ORIGINAL RESEARCH PAPER
Volume-9 | Issue-4 | April-2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A STUDY OF SEVERITY OF DEPRESSIVE DISORDER WITH IRON DEFICIENCY ANEMIA WITH EFFECT OF TREATMENT IN FEMALE OF REPRODUCTIVE AGE GROUP

Psychiatry

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ABSTRACT

INTRODUCTION - Anemia is a common nutritional deficiency which has symptoms as lethargy, easy fatigability, decrease interest in work etc. A patient of anemia show signs and symptoms of behavioural and mood disorders like depressive disorder.

METHODOLOGY- One hundred thirteen female patients at Psychiatric centre, S.M.S medical college and Hospitals, Jaipur, diagnosed with depressive disorder in accordance with ICD-10 criteria were selected after taking informed consent and screened with the entire inclusion and exclusion criteria. In all patient's socio-demographic profile and clinical profile were recorded. In all patients Standard Beck's Depression Inventory(BDI) Hindi version was used to evaluate severity of depression. Blood samples were taken for CBC, Haemoglobin (Hb), MCV and serum ferritin. Two groups (1) Depressive disorder with anemia (test group) and (2) Depressive disorder without anemia (Control group) were made and given treatment for their respective elements. The results were compared with BDI scores (co-relation coefficient) before and after treating for specific disorders (paired t- test).

RESULT & CONCLUSIONS- In our study, negative co-relation was observed between Hb levels, and BDI scores. It demonstrates the effect of Hb decrease, anemia occurrence on depressive disorder severity. iron deficiency anemia accentuate the existing depressive disorder and contributes to the psychopathology in depressive disorder.

KEYWORDS

Depression, Women, Iron Deficiency Anemia.

INTRODUCTION

According to a study done by WHO 'Global burden of disease'2017 ranked according to parameters such as DALY* and PQLI** depressive disorders were ranked 'third' and iron deficiency anemia 'seventh'. These two disorders coexist in our society and alleviates each other symptoms and severity [1]. In India, prevalence rate of depressive disorder (unipolar) is 2.7% and prevalence of anemia in females in reproductive age group (15-49 years) are in pregnant 50.4% and in non-pregnant reproductive age group (15-49years) is 53.2% [2,3]. Depressive disorder afflicts one out five women and one out of ten men at some time during their life years and with the rate of suicide around 15% in depressive disorders, explains the severity of illness [4].

Menstrual blood loss plays a major role in iron metabolism. The iron has an important role in neurologic functions and developments [5,6]. Iron is required for proper myelination of the spinal cord and brain white matter of cerebellar folds, and it is a cofactor for a number of enzymes involved in neurotransmitter synthesis, such as tryptophan hydroxylase (serotonin) and tyrosine hydroxylase (norepinephrine and dopamine) [7,8].

In human brains oligodendrocytes cell comprise iron, which are responsible for the production of myelin. In Iron deficiency anemia, failure to deliver iron to these oligodendrocytes' cells could be causally related to delay motor maturation and perhaps behavioural alterations during particular periods of early brain development. Iron-containing proteins that may directly or indirectly alter brain function through peroxide reduction, amino acid metabolism, fat desaturation, and altering membrane function [9].

Patients, who are suffering from iron deficiency anemia, show signs and symptoms of mood disorders like depressive disorder. Many of depressive symptoms in patients with iron deficiency anemia can be resolved by iron supplementation even before any improvement in red blood cell count or other indicators improvement. It seems that this phenomenon is due to improved levels of neurotransmitters, and iron-dependent enzyme that is not related to haemoglobin (Hb) concentration [10,11]. Iron deficiency anemia can cause depression, irritability, fatigue, sleepiness, and it effects on quality of life, the symptoms of depressive disorder and anemia can cause a range of similar symptoms, and each has its own special treatment, but simultaneous therapy is useful and alone treatment of them sometimes is not enough.

The aim of the study is to associate iron deficiency anemia with depressive disorder and effect on severity of depressive disorder post treatment of both co-existing disorders.

Objectives

- To substantiate the effect on severity of depressive disorder, co-existing with iron deficiency anemia.
- To corroborate the effect of treatment of iron deficiency with treatment of depressive disorder.

METHODOLOGY

One hundred thirteen female (aged between 15-45 years) patients presenting in outpatient department at Psychiatric centre, S.M.S medical college and Hospitals, Jaipur, India, diagnosed with depressive disorder in accordance with ICD-10 criteria and confirmed by a senior psychiatrist, were selected after taking informed consent and screened with the entire inclusion and exclusion criteria. The permission to conduct the study was obtained from the ethical committee of the institution.

In all patients socio-demographic profile and clinical profile were recorded. In all patients Standard Beck's Depression Inventory(BDI) Hindi version was used to evaluate severity of depressive disorder [14]. Blood samples were taken for complete blood count difference analysis, Haemoglobin (Hb), MCV and serum ferritin.

SELECTION CRITERIA

Criteria Of Inclusion

- Female with reproductive age group 15-45 years, diagnosed with depressive disorder (according to ICD-10 criteria).
- Literate, to able to comprehend in Hindi (at least till secondary)
- Written Consent to participate in a follow up study for two months.

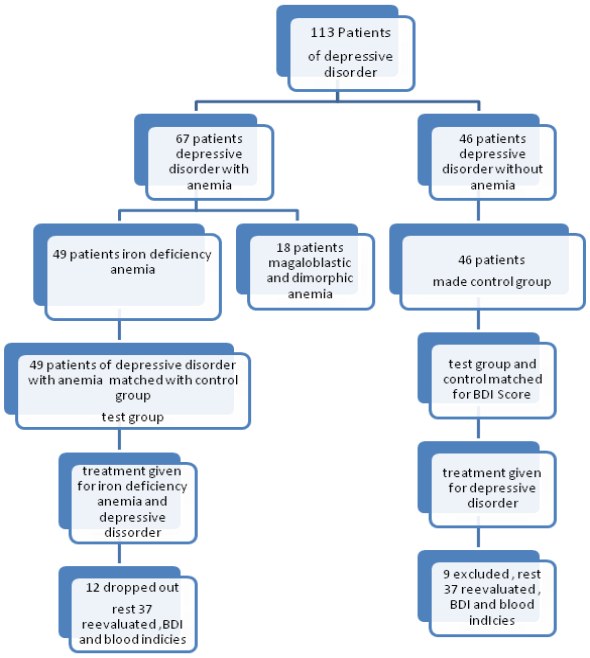
Criteria Of Exclusion

- Patients diagnosed with bipolar affective disorder either in depressive disorder or mania.
- Chronic medical or surgical illness.
- History of any drug intake in past two week.
- History of any substance abuse in past six months.
- Female in gestation period or lactating.
- Femalewithsevereanemia(<7.0gm/dl).

In this prospective study, treated selected patients (using above selection criterions) for a time period of two months for depressive disorder and

anaemia, according to guidelines of current medical diagnosis and treatment (CMDT 2019) and Maudsley Prescribing Guidelines in Psychiatry 13th Edition [15,16]. We followed up the same group of patients on treatment and re-evaluated the patients on the above-mentioned parameters after two months. The results were compared with BDI scores before and after treating for specific deficiencies.

Study Design



Statistical tools and analysis

The test group and control group were matched on the basis of various socio-demographic indices using independent t-test. Correlations between two variables (BDI score with haematological indices) using Pearson co-relation co-efficient. The results were compared with BDI scores before and after treatment using paired t-test. The changes in all haematological indices before and after treatment were compared using paired t-test. The degree of changes in BDI score and haematological indices were also compared.

OBSERVATIONS AND RESULTS

A total 113 patients diagnosed with depressive disorder and evaluated on OPD basis, out of which 67 patients were diagnosed with anemia and depressive disorder. Eighteen patients (out of 67) were diagnosed with megaloblastic/ di-morphic anemia, rest 49 were taken as test group (depressive disorder with anemia) and 46 patients (out of 113) having depressive disorder (no anemia) as control group.

The test group (n=49) were given treatment for anemia and depressive disorder for 2 months. The control group was treated only for depressive disorder for 2 months. Twelve patients dropped out in test group rest 37 re-evaluated for BDI score and blood indices. Thirteen seven patient of test group matched on sociodemographic profile re-evaluated after treatment. The BDI score scores and blood indices haemoglobin (Hb), mean corpuscular volume (MCV) and serum ferritin before and after treatment were compared and co-related.

Mean age of study group(n=49) was **28.86±7.93** years and mean age of control group(n=46) was **29.91±8.42 years** . Thirty-seven patients (75.51%) female were married in the test group and 32 (69.5%) in the control group. All female were educated till secondary level or above .

Table 2 shows the relationship between Hb values with BDI scores, before and after treatment of test and control groups. The probable relationships between levels of BDI scores with Hb, using pearson

Table 1: Comparison Of Socio-demographic Profile Of Study And Control Group

Variable	Depressive disorder with anemia (test group) (N=49)	Depressive disorder without anemia (Control group)(N=46)	t-value	df	p-value
Age(years) Age groups 15-25 26-35 36-45	Mean± SD= 28.86±7.93 16 21 12	Mean±SD= 29.91±8.42 14 17 15	0.629	93	0.531 (NS)
Parity No child One child 2 or more child	Mean± SD= 1.57±1.90 18 8 23	Mean± SD= 1.30±1.22 20 12 14	1.077	93	0.284 (NS)
BMI (Kg/M^2) <18 18-25 25-30	Mean± SD= 23.99±3.95 8 19 22	Mean± SD= 24.50±4.40 6 27 23	0.588	93	0.553 (NS)

NS= Non significant, S= significant

correlation were studied in patients depressive disorder with anemia (test group) and found a significant negative correlation between Hb levels and BDI scores (P coeff. = -0.430, p = 0.008) after treatment, this co-relation decreased and was not significant (P coeff. = -.166, p value = 0.327). Relationships between BDI scores and Hb in patients depressive disorder without anemia (control group) was not significant, before treatment (P coeff. = .299, p = 0.073) and after treatment (P coeff. = 0.356, p value=0.031).

Table 2: Co-relation of BDI -score and HB before and after treatment

Group		BDI Mean± SD	Hb Mean± SD	Pearson coefficient	p-valve
Test (n=37)	Before treatment After treatment	21.054±5.12 14.76±3.92	9.378±.59 10.286±.743	-.430 -.166	0.008 .327
Control (n=37)	Before treatment After treatment	20.757±4.91 18.68±4.5	12.343±.50 12.29±.57	0.299 0.356	0.073 0.031

Significant at 0.01 level (2-tailed)

Table 3 shows the relationship between serum ferritin levels with BDI scores, before and after treatment of test and control groups. The relationships between BDI scores with s. ferritin using pearson correlation were studied test group and also found a significant negative correlation (P coff. = -.412, p-value = 0.011), after treatment this co-relation decreased but was significant (P coff. = -.341, p-value = 0.039). The relationship between BDI scores and S. ferritin in control group found a negative significant correlation before treatment (P coff. = -.716, p-value = 0.001) and after treatment (P coff. =-.457, p-value = 0.003) .

Table 3: Co-relation Of BDI -score And Serum Ferritin Before And After Treatment

Group		BDI Means± SD	S.ferritin Mean± SD	Pearson Co-efficient	p-valve
Test (n= 37)	Before treatment After treatment	21.054±5.142 14.76±3.92	16.73±16.153 28.16±22.28	-.412 -.341	0.011 .039
Control (n= 37)	Before treatment After treatment	20.757±4.91 18.68±4.50	55.84±29.162 60.32±28.84	-.716 -.457	0.001 0.003

Significant at 0.01 level (2-tailed)

Table 4 shows the relationship between MCV values with BDI scores, before and after treatment of test and control group. The relationship between BDI scores with MCV using pearson correlation were studied in test group and found no significant correlation (P coff. = -.069, p-value = 0.686), and after treatment this co-relation was also insignificant (P coff. = .068, p-value = 0.690). Relationships between BDI scores and MCV levels in control group also found no significant correlation before treatment (P coff. = -.139, p-value = 0.412) and after treatment (P pcoff. =-.283, p-value = 0.089).

Table 4: Co-relation of BDI- score and MCV before and after treatment.

Group		BDI Mean± SD	MCV Mean± SD	Pearson coefficient	p-valve
Test	Before treatment	21.054±5.142	77.68±4.26	-.069	.686
	After treatment	14.76±3.92	80.19±3.4	.068	.690
Control	Before treatment	20.757±4.91	85.46±8.41	-.139	.412
	After treatment	18.68±4.5	86.22±7.63	-.283	.089

Significant at 0.01 level (2-tailed)

Table 5 show change and co relation in all indices before and after treatment in both groups (n=37). Mean BDI score of test group was 21.054±5.142 before treatment and 14.76±3.92 after treatment and found a significant association using paired t- test (t-value= 11.182, df=36, p= .0001). Mean BDI score of control group was 20.757±4.91 before treatment and 18.68±4.58 after treatment and found significant association (t- value= 6.448, df=36, p= .001).

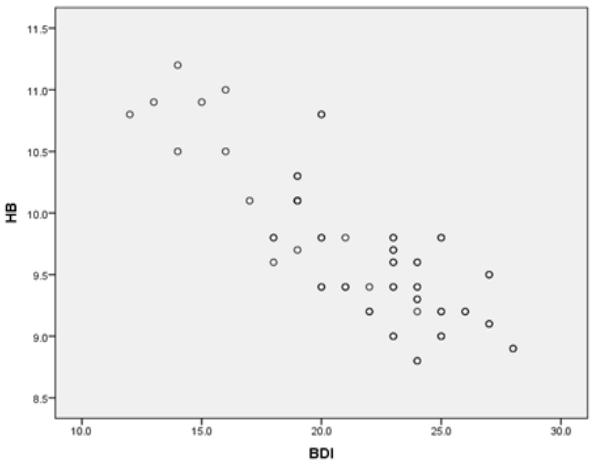
Mean Hb of test group was 9.378±0.596, before treatment and 10.286±0.76, after treatment. These values found a significant association (t- value= -9.182, df=36, p= .0001). The other blood indices MCV and S. ferritin had significant values on paired t-test in test group .

Table: 5 Blood Indicators And BDI- score and MCV before And After Treatment In Test Group And Control Group

Variable N=38	Mean±SD before treatment	Mean±SD after treatment	t-test value	df	p-value
BDI score					
Test	21.054±5.142	14.76±3.92	11.182	36	.0001
Control	20.757±4.91	18.68±4.58	6.448	36	.001
HB (gm/dl)					
Test	9.378±.596	10.286±.743	-9.182	36	.0001
Control	12.343±.50	12.295±.57	.486	36	.630
S. ferritin					
Test	16.73±16.153	28.16±22.28	-6.44	36	.001
Control	55.84±29.162	60.32±28.84	-1.7	36	.098
MCV					
Test	77.68±4.26	80.19±3.4	-5.882	36	.001
control	85.46±8.41	86.22±7.6	-.789	36	.436

Significant at 0.01 level (2-tailed)

FIGURE-1
Graph: Shows Correlation Severity Of Depressive Disorder And Hb Level In Test Group



DISCUSSION

Iron deficiency is one of the most common nutritional problems in the world both in developed and developing countries. Relationship of iron with brain function, cognition, and behaviour (including emotional behaviour) has been the subject of interest for researchers over the past decade [17].

This study evaluated the relation between levels of haemoglobin with the severity of depressive disorder in reproductive age group (15-45 years). Anemia was observed in 59.2% of the participants.

In the test group, there was a significant negative association between BDI scores and level of Hb (table-2, figure-1). This association became insignificant after treatment. When we compared BDI score of test group and control group, before and after treatment respectively, using paired t-test, the values were significant (P value< 0.05) but t- value was more in test group than control group. Which showed significant association and probability of improvement on treating for anemia co existing with depressive disorder. Our study is supported by Noorazar SGh, et al found negative correlation between Hb levels and HDRS score. It demonstrates the effect of Hb decrease and anemia occurrence on depressive disorder severity [18]. Madiha Shafi et al concludes that there is relationship between iron deficiency anemia and depressive disorder, and severity of symptoms of depressive disorder increases with degree of iron deficiency anemia[19] It seems that this phenomenon is due to the recovery of neurotransmitters and enzyme levels, dependent on iron, unrelated to haemoglobin concentration [20]. With the identification of the use of iron supplements along with antidepressant medicine in treatment of depressive disorder and iron deficiency anemia, extended knowledge is needed to identify any relationship of iron deficiency with Depressive disorder and the usefulness of iron supplements in its treatment, in particular. Iron is a cofactor for a number of enzymes involved in neurotransmitter synthesis, such as tryptophan hydroxylase (serotonin) and tyrosine hydroxylase (norepinephrine and dopamine)[21,22].

In our study, a significant negative co-relation obtained between BDI scores and S. ferritin levels in test group (table-3). This co-relation remained same but P coeff. decreased after treatment. When we compared S. Ferritin levels before and after treatment using paired t-test, the values were significant. Bart Alena et al. shows that ferritin level was significantly lower in non-anaemic women with untreated major depressive disorder compared to healthy control group [23].

Furthermore, increasing in serum ferritin levels was associated with an improvement in depressive symptoms in treatment-resistant depressive disorder in chronic haemodialysis patients with major depressive disorder [24]. Vahdat et al determined that the mean serum ferritin was significantly lower in patients with depressive disorder [25].

These results are consistent with those of the study conducted in Iran on medical students showing that Spearman correlation coefficient for ferritin and depressive disorder was -0.167 and statistically significant [26].Similar results were observed in a study on Japanese male population [27].

Changes in iron metabolism has been suggested as potential pathological markers in patients with depressive disorder. Ferritin as an intracellular iron storage plays an important role, and this issue has become the subject of extensive investigation [28].

CONCLUSION

This study concludes that iron deficiency anemia co-existence with depressive disorder has high prevalence. Iron deficiency anemia exacerbates the existing depressive disorder and contributes to the psychopathology of depressive disorder. The treatment of both the disorders with holistic approach shows improvement multiple folds and treating body and mind together with at most efficiency and effect. At prevalence level, co-existence of iron deficiency anemia and depressive disorder specially in reproductive age group always kept in mind. At diagnostic level, all female presenting with features of depression should always be evaluated for anemia, clinically or haematological level.

Limitations

1) The sample size, even with best efforts could not be increased due to drop outs during follow up.
2) We had to exclude patients with severe anemia as they needed urgent medical attention.

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Reference values[29]

Variable	Values
Haemoglobin	
Mild anemia	10-12 gm/dl
Moderate anemia	7-9.9 gm/dl
Severe anemia	<7 gm/dl
Mean corpuscular volume (MCV)	77-93 fl
Serum ferritin (S. ferritin)	10-150ng/ml