

A Study To Compare And Correlate The Effect On Iron Deficiency Anaemia On Cognition In Young Adult Females

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ABSTRACT

Background: The prevalence of iron deficiency anaemia (IDA) in young Indian women especially the urban population is on a rise since a past few years due to various factors including inclination towards processed food. Anaemia, particularly iron deficiency anaemia (IDA), is a prevalent public health issue in India, affecting a significant portion of the population, including children, adolescents and women. Recent data from 2024 indicates that anaemia continues to be a challenge, with substantial implications for cognitive function among adolescents. Mild cognitive impairment (MCI) has been observed in individuals with anaemia, suggesting a potential link between iron status and cognitive performance.

Methods: The study was an analytical correlational study conducted at the Central Neuro-Physiology Lab, Acharya Vinoba Bhave Rural Hospital (AVBRH) in Wardha, focusing on adult females of reproductive age, ranging between 18 and 30 years old. The total sample size for this study was determined to be 260, with 130 women diagnosed with Iron Deficiency Anaemia (IDA) and 130 non-anaemic healthy women. Purposive sampling techniques were utilized for participant selection. Hematological evaluation was conducted through Complete Blood Count and serum ferritin analysis. Cognitive assessment was performed using the Montreal Cognitive Assessment (MoCA). The Student's t-test and Pearson's correlation were used to examine the association between haemoglobin, serum ferritin levels and cognition.

Results: The findings suggest that there was no statistically significant difference in age, weight, height, and BMI between females with iron deficiency anaemia and healthy females ($p > 0.05$). However, hemoglobin and serum ferritin concentrations were notably lower in anaemic females compared to healthy females ($p < 0.001$). Additionally, the total MoCA score was significantly lower in anaemic females compared to healthy females ($p < 0.001$). MoCA score showed significant positive correlation with haemoglobin ($r = 0.667$, $p < 0.001$) and ferritin levels ($r = 0.652$, $p < 0.001$) indicating that cognitive function diminishes with severity of anaemia. Specifically, individuals with moderate anaemia exhibited the lowest MoCA score of 22.94 ± 2.479 , while those with no anaemia displayed the highest MoCA score of 26.48 ± 2.175 . This disparity was found to be statistically significant ($p < 0.001$). The linear regression model indicated that a unit decrease in ferritin decreases the MoCA score by 0.145 (95%CI: 0.124-0.166), and a unit decrease in the hemoglobin decreases the MoCA score by 1.182 (95%CI: 1.020-1.344), which was statistically significant.

Conclusions: In this study, it was found that anaemic women had significantly lower cognitive scores compared to the healthy non-anaemic group. High levels of hemoglobin and ferritin showed a moderate positive correlation with higher cognitive performance. These findings suggest that cognitive function in young females is moderately influenced by IDA, highlighting that IDA is one of the potential risk factor for cognitive impairment.

Keywords: Iron Deficiency Anaemia (IDA), Cognitive function, MoCA, Serum Ferritin

Introduction

Anaemia is a serious global public health problem that particularly affects young children, menstruating adolescent girls and women, and pregnant and postpartum women. WHO estimates that 40% of children 6–59 months of age, 37% of pregnant women, and 30% of women 15–49 years of age worldwide are anaemic.¹

Anaemia in adolescents not only leads to impairment of physical growth but also affects behavioural and mental functions, such as lack of concentration, increased mood changes, irritability, and impairment of academic performance among students, mainly due to a reduction in energy level, endurance, and activity.^{2,3} It is an independent risk factor for poor cognition as shown by the effect of anaemia on age-related cognitive decline. And also linked with a 41-61% increased risk of dementia, especially in the elderly.^{4,5} Reduced haemoglobin levels in anaemia cause tissue hypoxia and reduced oxygen delivery to the brain, producing brain ischaemia, which is the most crucial factor in developing cognitive dysfunction and dementia.⁶⁻⁹ It has also been found that increased haemoglobin results in improved CNS functions.¹⁰ Past studies have concentrated on cognition and anaemia in middle-aged adults or the geriatric population.^{11,12} However, there exists a significant gap in understanding the relationship between cognition and anaemia among young adults, especially females. Iron deficiency anaemia (IDA) is a prevalent condition that can significantly impact cognitive function, particularly in young women. Iron is crucial for brain development and maintenance of its function, and its deficiency can lead to impairments in attention, memory, and learning.¹³ Hence, this comparative study aims to investigate the cognitive differences between young women with and without IDA.

Various studies showed the correlation of IDA and central nervous system pathologies including cognitive deficits in developmental stages like infants, children and adolescents. Very less studies have evaluated the relationship between IDA and cognitive performance in young adults using MoCA. Women of reproductive age are at higher risk for IDA due to inadequate dietary intake, high menstrual loss and pregnancy. Therefore, it is important to reveal the effects of IDA on cognition in young women.¹⁴

By comparing cognitive performance in these two groups, this study seeks to highlight the importance of addressing iron deficiency to improve cognitive outcomes in young women. Therefore, the present study was designed to emphasize on the significance of addressing iron deficiency to enhance cognitive outcomes in young women by comparing cognitive performance in two distinct groups. The present study was specifically designed to assess and compare cognition using the Montreal Cognitive Assessment (MoCA) in anaemic and non-anaemic women. Additionally, the study seeks to evaluate the correlation between MoCA scores and levels of haemoglobin and serum ferritin.

Methodology

Study design and setting

This study was an analytical correlational study conducted at the Central Neuro-Physiology Lab, Acharya Vinoba Bhave Rural Hospital (AVBRH) in Wardha. The study focused on adult females of reproductive age, ranging between 18 and 30 years old. The research took place from January 2018 to February 2022.

Sample size: The total sample size was calculated at 260; 130 women with IDA and 130 non-anaemic healthy women.

Sampling technique – Purposive sampling/ convenience sampling technique was used.

Study Participants: Women from the Department of General Medicine, Obstetrics & Gynaecology at AVBRH in Wardha, along with community volunteers, were recruited for this study. Prior to enrolment, informed consent was obtained from each participant with approval from the Institutional Ethics Committee [DMIMS (DU)/IEC/2017-18/6569].

The participants underwent interviews and examinations as per a structured proforma. Haematological evaluation, including Complete Blood Count and serum ferritin levels, was done. Based on their Haemoglobin and serum ferritin levels, the participants were categorized as either anaemic or non-anaemic healthy women. Red cell indices and peripheral smear were utilized to rule out other forms of anaemia.

Furthermore, cognitive assessment was performed using the Montreal Cognitive Assessment (MoCA) tool. This comprehensive approach allowed for a thorough evaluation of the participants' health and cognitive function.

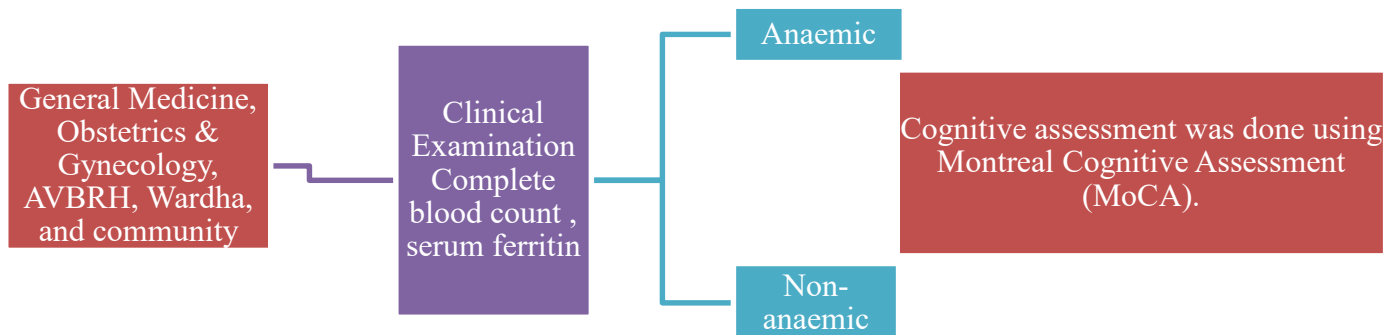


Fig 1: Flowchart depicting study design

The participants were grouped based on the following inclusion and exclusion criteria:

Inclusion criteria for the anaemic group (females with IDA):

1. Females in the age group of 18 -30 years
2. Hemoglobin levels between 8 - 12g/dl
3. Serum ferritin level < 15ng/mL (0 -14.9 ng/mL)

Inclusion criteria for non-anaemic group (healthy females without IDA):

1. Females in the age group of 18 -30 years
2. Hemoglobin level between 12 – 15g/dl.
3. Serum ferritin level 15 – 150 ng/mL

Exclusion criteria:

1. Body mass index <18.5 or >22.9 kg/m²
2. Current pregnancy or pregnancy within the previous year, currently lactating, on hormonal contraceptives, irregular menstrual cycles.
3. Recent blood donation
4. Known cases of endocrine disorders (e.g.: Diabetes Mellitus, Thyroid dysfunction) and neurological diseases
5. Use of medications – iron supplements, major or minor tranquilizer that may alter cognitive and neurophysiological measures.

Materials and methods: Blood samples were collected from the subjects for estimating complete blood count (CBC)

and serum ferritin. 3ml of blood sample was collected by venipuncture, of which 2ml was transferred in EDTA bulb for complete hemogram estimation and 1ml sample was transferred in the red top vacutainers for serum ferritin estimation.

1. Blood hemoglobin was analyzed by spectrophotometry using Beckman Coulter UniCel DxH 800 [International Council for Standardization in Hematology (ICSH)]¹⁵

2. Serum ferritin was estimated by Electrochemiluminescence assay (ECLIA) using Vitros 5600 [NIBSC Code 94/572 3rd International Standard for Ferritin] ¹⁶

The Standard Operating Procedure (SOP) was diligently adhered to. Age-adjusted values for Hemoglobin and Serum Ferritin were utilized in the analysis. Subjects were categorized as anaemic or non-anaemic based on their Hemoglobin concentration, following WHO classifications.

Height (meter) was measured using a stadiometer to the nearest 0.1cm and body weight (kilograms) was measured using a weighing scale to the nearest 0.1kg. BMI was calculated as Weight (kg)/ Height (mt)². ¹⁷

Cognitive Assessment: We used a validated, 30- point, Montreal Cognitive Assessment (MoCA) screening tool for cognitive assessments. It is a rapid screening instrument for mild cognitive dysfunction requiring approximately 10 minutes of administration. Due to its high sensitivity and validity, MoCA is a standard scale used in scientific research for detecting cognitive decline and MCI. Training and certification are preferable to administer MoCA. ^{18,19}

The study participants were allowed to sit comfortably in a dedicated room of the hospital in a comfortable and calm environment. After filling in the participant details, verbal instructions were given to the subject to perform the various tasks of the MoCA. The MoCA test version 7.1 in English and Hindi language was used. ²⁰ For the test and detailed instructions on administration, please refer to www.mocatest.org. ²¹

The following cognitive domains were assessed and accordingly points were assigned : visuospatial and executive functioning: 5 points, naming: 3 points; attention: 6points, language:3 points, abstraction: 2 points, delayed recall: 5 points, orientation: 6 points, and education level: 1 point was added to the subject’s score if they had 12 years or less formal education. A maximum of 30 points are attainable, and a score between 26-30 indicates normal cognition while 18-25 indicates mild cognitive impairment, 10-17 indicates moderate cognitive impairment and a score of < 10 indicates severe cognitive impairment. ¹⁹

Results

Table 1: Comparison of baseline characteristics and hematological parameters

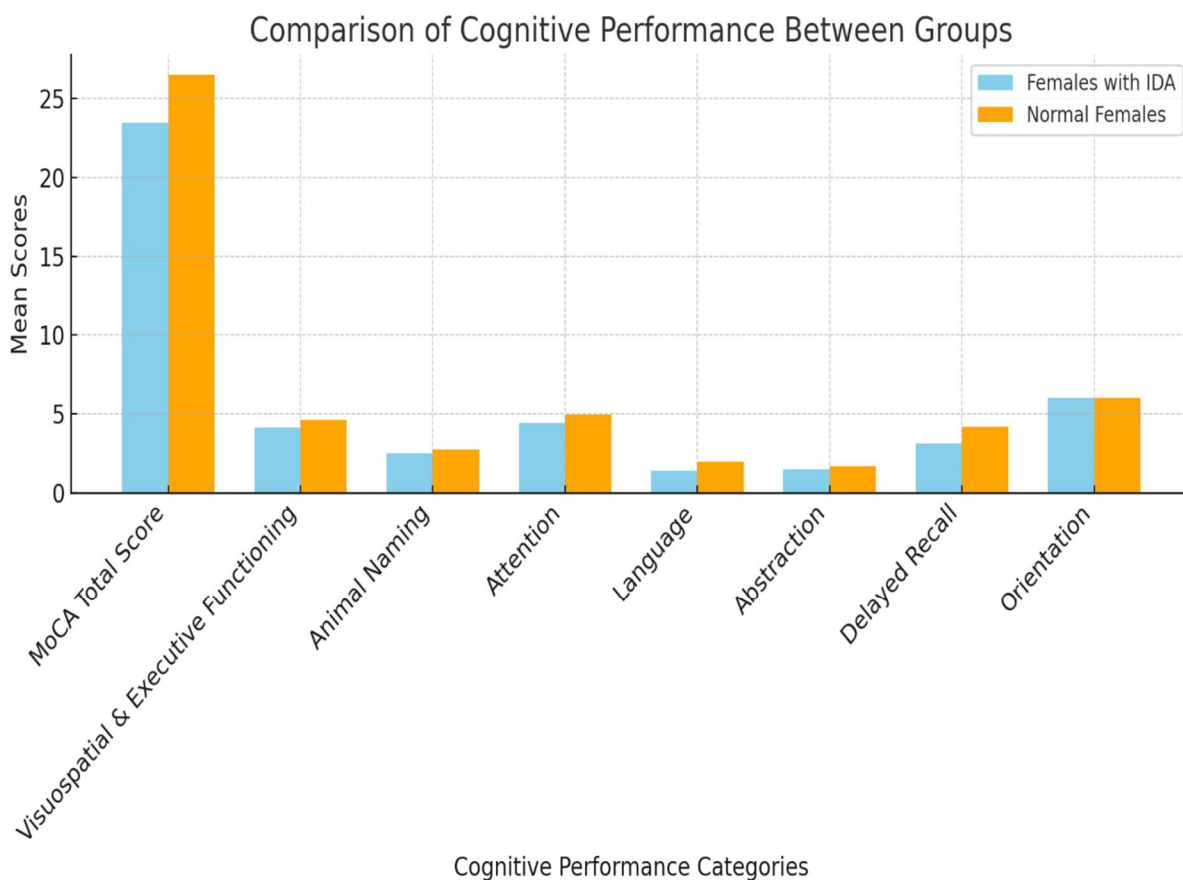
Parameters	Females with IDA (Mean±SD) N = 130	Normal Females (Mean±SD) N = 130	t value	p value
Baseline characteristics				
Age (years)	23.88±3.67	24.09±3.41	-0.472	0.637
Body Weight (kg)	60.67±5.72	61.60±5.33	-0.483	0.630
Height (mt)	1.66±0.05	1.65±0.05	1.390	0.166
BMI (kg/m ²)	22.10±1.95	22.48±1.89	-1.593	0.112
Hematological parameters				
Hemoglobin (gm %)	10.37±0.95	13.02±0.69	-25.869	0.001
Serum Ferritin (ng/ml)	8.55±3.78	27.61±10.52	-14.933	0.001

Table 1 displays the baseline characteristics and hematological parameters, which were compared using Student's t-test. The results indicate that there was no statistically significant difference in age, weight, height, and BMI between females with iron deficiency anaemia and healthy females (p>0.05). However, hemoglobin and serum ferritin concentrations

were significantly lower in anaemic females compared to healthy females ($p < 0.001$).

Table 2: Comparison of Cognitive performance – MoCA Score

Cognitive performance	Females with IDA (Mean±SD)	Normal Females (Mean±SD)	t value	p value
MoCA total Score	23.44±2.45	26.48±2.18	-10.602	0.001
Sub Scores				
Visuospatial & executive functioning (5 points)	4.12±0.67	4.60±0.59	-6.200	0.001
Animal Naming (3 points)	2.51±0.52	2.73±0.46	-3.667	0.001
Attention (6 points)	4.42±1.01	4.96±0.89	-4.620	0.001
Language (3 points)	1.38±0.89	1.98±0.82	-5.656	0.001
Abstraction (2 points)	1.47±0.50	1.68±0.47	-3.449	0.001
Delayed Recall (Short term memory) (5 points)	3.14±1.19	4.19±0.96	-7.857	0.001
Orientation (6 points)	6.00±0.00	6.00±0.00	-	-



Graph 1: Comparison of Cognitive performance – MoCA Score

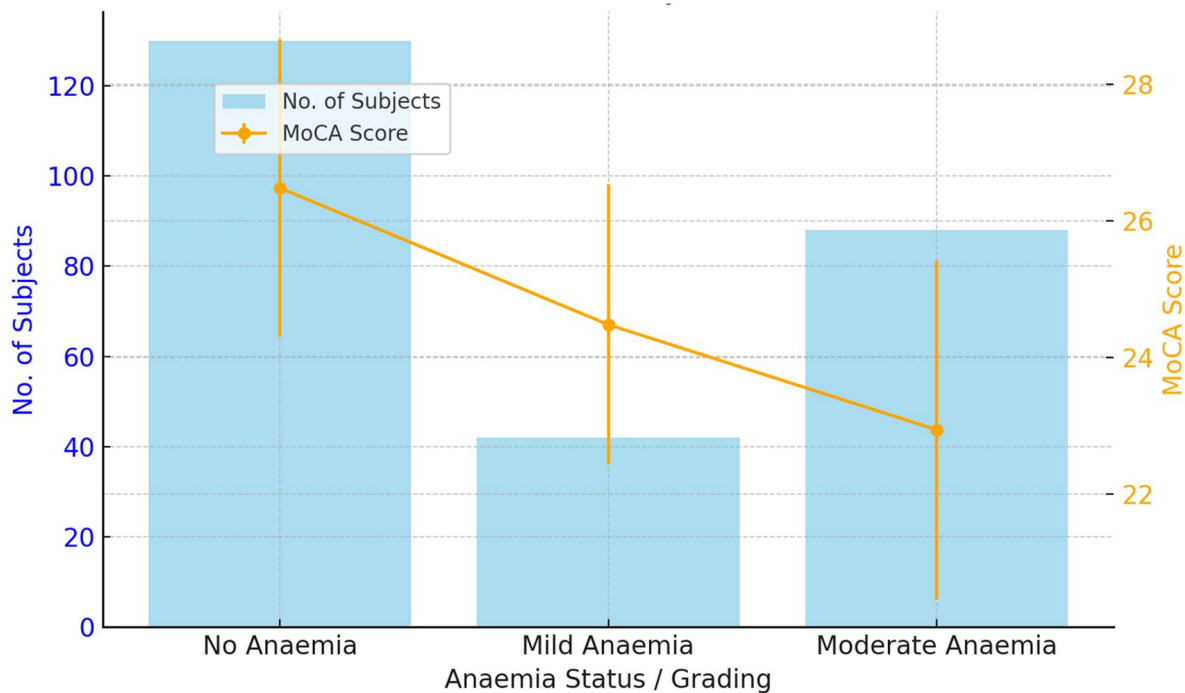
The table-2, and graph 1 the cognitive function assessed using MoCA test were compared in anaemic and healthy females using student's t test. The total MoCA score was significantly higher in healthy females

compared to anaemic females ($p < 0.001$). Similarly, the sub scores assessing visuospatial and executive functioning,

naming, attention, language, abstraction and short term memory were significantly reduced in anaemic females compared to healthy females ($p < 0.001$) while there was no difference in the orientation between the two groups.

Table 3: Relationship of Hemoglobin and the Cognitive Status (Cognitive status in different grades of anaemia)

Anaemia status / grading	No. of Subjects	Hemoglobin (g/dl)	MoCA Score
No Anaemia	130	≥ 12	26.48 ± 2.175
Mild Anaemia	42	11-11.9	24.48 ± 2.051
Moderate Anaemia	88	8-10.9	22.94 ± 2.479
One way ANOVA: $p = 0.001$			



Graph-2 Relationship of Hemoglobin and the Cognitive Status (Cognitive status in different grades of anaemia)

Table 3 and graph-2 illustrates a comparison of cognitive scores across various grades of anaemia using a one-way ANOVA analysis. The results indicate a relation between hemoglobin levels and cognitive function, with a noticeable decrease in MoCA scores as hemoglobin levels decrease. Specifically, individuals with moderate anaemia exhibited the lowest MoCA score of 22.94 ± 2.479 , while those with no anaemia displayed the highest MoCA score of 26.48 ± 2.175 . This difference was found to be statistically significant ($p < 0.001$), suggesting that higher hemoglobin levels are associated with better cognitive function.

Table 4: Relationship of Ferritin and the Cognitive Score

Ferritin levels	No. of Subjects N = 260	Serum Ferritin (ng/ml)	MoCA Score
Non Iron Deficient	94	≥ 15	27.14 ± 1.79

Iron Deficient	166	< 15	23.73±2.45
Independent t test: t = 11.812; p = 0.001			

The Table - 4 shows the relationship between ferritin levels and cognitive performance, as measured by the Montreal Cognitive Assessment (MoCA) score, in 260 subjects. The results reveal a statistically significant difference in cognitive scores between individuals with normal ferritin levels (≥ 15 ng/ml) and those with iron deficiency (< 15 ng/ml). Participants without iron deficiency ($n = 94$) demonstrated significantly higher MoCA scores (27.14 ± 1.79) compared to iron-deficient individuals ($n = 166$), who scored 23.73 ± 2.45 . The independent t-test yielded a highly significant result ($t = 11.812, p = 0.001$), indicating that iron deficiency is strongly associated with lower cognitive function.

Table 5: Correlation of hemoglobin and ferritin with MoCA score

Parameter	Hemoglobin		Ferritin	
	r value	p value	r value	p value
MOCA score	0.667	0.001	0.652	0.001

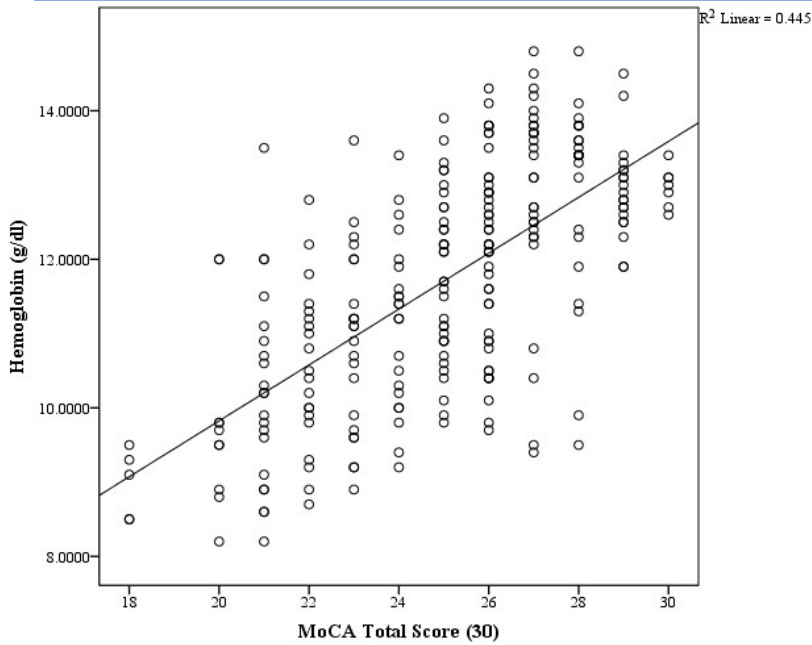
Table 5 shows the correlation between cognitive performance (MoCA score) with hemoglobin and ferritin levels. The analysis reveals significant moderate positive relationships between these biomarkers and the Montreal Cognitive Assessment (MoCA) score.

Table 6: Linear regression model for the relation of hemoglobin with MoCA

Hemoglobin \rightarrow MoCA

Model	B	95.0% Confidence Interval for B		p value	
		Lower Bound	Upper Bound		
1	(Constant)	11.146	9.236	13.056	
	Hemoglobin	1.182	1.020	1.344	0.001

The above table shows the linear regression model of hemoglobin with MoCA. A unit decrease in the hemoglobin decreases the MoCA score by 1.182 (95%CI; 1.020-1.344) that was found to be statistically significant. Hence, anaemia decreases the cognitive scores. (Graph -3)



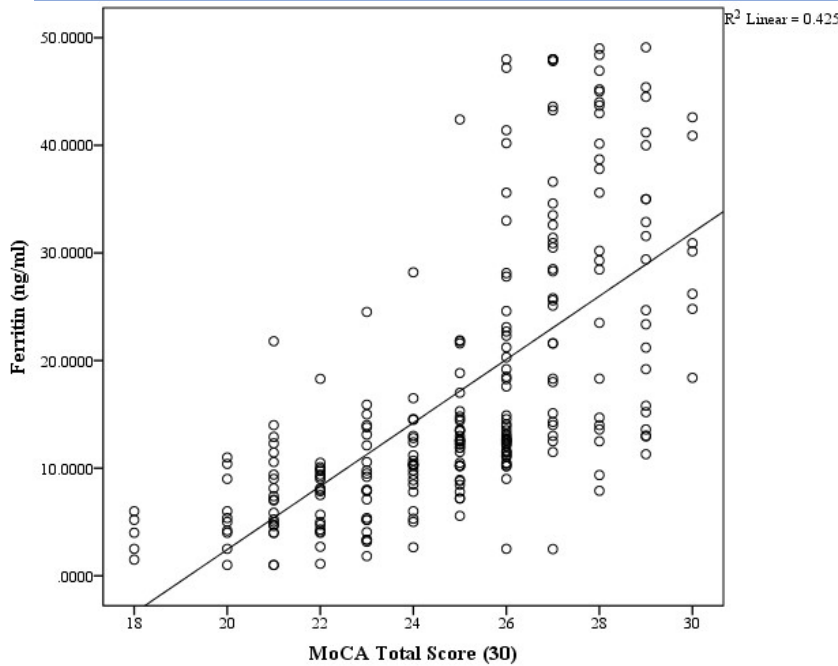
Graph 3: Scatter plot showing the linear regression of MoCA Score and hemoglobin levels

Table 7: Linear regression model for the relation between serum ferritin and MoCA score

Ferritin → MoCA Score

Model		B	95.0% Confidence Interval for B		p value
			Lower Bound	Upper Bound	
1	(Constant)	22.34	21.882	22.796	
	Ferritin	0.145	0.124	0.166	0.001

The linear regression model for the relation between serum ferritin and MoCA score in the above table shows that, a unit decrease in the ferritin decreases the MoCA score by 0.145 (95%CI; 0.124-0.166) and it was found to be statistically significant. Hence, with the rise in levels of ferritin there is an improvement in the MoCA score (Graph - 4).



Graph 4: Scatter plot showing the linear regression between MoCA Score and ferritin levels.

Discussion

In our study it was observed that there was notably lower hemoglobin and serum ferritin levels in anaemic females in comparison to their healthy counterparts ($p < 0.001$). However, there was no statistically significant difference in age, weight, height, and BMI between females with iron deficiency anaemia and healthy females ($p > 0.05$). The MoCA scores were significantly lower in anaemic females compared to healthy females ($p < 0.001$). And the MoCA scores correlated positively with haemoglobin ($r 0.667$) and serum ferritin ($r 0.652$) levels that was statistically significant ($p < 0.001$). The results of our study align with research conducted by Felek D evaluated the cognitive functions of patients with anaemia found that cognitive scores were significantly lower in individuals with iron deficiency anaemia compared to healthy individuals. The study included 112 participants, with 56 in the test group (iron deficiency anaemia) and 56 in the control group (healthy individuals). Montreal Cognitive Assessment (MoCA) scores were recorded for each participant, along with their hemoglobin levels and history of recurrent anaemia. The results showed that the mean MoCA score for the test group was 19.80 ± 3.46 , while the control group had a mean score of 22.98 ± 3.59 . This difference in cognitive function between the two groups was found to be statistically significant.²²

Additionally, studies by Khedr et al.²³, Jaleel et al.²⁴, and Kavitha et al.²⁵ utilized MMSE to assess cognition and found lower MMSE scores in young adults with iron deficiency anaemia compared to controls, with a positive correlation between anaemia and cognitive scores.

Furthermore, More et al.²⁶ discovered that cognitive scores in girls decreased in relation to the severity of iron deficiency. A study conducted by M Sharma et al.²⁷ demonstrated that MoCA scores in anaemic females improved proportionately with the supplementation of iron and folic acid tablets aimed at improving their anaemic status.

In another study done by Astri et al, it was observed that 61.5% of the female students were anaemic, while 38.5% were not. Additionally, 66.7% of the students failed to meet academic standards, compared to 33.3% who passed. Statistical analysis using the chi-square test indicated a weak correlation between anaemia and learning achievement ($p = 0.005$).

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S. Qairunnisa et al in young individuals (18-20 years) that revealed a statistically significant difference between the anaemic and healthy groups on Digit Symbol Substitution Test scores (21.10 ± 2.99 versus 32.60 ± 14.69), letter

cancellation test (25.80 ± 4.63 versus 35.80 ± 4.56), and Stroop test (132.10 ± 8.15 versus 123.56 ± 10.52).²⁹

A study conducted by Engin Kelkitli and Demet ArslanYazıcıoğlu aimed to evaluate cognitive performance in patients with iron deficiency anaemia (IDA) using the Montreal Cognitive Assessment (MoCA). The study included 40 patients diagnosed with iron deficiency anaemia who underwent cognitive assessment with MoCA, as well as laboratory analysis that included a complete blood count, iron levels, total iron binding capacity, ferritin levels, and transferrin saturation. Univariate and multivariate analyses were performed to identify the variables associated with MoCA scores. The mean MoCA score was found to be 23.73 ± 4.00 (range 11–30). Iron levels ($r=0.37$, $p<0.01$), transferrin saturation ($r=0.42$, $p<0.007$), and ferritin levels ($r=0.56$, $p<0.001$) were significantly correlated with MoCA scores, which are nearly similar to our findings.³⁰

A cross-sectional observational community-based study conducted by Vedpal et al.³¹ was carried out in a rural block, Sampla, in Haryana. Non-probability sampling was utilized to select 1951 adolescent girls. The study focused on the effects of iron deficiency anaemia on the cognitive assessment of adolescent girls. It was found that iron deficiency anaemia negatively impacts cognitive functions.

Similar results were observed in studies conducted by Sarika More et al.³² in Maharashtra, India, and by Suzan O Mousa³³ and her colleagues in Egypt. Their findings suggest that the prevalence of anaemia is high in various parts of the country and globally. This highlights the importance of addressing iron deficiency anaemia in adolescent girls to improve their cognitive abilities and overall well-being.

A study conducted by Wender MJ, as a post-hoc analysis of a randomized controlled trial involving 246 adolescents aged 12-16 in Maharashtra, India, revealed a noteworthy correlation between serum ferritin levels (as a predictor) and hemoglobin (Hb) levels (as a moderator) on the cognitive function of the adolescent brain. It suggests that the influence of ferritin on cognitive function is contingent upon the level of hemoglobin present in the body.³⁴ Similarly, Yeboah et al.³⁵ revealed a noteworthy positive correlation between ferritin levels and cognitive performance test scores (CPTS) ($r = 0.451$, $p < 0.001$). Additionally, a significant positive correlation was observed between hemoglobin levels and CPTS ($r = 0.402$, $p < 0.001$).

Anaemic status affects the cortical cognitive processing indicative of possible role of serum ferritin and hemoglobin. Serum ferritin is an indicator of body's iron level and iron is associated with the integrity of neurotransmitter metabolism especially dopamine while hemoglobin is associated with energy requirements.³⁶ Iron is an important hematopoietic factor plus plays a key role in various functions in the nervous system including neurogenesis, myelination, synaptogenesis, neuroplasticity, neurotransmitter, and brain energy metabolism.^{37,38} Additionally, its critical role in oxygen transport leads to cerebral hypoxia leading to cognitive decline.³⁹ Hence, the severity of IDA is associated with deviation in cognitive functions, a potential risk factor for cognitive decline.

Conclusion

In this study, it was found that anaemic women had significantly lower cognitive scores compared to the healthy non-anaemic group.

Moreover, the MoCA scores were found to have a positive correlation with hemoglobin and ferritin levels. This indicates that as hemoglobin and serum ferritin levels decreased, the cognitive score also decreased significantly.

Limitations

The small sample size in this study necessitates further follow-up after correction of anaemia. It is important to note that the prevalence of anaemia in this younger group may not accurately reflect that of the general population. Similarly, the cognitive scores measured in this younger group may not be indicative of the general population as a whole. Further research and analysis are needed to draw more conclusive and representative results.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee [DMIMS (DU)/IEC/2017-18/6569].

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