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Original Article

Relationship between severity of depression symptoms and iron deficiency anemia in women with major depressive disorder

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Abstract

Introduction: Iron deficiency (ID) is a common nutritional problem lead to many unintended consequences such as decrease energy, immune system problems, and neurological dysfunction. The most common psychological disorder is depression. A patient with ID anemia (IDA) show signs and symptoms of behavioral and mood disorders like depression.

Methods: In this study, 100 female patients with diagnosed major depression in years 2010 and 2011 were studied. In all patients standard Hamilton depression rating scale (HDRS) was used to evaluate depression severity. Blood samples were taken for complete blood count difference analysis and evaluating anemia and in those with hemoglobin (Hb) < 12 mg/dl, ferritin, and total iron binding capacity were checked to evaluate IDA.

Results: Patients mean age was 36.34 ± 10.43 years old. Mean HDRS score was 32.20 ± 4.07. 19 had anemia, and among them 8% had IDA. Mean HDRS score in patients with IDA (33.37 ± 1.90) was higher than those without (32.09 ± 4.19), but the difference was not significant (P = 0.39). There was no difference between patients with and without anemia in HDRS score. The negative relation was observed between Hb levels, and HDRS score (Pearson correlation = -0.21, P = 0.03).

Conclusion: We observed that the negative correlation between Hb levels and HDRS score. It demonstrates the effect of Hb decrease and anemia occurrence on depression severity; however, it needs more studies.

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Introduction

Iron deficiency (ID) and iron deficiency anemia (IDA) is the most common nutritional deficiency that affected most of the 3.5 billion people in developing countries.[1] The IDA is the most current cause of anemia in different age groups, including women of reproductive age.[2] Decreased productivity, decreased academic performance, immune system disorders and neural dysfunction in vulnerable groups is adverse consequences of IDA.[3]

Among the wide different biological effects of iron, there is remarkable evidence that iron has an important role in neurologic

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functions and developments.[4,5] 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).[6,7]

The major cell types that comprise iron in human brains are oligodendrocytes, which responsible for the production of myelin. Therefore, alterations in the functioning of these cells are associated with hypomyelination. In ID, oligodendrocytes appear immature. The failure to deliver iron to these cells could be causally related to delay motor maturation and perhaps behavioral alterations during particular periods of early brain development. Iron has different roles in brain metabolism like incorporation into enzymes of oxidation-reduction or electron transport; synthesis and packaging of neurotransmitters; and uptake and degradation of the neurotransmitters into other iron-containing proteins that may directly or indirectly alter brain function through peroxide reduction, amino acid metabolism, fat desaturation, and altering membrane function.[8]

Depression is the most common mental disorder.[9] The overall prevalence of mood disorders was reported 25% [25-10% for major depressive disorder (MDD) in women and 12.5% in men].[10] Prevalence of women's depression in reproductive ages is two times more than men.[11,12] Current estimates suggest that 16% of the population will experience a type of depression during their life.[13] Approximately, 121 million people suffer from depression worldwide, and it will be the third cause of disability up to 2020.[14]

Some causes of depression such as genetics couldn't be changed, but others can be modified. Nutrition may play an important role in preventing depression. In fact, nutritional deficiencies can affect the psychological state and brain mechanisms that can lead to mood disorders such as depression.[15] The association of depression with some vitamin deficiencies (folic acid, vitamin B_{12}, niacin and vitamin C) has been established.[11] Patients, who are suffering from IDA, show signs and symptoms of mood disorders like depression.

Many of depressive symptoms in patients with IDA can be resolved by iron supplementation even before any improvement in red blood cell count or other indicators improvement.[2] It seems that this phenomenon is due to improved levels of neurotransmitters, and iron-dependent enzyme that is not related to hemoglobin (Hb) concentration.[16,17]

IDA can cause depression, irritability, fatigue, sleepiness, and it effects on quality of life, the symptoms of depression 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. Therefore, such a study to understand the relationship of depression with anemia and the effect of anemia on the severity of symptoms should be required.

Methods

This cross-sectional study was conducted in 2010-2011 on 100 women diagnosed with MDD, according to psychiatric diagnosis and Hamilton depression rating scale (HDRS) and also HDRS was used for evaluation of depression severity. Convenience sampling was used to select patients from clinics of Tabriz University of Medical Sciences, Iran. Inclusion criteria of the study were psychiatric diagnosis of major depression according to Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR) criteria, Age over 18 years, being female and exclusion criteria were history of mania, depression due to other physical illnesses, Specific drug intake (or provide 2-week washout period for patients who received the drug), Alcohol consumption during the past 6 months, other severe illnesses such as liver disorders, Pregnancy, lactation, vegetarian diet and vitamins or iron supplementation during 6 months.

After diagnosis by a psychiatrist, all participants were taken tests of thyroid and liver function test. Beta human chorionic

gonadotropin (Beta-hCG) test was evaluated in women with they don't know "are they pregnant or not" and enrolled if there was not an impairment in performed tests. In the remained 100 patients, to assess the severity of depression HDRS was used to determine the severity of depression.

Demographic features as age, education level, occupation, marital status, and a number of children were assessed at baseline, and informed consent was obtained. 7 ml blood samples were collected from all patients included in 2 ml citrated and 5 ml clot in two separate glasses and delivered in maximum two hours. The clot samples were centrifuged immediately after clotting for serum separation, and maintained in -20 °C. In this study, Hb < 12 g/dl considered as anemia. If the Hb is < 12 g/dl, Fe and total iron binding capacity (TIBC) were also tested. TIBC levels > 360 µg/dl and Fe < 30 µg/dl were considered as IDA. Because levels of mean corpuscular volume (MCV), mean corpuscular Hb (MCH) and mean corpuscular Hb concentration (MCHC) have changed in the early stages of ID, these indicators were also evaluated.

The data were analyzed by SPSS software (version 16, SPSS Inc., Chicago, IL, USA). Statistical significance level was considered P < 0.05. Frequency, percentage, Student's t-test, one-way ANOVA, and Pearson correlation test were used.

Results

All participants were in their reproductive ages with a mean age of 36.34 years. 75 patients (75%) were householder, and 25 patients (25%) were employed. 15 patients (15%) were single, 80 (80%) were married, and 5 (5%) were divorced or widowed. The mean number of their children was 1.76 ± 1.36. Minimum and maximum were 0 and 9, respectively. Only 12% of patients were illiterate.

Table 1 shows the relationship between blood sample indicators with HDRS scores, and there were not any significant association. The lowest and highest Hb level was 9.40 and 15.90 mg/dl, respectively. Hb levels in 18 patients (18%) were low and in 82 cases (82%) were normal. The mean hematocrit level was 40.73 ± 4.54, and the median was 41. The minimum and maximum rates were 24 and 49, respectively.

MCV levels in 72 cases (72%) were between 90 and 60 and this is a sign of IDA. In 28 cases (28%) MCV was normal. MCH levels in 82 cases normal and in 18 were decreased. MCHC level in 90 cases normal and in 10 was reduced.

Table 1. Comparison experimental variables based on Hamilton depression rating scale (HDRS)

Variables	HSRD	P (t-test)
Hb ≤ 12 (g/d1)	32.50 ± 3.38	0.73
Hb ≥ 12 (g/d1)	32.00 ± 4.10	
Hct ≤ 37%	32.36 ± 3.33	0.84
Hct ≥ 37%	32.16 ± 4.40	
MCV ≤ 80	33.00 ± 4.40	0.53
MCV ≥ 80	32.12 ± 4.10	
MCH ≤ 27	33.05 ± 3.89	0.29
MCH ≥ 27	31.98 ± 4.11	
MCHC ≤ 32	33.00 ± 3.16	0.28
MCHC ≥ 32	32.04 ± 4.34	

Hct: Hematocrit; Hb: Hemoglobin; HDRS: Hamilton depression rating scale; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration

TIBC and ferritin levels were checked in 18 patients. The mean of TIBC was 376.67 ± 89.43 with a median of 384.05. The minimum and maximum TIBC were 168 and 510, respectively. In this cases, TIBC levels in 7 patients (38.9%) were normal and in 11 patients (61.1%) was high. The mean of ferritin was 28.36 ± 26.47 with a median of 22.60. Minimum and maximum ferritin were, respectively, 4.40 and 97.20. Ferritin levels in 4 patients (22.2%) were normal and in 14 patients (77.8%) was low. According to the criteria of anemia 8 patients (8%) had IDA, that in 7 cases there was lower Hb level and 1 patient had normal Hb, but could be considered as mild anemia. Anemia was found in 19% of total patients.

HDRS compare scores among different variables

HDRS scores were 31.08 ± 4.23 in householder patients and 33.40 ± 3.32 in employed patients and the difference between the two groups was not statistically significant (P = 0.08). Figure 1 shows the patient's HDRS scores based on

marital status. HDRS scores were the higher in unmarried patients compared with married patients and in married patients was higher compared with divorced or widowed patients. However, the difference between groups Were not statistically significant (P = 0.70).

HDRS scores in patients with and without anemia were 33.37 ± 1.99 and 32.09 ± 4.19, respectively. It was observed that patients with IDA had higher scores than the normal group. However, the difference between groups was not statistically significant (P = 0.39). Figure 2 shows HDRS scores between patients with and without anemia. It is observed that the mean HDRS is higher in patients with anemia. However, the difference between groups was not statistically significant (P = 0.70).

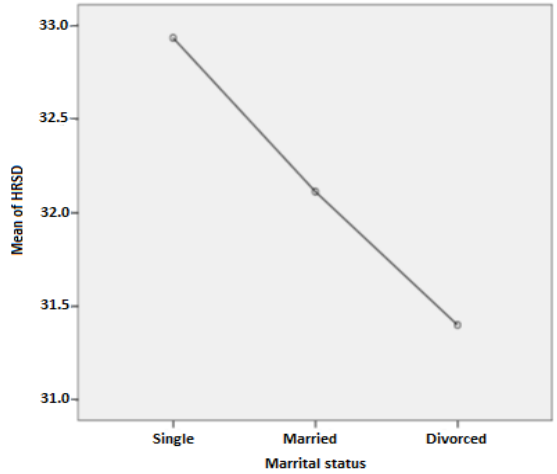

Figure 1. Hamilton depression rating scale (HDRS) scores based on the marital status of patients

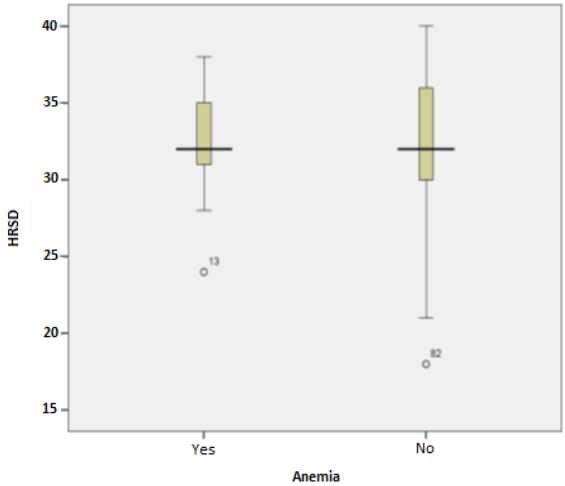

Figure 2. Hamilton depression rating scale (HDRS) scores between patients with and without anemia

HDRS scores in patients with normal and low Hb were 32.50 ± 3.38 and 32.13 ± 4.22, respectively. However, the difference between groups was not statistically significant (P = 0.73).

The probable relationships between different levels of scores HDRS using Pearson correlation across all participants were examined, and a significant negative correlation was found between Hb levels and HDRS scores (Pearson correlation = 0.21, P = 0.03). The probable relationships between different levels of HDRS scores using Pearson correlation were studied in patients with IDA and also found a significant negative correlation between Hb levels and HDRS scores (Pearson correlation = 0.77, P = 0.02). The possible relationships between different levels of HDRS scores using Pearson correlation was studied in patients with anemia and also found a significant negative correlation between Hb levels and HDRS Scores (Pearson correlation = 0.48, P = 0.03) and there was no significant correlation between serum ferritin and TIBC level with HDRS scores (Pearson correlation = 0.22, P = 0.39), (Pearson correlation = 0.01, P = 0.96).

Discussion

ID is one of the most common nutritional problems in the world both in developed and developing countries.

Relationship of iron and brain function, cognition, and behavior (including emotional behavior) has been the subject of interest for researchers over the past decade.[4] Changes in iron metabolism has been suggested as potential pathological markers in patients with depression. Ferritin as an intracellular iron storage plays an important role, and this issue has become the subject of extensive investigation.[18] Bartalena et al.[19] shows that ferritin level was significantly lower in non-anemic women with untreated major depression compared to healthy control group. Furthermore, increasing in serum ferritin levels was associated with an improvement in depressive symptoms in treatment-resistant depression in chronic

hemodialysis patients with major depression.[20]

In the current study, 19% of women with depression were anemic and about 8% were suffering from IDA. The study of Onder et al.[21] shows that 15% of people with depression were anemic. In the study of Kolahi et al. prevalence of anemia in women living in the North West of Tabriz was reported 9.7% and 75.3% of anemic patients had IDA.[22] Furthermore in our study, it was found that anemia was significantly higher in patients with depression and HDRS significantly increased with decreased Hb levels, however, Lever-van Milligen et al.[23] showed that there is no association between depressive and/or anxiety disorders and Hb levels or anemia status. Benton and Donohoe[15] showed that depression significantly associated with early fatigue and apathy and the symptoms were exacerbated by IDA.

In the present study, there is no significant association between depressive symptoms and serum ferritin levels. The results of this research are consistent with the study of Yi et al.[20] The findings of these researchers showed that there is not significant relationship between serum ferritin levels and depression in women, however, in men significantly increased depression severity with reduced serum ferritin levels. But Vahdat et al.[17] determined that the mean serum ferritin was significantly lower in patients with depression.

Limitations

We did not have control group but as mentioned above in the North West of Tabriz anemia was reported 9.7% that 75.3% of anemic patients had IDA.[23]

Conclusion

There is negative correlation between Hb level and HDRS score in total patients, anemic patients, and IDA group, and it demonstrate the effect of Hb decrease and anemia on depression severity, however, it needs more studies.

Conflict of Interests

Authors have no conflict of interest.

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