Original Article

The Role of Iron Deficiency as Trigger for Depression: A Biochemical and Psychological Perspective

Jaafar S Al-Showaily, Mohand Kareem Razzaq, Hussein Flayyih Hassan and Qayssar A. Obaid

ABSTRACT

Objective: To investigates the role of iron deficiency as a determinant of depression as perceived from both a biochemical and a psychological perspective.

Study Design: Case control study

Place and Duration of Study: This study was conducted at the Al-Rifai Teaching Hospital in Dhi Qar, Iraq from 1st November 2024 to 30th June 2025.

Methods: 162 participants were enrolled. Self-inventory instrument has been used which included two domains, psychological domain by using Beck`s depression inventory to assess depression level and the other domain is the biochemical domain which include biochemical sample and analysis of 5 ml venous blood samples were collected from participants and placed in a 2 ml anticoagulated tube for complete blood count measurement, which included white blood cell, red blood cell, Hemoglobin A1c and hematocrit only, and 3 ml in a yellow gel tube for ferritin and B12 measurement. Participants were divided into two groups; control group those with no depression and depressed group (cases) those with depression.

Result: Depression level among depressed group was high 65%. The differences between control subjects either moderate or severe anemia regarding age, gender and body mass index. Ferritin showed significant decreases among patients who had either moderate anemia or severe anemia when compared to participants in the control group ($p<0.01$) which proved iron deficiency as a primary condition within these groups. The anemic groups exhibited diminished levels of all three markers (hemoglobin, hematocrit and red blood cell) which confirm the clinical presentation of anemia.

Conclusion: Biochemical and psychological investigation support highly-converging evidence for a role of iron deficiency in depressive symptoms, and as anemia and depression increase ferritin decrease and as response to the inflammatory process white blood cell also increases.

Key Words: Depression, Iron deficiency, Biochemical perspective, Psychological perspective

Citation of article: Al-Showaily JS, Razzaq MK, Hassan HF, Obaid QA. The Role of Iron Deficiency as Trigger for Depression: A Biochemical and Psychological Perspective, Med Forum 2025;36(9):55-59. doi:10.60110/medforum.360910.

INTRODUCTION

The bio-psycho relationship between iron and depression, the goal of the research is to explore this relationship in an integrated bio-psycho manner and are expected to reveal the biopsychological mechanisms of iron's influence on depression and provide evidence-based references for clinical management.[1-3]

Department of College of Medicine, University of Sumer, Thi-Qar, Iraq.

Correspondence: Jaffar S. Al-Showaily, College of Medicine, University of Sumer, Iraq.
Contact No: 07814574612
Email: jaafar.sadiq@uos.edu.iq

Received: July, 2025
Reviewed: August, 2025
Accepted: August, 2025

Depression is one of the most commonly reported mental health problems. It is related to the loss of interest in normal daily activities and is characterized by sadness, discouragement, hopelessness, guilt, decreased energy, and concentration and sleep disorders. Depression has been the main cause of disability globally, affecting an estimated 300 million people in 2015.[4] If significant steps are not taken, by 2030, it is anticipated that it will undermine the productive abilities of individuals more than all other diseases, culminating in economic losses at the level of trillions of USD. Depressive disorders have also caused an increase in suicide rates. Globally, more than 800,000 individuals committed suicide in 2012, while kin suicide caused 50% of all deaths. In addition, the direct economic burden for depression therapy is enormous and amounts to millions of dollars.[5,6]

Rapid industrialization has brought about an obvious change in the structure and nutrition of diets, with iron deficiency appearing as the main public health issue. In fact, iron deficiency is the most prevalent public

nutritional problem, impacting anemia's occurrence. It is well established that there is a reciprocal relationship between anemia and depression. In a group of over 2,500 women in the USA, anemia evolved prior to a depressive episode and thus increased the likelihood of having health problems. 3,491 women aged 18-65 in the USA suggested anemia is always likely to be correlated to the symptoms of depression. A similar conclusion was drawn from a longitudinal, epidemiological cohort study of 3,770 men and 4,093 women joining the army in between the years 2000 and 2003, who did not submit psychiatric medical backgrounds before.[7,8]

Currently, mental disorders comprise the leading cause of non-fatal illness worldwide. Depression is a common mood disorder characterized by fatigue, suicidal ideation, anhedonia (reduced pleasure response), feelings of worthlessness and guilt, and dysphoria. Depression causes a significant decrease in people's quality of life, and currently, the pathophysiology of this complex and heterogeneous disorder is still not fully understood.[9,10] Considering the considerable global burden of disability related to depression and iron deficiency, the research not only contributes to a better understanding of negative mood states but also could provide a potential preventative strategy for the clinical treatment of depression, and especially in a country like China where the increasing frequency of smog events is related with oxidative stress and other severe mental health problems.[11] It is interdisciplinary research on the biochemistry and psychology of nutrition in relation to emotional well-being. Reduced costs will improve the efficiency and analytical focus of current biochemical research, while broadening the horizons of this laboratory. Regarding the biochemical perspective, the clinical management of iron deficiency, along with the capacity of specific psychological states to be biochemically quantified, will be investigated. The psychological perspective examines the nutritional factors of mental health. Benefits for students also include an opportunity for mentoring, laboratory training in advanced equipment and techniques, and the development of an original and substantial piece of research. It is anticipated that this study will make a significant contribution to the knowledge and understanding of how iron impacts the depressive state. In each instance, the biochemical and psychological paradigms becomes a lens in understanding issues related to mental health. Such a rigorous two-sided strategy towards depression will serve as a benchmark and many paths for future inquiry.[12-14]

METHODS

This case control study was conducted at Al-Rifai Teaching Hospital in DhiQar, Iraq from 1st November 2024 to 30th June 2025 and 162 samples were collected and using non-random purposive sampling method. The sample size was calculated the standard equation used (z×pq)/d. The samples were divided into three groups: the first group consisted of 41 healthy individuals as a control group (C (male = 21, female = 20), aged 35–65 years); 42 patients with moderate anemia (male = 21, female = 21), aged 37–65 years); and 79 patients with severe anemia (male = 40, female = 39), aged 43–65 years. To collect data, all study participants underwent an annual medical examination at Al-Refai Teaching Hospital. Patients have chronic kidney diseases, chronic liver disease, tuberculosis, arthritis, systemic lupus erythematosus, mononucleosis, Bechet's disease, and cancer have been excluded. A standard scale (Beck`s depression inventory (BDI)has been used, it has been translated and modified according to the Iraqi community standards, it is 21 items scale it has been merged to three levels of diagnosis, control, moderate and high depression (0-13) represent control, (14-28) moderate depression and (29-63) represent high depression. On the other hand, biochemical sample and analysis5 ml venous blood samples were collected from all participants and placed in a 2 ml anticoagulated tube for CBC measurement, which included WBC, RBC, HbA1c, and Hct only, and 3 ml in a yellow gel tube for ferritin and B12 measurement.

The data was analyzed using SPSS-26. The Kolmogorov-Smirnov test was used to divide the variables across the research groups. The one-way ANOVA test was used to compute and compare the means and standard deviations. The P value $P<0.05$ was considered significance, while the receiver operating characteristic curve (ROC) was used to ascertain the ideal specificity and sensitivity of a diagnostic test.

RESULTS

Table 1 demonstrate depression levels among participants which present that about half of the participants have high depression (48.8%) while no depression (control) and moderate depression each with about 25% of all participants which constitutes the other half of participants.

Table 2 showed the parameter age when compared group control with moderate showing no significant ($p<0.05$) also when compared control with high and moderate with high showing no significant ($p<0.05$), also gender and BMI showing no significant when compared control with all groups.

Table 3 showed the parameter B12 when compared group control with moderate showing no significant ($p <0.05$) also when compared control with high and moderate with high showing no significant ($p <0.05$), as well as Ferritin showing highly significant increase when compared control with moderate ($p > 0.01$) also showing highly significant increase ($p>0.01$) when compared control with high and moderate with high showing highly significant increase ($p>0.01$), and WBC and RBC the results showing when compared control

with moderate (p>0.01) also showing highly significant increase (p>0.01) when compared control with high as well as when compared moderate with high showing no significant increase (p<0.05), and Hgb showing highly significant increase with all groups (p>0.01), HCT the results showing when compared control with moderate (p>0.01) also showing highly significant increase (p>0.01) when compared control with high as well as when compared moderate with high showing no significant increase (p<0.05).

Table No.1: Depression level among participants (n=162)

Depression levels	No.	%
Control (no depression)	41	25.3
Moderate	42	25.9
High depression	79	48.8

Table No. 2: Comparison of Age, Gender and BMI among different groups (n=162)

Parameter	C (n=41)	M (n=42)	H (n=79)	Group	P value
Age	31.56±14.51	31.35±15.43	26.98±11.43	C* M	0.997
				C* H	0.180
				M* H	0.204
Gender	1.92±0.26	1.95±0.21	1.83±0.37	C* M	0.927
				C* H	0.285
				M* H	0.126
BMI (Kg/m^2)	24.02±2.50	25.62±3.29	24.63±2.92	C* M	0.036
				C* H	0.525
				M* H	0.183

**p<0.01 is extremely significant, *p<0.05 is significant, and p > 0.05 is no significant.
C for Control, M for Moderate anemia and H for High anemia

Table No.3: Comparison of B12, Ferritin, WBC, RBC, Hgb and HCT among different groups (n=162)

Parameter	C (n=41)	M (n=42)	H (n=79)	Group	P value
B12	272.90±56.77	248.98±112.70	269.80±137.78	C* M	0.615
				C* H	0.989
				M* H	0.615
Ferritin	50.105±28.12	25.72±12.87	14.79±5.29	C* M	0.000**
				C* H	0.000**
				M* H	0.001**
WBC	5.72±2.91	7.52±2.58	7.89±2.60	C* M	0.007
				C* H	0.000**
				M* H	0.755
RBC	4.03±0.60	4.52±0.55	4.50±0.66	C* M	0.001
				C* H	0.000**
				M* H	0.988
Hgb	12.69±1.05	10.09±0.95	8.45±1.39	C* M	0.000**
				C* H	0.000**
				M* H	0.000**
HCT	36.33±4.02	26.41±4.53	23.69±8.32	C* M	0.000**
				C* H	0.000**
				M* H	0.081

**p <0.01 is extremely significant, *p < 0.05 is significant, and p > 0.05 is no significant
C for Control, M for Moderate anemia and H for High anemia

DISCUSSION

In the present study, the control group matched the other groups regarding both age and gender demographics per statistical analysis (p>0.05). Body mass index measurement demonstrated an increased value in the moderate anemia group to the extent that it produced a statistically meaningful correlation versus the control group (p = 0.036) indicating a link between body mass and anemia severity.[15]

The biochemical indicators of table 3 showed significant decreases among patients who had either moderate anemia or severe anemia when compared to participants in the control group (p<0.01), which proved iron deficiency as a primary condition within these groups. The anemic groups exhibited diminished levels of all three markers (Hgb and HCT and RBC) which confirm the clinical presentation of anemia. The elevated white blood cell count in anemic groups can be attributed either to an immune response or the stress

that accompanies anemia state. The Vitamin B12 amounts collected from testing remained equal for all participant groups.[16]

Depression levels among participants as it reveals highest percentage (48%) are high and severe depression which is can be considered as indicator for the connection between depression and anemia, the interplay between mental health and hematological picture, as it has been stated, anemia have high connection with mood disorders, cognitive of the individual and other aspects like fatigue.in fact, having this percentage of depression may make the connection picture is clearer.[17] Liu et al[18] find same result as about half of the participants have high depression level.

The correlation between depression and iron deficiency have been studied in many articles as attempt to prove the exact relationship between depression and iron deficiency.[19,20] Iron deficiency is affecting hippocampus, and some neurotransmitters, and as the hippocampus is responsible for learning and memory and by it is need to iron, any disturbance will lead to psychological disorders. Same idea is a about corpus stratum which is affected by iron shortage and as it is responsible for controlling executive activities like, sustaining attention, regulation of emotion and other purposes. As for neurotransmitters iron deficiency have great impact on dopamine, serotonin and noradrenaline which they have direct impact on mood and play a major role in depression.[20]

The research supports existing evidence for the biopsychosocial model of depression by showing that iron deficiency plays an essential part in initiating and worsening psychological symptoms. Health authorities of developing and industrializing societies should establish integrated screening services which protect both mental wellness and nutritional health because their populations face rising mental health burdens alongside changes in dietary patterns.

CONCLUSION

The results of this biochemical and psychological investigation support highly-converging evidence for a role of iron deficiency in depressive symptoms, advancing the field by revealing this association in a younger population in a country of rapid Westernization. Iron deficiency has long been associated with fatigue, which is a common and characteristic symptom of depression. The important role of iron in the brain has been increasingly acknowledged, with some going as far as to consider the brain a "privileged" organ for iron in terms of metabolism. Iron acts as a co-factor in the synthesis and reuptake of several important neurotransmitters, including dopamine, norepinephrine, glutamate, and serotonin. The elucidation of the close association between iron deficiency and depressive symptoms may have urgent implications for public health, particularly in non-Westernized countries of rapid industrialization that currently have a relatively low prevalence of mental disorders and receive little attention with regard to mental health care and research. It is recommended that further biomedical studies be conducted on a larger scale within the socio-cultural context of such industrializing regions, and that these studies focus on the organization of multi-ethnic cohorts of younger populations as a priority area for the field.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Jaafar S Al-Showaily, Mohand Kareem Razzaq
Drafting or Revising Critically:	Hussein FlayyihHassan, Qayssar A. Obaid
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

Conflict of Interest: The study has no conflict of interest to declare by any author.

Source of Funding: None

Ethical Approval: No. 2/8/2400 dated 18.11.2024

REFERENCES

1. Li W, Huang X, Wei Y, Yin T, Diao L. Connecting the dots: the role of fatigue in female infertility. Reprod Biol Endocrinol 2024;22(1):66.
2. Goldberg RC. Exploring the relationships among bio-psycho-social measures of stress: a multifactorial approach towards the evaluation and reduction of stress. California Institute of Integral Studies 2022; 45-60..
3. Ma L, Yuan J, Yang X, Yan M, Li Y, Niu M. Association between the adherence to Mediterranean diet and depression in rheumatoid arthritis patients: a cross-sectional study from the NHANES database. J Health Popul Nutr 2024;43(1):103.
4. Richardson AC, Heath AL, Haszard JJ, Polak MA, Houghton LA, Conner TS. Higher body iron is associated with greater depression symptoms among young adult men but not women: observational data from the daily life study. Nutr 2015;7(8):6055-72.
5. Liu J, Liu Y, Ma W, Tong Y, Zheng J. Temporal and spatial trend analysis of all-cause depression burden based on Global Burden of Disease (GBD) 2019 study. Sci Rep 2024;14(1):12346.
6. Liu J, Ning W, Zhang N, Zhu B, Mao Y. Estimation of the global disease burden of depression and anxiety between 1990 and 2044: An analysis of the global burden of disease study 2019. Healthcare 2024; 1721.

7. Kumar SB, Arnipalli SR, Mehta P, Carrau S, Ziouzenkova O. Iron deficiency anemia: efficacy and limitations of nutritional and comprehensive mitigation strategies. Nutr 2022; 14: 2976.
8. Brittenham GM, Moir-Meyer G, Abuga KM, Datta-Mitra A, Cerami C, Green R, et al. Biology of anemia: a public health perspective. J Nutr 2023; 153: S7–28.
9. Klein DN, Goldstein BL, Finsaas M. Depressive disorders. Child Adolesc Psychopathol 2017; 610-41.
10. Wainberg ML, Scorza P, Shultz JM, Helpman L, Mootz JJ, Johnson KA, et al. Challenges and opportunities in global mental health: a research-to-practice perspective. Curr Psychiatry Rep 2017; 19: 28.
11. Mills NT, Maier R, Whitfield JB, Wright MJ, Colodro-Conde L, Byrne EM, et al. Investigating the relationship between iron and depression. J Psychiatr Res 2017; 94: 148–55.
12. Weye N, Momen NC, Whiteford HA, Christensen MK, Iburg KM, Santomauro DF, et al. The contribution of general medical conditions to the non-fatal burden of mental disorders: register-based cohort study in Denmark. BJP 2022; 8: e180.
13. Melo APS, Dippenaar IN, Johnson SC, Weaver ND, de Assis Acurcio F, Malta DC, et al. All-cause and cause-specific mortality among people with severe mental illness in Brazil's public health system, 2000–15: a retrospective study. Lancet Psychiatr 2022; 9: 771-81.
14. Ali S, Santomauro D, Ferrari AJ, Charlson F. Excess mortality in severe mental disorders: a systematic review and meta-regression, J Psychiatr Res 2022; 149: 97-105.
15. Fried EI, Flake JK, Robinaugh DJ. Revisiting the theoretical and methodological foundations of depression measurement. Nat Rev Psychol 2022; 1: 358-68.
16. Portugal-Nunes C, Castanho TC, Amorim L, Moreira PS, Mariz J, Marques F, et al. Iron status is associated with mood, cognition, and functional ability in older adults: a cross-sectional study. Nutr 2020;12: 3594.
17. García-Montero C, Ortega MA, Alvarez-Mon MA, Fraile-Martinez O, Romero-Bazán A, Lahera G, et al. The problem of malnutrition associated with major depressive disorder from a sex-gender perspective. Nutr 2022;14:1107.
18. Sweileh WM, Abu-Hadeed HM, Al-Jabi SW, Zyoud WH. Prevalence of depression among people with type 2 diabetes mellitus: a cross sectional study in Palestine. BMC Public Health 2014;14:163.
19. Kohsari M, Moradinazar M, Rahimi Z, Najafi F, Pasdar Y, Moradi A, et al. Association between RBC indices, anemia, and obesity-related diseases affected by body mass index in Iranian Kurdish Population: results from a cohort study in Western Iran. Int J Endocrinol 2021;2021: 9965728.
20. Zheng H, Long W, Tan W, Yang C, Cao M, Zhu Y. Anaemia, iron deficiency, iron-deficiency anaemia and their associations with obesity among schoolchildren in Guangzhou, China. Public Health Nutr 2020;23:1693-1702.