

Research Article

A study of correlation between iron deficiency anaemia and serum lipid profile in Indian adults in BRIMS, Bidar

Vijaykumar B. Antappanavar^{1*}, Shivraj G. Biradar¹, Veerendra Patil²,
Prithviraj M. Biradar¹, Shivkumar Mithare¹, Ashish Kumar Sharma¹

¹Department of Medicine, BRIMS, Bidar, Karnataka, India

²Department of Pathology, BRIMS, Bidar, Karnataka, India

Received: 10 July 2014

Accepted: 19 July 2014

*Correspondence:

Dr. Vijaykumar B. Antappanavar,
E-mail: Vijayvb8@gmail.com

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ABSTRACT

Background: Both iron deficiency anemia and dyslipidaemia are widely prevalent public health problems, especially in the Indian population. Some link has been suggested between the two potentially morbid conditions but a sufficient Indian study could not be found in this regard.

Methods: This study was planned to find the changes in serum lipid profile in adult Indian patients with iron deficiency anemia and the effect of oral iron therapy on them. 100 iron deficiency anemia and 70 age and sex matched healthy controls, in the age group 18-35 years were investigated for any possible changes in serum lipid profile i.e., triglycerides, total cholesterol, high density lipoprotein cholesterol, very low density lipoprotein cholesterol. The patients were followed up after 3 months of oral iron therapy.

Results: The results are shown as mean ± standard deviation. Triglycerides and very low density lipoprotein cholesterol levels were found to be significantly ($P < 0.001$) elevated in the iron deficiency anemia group (151.87 ± 48.06 mg/dl and 30.40 ± 9.71 mg/dl) as compared to controls (109.99 ± 30.81 mg/dl and 21.96 ± 6.69 mg/dl), whereas level of low density lipoprotein cholesterol were found to be significantly ($P = 0.02$) lower in patients (90.96 ± 41.55 mg/dl) as compared to controls (105.24 ± 26.45 mg/dl). However, after treatment (in 43 patients) there was significant ($P < 0.001$) reduction in the levels of triglycerides and very low density lipoprotein cholesterol (111.56 ± 26.87 mg/dl and 22.30 ± 5.36 mg/dl) when compared to their pretreatment level (154.70 ± 53.89 mg/dl and 30.93 ± 10.84 mg/dl), whereas low density lipoprotein cholesterol levels did not show any significant change.

Conclusion: These findings indicate that iron deficiency anemia in Indian adults is attended by abnormal serum lipid profile, which responds significantly to iron therapy.

Keywords: Iron deficiency anaemia, Serum lipid, Dyslipidaemia, Hyperlipidaemia

INTRODUCTION

Both Iron Deficiency Anemia (IDA)¹⁻³ and dyslipidemia⁴ are widely prevalent problems in the Indian population, irrespective of the socio-economic status of the people.^{3,5}

Various studies, both in animals^{6,7} and in humans^{8,9} have linked IDA with altered blood lipid profile. Lewis and

Iammarino¹⁰ reported increased triglycerides (TG) and chylomicron levels in male Sprague-Dawley rats, made iron deficiency by dietary iron lack. A study done by Choi et al.¹¹ in young Korean girls with severe IDA, reported low levels of triglycerides and total cholesterol (TC) which, returned to normal after the iron therapy. Despite such a high prevalence of both IDA and dyslipidemia, no relevant study could be found, linking

the two with reference to the Indian population. Recognition of altered blood lipid levels as risk factors in Coronary Artery Disease (CAD) has stimulated research to identify the extent to which they are influenced by both physiological and environmental factors. Since IDA is recognized as major public health problem, the suggested relationship between the two assumes clinical importance. The present study is an attempt to investigate the relationship between IDA and blood lipid levels in Indian adults.

METHODS

The study was carried out from June 2011 to January in 2013 in BRIMS, Bidar.

The subjects were selected randomly after a thorough history taking and clinical examination. Subjects with any history of smoking, chronic alcoholism, chronic infection/disease, disease of heart, kidney, liver or thyroid, diabetes mellitus, history of drug therapy, both long term and those affecting serum lipid level, steroids, hematinic therapy especially during past on year, hospitalization or any surgical procedure performed within past 2 months, active bleeding, hematological disorder, recurrent jaundice, any recent or recurrent blood transfusion, current pregnancy and passage of worms in stools were excluded from the study. Only subjects with Body Mass Index (BMI) between kg/m^2 to 24.99 kg/m^2 were selected for the study.

The selected subjects were informed about the project both in written and in person. Formal consent letters from them were obtained in writing, permitting their participation in the project and ensuring a compliance with the therapeutic regime. They were allotted specific days, on which venous blood samples were collected early in the morning, following overnight fasting.

The reference values of the hematological and the biochemical tests were based on the hospital laboratory reference data. Complete hemogram, Erythrocyte Sedimentation Rate (ESR), serum iron, Total Iron Binding Capacity (TIBC) and serum ferritin were determined and Transferring Saturation (TS) was calculated in all subjects.

The diagnosis of IDA was confirmed when hemoglobin (Hb), serum iron and TS levels were lower than the expected ranges for the selected group. Only those subjects with serum ferritin levels $<15 \text{ mg/l}$ were, selected from the IDA group.

Analysis of serum lipid levels, which included TC, TG, High Density Lipoprotein (HDL) cholesterol, Low Density Lipoprotein (LDL) cholesterol and Very Low Density Lipoprotein (VLDL) cholesterol were done in all subject, using the enzymatic method (auto analyzer, Beckmen Synchron Clinical System CX4, Beckman Coulter, Inc, California, USA).

The IDA subjects were given oral iron therapy in the form of ferrous sulphate tablets 200 mg three times a day and were re-investigated after 3 months. The controls were also followed up after 3 months.

The statistical analysis (sing SPSS software, version 10.0) was done utilizing the unpaired Student's 't' test to compare control and IDA group, while the paired 't' test was used to compare the effects of oral iron therapy and to compare the controls various parameters changes in parameters were determined with the help of the Pearson method. Results were given as means \pm Standard Deviation (SD). The statistical significance level was accepted at P value less than 0.05.

RESULTS

The study group comprised 100 confirmed IDA adults (27 males and 73 females) in the age group of 18-35 years (means 25.34 ± 6.27 years). Seventy healthy sex matched adults within the same age group (mean 25.03 ± 6.02 years) were enrolled as the control group. After iron therapy from 3 months, 61 patients (18 males and 43 females) followed up. The mean age of the post-therapy group was 26.46 ± 6.46 years.

Table 1: Baseline hematological and lipid parameters of IDA patients and controls.

Parameters	IDA (n=100)	Controls (n=100)
Hematological		
Hb (g/dl)	$8.79 \pm 1.42^{***}$	13.77 ± 1.44
Serum iron ($\mu\text{g/dl}$)	$39.33 \pm 6.22^{***}$	97.14 ± 19.58
TIBC ($\mu\text{g/dl}$)	$389.03 \pm 40.56^{***}$	292.72 ± 26.02
TS (%)	$10.33 \pm 1.91^{***}$	50.4 ± 30.33
Serum ferritin ($\mu\text{g/dl}$)	$8.93 \pm 3.5^{***}$	50.4 ± 30.00
Lipids		
TC (mg/dl)	160.17 ± 45.81	168.21 ± 26.44
LDL (mg/dl)	$90.96 \pm 41.55^*$	105.24 ± 26.45
VLDL (mg/dl)	$30.40 \pm 9.71^{***}$	21.96 ± 6.69
TG (mg/dl)	$151.87 \pm 48.06^{***}$	109.99 ± 30.81
HDL (mg/dl)	39.01 ± 8.84	41.20 ± 8.66
***Significant (P <0.001), *Significant (P <0.02)		
<ul style="list-style-type: none"> • Plus - minus values are means \pm SD. IDA denotes iron deficiency anemia group, HB hemoglobin concentration, TIBC total iron binding capacity, TS serum transferrin saturation, TC serum total cholesterol concentration, LDL serum low density lipoprotein cholesterol concentration, VLDL serum very low density lipoprotein cholesterol concentration. TG serum triglycerides concentration and HDL serum high density lipoprotein cholesterol concentration. • P-values were calculated with use of student's 't' test and values ≥ 0.01 have been rounded off to 2 decimal places. 		

The baseline hematological parameters of the IDA patients were found to be significantly different from controls (Table 1). The IDA subjects had significantly

lower Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH) and Mean Corpuscular Hemoglobin Concentration (MCHC) values as compared to the control group. The comparison serum lipid profile between the IDA and the control group is also summarized in Table 1. The levels of serum TG and serum VLDL were significantly ($P < 0.00$) higher in the IDA group, whereas the levels LDL were significantly ($P = 0.02$) lower.

After the iron therapy there was significant ($P < 0.001$) increase in the levels of hemoglobin, serum iron, TS and serum ferritin, while TIBC levels showed a significant fall (Table 2). These subjects also showed a significant increase their red blood cell indices.

When the serum lipid profile of IDA subjects was analysed after the iron therapy significant ($P < 0.001$) reduction in serum TG and VLDL levels was noted. The other parameters however, did not show any significant change (Table 2).

Table 2: Effect of iron therapy on the hematological and lipid parameters after 3 months.

Parameters	Pre-therapy IDS (n=4)	Post therapy IDA (m=61)
Hematological		
Hb (g/dl)	9.13 ± 1.47	13.36 ± 1.21***
Serum iron (µg/dl)	40.26 ± 6.67	112.30 ± 17.01***
TIBC (µg/dl)	393.16 ± 41.87	313.79 ± 44.43***
TS (%)	10.52 ± 2.06	35.57 ± 6.03***
Serum ferritin (µg/dl)	9.56 ± 2.89	48.00 ± 25.73***
Lipids		
TC (mg/dl)	160.67 ± 47.31	152.70 ± 40.51
LDL (mg/dl)	91.40 ± 40.47	91.74 ± 36.63
VLDL (mg/dl)	30.93 ± 10.84	22.30 ± 5.36***
TG (mg/dl)	154.70 ± 53.89	111.56 ± 26.87
HDL (mg/dl)	38.56 ± 9.57	38.70 ± 13.25
***Significant ($P < 0.001$)		
<ul style="list-style-type: none"> • Plus - minus values are means ± SD. Pre-therapy IDA denotes iron deficiency anemia group before treatment whereas, post-therapy IDA is the same group after 3 months of oral iron therapy HB hemoglobin concentration, TIBC total iron binding capacity, TS serum transferring saturation TC serum total cholesterol concentration, LDL serum low density lipoprotein cholesterol concentration, VLDL serum very low density lipoprotein cholesterol concentration, TG serum triglycerides concentration and HDL serum high density lipoprotein cholesterol concentration. • P-values were calculated with use of student's 't' test. 		

When changes in parameters (before and after iron treatment) were correlated with each other. A significant negative correlation ($r = -0.31$, $P = 0.04$) was found between transferring saturation with TG levels and a

significant positive correlation ($r = 0.38$, $P = 0.01$) was found between serum ferritin with serum HDL levels.

DISCUSSION

Micronutrient deficiency, with is due to lack of essential minerals in the diet, is a serious public health concern in most developing countries. Even though these elements are needed only in minute quantities, their deficiency leads to malnutrition syndromes with clinical sings leading to high social and public costs through increased public expenditure on health services. This results in suboptimal returns on investment in education and training by decreasing the working capacity of the population due to high rates of illness and disability thus constituting the tragic loss of human potential. Overcoming micronutrient malnutrition is a precondition for ensuring a rapid and high overall development of the country and its people.¹²

Iron Deficiency (ID) is the world's most widespread nutritional disorder, regardless of age, gender and socioeconomic status, affecting both industrialized and developing countries; it is the most common cause of anemia. On a worldwide basis WHO has estimated that about a affecting over twice as many. ID is an important public health problem because of its complications.¹³

In developing countries like India, anemia is highly prevalent with most cases being those of IDA. WHO reports on IDA, using anemia prevalence as an indirect indicator of ID, estimated the prevalence of ID as being 42.3% in women (15-59 years) and 30% in men (15-59 years) in the developing world. The report also estimated that 88% of pregnant females and 74% of non-pregnant females in are anemic.¹⁴ The present study, besides collecting the complete data from 100 adult's subjects with IDA, excluded nearly three times this number with either ID without anemia or with IDA under the various exclusion criteria.

Dyslipidemia is one of the major risk factor in the development of CAD. Various studies.^{15,16} have reported elevated plasma levels as risk factors in emergence of CAD. Else are widely prevalent problems even in the normal Indian population.^{4,5}

Since krause¹⁷ showed hyperlipidemia in patients with acute hemorrhage in 1943, several experimental studies were performed to find out the relation between ID and dyslipidemias, as well as to find out the biochemical mechanisms explaining them. Yet, the authors of the present study couldn't find any significant data about the relationship, in references, in reference to the Indian population, where both the conditions are rampant.

The present study found significantly raised levels of both TG and VLDL cholesterol levels in the IDA subjects, as compared to healthy controls. Similar results were observed by Tanzer et al. in Turkish children.

Animal studies reporting elevated TG levels, were performed by Guthrie¹⁸ in ID Male Sprague-Dawley rats. However a study on ID Korean girls (14-19 years) found reduced levels of TG in severe IDA while another study⁹ on Turkish children with IDA found no effect on either TG or VLDL levels.

The present study observed significant reduction in the levels of both TG and VLDL after 3 months of oral iron therapy in the IDA groups. Furthermore, in response to iron treatment, significant correlations were found between changes in transferrin saturation with TG levels and between changes in serum ferritin with HDL levels. Lewis and Iammarino¹⁰ and Masini et al.¹⁹ in 1994 observed reduction in the levels of TG after iron therapy in ID rats. However, Choi et al.¹¹ found increase of TG levels over their pretreatment values in young ID Korean girls. They also reported significant positive correlation between blood hemoglobin concentration with the total cholesterol and the triglycerides levels in severely anemic (Hb 8 g/dl) subjects.

The present study observed reduced levels of LDL Cholesterol in the IDA group as compared to controls, but after iron therapy there was no significant change in the levels of this lipoprotein. However, Ece et al.⁹ in a study on IDA children reported reduced LDL levels, which returned to control levels after the iron therapy. Serum TC did not show any significant alteration in the IDA group while previous studies have reported variable results in relation to TC, with some studies reporting it as normal,^{10,20} while others reporting low levels.^{8,9}

Various studies have been performed to define the related mechanisms underlying dyslipidemias in IDA. High TG levels have been explained on the basis of impaired carnitine biosynthesis together with increased TG synthesis and decreased TG degradation^{8,10,21} in IDA while lower serum cholesterol has been related to be due to decreased hepatic synthesis⁶ or dilutional effects of serum.^{6,10,21,22} The exact mechanism by which iron regulates or functions in lip metabolism has not yet been established.

The significance of the results obtained by this study is, at present, unclear, perhaps due to small data. The authors feel that in future a larger randomized controlled trial with iron can be planned, by adopting more vigilant screening for anemia and motivating those suspected of the condition (who could even be asymptomatic) follow up in the hospital, where relevant cardiovascular and biochemical investigations could be performed on them.

Since hyperlipidemia is recognized as a risk factor in the development of CAD, all nutritional influences on the serum lipids' concentrations assume considerable

importance and warrant further study to enable us to more clearly understand the etiology of this disease. The role of iron in blood lipid metabolism has received little attention, especially in India, and must be explored to establish if ID is a contributing factor in the etiology cardiovascular disease in humans. In addition, the consequences of ID in relation to cardiovascular morbidity must be considered seriously and hence all attempts should be made to treat this micronutrient deficiency promptly.

These findings indicate that iron deficiency anemia in Indian adults is attended by abnormal serum lipid profile, which responds significantly to iron therapy.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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DOI: 10.5455/2349-3933.ijam20140811

Cite this article as: Antappanavar VB, Biradar SG, Patil V, Biradar PM, Mithare S, Sharma AK. A study of correlation between iron deficiency anaemia and serum lipid profile in Indian adults in BRIMS, Bidar. *Int J Adv Med* 2014;1:96-100.