Section: Physiology

Original Research Article

COGNITIVE PROFILES OF ANEMIC IRON DEFICIENT AND NONANAEMIC IRON DEFICIENT YOUNG WOMEN: EVALUATION WITH MINI MENTAL STATE EXAMINATION (MMSE)

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ABSTRACT

Background: Iron Deficiency leading to severe stages of Iron Deficiency Anemia in young women interferes with Cognitive function. Iron deficiency, being the Worldwide most common Nutritional deficiency has an unfavourable impact on the human brain. The objective is to evaluate and compare the Mathematical Test score of Anemic Iron deficient and Non anemic iron deficient study group with the Non anemic Non-iron deficient control group in order to rule out the impact of Iron deficiency on cognition in the present study.

Materials and Methods: This case control study was conducted at Hospital. Informed written consent was taken from the participants.

Results: On scholastic assessment the difference in the Mathematical score was highly significant between the Non anemic Non-iron deficient control (Group 1) &Anemic Iron deficient(Group 2), and also between Non anemic Non-iron deficient control (Group 1) & Non anemic iron deficient (Group 3), in all the subsets S1,S2,S3,S4,S5,TOTAL SCORES.

Conclusion: Neurocognitive insufficiency of iron in young women influences the cognitive functions of the study participants in terms of reduction in mathematical score, reduction in test scores on various domains of cognition like Logical memory,Immediate Recall,Digit forward,Digit backward were noticed.

Keywords: Hemoglobin and Serrum Ferritin levels, Mathematical score.

INTRODUCTION

Iron deficiency is the most widely prevailing micro nutrient deficiency, gaining an accelerated momentum in developing serious cognitive risks in young women on a Global Front, and is the leading cause of Iron deficiency anemia.[1]

WHO estimates that over 2 billion people across the world are anemic, out of which approximately 50% is due to iron deficiency. In India out of 64 million Adolescent girls, 56% is found to be anemic, hence the prevalence of Iron deficiency is 2.5 times greater than Iron deficiency anemia.[2]

Functionally, Iron deficiency is an imbalance in intake of iron, absorption, and the iron loss.[3] Iron deficiency anemia is a condition arising due to insufficient iron to form normal red blood cells (RBC).[3]

Evidences show a modest improvement in cognition in patients with chronic kidney disease and cancer following treatment with erythropoietin indicating a strong relationship of iron deficiency and impaired cognitive performance.[4]

MATERIALS AND METHODS

To analyse the effects of Iron deficiency on cognitive functions in young women this case control study is been done. For this study 81 female subjects in the age group of 18-35 years were chosen divided in to three groups.

- Group I-27 subjects in (Non anemic Non Iron deficient control group)
- Group II-27 subjects in (Anemic Iron deficient study group)

- Group III-27 subjects in (Non anemic Iron deficient study group)

This case control study study was conducted at Hospital,.Informed written consent was taken from the participants.

Inclusion Criteria

Young Women with Iron Deficiency Anaemia

Exclusion Criteria:

- Cardiovascular disease
- Chronic illness
- Diabetes Mellitus
- Hypertension
- Chronic Infection
- Chronic inflammation
- Postmenopausal Women
- Recent Blood donation
- Pregnancy Related Condition (Abortion, Postpartum Period)
- Neurological disorder/Seizures
- Mental retardation
- Psychiatric Illness.

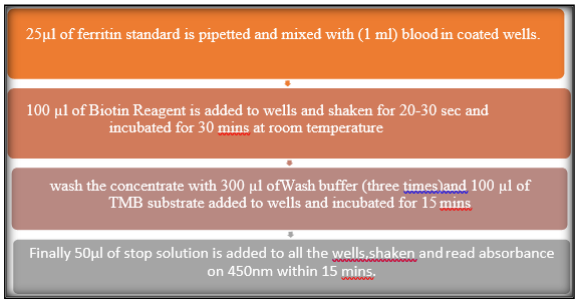
Method of Estimation of Parameters: Blood samples (2ml) were taken from the study participants and evaluation of the hemoglobin concentration was done by Automated analyzer – Beckman coulter counter.

Ferritin Estimation: Estimation of serum Ferritin concentration to rule out iron deficiency was done by ELISA method.

Reagent Used

- Ferritin standard-0.5ml
- Anti-ferritin Biotin Reagent-12ml.
- Anti-ferritin Enzyme Reagent-12ml
- Wash concentrate-25ml
- TMB Substrate-12ml
- Stop solution -12ml.

ASSAY PROTOCOL



Parameter	Unit	Normal Range
Hemoglobin	gm%	12.0 to 17
Serum Ferritin	ng/ml	Women-10-200

Method of Assessing Cognitive Function

Scholastic Assessment of Cognition (Mathematical Score)-Mini Mental State Examination(Folstein).

For assessing the performance of the participants, various questions were put forward from the questionnaire, the arithmetic scores are evaluated finally and cognitive impairment is assessed.

Statistical Analysis

Data analysis in this Case-Control Study was done by using IBM SPSS (Statistical Package for Social Sciences) software version 16.0 for windows 10.0. Statistical analysis done using Independent t-test was done to find out the significance of difference between Groups I and II and between Groups II and III. One-way Analysis of Variance (ANOVA) was applied to compare means within and between the three groups. The confidence interval was set at 95% and p-value< 0.05 was considered significant.

RESULTS

As mentioned in the materials and methods 81 female subjects were divided into three groups.

- GROUP 1- 27 subjects in control group (Non anemic Non Iron deficient)
- GROUP 2-27 subjects (Anemic Iron deficient study group)
- GROUP 3-27 subjects in (Non anemic Iron deficient study group

Age compared between the control and study groups, did not show a statistical significant difference.

Hemoglobin concentration were predominently lower in the study groups, Anemic iron deficient (Group 2) (mean-10.21) and Non anemic iron deficient (Group 3) (mean-12.31)compared to the Non anemic Noniron deficient control (Group1) (mean-12.99).

Serum Ferritin concentration were comparatively lower in the study groups the Anemic iron deficient (Group 2) (mean-7.81) &Non anemic iron deficient (Group 3)(mean-9.011) than the control group Non anemic iron deficient (Group 1)(mean-25.303) proving a statistical significance.

Hemoglobin and serum ferritin concentration compared between control (Group1) and study (Group 2) showed a statistical significance (p<0.000) and on comparision of the same parameters among (Group 1 and Group 3) alsoproved to be statistically significant.

Table 1: Descriptive Statistics and Comparision of Age, Hemoglobin and Serum Ferritin Levels of Control Group (1) & Study Groups (2 & 3)

	n	Mean	S.D	Min.	Max.	F	p Value
Age						.000	1.000Not Significant
GROUP 1	27	19.0370	.93978	18.00	21.00		
GROUP 2	27	19.0370	.93978	18.00	21.00		
GROUP 3	27	19.0370	.93978	18.00	21.00		
Total	81	19.0370	.92796	18.00	21.00		

Hb (g %)						163.239	.000** Significant
GROUP 1	27	12.9926	.46403	12.20	13.70		
GROUP 2	27	10.2111	.77327	8.60	11.20		
GROUP 3	27	12.3148	.48015	11.60	13.40		
Total	81	11.8395	1.32634	8.60	13.70		
Serrum Ferritin(ng/ml)						253.428	.000** Significant
GROUP 1	27	25.3037	5.46425	15.90	32.80		
GROUP 2	27	7.8074	.69776	6.70	8.90		
GROUP 3	27	9.0111	.42366	7.90	9.70		
Total	81	14.0407	8.62467	6.70	32.80		

***significant at the 0.01 level, * significant at the 0.05 level*

This table indicates that Hemoglobin and serum ferritin levels are found to have statistical significant differences between the Non Anemic Non-iron deficient control (Group 1), Anemic iron deficient (Group 2), and as well as in Non Anemic iron deficient (Group 3).

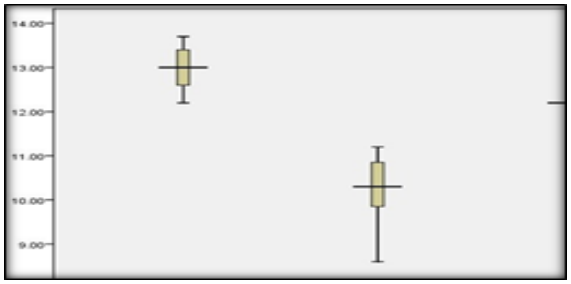


Figure 1: Box Plot Summarizing the Distribution of Hemoglobin Levels in The Non Anemic Non Iron Deficient Control (Group 1), Anemic Iron Deficient (Group 2) & Non Anemic Iron Deficient (Group 3)

- The median is marked by a horizontal line inside the box.
- Whisker's are the lines extending at the end of the box placed vertically extending to maximum and minimum levels of Hemoglobin for the particular group.
- The ends of box denote the upper and lower quartile of Hemoglobin levels of that specific group.

We visualize that in the above plot Hemoglobin levels are significantly higher in the Non anemicnon-iron deficient control (Group1) compared to the Anemic iron deficient group 2 and Non anemic iron deficient (Group 3).

The Hemoglobin level in the Group 1 is significantly lower as indicated by the upper and lower quartiles in Boxplot.

Hemoglobin levels in the Group 2 is comparatively lower than Group 3 indicating that subjects in this group is Non anemic iron deficient rather than anemic iron deficient of Group 2.

Graphical Representation of Serum Ferrtin Levels in Non.

AnemicNon Iron Deficient Control (Group 1), Anemic Iron.

Deficient (Group 2) &Non Anemic Iron Deficient (Group 3).

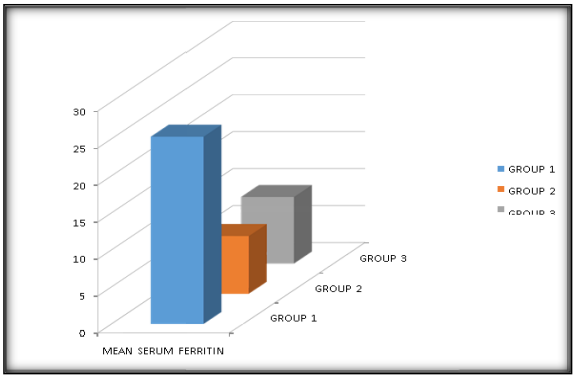


Figure 2: This Bar Diagram shows that the Serum Ferritin Levels Are Higher in the Non Anemic Non Iron Deficient Control (Group 1) compared to The Anemic Iron Deficient (Group 2) & Non Anemic Iron Deficient (Group 3).

Table 2: Comparision of Age, Hemoglobin and Serum Ferritin Levels of Non Anemic Non Iron Deficient Control (Group 1) And Anemic Iron Deficient (Group 2)
(Independent T-Test)

	n	Mean	S.D	p value
Age				
GROUP 1	27	19.04	.940	1.000>0.05
GROUP 2	27	19.04	.940	Not Significant
Hb(g%)				
GROUP 1	27	12.99	.464	.000<0.05
GROUP 2	27	10.21	.773	Significant
Serrum Ferritin(ng/ml)				
GROUP 1	27	25.304	5.464	.000<0.05
GROUP 2	27	7.807	.698	Significant

This table depicts that the Hemoglobin(mean - 12.99) is seen in control (Group 1) and Hemoglobin levels of study (Group 2) showed a (mean-10.21) showing a significant difference. In Serum ferritin levels there is a significant difference between Non anemic iron deficient Control (Group 1) and Anemic iron deficient study (Group 2).

The above table shows that,the statistical significant differences in not seen in the age, whereas significant differences (p<0.000) is observed in

terms of Hemoglobin and serum Ferritin levels between Non anemic non-iron deficient Control (Group 1)and Non Anemic iron deficient (Group 3). Comparision of Mean Hemoglobin and Mean Serum Ferritin Levels of Non Anemic Non Iron Deficient Control (Group 1) And Non Anemic Iron Deficient (Group 3).

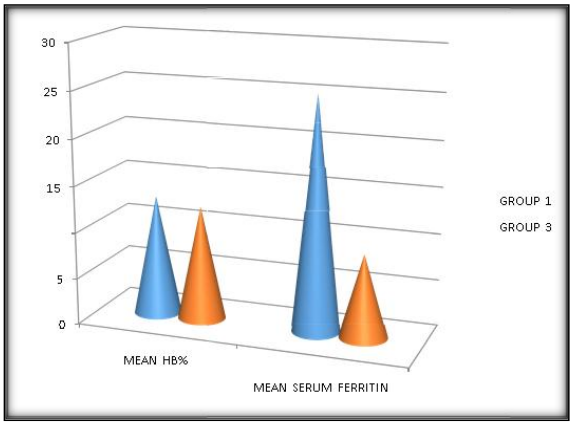


Figure 3: This graphical representation explains the fact that the Mean Hemoglobinlevels and mean serum ferritin levels of control (Group 1) is significantly higher compared to the study (Group 3)

On scholastic assessment the difference in the Mathematical score was highly significant between the Non anemic Non-iron deficient control (Group 1) &Anemic Iron deficient(Group 2),and also between Non anemic Non-iron deficient control (Group 1) & Non anemic iron deficient (Group 3), in all the subsets S1,S2,S3,S4,S5,TOTAL SCORES.
This table shows that the mathematical scores between and within the groups are found to be statistically significant($p<0.000$).

This table shows that the difference in mathematical scores is found to be statistically significant ($p<0.000$) between the Non anemic Non-iron Deficient control (Group 1) and the Anemic iron Deficient (Group 2) with respective to S1,S2,S3,S4,S5 and total scores.
This table shows that the difference in the mathematical scores is found to be highly significant between Non anemic Non-iron deficient control(Group 1)& Non Anemic iron Deficient(Group 3) in all the subsets of S1,S2,S3,S4,S5 and TOTAL SCORES.
Comparision of Total Mean Mathematical Score between the Non Anemic Non Iron Deficient Control (Group 1) And Anemic Iron Deficient (Group 2) & Non Anemic Iron Deficient (Group 3).

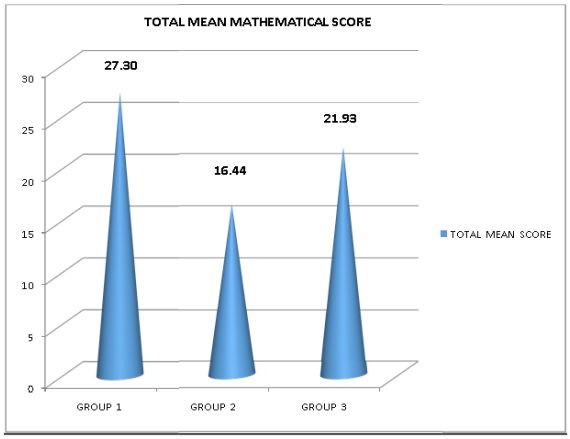


Figure 4: This graph shows that the Mean mathematical score of control Group 1 is (mean-27.30)Which is profoundly higher compared to the Anemic iron deficient Group 2 (mean-16.44) and the Non anemic iron deficient Group 3(mean-21.93).

Table 3: Comparision of Age, Hemoglobin and Serum Ferritin Levels of Non Anemic Non Iron Deficient Control (Group 1) and Non Anemic Iron Deficient (Group 3) (Independent T-Test)

	n	Mean	S.D	p value
Age				
GROUP 1	27	19.04	.940	1.000>0.05
GROUP 3	27	19.04	.940	Not Significant
Hb(g%)				
GROUP 1	27	12.99	.464	.000<0.05
GROUP 3	27	12.31	.480	Significant
Serrum Ferritin(ng/ml)				
GROUP 1	27	25.30	5.464	.000<0.01
GROUP 3	27	9.01	.424	Significant

Table 4: Descriptive Statistics &Comparision of Cognitive Domains in Control (Group 1) & Study Groups (2&3). (One-WayAnova)

	[n=81]				
Mathematical Score	**Group 1 (Mean±Sd)**	**Group 2 (Mean±Sd)**	**Group 3 (Mean± Sd)**	**F Value**	**P Value**
S1	5.59±0.500	3.44±1.013	4.70±1.102	37.856	.000< 0.05 Significant
S2	5.44 ±.640	3.37±1.115	4.56±.934	34.745	.000< 0.05 Significant
S3	5.44 ±.698	3.11±.934	3.96±.940	50.365	.000< 0.05 Significant
S4	5.26 ±.656	3.37±.629	4.30±.993	39.879	.000< 0.05 Significant
S5	5.67 ±.953	3.15±.718	4.41±1.010	72.716	.000< 0.05

					Significant
Total Score	27.30± 0.953	16.44± 0.841	21.93± 0.917	966.579	.000< 0.05 Significant

Table 5: Comparision of Scholastic Assessment of Mathematical Score in Non Anemic Non Iron Deficient Control (Group 1) & Anemic Iron Deficient (Study Group 2) (Independent T Test)

	(MEAN±SD)		
MathematicalScore	**Group 1(N-27)**	**Group 2(N-27)**	**P Value**
S1	4.70±1.102	3.44±1.013	.000< 0.05 Significant
S2	4.56±.934	3.37±1.115	.000< 0.05 Significant
S3	3.96±.940	3.11±.934	.000< 0.05 Significant
S4	4.29±.993	3.37±.629	.000< 0.05 Significant
S5	4.41±1.010	3.15±.718	.000< 0.05 Significant
Total Score	27.30±0.953	16.44±0.841	.000< 0.05 Significant

Table 6: Comparison of Scholastic Assessment of Mathematical Scores InNonanemic Non Iron Deficient Control (Group 1) &Non Anemic Iron Deficient (Group 3) (Independent T Test)

	(MEAN±SD)		
MathematicalScore	**Group 1(N-27)**	**Group 3(N-27)**	**P Value**
S1	5.59±0.501	4.71±1.103	.000< 0.05 **Significant**
S2	5.44±.641	4.56±.934	.000< 0.05 **Significant**
S3	5.44 ±.698	3.96±.940	.000< 0.05 **Significant**
S4	5.26±.656	4.30±.992	.000< 0.05 **Significant**
S5	5.67 ±.953	4.41±1.010	.000< 0.05 **Significant**
Total Score	27.30± 0.953	21.93± 0.917	.000< 0.05 **Significant**

DISCUSSION

Following the eminent study of Elena Zhukovskaya et al,[5] numerous studies was carried out to Evaluate the role of iron deficiency on cognitive functions. Iron deficiency & Anemia owing to iron deficiency, has been reported to majorly affect the general energy levels ,performance of activity, and most significantly it affects many Cognitive and Behavioural tests scores when performed on these Young women.[6]

We evaluated the causal role of iron in causing poor cognitive outcome in young women. Numerous iron studies was done assessing various iron parameters like, serum ferritin, Transferrin saturation, Bone marrow iron, TIBC, NTBI and Hemoglobin concentration. Serum ferritin and Hemoglobin are the definite important indicators of iron deficiency and iron deficiency anemia.

We used Hemoglobin and the serum ferritin levels to identify the participants with Iron deficiency anemia and Iron deficiency and to study their impact on cognitive decline in young women. Accordingly,we divided the study population in to three groups-Non anemic Non-iron Deficient (group 1)-Healthy controls,Anemic iron deficient (group 2) & Non anemic iron deficient (group 3).Serum ferritin is one of the major key protein regulating Iron Homeostasis and is a significant Biomarker of iron status. Serum ferritin, being a highly reliable tool is often used as a surrogate variable to reflect the iron stores.[7]

F.P.N.Arcanjo et al,[8] in his case control study found that Hemoglobin and serum ferritin levels were significantly lower in anemic iron deficient group compared to Non anemic counterparts which matches with the results of our study were the Hemoglobin and serum ferritin levels were decreased in Anemic iron deficient (group 2) compared to the control group (Non anemic non-iron deficient (group 1).

In our study, serum ferritin levels in Anemic iron deficient group (mean-7.8074) were significantly lower ,compared to the Non anemic iron deficient (mean-9.0111) & as well as the Non anemic non-iron deficient groups (mean-25.3037).

In our study,we also found that Hemoglobin levels in Anemic iron deficient group(mean-10.2111) were significantly lower than the Non anemic iron deficient (mean-12.3148)and Non anemic Non-iron deficient Control groups(mean-12.9926).

Low Hemoglobin levels is associated with decrease in oxygen carrying capacity of blood majorly resulting in severe hypoperfusion of brain further

causing an stress and influential changes in vessel wall and inflammatory cellular response leading on to neurodegenration.Increased risk of neural damage seen in renal dysfunction occurs due to the decline in Erythropoietin levels in anemic individuals.

M.Gopi et al,[9] based on his cross sectional study over 304 subjects, reported that lower Hemoglobin Levels lead to worst global cognition and often indicated as a magnamious marker for many conditions such as ischemia,(Cerebro vascular diseases,Oxidativestress(Irondysregulation),Hypoxi a(Hypoxia –inducible factor and change in normal Erythropoietin levels).Low Hemoglobin is decremental to memory domains like immediate and delayed verbal memory,proving that anemia in young women is most often associated with low performance on many psychological memory tests.

Raj C.Shah et al,[10] in his study also noticed the similar effect that Lower Hemoglobin concentration was associated with worst cognition and also insisted that it was leading to greater decline in semantic memory and perceptual speed of an individual.

On analyzing typically the age adjusted means stratified by gender Women showed lower performances of cognitive test scores in many domains compared to men.

Martha Dlugaj et al,[11] did a cross sectional study which showed that Women with anemia showed a significant worse scores in Problem solving, Speed of processing ,Verbal fluency task compared to men supporting the fact that Iron deficiency and decline in cognitive outcomes are more common in women which is similar to the findings of our study were women predominantely showed a greater degree of declining cognitive function in many subsets.

Lura E Murray-Klob et al,[12] in his interventional study showed a strong evidence that IDA is associated with poorer scores in cognitive function tests in childrens,whereas in adolesents the cognitive test scores is impaired even in absence of overt anemia.

In Iron deficient individuals multitude of causative factors work in bringing about a change in the resultant brain functioning, Brain energy metabolism,Neurotransmitter synthesis and function promptly leading to defective performance or slowness in performing cognitive domain tasks in everyday life.

Sarika more et al,[13] explored that in Iron deficient young women, the scholastic assessment of mathematical score showed a statistical significant difference in Non anemic non-iron deficient control group & Anemic iron deficient (group 2)Similarly differences in mathematical score also existed between the Non anemic Non-iron deficient control group & Non anemic iron deficient (group 3)whose results were in favour of our study where the scholastic assessment of mathematical score revealed a significant difference between Non anemic Non iron deficient control group & Anemic iron deficient (group 2).

KavithaUkkarapandian et al,[14]in their Descriptive cross sectional study, used the following test MMSE and Weschler's Memory scale IV to assess the cognitive function among the anemic subjects and controls and later found that the cognitive function test scores was low in anemic adults which is all the way similar to our study findings were Scores of MMSE and Weschler's Test in Anemic iron deficient group is comparatively much lower than the control group.

Ann B Bruner et al,[15] in his double blinded placebo controlled clinical trial assessed the effects of iron supplementation on cognitive function in adolescent girls with Non anemic iron deficiency and the study showed that girls who received iron supplementation performed much better on tests of Verbal Learning and memory than the girls in control group.

Thus Decremental decrease in scores of cognitive function tests is seen in Anemic iron deficient and Non anemic iron deficient study participants proving that Iron deficiency and Anemia due to Iron deficiency brings about a cognitive decline on one or more of the cognitive domains indicating strongly that the Iron deficiency is the major cause of worst cognitive functions in young women.

Limitation: In our study, we used Hemoglobin and Serrum Ferritin levels, as they are the significant markers that directly reflect the body iron stores. The former evaluates Anemia and the Later identifies the Iron deficiency of participants of our study.Apart from Ferritin and Hemoglobin, other parameters for iron Estimation like Serum iron,Total Iron Binding capacity(TIBC), Transferrin saturation, Trans ferritin receptor-Ferritin index and their relation to cognition should be performed in future studies which would further enhance the study and strengthen them.

The Memory Quotients(MQ) obtained from them are directly comparable to the subject's Intelligence Quotient(IQ).On the contrary, it is relatively lengthy and failed to assess one of the Cognitive Domain like the Executive function as a part.

CONCLUSION

The findings of the our study supports the fact that Neurocognitive insufficiency of iron in young women influences the cognitive functions of the study participants in terms of reduction in mathematical score, reduction in test scores on various domains of cognition like Logical memory,Immediate Recall,Digit forward,Digit Backward,Associative Learning,which on long term distrupts the level of IQ. This impairment in young women can have a negative influence on a multistage approach were women are expect to do multitasking being a mother,be at work,or be it in a family environment.

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