

Impact of Magnesium and Ferritin Deficiency on Depression Among Adolescent Students

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Abstract

Background: Depression is considered the fourth-leading cause of health problems. It is the fourth-leading cause of health problems and disability, which causes 16% of the worldwide burden of disease and injury among adolescents. **Objective:** The aim of the present study was to evaluate the possible association of magnesium (Mg) and ferritin deficiency with depression in adolescent students. **Patients and Methods:** This case control study in secondary schools at Al-Ghanayem discrete. The total number included was 358 students. All were screened for depression by the Arabic version of the Beck questionnaire. The students who had positive score was selected as cases 86 and a matched same number of students with negative score was selected as controls. Serum level of ferritin and magnesium was measured in the 2 groups. **Results:** There was statistically significant difference between the studied groups when comparing depression grade with each of ferritin and Mg. Depressed group cases had lower mean values of ferritin and Mg. The ferritin cut-off level for the prediction of depression was (35.5 µg/dL, which had a sensitivity of 74.4% and a specificity of 75.6%. The magnesium cut-off levels for the prediction of depression were 1.95 mg/dL and 104.5 ng/dL which had a sensitivity of 70% and 64%, respectively. **Conclusion:** There was a statistically significant negative correlation between depression severity and each of socio-economic status ferritin and Mg. Each of ferritin and Mg were predictors for depression.

Keywords

depression, ferritin deficiency, magnesium, adolescent

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Introduction

Depression is the fourth greatest cause of health problems and impairment among adolescents, accounting for 16% of the global burden of disease and injury. Globally, 17% of 10- to 19-year-olds suffer a mental illness, accounting for the whole disease burden of this age group.¹ At all ages, depression is a prevalent mental health condition.² As a result of hormonal changes that teens encounter, true depression in teens is frequently challenging to detect because typical adolescent behavior is characterized by both up and down moods.³

It is a significant contributor to adolescent impairment and suffering and is viewed as a significant, preventable risk factor for suicide that is currently the second leading cause of adolescent death.⁴

The risk of developing depressive illnesses passes through generations and can run in families. Children with

depressed parents and sad grandparents had the highest rates of major depressive disorder in a multigenerational study.⁵ Genetic and environmental factors, including diet and nutrition, can influence the etiology and psychological treatment of depression, which is a complicated problem.⁶

Evidence from epidemiology points to a link between vitamin deficiencies and mental diseases like depression.⁷

There were many mechanisms that may underlie the link between magnesium and depression: Dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis is related to

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depression. Lack of magnesium causes corticotropin-releasing hormone to be released, which raises the level of adrenocorticotropin hormone.⁸

Although consuming magnesium supplements was proven to cause a reduction in depressive symptoms, there was no agreement on the link between magnesium and depression.^{9,10} The level of iron in the body has a significant impact on how the brain works, how people think and behave, and how depressed people behave. A common clinical biomarker to assess iron status is ferritin, an intracellular protein with the ability to store and release iron.¹¹ Most of the research in the field of nutritional psychiatry now focuses on adults, which limits its application.⁸

Therefore, this study aimed to evaluate the possible association of magnesium and ferritin deficiency with depression in adolescent students.

Psychiatry illness in adolescents had higher comorbidity, decreases life quality, and increases burden on individual, family, and community. So, investigate nutritional role in adolescent could help in reduce severity of illness and increase recovery rate.¹²

We are hypothesizing that magnesium and ferritin serum level have negative correlation with depression score. And the research question was “Is their difference between magnesium and ferritin serum level between depressed and normal adolescents?”

Methods

This case control study included adolescent students at Al-Ghanayem city; Assiut Governorate in the period between 2021 and 2022. There were 6 secondary schools in this city. We selected secondary schools only as the secondary students can easily understand the questionnaire (according to our pilot study) to represent the sample.

In the process of conducting study involving secondary schools, a stratified randomization approach was employed to ensure a representative sample. The study focused on a particular district comprising 6 secondary schools. From this pool, 2 schools were randomly selected to participate.

Within each of the chosen schools, a further stratification method was implemented. Both schools followed a structure of 3 grade levels, ranging from the first to the third year of secondary education. Notably, each grade level consisted of 5 classes, totalling 15 classes per school.

To obtain a diverse and unbiased sample, 1 class was randomly selected from each grade level at both schools. This random selection process aimed to capture a microcosm of the student population, as each class typically consisted of 40 to 50 students.

The researcher and 4 trained assistants entered the classes at the same time. After explaining the aim of the study and the way of filling the questionnaire in each classroom to the students, he/she fills the questionnaire by him/

herself. All the students in the class filled in the questionnaire at the same time.

The total number of students was 358 students, 192 of them from school 1 and 166 from school 2 (Figure 1).

The Arabic version of a 21-question Beck's questionnaire was used. This self-report tool is used to evaluate the intensity and breadth of depression symptoms. This tool is recommended by The United States Preventive Services Task Force.¹³

The questionnaire consists of 21 questions, each item rated from 0 to 3. The score was as follows (0-9: no depression, 10-15: mild depression, 16-23: moderate depression, 24-36: severe depression, and more than 37 very severe depression).

Of the 358 students 109 students had depression according to the used questionnaire (23 of them excluded as they refused to do any investigations) and 249 of them were no depression (normal).

Sample size was calculated using G power version 3.1.9.7 software (SPECS, 2020) power 95% based on a study done in University of Tehran¹⁴ the mean of serum ferritin in depressed patients was 26.95 ± 11.3 and in the control 38.6 ± 17.1 . The calculated sample is 86 students (43 cases and 43 controls) the sample will be multiplied χ^2 design effect due to design drop out and analysis of multi-variable to become 172 students (86 cases and 86 control).

According to the calculated sample size 86 cases and matched 86 controls were included. Students in the preparatory and secondary schools who aged between 12 and 18 years old were included. Students taking medications for depression, or any long-term medications were excluded. The school manager sent a letter to the care giver including the study title and the aim and the study then the care giver sent back with the approval of participation. A telephone call was also made by the research team to the care giver to confirm the attendance time to come to a certain laboratory in the district to take the venous blood samples from studied students.

A written consent from the students' guardians who agreed to participate in the research was taken to get from each case and control student to take 5 mL of venous blood samples from studied students using a plastic syringe and a stainless-steel needle. The blood was drawn into a metal-free plastic tube, allowed to clot at room temperature for 30 min, and then centrifuged for 15 min at 3000rpm in a room with no dust. Prior to analysis, serum samples were shielded from light and kept at 80°C. The normal range of magnesium was 1.6 to 2.5 mg/dL, and ferritin level was 16 to 220 ng/dL. The analysis was done by Robotnik Readwell Microplate Elisa Reader made in China 2016.

The Gilani socioeconomic questionnaire was completed by parents of the students.¹⁵ It was composed of 84 points. The score (0-21 are very low level, 22-42 are low level, 43-63 are middle level, and more than 63 are high level).

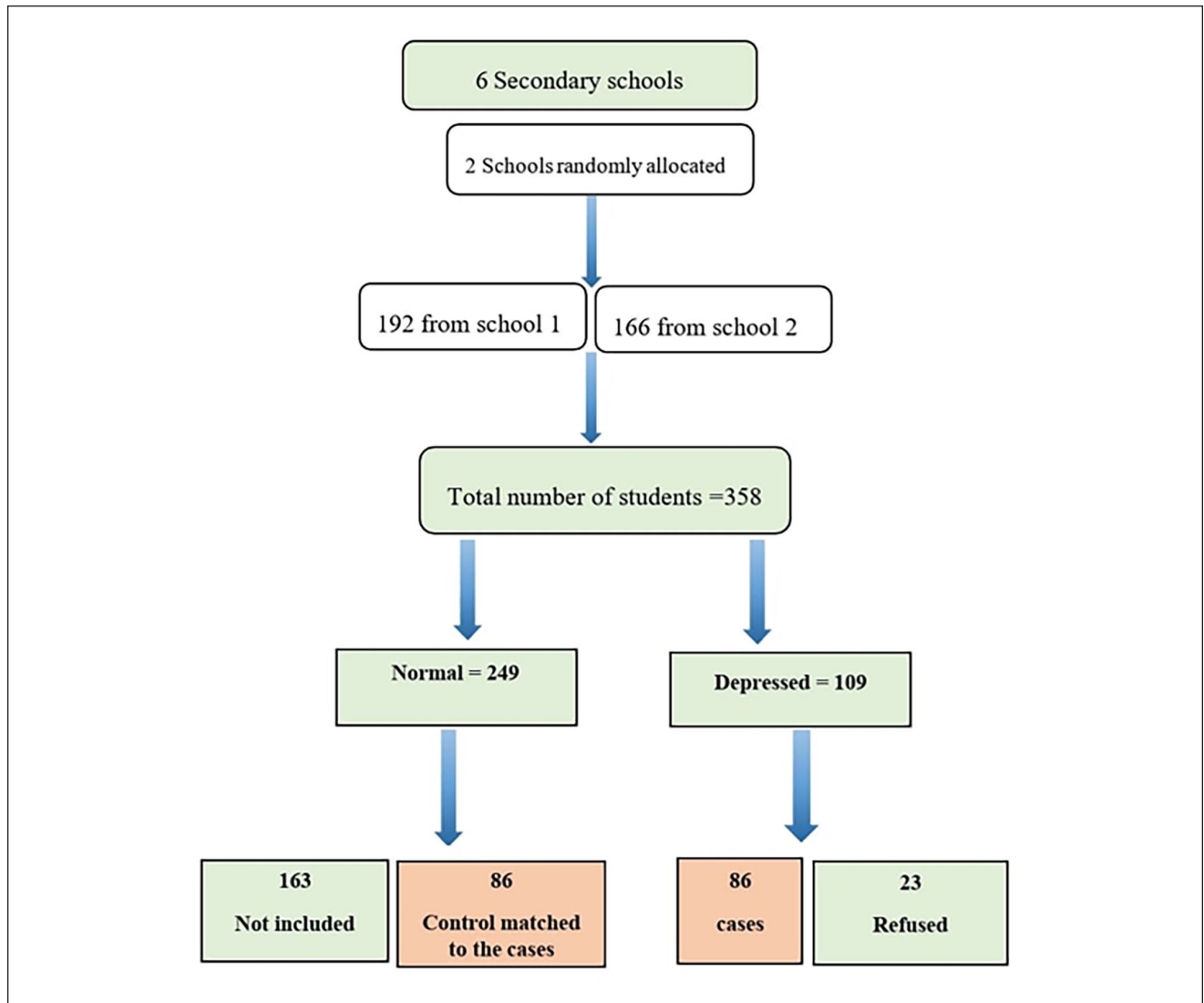


Figure 1. Flow chart of the study sample.

The cases diagnosed with mild depression were reassured and had at least 2 sessions of psychotherapy and follow up. Those with moderate depression referred to the outpatient clinics of psychiatry in Assiut University Hospitals.

Statistical analysis

Data entry was done using excel program. SPSS 26.0 for Windows (SPSS Inc., Chicago, IL, USA) was used to statistically analyze all data. The mean and standard deviation were used to convey quantitative data, while absolute frequencies (number) and relative frequencies (percentages) were used to express qualitative data. Independent samples Student's *t*-test, 1 way ANOVA test, and Chi square test were used. Pearson rank correlation coefficient was

calculated to assess relationship between various study variables, (+) sign indicate direct correlation and (–) sign indicates inverse correlation, values near to 1 indicate strong correlation and values near 0 indicate weak correlation. Validity of the tested variables was done by ROC curve to detect sensitivity, specificity, PVP, and NPV. Logistic regression analysis was used to analyze significant depression predictors. All tests were 2 sided. *P*-value <.05 was considered statistically significant (S), *P*-value ≥.05 was considered statistically insignificant (NS).

Results

The present study showed a statistically significant difference between the depression classifications regarding mean SES total score and sex (Table 1).

Table 1. The Basic Characteristics of the Studied Group and Its Relationship With Depression Severity.

Characteristic	Control (n=86)		Cases (n=86)				Test	P value	Post hoc
			Mild (n=66)		Moderate (n=20)				
Age (years)									
Mean ± SD	16.26 ± 0.80		16.25 ± 0.73		16.05 ± 0.90		0.758	.469	PI = 0.934 P2 = 0.221 P3 = 0.272
SES (total score)									
Mean ± SD	54.14 ± 13.71		46.70 ± 14.82		46.73 ± 14.64		10.626	<.001	PI < 0.001* P2 = 0.018* P3 = 0.994
Category		N	%	N	%	N	%	χ ²	P value
Sex	Male	34	39.5	15	17.2	1	4.5	9.427	.009
	Female	52	60.5	72	82.8	21	95.5		
Grade	1	41	47.7	55	63.2	11	50	6.479	.166
	2	42	48.8	30	34.5	9	40.9		
	3	3	3.5	2	2.3	2	9.1		
School	1	41	47.7	55	63.2	11	50	4.251	.119
	2	45	52.3	32	36.8	11	50		
Socio economic status (SES level)	Low	23	26.7	44	50.6	9	40.9	19.847	.001
	Middle	41	47.7	28	32.2	11	50		
	High	22	25.6	15	17.2	2	9.1		

Abbreviations: (χ^2) Chi-Square tests, 1-way ANOVA test, Post Hoc Test; P1, mild depression group versus control group; P2, moderate depression group versus control group; P3, mild depression group vs moderate depression group.

Table 2. Level of Ferritin and Mg Between Cases and Control.

Characteristic	Cases (n=86)	Control (n=86)	Test	P value
Ferritin			-6.601	<.001
Mean ± SD	43.31 ± 12.47	27.71 ± 16.95		
Mg			5.809	<.001
Mean ± SD	2.05 ± 0.21	1.86 ± 0.23		

Mann-Whitney U test; Independent Samples Test.

The mean value of Ferritin was 35.51 ± 16.77 , ranging from 7 to 80 ng/mL. The mean value of Mg was 1.96 ± 0.24 , ranging from 1.36 to 2.70 mg/dL. Most of the cases and controls have Mg and Ferritin within normal level.

There was statistically significant difference between the studied groups when comparing depression grade and each of ferritin, Mg and depressed group cases had lower mean values of trace elements (ferritin and Mg; Table 2).

There was statistically significant difference between the depression classifications and each of ferritin and Mg as cases with moderate depression had lower mean values of ferritin. On the other hand, there was no significant difference between cases with mild and moderate depression (Table 3).

Regarding Validity of magnesium in predicting depression, Sensitivity was (70.9%), specificity=59.3%), predictive value for positive (PVP)=(63.5%), predictive value for negative (PVN)=(67.1%), and (65.1%) accuracy.

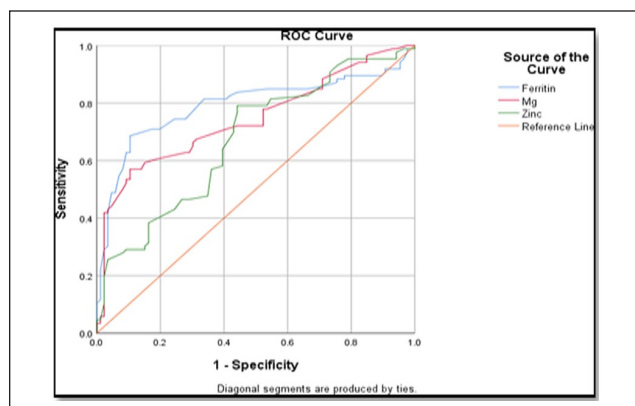
Analysis by the ROC curve was performed to test the predictive power of ferritin along with other relevant factors for depression where ferritin level was found to be the most superior as it achieved an area under the curve (AUC) of 0.791 while Mg had an AUC of 0.743. The best ferritin cut-off level for the prediction of depression was (35.5 ng/dL; Figure 2).

There was a statistically significant negative correlation between depression severity and each of socio-economic status (SES level), ferritin and Mg (Table 4).

Table 3. Relation Between Depression Severity and Patients' Trace Elements (ferritin, Mg) of the Studied Groups.

Characteristic	Control (n = 86)	Cases (n = 86)		Test	P value	Post hoc
	Normal (n = 86)	Mild (n = 66)	Moderate (n = 20)			
Ferritin				23.783	<.001	P1 < 0.001
Mean ± SD	43.31 ± 12.47 (-)	28.29 ± 16.79	25.80 ± 17.77			P2 < 0.001 P3 = 0.514
Mg				16.830	<.001	P1 < 0.001
Mean ± SD	2.05 ± 0.21	1.85 ± 0.22	1.87 ± 0.25			P2 = 0.001 P3 = 0.758

Post Hoc Tests, I-way ANOVA test, P1, mild depression group versus control group, P2, moderate depression group vs control group, P3, mild depression group vs moderate depression group.

**Figure 2.** Roc curve illustrated predictive values of the relevant factors different trace elements in depression prediction.**Table 4.** Correlation Between Depression, SES Score, and Different Parameters.

Variables		Depression severity
Age (years)	R	-.028
	P	.602
Ferritin	R	-.436
	P	.000
Mg	R	-.362
	P	.000
SES (level)	R	-.190
	P	.000

[R = Pearson correlation], [P = Sig. (2-tailed)].

Higher levels of ferritin, Mg are protective factors against depression. They were still predictors for depression after adjustment of age and sex (Table 5).

Discussion

By using the Arabic version of Beck Questionnaire of Depression, the prevalence of depression was 30.4% of

Table 5. Logistic Regression for Evaluating of Depression Among Adolescents After Adjustment of Age and Sex.

Variables	B	SE	Wald	Df	Sig.	Exp (B)	95%CI for Exp(B)	
							Lower	Upper
Ferritin	-0.065	0.014	22.445	1	.000	0.937	0.913	0.963
Mg	-3.089	0.959	10.366	1	.001	0.046	0.007	0.299

Variable(s) adjusted: Age (years) and Sex.

which (24.3%) had mild depression, (6.4%) had moderate depression, and 0% had severe depression as the severe depression usually cannot attend the school except 1 student and refused to participate in the study. when compared to similar studies, is relatively high since teenagers in impoverished countries have a greater chance of acquiring mental health problems. This finding is in line with a study conducted in Qatar Al-Kaabi et al¹⁶ revealed that prevalence of depression between the participants (34.5%), of which (14.9%) were mildly depressed, (11.2%) were moderately depressed, and (8.4%) were severely depressed. So, these results revealed that the importance of screening of depression among adolescents.

Daryanavard et al¹⁷ showed that the prevalence rate of depressive symptoms among secondary school students in Dubai was 17.5%. This variation in prevalence rates may be explained by variations in the techniques and metrics used to quantify depression, sampling techniques, the time, and age.

The current study revealed that the mean Mg was 1.96 ± 0.24 ranging from 1.36 to 2.70 mg/dL. There was statistically significant difference between the studied groups when comparing depression grade and Mg as depressed group cases had lower mean values of Mg. Although the majority of cases and controls have normal levels of Mg.

Regarding Validity of Mg in predicting depression, Sensitivity was (70.9%), specificity=(59.3%), predictive value for positive (PVP)=(63.5%), predictive value for negative (PVN)=(67.1%), and (65.1%) accuracy.

Although the exact biological mechanisms underlying the link between low blood magnesium levels and depression are yet unknown, they may involve oxidative pathways, the stress axis, and the central nervous system. According to Peng et al,¹⁸ there is evidence that magnesium insufficiency alters the way the central nervous system (CNS) functions, particularly regarding glutamatergic transmission in the limbic system and cerebral cortex. Different parts of the brain are involved in the etiopathogenesis of depression.

This was in accordance with Rajizadeh et al¹⁹ measured the level of magnesium in blood serum taken from depressed patients in Iraq found that the mean total serum magnesium level was 2.1 ± 0.26 mg/dL. Hypomagnesemia occurred in 13.7% in the study group, Depression and the Mg concentration in blood serum had a strong correlation. This strongly shows that magnesium plays a substantial role in the pathophysiology of depression.

Similar results were obtained by Tarleton et al²⁰ reported an inverse relationship between depressive symptoms and magnesium levels and magnesium intake, which persisted after adjustment for age, body mass index, and education.

On the other hand, prospective cohort studies have failed to find an association between magnesium status and later risk of depression. Martinez et al²¹ performed a study among people without any history of depression and found no significant association between magnesium intake, as assessed by diet, and risk of depression 10 years later.

The current study revealed that the mean value of Ferritin is 35.51 ± 16.77 , ranging from 7 to 80 ng/mL. There was statistically significant difference between the studied groups when comparing depression grade and ferritin as depressed group cases had lower mean values of Ferritin. Cases with moderate depression had lower mean values of ferritin. Berthou et al²² demonstrated that proper neurotransmitter synthesis (serotonin, dopamine, and noradrenaline) requires brain capture of blood iron and neuro-bioavailability. These neurotransmitters, which play a role in emotional actions, rely on neuron aromatic hydroxylases that require iron as a necessary cofactor to function.

Students with depression had a mean ferritin level that was noticeably lower than that of healthy students. The odds of depression increased by 1.92 when the ferritin level was changed from normal to low. Yi et al²³ illustrated that there was no significant association found between serum ferritin concentrations and prevalence of depressive symptoms in women.

The study had limitations as small number of sample size, a study with a large number was needed. This study researched only ferritin and Mg we recommend more studies on the other micronutrients. Weight and body mass index should be measured in the next studies.

Conclusion

Depression is a common prevalent mental illness; about third of students in our study were diagnosed with depression. There was difference between the studied groups when comparing depression grade and each of ferritin and Mg. The ferritin cut-off level for the prediction of depression was 35.5 µg/dL, which had a sensitivity of 74.4% and a specificity of 75.6%. The Mg cut-off levels for the prediction of depression was 104.5 ng/dL which had a sensitivity of 64%.

Author Contribution

Authors contributed equally to the study.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Consideration

Written consent from the parent or guardian of the students to allow to perform the serum Mg and ferritin level in blood. The ethical and research committee in faculty of medicine, Cairo University and the ethical and research committee of Family Medicine Department were the 2 institutions that ethical approvals were obtained from. The approval was on 21/12/2020 and the code of approval is (MD-315-2020).

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