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The association between iron deficiency anemia and cognitive abilities among female university students

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ABSTRACT

Introduction: Iron deficiency is a serious condition occurring when the human body's total iron is less than the normal amount (three-four g). This study aimed to find the prevalence of iron deficiency anemia (IDA) and its association with cognitive abilities among female students. A cross-sectional study was carried out on 198 female students recruited using convenience sampling from Imam Abdulrahman Bin Faisal University.

Materials & methods: A food frequency questionnaire and cognitive abilities tests were used to collect the required information.

Results: The results showed that the prevalence of IDA was 27.4%. The cognitive abilities parameters of immediate memory, working memory, speed of attention, and accuracy of attention for 50.0% of the students were 24, 16, 194, and three, respectively.

Conclusions: No significant association between IDA and cognitive abilities was noted. Therefore, more studies are needed to explore the association between iron-supplemented diet and cognitive function.

Keywords: iron deficiency, cognitive, prevalence, Saudi Arabia

INTRODUCTION

Iron is one of the most essential elements in blood production. Red blood cells (RBC) contain about 70.0% of the body's total iron. Iron is found in blood cells (hemoglobin [Hb]) and muscle cells (myoglobin). Hb is important for oxygen transportation from the lungs to the body's tissues, and it is stored mostly in the liver as ferritin. Moreover, iron has an essential role in brain development, attention span, intelligence, and sensory perception functions in the brain. The average concentration of iron in the brain is higher than all the other minerals, as iron is required by the enzymes involved in the function of the brain, including myelination. It is also required for mitochondria electron transport, protein synthesis, and neurotransmitter synthesis and degradation. The adult male has 1,000 mg of iron storage in contrast, the adult female has 300 mg. Hb synthesis can be decreased if iron stores are depleted, which results from chronically low iron intakes [1].

Iron deficiency occurs when the body's requirements are not met. Deficiency is associated with low levels of iron storage in the body that leads to depletion in the count of RBC and reduction of the iron supply in tissues. The severity of an iron deficiency is associated with anemia. Iron deficiency can cause changes in neurotransmitter homeostasis, decrease myelin production, impair synaptogenesis, and decline the function of the basal ganglia. Therefore, iron deficiency anemia (IDA) adversely affects cognitive functions and psychomotor development [2]. World Health Organization has recognized IDA as the most common nutritional deficiency in the world, with 30.0% of the population being affected with this condition. [3]. In two Saudi studies, the prevalence of IDA among female students were 34.0% [4] and 64.0% [5], respectively. In a recent study [6], it was reported that Saudi women could be more prone to IDA than men. Study conducted in China showed Students without anemia had a higher average test score than students with anemia ($p<0.001$), and findings also highlighted anemia affected academic performance both directly ($p<0.050$), and indirectly by decreasing the cognition score ($p<0.050$) [7]. Studies from countries like India with high rates of poverty and malnourished individuals, especially females and children due to gender discrimination, that deprives women of nutritious food, showed the deterioration of cognitive scores in females and children with iron deficiency [8].

Children under five years of age are especially at risk, and the major concern is that IDA may affect cognitive and

psychomotor development [9]. However, iron supplements can be highly effective at improving iron status and preventing IDA, iron may adversely affect growth and development, and may increase risk for certain infections [10]. Whereas, in low- and middle-income countries iron supplementation for IDA Oral iron intake can improve the intelligence test scores of children and adolescents and should be considered for future nutritional interventions [11]. IDA is also common in geriatric patients and may affect their physical abilities and their day-to-day activities; thus, iron replacement treatment has had a positive effect on the functional, cognitive, and nutritional status of older patients with iron deficiency and IDA [12]. Therefore, this study aimed to estimate the prevalence of IDA among female students and to evaluate the correlation between IDA and cognitive abilities also between the food intake and cognitive abilities among female university students.

MATERIALS & METHODS

Study Design & Data Collection

In this cross-sectional study, participants were recruited using convenience sampling from Imam Abdulrahman Bin Faisal University (IAU) female students. The study included n=198 participants n=113 control and n=85 IDA. The inclusion criteria were female IAU students between the ages of 19 and 24 years old [13]. The exclusion criteria were females with a history of neurological diseases, pregnant women; women with chronic diseases (e.g., autoimmune gastritis and celiac disease); bariatric surgery patients, females with visual problems other than refractive errors; and those with hereditary blood disorders (e.g., sickle cell anemia and thalassemia). All participants were given a consent form to sign and were informed of the aim of the study. All records were collected by datasheet.

Assessment of Dietary & Biochemical Variables

A pilot study was done by distributing the survey among 20 female students then the distributed surveys get assessed by experts in the field to ensure the quality of the survey, samples were performed to measure the reliability and validity of the questionnaire. After obtaining the informed consent, students were interviewed regarding their socio-demographic background, anthropometric indices (bodyweight and height) were measured, body mass index was calculated using the following equation: body mass index=weight (kg)/height (m^2) [14], a questionnaire about food habits, family history, and their knowledge was collected from all participants, food frequency questionnaire (FFQ) based on iron intake was estimated by using FFQ, which was based on iron content of different food items n=82 items, divided into three groups (high n:23, moderate n:32, and mild n:27 iron content) [15]. Cognitive abilities tests, Wechsler memory scale (WMS) and digit cancellation test (DCT), are used. Each participant was placed in an empty quiet room to avoid distractions. First, digit span test (DST) was prepared by [16], it is sub-scales of WMS. Forward and backward DST are among the oldest and common widely used neuropsychological tests of short-term verbal memory. digit span is measured for forward and reverse-order (backward) recall of digit sequences. Digit sequences are presented beginning with a length of four digits (forward) and three (backward) and two trials are presented at each increasing list length. Thus, there are two scores of the test, the first part is forward digit span that measures short-term memory (and the instructions of this part “I will tell you some numbers and after finishing them directly, I want you to repeat this numbers exactly”) and the second part is the trend and measures the working memory this part is backward digit span (and the instructions of this part “I’ll read you a series of numbers and after I finish them, I want you to repeat these numbers but in a backward, For example: if I told you five-nine-one, you would say one-nine-five”). The test stops when the participant fails to remember two trials for the same sequence. The score is calculated by the sum of the correct trials.

Second, DCT was prepared by [17], on a sample of the university’s 200 students (102 males and 98 females). The average age is 20.67 years with a standard deviation of 2.04 and their intelligence is normal. It measures visual attention and consists of 323 randomly recorded numbers on printed paper. It requires the participant to write off a number three preceded by an even number, and each number seven preceded by an odd number. Two scores of this test are extracted: speed score is time taken by the participant in the test performance. Calculates time in seconds, accuracy score is number of errors + numbers that should have been written off [18]. These two tests were used, a meeting was done with a psychiatry doctor to get the cognitive ability test, know how to apply it on the participants, and how to confirm and calculate the result. Biochemical analysis complete blood count, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), Hb, fasting blood glucose, folate, vitamin B12, serum ferritin, hematocrit, iron, and total iron binding capacity (TIBC) were analyzed at the laboratory of Family and Community Medicine Center (FAMCO) at IAU.

Sample Size Calculation

With expected prevalence of IDA as 38.0% and with absolute precision as 7.0%, the sample size for this study was calculated as 192, for a level of significance is 5.0% [19].

Statistical Analysis

The collected data were analyzed using IBM SPSS statistics (IBM Corp, Armonk, NY, USA) version 26, through the following statistical methods: frequencies with percentages, descriptive statistics, Chi-square test, and Kruskall-Wallis H test along with bar plot, histograms, and boxplots for the graphical representation. $p<.050$ was considered significant.

RESULTS

Demographic & Medical Data for Study Group

A total of 198 students between the ages of 19-24 years had met the inclusion criteria of the study. The demographic information of the participant shown in **Table 1**. The results showed that most of the study participants were from the age category 22-24 years (57.2%) and 42.7% were from the age category 19-21 years.

Table 1 illustrated that 170 (85.4%) of the participant had no diseases yet skin conditions and gland dysfunctions were mostly present 10 (5.0%). 107 (53.8%) of the participants had vitamin and minerals deficiency, where 92 (46.2%) do not. the participants were also asked if they take supplements, 160 (80.4%) do not take supplements, where 36 (19.3%) of the participants take supplements. Participants were asked if they

Table 1. Demographic & medical data for study group

Variable	Frequency (n)	Percentage (%)
Age		
19-21	85	42.7
22-24	114	57.2
Money income (SR)		
<5,000	24	12.1
5,000-10,000	37	18.6
>10,000	138	69.3
Do you suffer from any chronic disease?		
No disease	170	85.4
B12 deficiency anemia, thalassemia carrier, sickle cell anemia carrier, & iron deficiency anemia	4	2.0
Chronic pain due to past surgery	1	0.5
Migraine & epilepsy	2	1.0
Sinusitis &asthma	3	1.5
Eczema, psoriasis, & vitiligo	5	2.5
GERD, T1DM, cystic fibrosis, hypothyroidism, & hyperthyroidism	5	2.5
Do you have vitamins or minerals deficiency?		
Yes	92	46.2
No	107	53.8
Do you take any supplements?		
Yes	36	19.6
No	160	80.4
Do you suffer from memory, focusing, or attention problems?		
Yes	103	51.8
No	96	48.2

Table 2. Biochemical parameters for study participants

Biochemical parameters (unit)		Frequency (n)	Percentage (%)
B12 (pg/mL pmol/L)	<187	5	2.5
	187-883/normal	193	97.5
Iron (mcg/dL)	<50	68	34.3
	50-170/normal	130	65.7
TIBC (µg/dL)	<250	1	0.5
	250-450/normal	176	89.8
	>450	19	9.7
Folic acid (ng/mL nmol/L)	3.1-20.5/normal	195	99.5
	>20.5	1	0.5
Ferritin (ng/mL ug/L)	<4.63	35	17.8
	4.63-204/normal	162	82.2
Glucose (mmol/L)	70-99/normal	170	86.3
	>99	27	13.7
WBC (k/uL)	<4.0	37	18.7
	4.0-11.0/normal	160	80.8
	>11.0	1	0.5
RBC (mil/uL)	<4.1	31	15.7
	4.1-5.5/normal	158	79.8
	>5.5	9	4.5
Hb (g/dL)	<12.0	85	42.9
	12.0-16.0/normal	113	57.1
Hematocrit (%)	<37	113	57.1
	37-47/normal	85	42.9
MCV (fL)	<80	89	44.9
	80-94/normal	109	55.1
MCH (pg)	<27	99	50.0
	27-32/normal	99	50.0

face any memory, focusing, or attention problems. 103 (51.8%) had problems, where 96 did not face any complications.

The health condition of the individual can be affected by several factors, such as low monthly income, the family monthly income was determined for each participant 24 (12.1%) of them were getting <5,000 SR, 37 (18.6%) were getting between 5,000-10,000 SR and 138 (69.3%) were getting >10,000 monthly. Low consumption of iron-rich food sources per person may be caused by this factor.

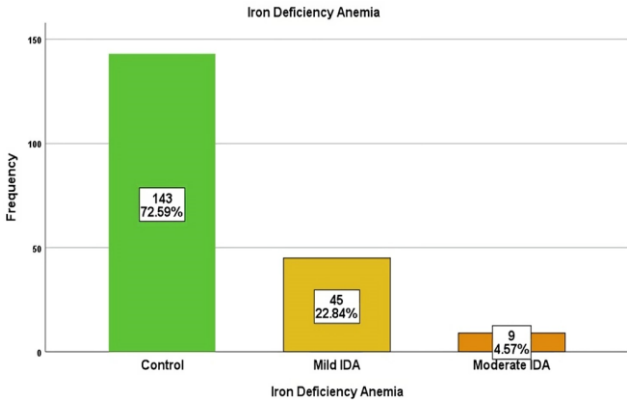

Figure 1. IDA prevalence among university students (Source: Authors' own elaboration)

The subjects have been classified depending on their hematologic measurement, as shown in **Table 2**. Most of the participants (99.5% to 65.7%) have normal ranges of vitamin B12, Iron, folic acid, ferritin. On the other hand, out of range values for hematology ranged between 0.5% and 57.1% with parameters such as Hb, hematocrit, RBC, white blood cell (WBC), MCV, and MCH.

Prevalence of Iron Deficiency Anemia Among Study Participants

As it is shown in **Figure 1**, the prevalence of IDA was 27.4%. Among the total, 45 (22.8%) were mild IDA and the remaining 9 (5.0%) were moderate. None with severe IDA.

Cognitive Abilities of Study Participants

The normality of the cognitive abilities parameters was tested using Shapiro-Wilks test and using histogram plots and it is found that all the four parameters follow a non-normal distribution. Hence, non-parametric approach was done for description and comparison of cognitive ability parameters.

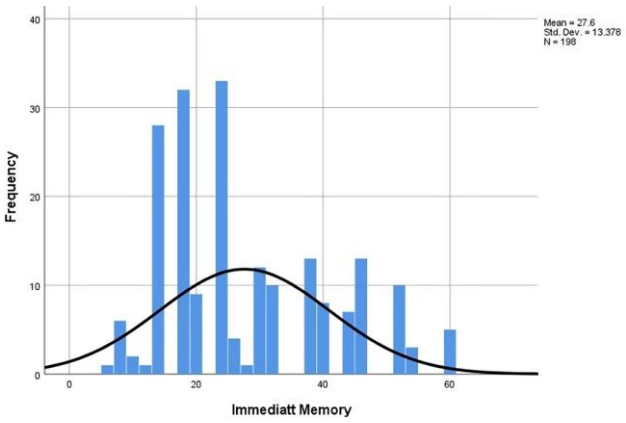

Figure 2. Histogram plot & normal curve to represent distribution of immediate memory of study participants (Source: Authors' own elaboration)

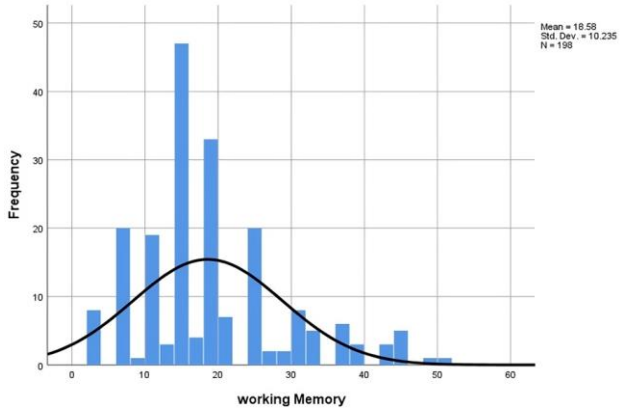

Figure 3. Histogram plot & a normal curve to represent distribution of working memory of study participants (Source: Authors' own elaboration)

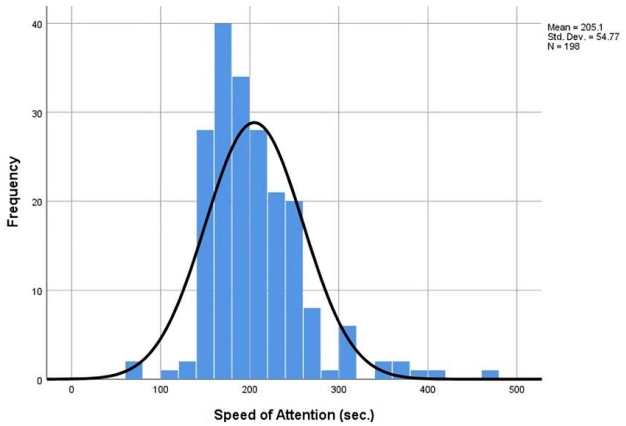

Figure 4. Histogram plot & normal curve to represent distribution of speed of attention of study participants (Source: Authors' own elaboration)

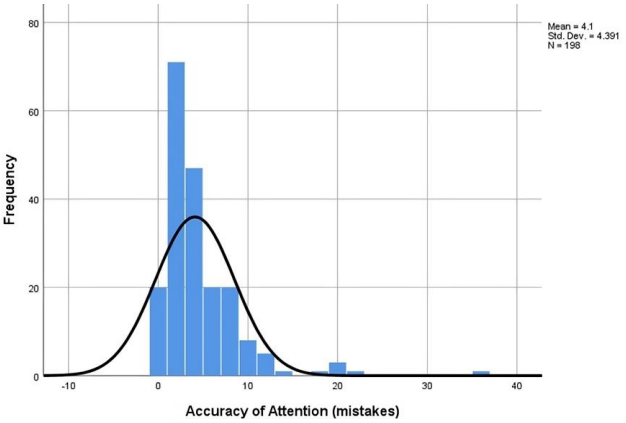

Figure 5. Histogram plot & normal curve to represent distribution of accuracy of attention of study participants (Source: Authors' own elaboration)

Table 3. Description of cognitive abilities using quartiles

Parameters	Quartile score		
	1st quartile	3rd quartile	Average
Immediate memory	18	38	24
Working memory	12	24	16
Attention spped	168	232	194
Attention accuracy	2	5	3

Description of cognitive abilities using quartiles

Figure 2 illustrated that 50.0% of the participant's immediate memory is between 18-eight and the average score is 24.

Similarly, for working memory is portraying that 50.0% of the participants are between 12-24 and their average score is 16 (**Figure 3**).

The same in **Figure 4** for speed of attention, where 50.0% of the participants, where between 168-232 and their average is 194.

Finally displaying accuracy and attention revealed that 50.0% of the participants were between two-five with an average of three (**Figure 5**).

Table 3 showed description of cognitive abilities using quartiles.

Table 4. Cognitive ability comparisons among IDA categories

Cognitive abilities	Median (IQR)			p
	Non-anemic (n=143)	Mild (n=45)	Moderate (n=9)	
Immediate memory	24 (18-38)	24 (18-37)	30 (19-41)	.771
Working memory	15 (14-24)	19 (7-26)	14 (9-25)	.719
Attention spped	193 (165-230)	189 (167-237)	218 (204-339)	.090
Attention accuracy	3 (2-5)	4 (2-7)	2 (1-4)	.216

Comparison of Cognitive Abilities Among Iron Deficiency Anemia Categories

To compare the cognitive abilities among IDA categories, the non-parametric method, Kruskal-Wallis H test is used.

Table 4 showed that there is no significant difference in cognitive abilities parameters. The boxplots represent the cognitive abilities among the study groups.

Figure 6 illustrated that the maximum values of immediate memory are higher among non-anemic and mild IDA than moderate IDA group. Even if there is no significant difference in working memory, as described in **Figure 7** more subjects are with higher working memory in non-anemic and mild IDA groups. There are no subjects with high working memory in the moderate IDA group. The speed of attention is significantly higher in the non-anemic and mild IDA groups. There is no

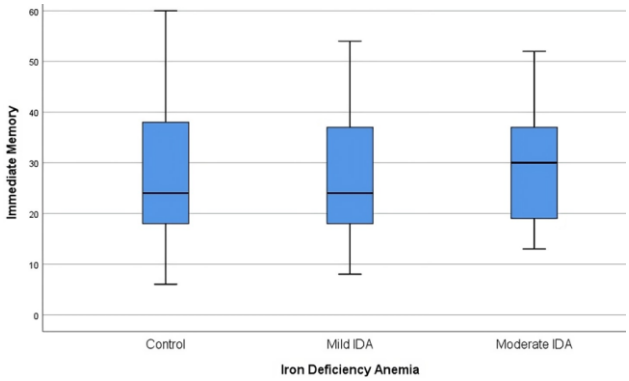

Figure 6. Distribution of immediate memory among non-anemic & anemic categories (Source: Authors' own elaboration)

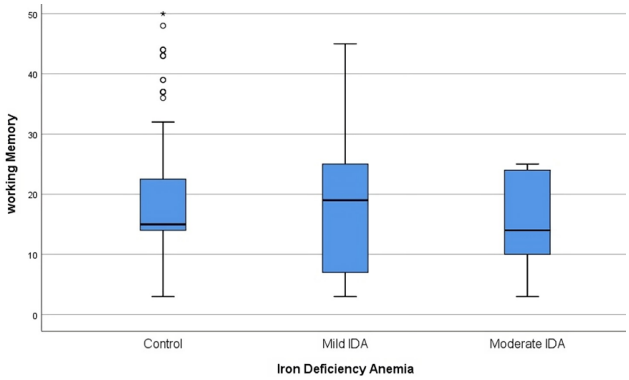

Figure 7. Distribution of working memory among non-anemic & anemic categories (Source: Authors' own elaboration)

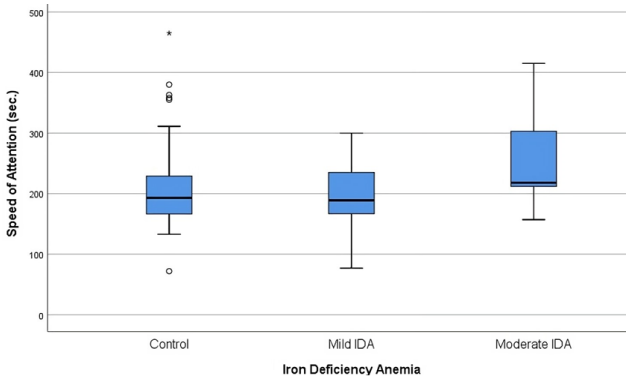

Figure 8. Distribution of speed of attention among non-anemic & anemic categories (Source: Authors' own elaboration)

significant difference in the accuracy of attention as illustrated in **Figure 8** and **Figure 9**, respectively.

Association Between Food Intake & Cognitive Abilities

Cognitive abilities were categorized as low and high on their median values. The association between the food items and cognitive abilities were performed using Chi-square test.

Food items that were associated with IDA were Arabic bread (pita) (p=0.014), canned pumpkin (p=0.004), sunflower seeds (p=0.016), sweet potatoes (p=0.003), rice (p=0.032), raisin (p=0.007), figs (p=0.000), sardine (p=0.021), fish (p=0.041), and beef meat (p=0.006). The food items were significantly associated with immediate memory chicken liver (p=0.022), fish (p=0.039), and white bread (p=0.049). The food items

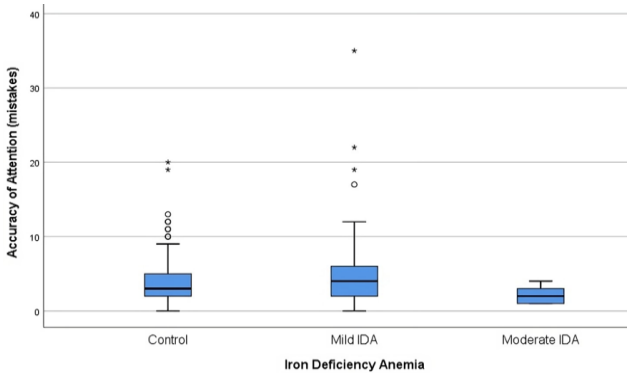

Figure 9. Distribution of accuracy of attention among non-anemic & anemic categories (Source: Authors' own elaboration)

significantly associated with working memory were almonds (p=0.024) and cashews (p=0.044). The food items found significantly associated with the speed of attention were lentil (p=0.042), sesame seeds (p=0.021), and zucchini (p=0.028). The therapeutic diet is significantly associated with the accuracy of attention (p<0.010). Also, the food items lamb meat (p=0.042), yellow beans (p=0.042), milk (p=0.044), and tomato juice (p=0.041) were significantly associated with the accuracy of attention.

DISCUSSION

Iron is an important mineral for the body that plays many roles, especially in brain development, attention span, intelligence, and sensory perception functions in the brain. The current research was aimed at estimating the prevalence of IDA among female university students and its association with cognitive abilities.

The participants of preset work were given a general questionnaire, which consisted of numerous questions on their economic status, demographics, food consumption habits, anthropometric characteristics, and health-related issues. It was investigated the effects of IDA on cognitive function among female adolescents in a rural area of central India [8]. The authors indicated that the health status of female adolescents are affected by not only poverty and literacy but also gender discrimination, which renders women prone to IDA development.

Similarly, a cross-sectional study conducted by [20] uncovered a high prevalence of IDA among children in 28 rural Indian states, among which bihar has the highest prevalent (77.9%). It was reported that most university students, especially females, have IDA that might become worse by malnutrition, lifestyle habits, and lack of awareness [21]. In a cross-sectional study conducted by [22] revealed that university female students specially those who attempting weight loss diet programs without professional guidance are more prone to the risk of the development nutritional disorders like IDA.

The current study found a 27.4% prevalence of IDA, similar to the findings derived in a few studies conducted in Saudi Arabia to estimate disease occurrence among female students. For example, it was found a prevalence of moderate 49.0% [5], whereas it was reported a 34.0% prevalence among female medical students [4]. It was estimated the prevalence of IDA

among female university students at 64.0% [5], whereas it was found a prevalence of 35.0% [23]. A study conducted in India found that the prevalence of IDA among adolescent girls is 50.0% [24], and another study in Yemen revealed a prevalence of 47.0% among university female students [21].

The results of the current research showed that 17.8% of the participants had low ferritin. These findings agreed with [25], it was reported that there is a correlation between low serum iron and ferritin levels among Jazan University students.

The most accurate initial diagnostic test for IDA is serum ferritin measurement. Serum ferritin values greater than 100 ng per mL (100 mcg per L) reflect adequate iron stores and a low likelihood of IDA. Among the participants in the present study, 42.9% had low Hb levels. Our results are confirmed by those of [26], who showed decreased Hb percentage levels by 13.0% with Hb concentration <12 g/dL among female medical students.

The current research was also intended to evaluate the correlation between IDA and cognitive abilities, but no significant association was found between the two. These results contradict the claim of [27] showed that low cognitive performance is associated with IDA and students with latent iron deficiency had moderate reduction in cognitive abilities.

Conversely, the present results support those derived by [28], who indicated a negative effect of both low and high iron concentrations on neurocognitive ability. The generalizability of the results in the present work is limited by differences in environments and lifestyles, which play a primary role in the development of human beings, both medically (iron and Hb status) and mentally (cognitive abilities).

Further research is needed to establish whether cognitive development occurs as an individual takes iron supplement. Although many studies have investigated this assumption [11]. Assessed cognitive function in young adults with IDA and the therapeutic effects of iron supplementation. The authors discovered that intelligence and cognitive function in adults aged 28 years seem to be lower in individuals who do not take iron supplements. It was inquired into the impact of iron deficiency and IDA treatments on cognitive function and other aspects among older patients [12]. It was recruited 81 patients, from whom CGA and blood samples were taken to diagnose iron deficiency [12]. The authors then re-evaluated the patients six months after iron supplementation. The results showed improvements reflected in assessment scales, such as Lawton-Brody instrumental activities of daily living scale, mini-mental state examination, and mini nutritional assessment short-form. They likewise found a positive impact on cognitive ability among the participants after treatment with iron supplements.

It was investigated the effect of iron supplementation on growth and cognitive functions and found no significant effect of iron supplementation on growth [29]. However, such treatment significantly influenced cognitive function. The authors concluded that iron supplementation significantly enhances cognitive function. Iron supplementation can increase iron balance in the body and maintain functions that involve this mineral.

CONCLUSIONS

Iron is an important mineral for the body, it has many roles, especially in brain development, attention span, intelligence, and sensory perception functions in the brain. The present study showed that the prevalence of IDA among female students was 27.4%. No significant correlation was observed between IDA and the cognitive abilities among the participants. While the consumption some food items that are high in iron may improve cognitive function. Thus, students should be more aware of their cognitive health and increase their diet supplemented with iron to improve cognitive function.

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Ethical statement: The authors stated that the Institutional Review Board approval for this study was granted by Imam Abdulrahman Bin Faisal University on 5 February 2020 (Serial Number: UGS-2020-01-051). Written informed consents were obtained from the participants.

Declaration of interest: No conflict of interest is declared by authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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