

# Iron Supplementation Intermittently in Reducing the Severity of Depression: Original Article

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## Abstract

To investigate the effect of iron supplementation on the severity of depression among anemic students. The study design was Quasi Experimental Trial and conducted in the Department of Allied health sciences, The University of Lahore, Lahore from May to December 2019. The severity and symptoms of depression was measured by Beck's depression scale. 781 female students were analyzed and 377 students were enrolled in the study. Written informed consent were taken from the students. A semi-structured proforma was used for documenting the outcome variables. Blood samples were taken for Hemoglobin (Hb) level. Iron supplementation significantly reduced the severity of depression ( $21 \pm 2.98$ ,  $p < 0.001$ ) at baseline versus post study ( $17.47 \pm 3.31$ ,  $p < 0.001$ ) by using Beck's Depression scale (BDI). The results showed that there was a significance improvement in post study hemoglobin (Hb) in comparison with baseline Hb (Hb at baseline =  $10.79 \pm 0.60$ ,  $P < 0.001$  vs Hb at post study =  $10.97 \pm 0.83$ ,  $P < 0.001$ ). After intervention, subjects with continued depression had high rate of iron deficiency anemia.

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These data are valuable as they enable us to conclude that iron supplementation can reduce the severity of depression in the iron deficient anemic students.

**Keywords:** depression; hemoglobin; iron deficiency anemia; supplementation.

## **1. Introduction**

Globally, Iron deficiency is the most prevailing micronutrient deficiency but still the psychological consequences of iron deficiency remain indistinct. Iron is a micronutrient which required in a minute amount for physiological functions [1]. It works as a co-factor in many reactions, such as the synthesis of tyrosine and tryptophan; precursors to the neurotransmitter serotonin, dopamine and norepinephrine [2]. The traditional hypothesis of monoamine and depression have been concerned with these neurotransmitters in which postulates that low level of dopamine, serotonin and norepinephrine concentrations might result in depression [3]. More recently, many clinical studies propose that pathophysiology of iron is related with dysfunction of the glutamatergic system, malfunction in the mechanisms and metabolism of cytoarchitectural and glutamate maladaptive variations in many of brain areas enabling cognitive–emotive behaviors [4]. Iron is necessary for the myelination of neurons and maintained the serotonin concentration in the brain [3]. Iron is an important element for the energy production, synthesis of DNA, neurotransmitter, myelination, phospholipid metabolism and brain iron accretion [5]. Iron deficiency is associated with depressive disorder in adults. Furthermore, IDA in children contributed to the development of fatigue, anxiety, depression, social and attention-deficit disorders [6]. Numerous evidences proposed that depression seemed a multifactorial disorder [7]. Aging, Genetics, sedentary life style and various other influences contribute to the development and surge of depression in people [8,9]. Evidences showed that depression is also accompanying by dietary factors, including, fruits, junk food, vegetables, fish and coffee [10,11,12]. Dietary components performed significant role in depression, those are vitamin D, vitamin B6, vitamin B12, iron, zinc and folate [13,14]. As essential micronutrients, iron and zinc are almost available in equivalent alimentary sources and their insufficiencies are frequently co-occur [15]. Iron and zinc are essential for regulation of cellular functions and neuromodulation [16]. Depression is a common illness worldwide and it is associated with iron deficiency anemia [17]. the relationship between poor nutrition and depression has been suggested in women of childbearing age who are vulnerable to depletion of nutritional factors, including iron [18,19]. According to previous studies, that anxiety or depression was more widespread in children with iron deficiency anemia as compared to healthy population. Similarly, there was an association between serum ferritin level, blood Hb and depression in adults [20]. However, the occurrence of anemia was 35% in individuals with psychiatric disorders, including depression, than in the general population [21]. According to World Health Organization depression has become a foremost cause of dysfunction by the year of 2020, in the aligning of Disability Adjusted Life Years considered for all ages. Hence, it was stated that by the year 2020 depression would be the primary reason of burden of illness in the under developed as well as developing countries [22]. Depression is a serious existing ailment with a high prevalence rate in which iron has been suggested as one variable [23]. Iron supplementation can improve various depressive symptoms in patients having iron deficiency anemia, can be resolved before any enhancement in RBCs count or any improvement in other index. Generally, it seemed that blood hemoglobin (Hb) concentration was mainly responsible for the improvement in the neurotransmitter's concentration and highly dependent on iron-dependent enzymes [24].

There are many studies, reported that iron deficiency anemia may cause various disorders such as depression, shortness of breath, irritability, brittle nails, fatigue, disrupted sleep, chest pain, heart failure and many worse consequences on quality of life. Similarly, depression and anemia may cause a variety of same sign and symptoms, and each required a particular treatment, but concurrent treatment is beneficial while alone treatment was occasionally not sufficient [23]. In summary, iron deficiency anemia was meaningfully related with a modification of neurotransmitters such as monoamine, serotonin, myelin and many more, the irregular myelination of neurons, and is perhaps associated to the onset of psychiatric ailments. There are many well documented suggestions in the literature that iron deficiency anemia has an important influence on intellectual development, aptitude, and growth-progressive delay which lead to many psychological problems including depression [25]. Further studies are needed to confirm this association. Therefore, the current study was intended to evaluate the consequence of iron supplementation, intermittently on the severity of depression in the female students having iron deficiency anemia.

## **2. Methodology**

### **1.1. Study setting**

This interventional study was conducted in 2019-2020 on 377 female students in The University of Lahore and The University of Lahore, Teaching Hospital.

### **1.2. Study design**

The study design was Quasi Experimental Trial and sampling technique was purposive sampling. The sample size was calculated by formula,  $n = Z^2 \frac{P(1-P)}{d^2}$ . Only female students were eligible for the study. The female students having blood hemoglobin  $\geq 8 \leq 11.9$  mg/dL. Mild to moderate depressive students were enrolled. The students who were taking any supplement or any other anti-depressive drugs were excluded from the study. Pregnant or those students who were participated in any other interventional program were also excluded. Demographic characteristics such as age, occupation, gender, education level, marital status and biochemical, dietary data and depression measurement were evaluated at baseline of study, and informed consent was taken from each participant. After taking informed consent in written form, the data was collected by the researcher with the help of self-administered questionnaire. At baseline of study 781 students were analyzed and 377 students were enrolled who fulfill the study inclusion criteria. The severity of depression was measured by Beck's Inventory Scale. The researcher drawn 3 cc of random venous blood to check the blood hemoglobin level by ELISA method in The University of Lahore, Teaching Hospital from all the depressive female students. At baseline anthropometric measurements (weight, height, body mass index), biochemical evaluation (blood Hb), dietary intake data and severity of depression (Beck's Score) were collected. The iron supplements (60mg of iron per supplement) were given to the participants twice a week on non-consecutive days for 12 weeks [26]. After twelve weeks the same protocol of baseline visit was conducted to compared the post study data to test the study hypothesis.

### **1.3. Ethical approval of study**

The rules and regulation set by the ethical committee of the university and followed by researcher while conducting this research. Students participated after a written informed consent.

### 3. Statistical Investigation

Data was analyzed with the help of SPSS version 25.0 and the results were presented in the form of descriptive and inferential statistics. The collected data was analyzed with Chi Squared Test and Friedman Test. The level of significance was <0.05.

### 4. Result

All of the students were in their reproductive age with the mean age ( $20.0 \pm 1.2$ ). 339 students (90%) were single, 35 were married (9.2%) but non pregnant, 1 was widow (0.3%) and 2 were divorced (0.5%). At baseline all the students were mild to moderate depressives with mean ( $21.23 \pm 2.98$ ), minimum value was 11 and maximum value was 30; and all of them were anemic having blood hemoglobin 8.0- 11.9mg/dL with mean ( $10.9 \pm 0.60$ ) before intervention. After intervention there was a significant decrease in the severity of depression with mean value ( $17.47 \pm 3.31$ ), the minimum score was 8 while the maximum score was 29. There was significantly increase in the blood hemoglobin with mean ( $10.97 \pm 0.83$ ) and minimum value was 9.0mg/dL while maximum value 12.3mg/dL shown in the Table I.

**Table 1:** Comparison of variables at baseline and post study

Variables	Mean	S.D	Minimum	Maximum	P value
Age (Years)	20.0	$\pm 1.2$	20	25	< 0.01
Depression (Baseline)	21.23	$\pm 2.98$	11	30	
Depression (Post study)	17.47	$\pm 3.31$	8	29	
Hemoglobin (Baseline) mg/dL	10.9	$\pm 0.60$	8	11.9	
Hemoglobin (Post study) mg/dL	10.97	$\pm 0.83$	9.0	12.3	

### 5. Discussion

Iron deficiency (ID) is a nutritional problem and a condition when there is not sufficient iron in the body which lead to many inadvertent outcomes such as decrease energy metabolism, weak immune responses, and nerve cells proliferation and maturation. The most common mental or psychological problem is depression. An anemic patient with particularly iron deficiency anemia (IDA) manifest symptoms of social, gestures and mood disorders similar with depression [23]. Similarly, an association between low serum ferritin levels, blood hemoglobin and depression has been reported and iron is vital for many biological functions [27,28]. Form many studies it has been suggested that iron and zinc are essential elements for proper physiological and psychological functions [29].

Association of iron and nervous system and habitual behavior has been an interesting topic for researchers over the previous decades. In depressive patients the improper iron metabolism pathway may result in possible

psychological and pathological indicators [30].

Our central nervous system needs a wide range of mineral and micronutrients. Such as, folic acid, zinc, particularly iron needed to produce myelin and vitamin B6 manifest precise roles in the biological processes that administer the integrity of proteins, deoxyribonucleic acid, phospholipids and monoamine and catecholamine neurotransmitters [31]. Micronutrient supplementation plays a beneficial role in the perceived stress or tension, mild to moderate psychiatric symptoms, and other aspects of average mood in seemingly healthy people [32]. According to the World Health Organization (WHO), depression is the second most prevalent problem after ischemic heart diseases by the year 2020 [33].

Research proposed many psychosocial aspects for postpartum depression but some studies examined the relationship between physiological factors, precisely anemia and depression. This topic of iron supplementation for depression is relatively innovative in the arena. There are many evidences in the literature on depression and other probable influences but most of them did not emphasis on iron supplementation for depression and its effects on iron deficiency anemia. The results of current study revealed that diagnosis of depression and treatment of physiological factors, particularly anemia, could diminish the hazard of stress or depression [34].

There is a positive relationship between iron supplementation and BDI score in all anemic students, IDA was reduced in students which demonstrate the effect of iron supplementation on blood Hb and decrease in the severity of depression in anemic students, however, it needs more studies. This is in keeping with previous findings that all the students will remained blind to the iron supplementation throughout the study [25].

The associations between dietary iron intake and risk of depression remain contentious. From previous studies it has been reported that, high rates for male students are particularly concerning since they are typically less willing to access support, although females are more at risk of depression [17]. Thus, we carried out a study to find the consequence of iron supplementation on the severity of depression among anemic female students. Furthermore, the current study emphasizes that depression is a common mental health problem in university students. In summary, there are consistent findings over an array of studies accomplished in various countries done by many researchers, that multivitamin or iron supplementation may improves many aspects of mood and a positive change in the aggressive behavior. A major aim of the current study was to determine the consequences of intermittent iron supplementation on the severity of depression among anemic students.

## **6. Limitation**

The current study was limited to female students who were depressive and suffering from iron deficiency anemia.

## **7. Conclusion**

These data are valuable as it enables us to conclude that iron supplementation intermittently, can reduce the severity of depression in the iron deficient anemic students. Further studies are required for consistency of these findings in different age groups.

## 8. Conflict of interest

None

## 9. Funding sources

None

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