificate No. BSAHS/CHP-1/IRB/22/1343). A total of 131 individuals were categorized into iron deficiency anemia (IDA) Group with ferritin (<15 µg/L) 8 and hemoglobin levels (<11g/dl) 9 (n = 51) and non-IDA Groups with healthy pregnant females or those having anemia of etiologies other than iron deficiency (n = 80). The sampling technique used for the study was non-probability convenient sampling technique. The sample size was calculated using World Health Organization (WHO) calculator by taking the proportion of Iron deficiency anemia as 21.2%10 with a 95% confidence level and 7% margin of error.

Inclusion Criteria: Ambulatory pregnant women with age ranging from 18-45 years willing to participate in the study were included.

Exclusion Criteria: The study excluded pregnant women who had any acute illnesses, obesity, hypertension, chronic diseases, history of blood loss during the current pregnancy, blood transfusions, and those who had already received a diagnosis of a psychological illness before pregnancy.

A questionnaire-based interview was held. After receiving consent from all participants, the researcher conducted all interviews in person. The researcher asked about the sociodemographic information, medical history (prior pregnancies, problems from previous pregnancies, usage of medications, and comorbidities), and clinical information (complications during this pregnancy, iron supplementation status, any blood loss and treatment received, tiredness, and trouble sleeping). The risk of psychological distress was assessed by using a scale adapted from Depression Anxiety Stress Scale-21 (DASS-21). It is the short version of DASS-42, a self-report questionnaire for evaluating the detrimental psychological state of stress, anxiety, and depression.[11]

Blood was drawn from selected individuals for the estimation of serum iron, total iron binding capacity (TIBC) and ferritin in a plain tube which was then centrifuged at 3500 revolutions per minute (RPM) for 3 minutes at room temperature for separating serum. Serum iron and TIBC were measured using fully automated Clinical Chemistry analyzer, ADVIA 1800 using photometry technique whereas serum ferritin was measured with Immulite 2000 XPi using chemi-luminescence immunoassay technique. Transferrin saturation was determined using the formula [TSAT = (Serum Iron/TIBC ×100].Whole Blood was taken for Hemoglobin (Hb), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin Concentration (MCHC), and Mean Corpuscular Hemoglobin (MCH) estimation in a tri-potassium ethylene diamine tetra acetic acid (K3EDTA) tube. For the measurement of these hematological parameters, an automated hematology analyzer Sysmex XP 100 working on the principle of electrical impedance was used.

Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 26. To check the normality of the data, Shapiro-Wilk test was applied and then all the results were subjected to descriptive statistics. Quantitative data was analyzed as median ± Inter quartile range (IQR) as the data was non-parametric. Mann-Whitney U test was used to compare biochemical parameters between the Groups. The correlation between psychological distress and biochemical parameters was analyzed using spearman correlation coefficient. For risk estimation, the odds ratio was calculated with a confidence interval of 95%. The p value ≤0.05 was considered statistically significant.

RESULTS

The flow diagram for screening, allotment and evaluation of the data is shown in (Figure 1).

The study participants demographic details are listed in (Table-I). IDA was more prevalent in unemployed pregnant women with age between 25-34

years and who were in their 2nd trimester of pregnancy with sleep time less than 8 hours. There was a significant difference (p < 0.001) in antenatal depression, anxiety and stress in the IDA (86.3%, 84.3%, and 91.1%) as compared to non-IDA Group (43.8%, 51.2%, and 66.3%) respectively.

Table-I: Demographic details of the study participants and prevalence of depression, anxiety and stress among Iron Deficiency Anemia and non- Iron Deficiency Anemia Groups (n=131)

Characteristics		Iron Deficiency Anemia Group n = 51 n(%)	Non- Iron Deficiency Anemia Group n = 80 n(%)	*p*-Value
Age	≤ 24	8 (15.7%)	12 (15%)	
	25-34	39 (76.5%)	57 (71.3%)	0.584
	≥ 35	4 (7.8%)	11 (13.8%)	
Occupation	Employed	10 (19.6%)	20 (25%)	0.310
	Un-Employed	41 (80.4%)	60 (75%)	
Trimester	1st (<12weeks)	1 (2%)	3 (3.8%)	
	2nd(13-24weeks)	29 (46.9%)	32 (40%)	0.163
	3rd (>24 weeks)	21 (41.2%)	45 (46.3%)	
Iron supplementations	Yes	49 (96.1%)	74 (92.5%)	0.332
	No	2 (3.9%)	6 (7.5%)	
Tiredness	Yes	51 (100%)	75 (93.8%)	0.081
	No	0 (0%)	5 (6.3%)	
Sleep time	<8 hours	48 (94.1%)	66 (82.5%)	0.044
	>8 hours	3 (5.9%)	14(17.5%)	
Depression	Yes	44 (86.3%)	35(43.8%)	< 0.001
	No	7 (13.7%)	45 (56.3%)	
Anxiety	Yes	43 (84.3%)	41 (51.2%)	< 0.001
	No	8 (15.7%)	39 (48.8%)	
Stress	Yes	48 (94.1%)	53 (66.3%)	< 0.001
	No	3 (5.9%)	27 (33.8%)	

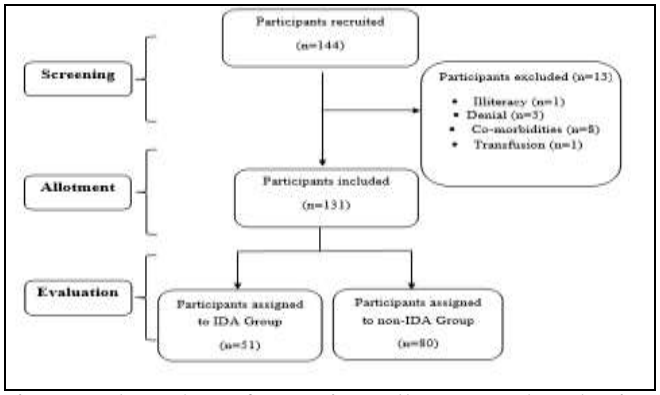

Figure-1: Flow Chart of Screening, Allotment and Evaluation of Data

Significant difference was found in case of biochemical parameters of the study participants in the both Groups (p-value < 0.001) (Table-II).

The Distribution of depression, anxiety and stress among IDA and non-IDA Group is shown in (Table-III). Most individuals in the IDA Group scored in the mild-moderate range for depression 23(45.1%) and anxiety 16(31.3%) and in the severe-extremely severe range for stress 30(58.8%), whereas most participants in the non-IDA Group scored in the normal range for depression 45(56.3%) and anxiety 39(48.8%) and in the mild-moderate range for stress 35 (43.75%).

Table-II: Distribution of biochemical parameters into Iron Deficiency Anemia and non- Iron Deficiency Anemia Group (n=131)

Parameters	Iron Deficiency Anemia Group n= (51) Median (IQR)	Non- Iron Deficiency Anemia Group n= (80) Median (IQR)	*p*-Value
Hb (g/dL)	10.4 (1.2)	11.5 (1)	< 0.001
MCV (fL)	81.6 (9.7)	88.1 (7.5)	< 0.001
MCH (pg)	27.4 (2.5)	29.8 (3.3)	< 0.001
MCHC (g/dL)	32.1 (1.6)	.33.5 (1.6)	< 0.001
Ferritin (µg/L)	9 (7)	22 (15)	< 0.001
Transferrin saturation (%)	10.4 (6.5)	17.1 (12.3)	< 0.001
Iron (µmol/L)	8.3 (4.6)	13 (7.5)	< 0.001
TIBC (µmol/L)	82 (20.9)	75 (16)	0.010

**IDA; Iron-deficiency anemia, IQR; Inter Quartile Range, n; Total number of participants, Hb; Hemoglobin, MCV; Mean Corpuscular Volume, MCH; Mean Corpuscular Hemoglobin, MCHC; Mean Cell Hemoglobin Concentration, TIBC; Total Iron Binding Capacity*

Table-III: Distribution of depression stress anxiety among Iron Deficiency Anemia and non- Iron Deficiency Anemia Group (n=131)

Variables		Iron Deficiency Anemia Group n(%)	Non- Iron Deficiency Anemia Group n(%)	*p*-value
Depression	Normal (0-4)	7(13.8%)	45(56.3%)	
	Mild- Moderate (5-10)	23(45.1%)	24(30%)	<0.001
	Severe-Extremely severe (≥11)	21(41.1%)	11(13.7%)	
Anxiety	Normal (0-3)	8(15.7%)	39(48.8%)	
	Mild- Moderate (4-7)	16(31.3%)	30(37.5%)	<0.001
	Severe-Extremely severe (≥8)	27(53%)	11(13.7%)	
Stress	Normal (0-7)	3(5.9%)	27(33.75%)	<0.001
	Mild-Moderate (8-12)	18(35.3%)	35(43.75%)	
	Severe-Extremely severe (≥13)	30(58.8%)	18(22.5%)	

The Correlation between biochemical parameters and psychological distress is listed in (Table-IV). It was found that Hb, Ferritin, Iron and Transferrin saturation had a significantly negative correlation with

Table-IV: Correlation between biochemical parameters and psychological distress (n=131)

	Depression		Anxiety		Stress	
Parameters	(r- value)	p-value	(r- value)	p-value	(r- value)	p-value
Hb (g/dL)	- 0. 36	< 0.001	- 0. 36	< 0.001	- 0. 30	< 0.001
Ferritin (µg/L)	- 0. 31	< 0.001	- 0. 35	< 0.001	- 0. 35	< 0.001
Transferrin saturation (%)	- 0. 27	0.002	- 0. 22	0.012	- 0. 25	0.003
Iron (µmol/L)	- 0. 22	0.012	- 0.19	0.029	- 0. 26	0.003
TIBC (µmol/L)	0.18	0.036	0.12	0.189	0.17	0.58

**Hb; Hemoglobin, TIBC; Total Iron Binding Capacity*

depression, anxiety and stress (p-value < 0.05). The correlation between TIBC and depression was significantly positive (r = 0.18, p = 0.036).

DISCUSSION

Iron Deficiency Anemia during pregnancy is still a significant public health issue and can contribute to maternal psychological distress, particularly in developing countries. There is a lack of information on this critical issue, which can be addressed timely. In the present study, participants who experienced psychological distress had lower ferritin levels than those who did not experience such distress. This association was supported by a study conducted by Hameed *et al.* in Palestinian mothers suffering from PPD to check its association with iron deficiency.[12] Depression, anxiety, sleep, and psychotic disorders were related to considerably greater rates of occurrence and risks in the IDA Group. (p < 0.05) in a study by Lee *et al*.[13]

Similarly, a hospital-based case-control study by Shafi et al. reported that IDA and depression were shown to be related. With the degree of IDA, the severity of depressive disorder symptoms grew. According to the reports, the Hb levels of the two Groups varied significantly from one another (p<0.001), in comparison to non-depressed individuals (16%), it was shown that depressed participants had a greater prevalence of iron deficiency anemia (73% p<0.001). Hemoglobin levels and depression had a Spearman rank correlation value of -0.429 (p <0.01), indicating a strong inverse relationship6. Similar results were reported in our study where this correlation was -0. 36(p<0.001).

In a web-based survey, IDA was linked to a self-reported history of depressive disorders.14According to a study by Patterson on young and middle-aged women who admitted to have a "low iron" at some point in their lives, reported significantly lower mean physical (PCS) and mental (MCS) component summary, and increased frequency of "continuous tiredness" than in women without a history of iron deficiency at baseline (67% and 63% vs 45% and 48%). 15 Similarly, in our study, it was reported that tiredness was found to be more in IDA Group participants as compared to non-IDA Group participants (100 % vs 93.1 %). In addition, a study conducted by Shariatpanaahi et al stated that, individuals with depression had mean ferritin levels that were notably lower than those of healthy participants (p <0.001) 16as also found in our study (p <0.001).

In contrast, a study by Kemppinen *et al.* showed that no conclusive evidence was found showing that prenatal or postpartum depression and gestational iron deficiency anemia are related. This study conflicts with the findings of our study, which demonstrated a substantial relationship between depression (p < 0.001) and IDA. However, there was only a tenuous link found between prenatal depression and gestational iron deficiency anemia. This could be because studies were modified to account for maternal age at birth, parity, maternal education and smoking during pregnancy.[17]

The presence of antenatal depression (p=0.02) was 45% in the iron-deficient Group and 25% in the iron-sufficient Group in a study conducted by Dama et al. whereas in our study it was 86.3% and 43.8% respectively.[18] A literature review by Wassef et al showed that in four out of five studies, iron supplementation after childbirth reduced the incidence of PPD, but it had no protective effect when administered during pregnancy.[19] This may be the reason why pregnant women who were taking Iron supplementation during pregnancy had both IDA and depression.

A study by Bouri et al. reports that in Iron Deficiency Anemia serum ferritin, and transferrin saturations decrease, but the TIBC increases. This study supports our results where in the IDA Group median (IQR) of ferritin was 9(7), p-value<0.001 and transferrin saturation was 10.4(6.5), p-value<0.001 which were found to be low except TIBC 82(20.9), p-value=0.032 which positively correlated with IDA.[20]

On the Other hand, Rinat Armony-Sivan et al stated regardless of the sample or time of the maternal iron status examination, depression ratings in anemic and non-anemic mothers with iron deficiency did not differ.[21] These results contradicted our study results which report that there is a significant difference between the scores of depression which is two times more in anemic women with iron deficiency.

There are several studies that support the considerable link between IDA and psychological distress that we found in our study, but there are also a few studies that contradict our findings in this respect. The results of our study and those of other research may differ because of the different scales used to evaluate stress, anxiety, and depression. It may also differ because of the devices and testing kits used to analyze the biochemical markers, since some normal ranges may vary from one kit to another.

LIMITATIONS OF STUDY

Firstly, the sample size was limited. A larger and more diverse sample size would have increased the study's sturdiness and generalizability. Secondly, it was a cross-sectional study so the change in psychological distress scores after correction of iron status cannot be known therefore further studies are required to study this possible change. Besides the limitations, the findings in this study will be used to focus on the burden of mental health problems during pregnancy caused by IDA, as well as to consider steps to scale up prenatal mental and physical health services in health care settings.

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CONCLUSION

According to the results of the current study, pregnant women with iron deficiency anemia had a higher risk of experiencing psychological distress i.e. depression, stress, and anxiety than pregnant women without iron deficiency anemia. Expectant women should prioritize receiving proper and appropriate nourishment, and they should be urged to regularly seek prenatal care. Unnecessary adverse effects can be prevented with appropriate prenatal care. Given the connection between maternal psychological distress and iron deficiency anemia, it's critical to recognize at-risk mothers and ensure that they receive the proper, prompt therapy.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SQ & ZHH: Data acquisition, data analysis, critical review, approval of the final version to be published.

MQAK & MUM: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MY & MA: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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