ORIGINAL ARTICLE

Relation between Depressive Disorder and Iron Deficiency Anemia among Adults Reporting to a Secondary Healthcare Facility: A Hospital-Based Case Control Study

Madiha Shafi[1], Fatima Taufiq[2], Humaira Mehmood[4], Saeed Afsar[3] and Ammarah Badar[5]

Abstract

Objective: To determine the relationship between iron deficiency anemia and depressive disorder; and identify the correlation between severity of anemia and depressive disorder.

Study Design: Descriptive, analytical study.

Place and Duration of Study: Department of Psychiatry and Medical Reception Center, Sindh Rangers Hospital, Karachi (a secondary healthcare facility), from January to July 2017.

Methodology: Depressive disorder was diagnosed by psychiatrist on ICD 10 criteria and severity of symptoms was assessed on HAM-D rating scale. Hundred cases and equal number of age and gender matched controls were enrolled in the study. A semi-structured proforma was used for documenting the socio-demographic factors and outcome variables. Blood samples were taken for Hemoglobin (Hb) level and peripheral film from both groups.

Results: Median Hb levels were 11.9 (IQR=1.27)) for depressed patients versus 12.9 (IQR=1.3) for healthy participants. Significant difference between Hb levels of two groups was found ($p<0.001$), i.e. depressed participants were found to have higher frequency of anemia (73%) as compared to non depressed participants (16%, $p=0.001$). Spearman rank correlation coefficient for Hb level and depression was -0.429 ($p<0.01$), showing significant negative correlation. The odds for Hb level were 0.487 (0.37-0.64), which showed that cases are less likely to be found with higher Hb levels as compared to controls ($p<0.001$).

Conclusion: This study concludes that there is relationship between iron deficiency anemia and depressive disorder; and severity of symptoms of DD increases with degree of IDA.

Key Words: *Adults. Depressive disorder. Iron deficiency anemia.*

INTRODUCTION

Depressive Disorder (DD) is one of the most common mental disorders worldwide. Approximately 300 million people are affected by DD globally.[1] Etiology of depressive disorder is broadly classified into two major categories, i.e. non-modifiable (genetic) and modifiable (environmental).[2] Nutrition is an important modifiable etiological factor. Many nutrient deficiencies (such as folic acid, vitamin B12) have been linked to causation as well as severity of DD, thus correction of these deficiencies can play significant role in prevention as well as treatment of DD.[3] No such specific causative relation has yet been established between iron deficiency and DD. However, there are some facts that force us to consider this factor. The clinical presentation of patients, affected by iron deficiency anemia (IDA), often mimics that of depressive disorder, such as lethargy, irritability and behavioural disturbances. Of note, many of these signs and symptoms precede the establishment of frank anemia.[4] Iron supplementation leads to improvement in depressive symptoms even before any visible improvement in RBC count is observed. It seems that this phenomenon is due to the recovery of neurotransmitters and enzyme levels, dependent on iron, unrelated to hemoglobin (Hb) concentration.[5] With the identification of the use of iron supplements in treatment of isolated depressive symptoms of IDA, extended knowledge is needed to identify any relationship of iron deficiency with DD, and the usefulness of iron supplements in its treatment, in particular.

If the association of IDA with DD is established, it can prove to be a breakthrough in effective management of the latter. Moreover, mental health professionals can be sensitised to the need of assessing the Hb status of patients of . Thus, the concept of holistic medicine will be satisfied,[6] which states that all the biological, psychological as well as social aspects of the patients must be considered during treatment. This cost-effective and easy treatment is not studied in Pakistan earlier.

The objective of this study was to determine the relationship between iron deficiency anemia and depressive

[1] *Department of Medical Education / Psychiatry[2] / Administration[3], Sindh Rangers Hospital, Karachi.*

[4] *Department of Community Medicine, Army Medical College, National University of Medical Sciences, Rawalpindi.*

[5] *Department of Psychiatry, Jinnah Postgraduate Medical Institute, Karachi.*

Correspondence: Dr. Madiha Shafi, Officer Incharge Training and Medical Education, Sindh Rangers Hospital, Karachi. E-mail: dr.madihashafi@gmail.com

Received: August 05, 2017; Accepted: March 27, 2018.

disorder; and identify the correlation between severity of anemia and depressive disorder.

METHODOLOGY

It was a hospital-based case control study, conducted at Sindh Rangers Hospital, Karachi, from January to July 2017. Cases and equal number of age and gender matched controls were enrolled by purposive sampling technique. Patients presenting to psychiatry OPD, aged between 18-60 years, were assessed. Cases were selected on uniformly accepted criteria as diagnosed patients of depressive disorder by consultant psychiatrist on ICD10 criteria,[7] with score of 8 and above on HAM-D rating scale (a standardised tool for indication and assessing severity of depressive disorder).[8]

Other psychiatric disorders were carefully excluded such as, schizophrenia, post-schizophrenic depression, bipolar affective disorder, and substance use disorders by psychiatrist. Chronic medical disorders (such as chronic liver disease, chronic renal disorders, hypothyroidism, and hyperthyroidism) were also excluded. Moreover, women who were pregnant or were in postpartum period were also excluded.

Age and gender matched controls, fulfilling the inclusion and exclusion criteria, were selected from other OPDs of the same hospital and from the attendants coming with the patients, as well. A semi-structured proforma was used for documenting the socio-demographic factors and outcome variables, i.e. score on HAM-D and hemoglobin (Hb) levels. The severity grouping were done on the basis of scores; participants having score 0-7 were labelled as without depression, 8-17 as mild depression, 18-24 moderate depression, and score more than 24 as severe depression.

Hemoglobin levels (Hb) were assessed in all the cases and controls. WHO criteria were used for the diagnosis of anemia.[9] In females, Hb $\geq$12 g/dL was considered as normal, 11 to 11.9 g/dL as mild anemia, 8 to 10.9 g/dL as moderate anemia, and <8 g/dL was considered as severe anemia. In males, $\geq$13 g/dL was taken as normal, 11 to 12.9 g/dL as mild anemia, 8 to 10.9 g/dL as moderate anemia, and <8 g/dL as severe anemia. Low Hb along with mean corpuscular volume (MCV) less than 80 fL, and microcytic picture on slide was taken as diagnostic standard for IDA. Other causes of microcytic anemia, i.e. sideroblastic anemia, thalassemia, and lead poisoning were ruled out on peripheral smear.

Sample size was estimated using Openepi sample size calculator version 3.01. Inserting mean and standard deviation of HAM-D scores of participants with anemia and without anemia; 32.09 ±4.19, 33.37 ±1.9 at 95% CI,[10] the sample size was found to be 204, i.e. 102 cases and 102 controls. From the initial sample of 204 participants, the patients with missing data of Hb and an equal number of controls were excluded making a final sample size of 200.

Ethical clearance was taken from institutional review board. Informed consent was obtained from the participants after informing them in simple and understandable language about the purpose of study. They were assured of confidentiality and allowed to withdraw at any point of study without mentioning the reason.

The data collected was analysed using computer packages, Statistical Packages of Social Sciences (SPSS version 22). Normality of Hb and HAM-D scores was assessed using Shapiro Wilk test, mean and standard deviation (SD) were computed for quantitative variable, e.g. age. Categorical variables were measured in frequencies and percentages. Stratification was done with regard to gender, age group, and socioeconomic status, for the outcome variables, (i.e. depressive disorder and anemia), in order to see the impact of these on the outcome variables by using Pearson Chi-square test of independence; p-value less than 0.05 were considered as significant. Mann-Whiteny U-test was used to compare median Hb levels between the two groups and median with interquartile range (IQR) was reported. Spearman rank correlation analysis was employed to examine the relationship between depression and Hb levels. In order to determine the degree of relationship between depression and Hb levels, logistic regression analysis was used, and odds ratio with p-value less than 0.05 were considered significant.

Table I: Characteristics of the patients with IDA and control subjects.

Characteristics	Control (n=100)	Cases (n=100)	P-value
Age			
18-25 years (n=34)	18	16	0.99
26-35 years (n=41)	21	20	
36-45 years (n=68)	33	35	
46-55 years (n=53)	26	27	
>55 years (n=4)	2	2	
Gender			
Female (n=130)	64	66	0.76
Male (n=70)	36	34	
Marital status			
Single (n=36)	23	13	0.125
Married (n=155)	75	80	
Widowed (n=5)	1	4	
Separated (n=4)	1	3	
Socioeconomic status (monthly income)			
Lower (Rs <14000 per month) (n=74)	39	35	0.81
Middle (Rs =14000-45000) (n=102)	50	52	
Upper (Rs > 45000) (n=24)	11	13	
Residence			
Rural (n=80)	40	40	1
Urban (n=120)	60	60	
Anemia			
Normal (n=111)	84	27	<0.001
Mild (n=82)	16	66	
Moderate (n=6)	0	6	
Severe (n=1)	0	1	

Table II: Association between anemia and score at HAM-D.

Anemia	Score at HAM-D								p-value
	Normal		Mild depression		Moderate depression		Severe depression		
	n	%	n	%	n	%	n	%	
Normal	84	84.0	14	26.4	8	29.6	5	25.0	<0.01*
Mild	16	16.0	36	67.9	18	66.7	12	60.0	
Moderate	-	-	2	3.8	1	3.7	3	15.0	
Severe	-	-	1	1.9	-	-	-	-	

**p<0.05 was considered significant using Pearson Chi-suare test of independence.*

RESULTS

Mean age of the 200 participants entering this study was 37.74 ±10 years with mean age of cases and controls as 38.19 ±10.2 years and 37.28 ±9.97 years, respectively; 65% (n=130) of the participants were female. Fifty percent (100) of the study participants were depressed with median HAM-D score 18 (IQR=10). Distribution of Hb and HAM-D scores was not normally distributed, the Shapiro Wilk test gives p-value less than 0.05 for both variables. Therefore, we used non-parametric test to compare the median of two groups. Other characteristics of the study population are described in Table I.

Median Hb levels were 11.9 g/dl (IQR=1.27) and 12.9 g/dl (IQR=1.3)) in depressed and healthy participants, respectively. The median differences of Hb between two groups were found statistically significant with p <0.01 (Figure 1). In depressed individuals, median HAM-D was 18 (IQR=10); and in healthy individuals the median HAM-D was 5 (IQR=3). Mann-Whitney U-test showed that median HAM-D scores of the two groups were significantly different (p<0.01).

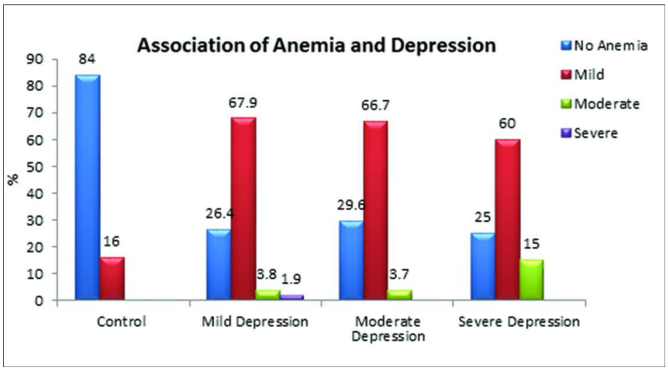

Figure 1: Relationship of anemia with depression (p <0.01) obtained using Pearson Chi-square test of independence.

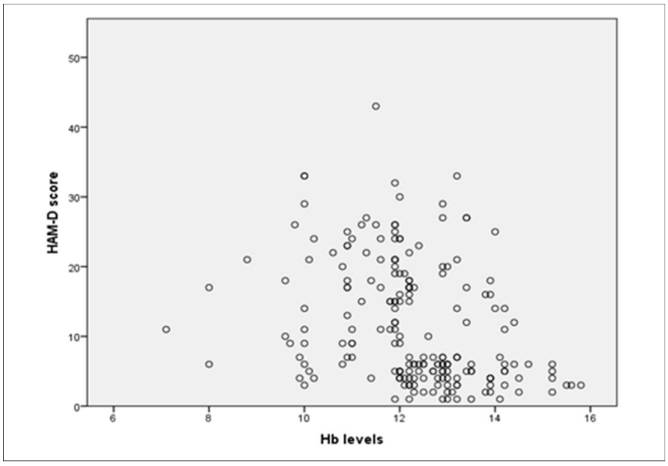

Figure 2: Spearman rank correlation between Hb concentration and HAMD rating scale in 200 adults (r = -0.429, p <0.01).

There was a significant association obtained between HAM-D scores and anemia, using Pearson Chi-square test with p-value less than 0.01. In this study, 67.9% cases of mild anemia were found with mild depression; and 3.7% cases of moderate anemia were found with moderate depression (Table II).

Spearman rank correlation coefficient for Hb level and depression was r = -0.429, and statistically significant (p<0.01) which showed negative relation (Figure 2).

The odds for Hb levels 0.487 (0.37 - 0.64) showed cases are less likely to be found with higher Hb levels as compared to controls, p-value was less than 0.05.

DISCUSSION

This study evaluated the relation between Hb levels and DD. Median Hb levels were 11.9 g/dl (IQR=1.27) and 12.9 g/dl (IQR=1.3) in depressed and healthy participants, respectively (p=0.01). IDA was observed in 44.5% of the participants, which seems higher than global estimates.[11] It might be due to the reason that 88% of our study population belongs to middle and low socioeconomic class in which IDA is more common, results similar to previous studies.[12,13] Higher frequency of IDA in depressed participants as compared to controls may indicate the role of iron in brain function and the development of DD. The scores at HAM-D raised significantly with decreasing Hb levels. These findings are similar to a study conducted in Iran.[10] In this study, although the correlation coefficient was low; but direction showed an inverse correlation between Hb level and severity of depression. These results are consistent with those of the study conducted in Iran on medical students showing that Spearman correlation coefficient for ferritin and depression was -0.167 and statistically significant.[14] Similar results were observed in a study on Japanese male population.[15]

The current study evaluated that IDA was associated with a significantly increased risk of DD, odds for Hb level 0.487 (0.37-0.64). These results supported by a

study conducted in Italy, showing strong association of anemia with depression in elderly population with odds ratio [OR] = 1.93; 95% confidence interval [CI], 1.19-3.13).[16] However, Yi *et al*. and Millingen *et al*. concluded that there was no association between IDA and depression.[15,17] This discrepancy may be due to sample differences, ethnic differences or different depression rating.

Future researchers could determine whether intervention with iron supplementation can relieve symptoms of depression in clinical trials. Future studies should also assess the multidimensional syndrome of depression by using an array of converging measures.

This study was limited by a small sample size and a hospital-based environment. The results need to be replicated ideally with large sample size. Moreover, to establish causal association between IDA and DD, role of iron supplements in patients with DD should be studied in clinical trials.

CONCLUSION

This study concludes that there is relationship between iron deficiency anemia and depressive disorder; and severity of symptoms of DD increases with degree of IDA. However, it needs validation with larger sample size and trials.

REFERENCES

1. http://www.who.int/mediacentre/factsheets/fs396/en. accessed on January 2017
2. Saveanu RV, Nemeroff CB. Etiology of depression: genetic and environmental factors. *Psychiatr Clin North Am* 2012; **35**:51-71.
3. Rao TSS, Asha MR, Ramesh BN, Rao KSJ. Understanding nutrition, depression and mental illnesses. *Ind J Psychiatry* 2008; **50**: 77-82.
4. Beard JD, Connor JR, Jones BC. Iron in the brain. *Nutr Rev* 1993; **51**:157-70.
5. Kathlen ML, Escott SS. Krauses food nutrition and diet therapy, 10th ed. Chapman and Hall: Philadelphia. 2004.
6. Havelka M, Lucanin JD, Lucanin D. Biopsychosocial model – the integrated approach to health and disease. *Coll Anthropol* 2009; **33**:303-10.
7. World Health Organization, The diagnostic criteria of major depression as defined by the ICD-10 classification of mental and behavioural disorders World Health Organization, Geneva, 1992; Jan 24, 2009.
8. Hedlund JL, Viewig BW. The Hamilton rating scale for depression: a comprehensive review. *J Oper Psychiatry* **10**: 149-65.
9. World Health Organization. Indicators and strategies for iron deficiency and anemia programs. Report of the WHO/UNICEF/ UNU consultation. Geneva, Switzerland. 1993.
10. Noorazar SGh, Ranjbar F, Nemati N, Yasamineh N, Kalejahi P. Relationship between severity of depression symptoms and iron deficiency anemia in women with major depressive disorder. *J Anal Res Clin Med* 2015; **3**:219-24.
11. Benoist BD, McLean E, Egli I, Cogswell M. Worldwide prevalence of anemia. WHO global database on anaemia. 1993-2005.
12. Kim JY. Relationship between socioeconomic status and anemia: prevalence in adolescent girls based on the fourth and fifth Korea national health and nutrition examination surveys. *Eur J Clin Nutri* 2014; **68**:2.
13. Animasahun BA, Temiye EO, Ogunkunle OO, Izuora AN, Njokanma OF. The influence of socioeconomic status on the hemoglobin level and anthropometry of sickle cell anemia patients in steady in steady state at the Lagos University Teaching Hospital. *Niger J Clin Pract* 2011; **14**:422-7
14. VahdatShariatpanaahi M, VahdatShariatpanaahi Z, Moshtaaghi M, Shahbaazi SH, Abadi A: The relationship between depression and serum ferritin level. *Eur J Clin Nutr* 2007; **61**:532-5.
15. Yi S, Nanri A, Poudel-Tandukar K, Nonaka D, Matsushita Y, Hori A, *et al.* Association between serum ferritin concentrations and depressive symptoms in Japanese municipal employees. *Psychiatry Res* 2011; **189**:368-72.
16. Onder G, Penninx BW, Cesari M, Bendinei S, Lauretani F, Bartali B, *et al*. Anemia is associated with depression in older adults: results from the InCHIANTI study. *J Gerontol A Biol Sci Med Sci* 2005; **60**:1168-72.
17. Lever-van Milligen BA, Vogelzangs N, Smit JH, Penninx BW. Hemoglobin levels in persons with depressive and/or anxiety disorders. *J Psychosom Res* 2014; **76**:317-21.