A Study of Lipid Profile in Iron Deficiency Anemia

Venkateshwarlu Nandyala[1*], Gandiah P.[2], Karthik R.S.[3], Sivarajappa P.[4], Indira G.[5], Krishna Prasad T.[6]

[1,4,5]Professor, [2]Professor and HOD, [3]Ex-Postgraduate Student, [6]Assistant Professor

Department of Internal Medicine, SVS Medical College, Mahabubnagar, Andhra Pradesh, INDIA.

[*]Corresponding Address:

venkatetreya@gmail.com

Research Article

Abstract: **Background & objectives:** Iron deficiency anemia (IDA) is common disorder of our nation. Dyslipidemia is widely prevalent in India without any socio-economic status. Association of IDA and dyslipidemias were reported in the same individuals or experimental animals. A prospective study was planned to find the changes in serum lipid profile in adult Indian patients with iron deficiency anaemia and the effect of oral iron therapy on them. **Material and Methods**: 100 patients with iron deficiency anemia and 50 age and sex matched healthy controls, in the age group of 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 and low density lipoprotein cholesterol. The patients were followed up after 3 months of oral iron therapy. **Observations and Results:** Total cholesterol, TG, LDL, VLDL levels were found to be significantly (<0.001) elevated in IDA group (165.9 ± 11.49, 175.32 ± 27.8, 93.53 ± 10.65, 31.74 ± 2.96) as compared to controls (149.04 ± 11.24, 103.28 ± 10.38, 80.02 ± 13.71, 20.92 ± 2.72) whereas HDL level was significantly(<0.001) decreased in IDA group (37.27 ± 3.07) compared to controls (48.34 ± 5.43). However after treatment there was significant reduction in TG and VLDL levels (87.78 ± 5.75 and 19.83 ± 1.95) when compared to their pre-treatment levels (175.32 ± 27.8 and 31.74 ± 2.96) and significant increase inHDL level (46.5 ± 3.58) as compared to pre-treatment levels (37.27 ± 3.07), whereas Total cholesterol and LDL levels (153.06 ± 15.2 and 88.76 ± 16.18) reduced insignificantly compared to pre-treatment levels (165.9 ± 11.49 and 93.53 ± 10.65). **Conclusion:** This study indicates that iron deficiency anaemia in Indian adults is attended by abnormal serum lipid profile, which responds significantly to iron therapy.

Key words: Indian adults, iron deficiency anaemia, cholesterol, triglycerides, iron therapy.

Introduction

Iron deficiency anemia (IDA) is common disorder of our nation[1,2,3]. Dyslipidemia is widely prevalent in India[4], without any socio-economic status[3,5]. Association of IDA and dyslipidemias were reported in the same individuals[6,7] or experimental animals[8,9]. Iron is an essential metal involved in a wide spectrum of physiological functions in the body, such as oxygen transport and enzymatic reactions. Nevertheless, excess iron can be harmful because it promotes the generation of free radicals, which lead to tissue damage [10,11,12,13]. Iron deficiency is commonly encountered in young infants and adolescent girls. In an epidemiological study, high body iron stores were related to an increased risk of coronary heart disease[14]. Subsequent studies have shown that low serum iron-binding capacity and high serum iron concentrations are risk factors for myocardial infarction[15,16]. Although associations have been found between dietary iron intake and serum lipid and lipoprotein concentrations in animal models[17,18], such relationships have not been investigated extensively in humans, and the available data are inconsistent. Knowledge about the effect of iron deficiency on serum lipid profiles is limited. A study done by Choi *et al*[19] in young Korean girls with severe IDA, reported low levels of triglycerides and total cholesterol (TC) which, returned to normal after the iron therapy. Therefore, in the present study, we investigated the changes in serum lipid concentrations that occur in patients of iron deficiency anemia (IDA).

Aims and Objectives

This study was planned to find the changes in serum lipid profile in adult Indian patients with iron deficiency anaemia and the effect of oral iron therapy on them

Materials and Methods

Study design and subject recruitment

This prospective study was carried out from August 2010 to September 2012 in MAHABUBNAGAR, India, among the adults attending Medicine outpatient clinics of Sri Venkata Sai Medical College hospital, Mahabubnagar, Andhra Pradesh. The Subjects were selected randomly after a through history and clinical examination. Patients of either sex aged between 18 to 40 years, with body mass index between 18.50 Kg/M^2 and 24.99 Kg/M^2. Smokers, chronic alcoholics, those with heart, liver, renal, haematological and thyroidal diseases were excluded so also diabetic patients. Pregnant cases and those on chronic treatment for any disease were not included in our study. The selected subjects were informed about the study both written and in person. A formal informed consent letters were obtained in writing, permitting their participation in the study and ensuring a compliance with 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 haematologicaland the biochemical tests were based on the hospital laboratory reference data. Complete haemogram, erythrocyte sedimentation rate (ESR), serum iron, total iron binding capacity (TIBC) and serum ferritin were determined and Transferrin saturation (TS) was calculated in all subjects.The diagnosis of IDA was confirmed when haemoglobin(Hb), serum iron and TS levelswere lower than the expected ranges for the selected group. Only those subjects with serumferritin levels < 15 mg/l were selected for the IDA group.Analyses of serum lipid levels, which included TC, TG, high density lipoprotein (HDLcholesterol, low density lipoprotein (LDL) cholesterol and very low density lipoprotein(VLDL) cholesterol were done in all subjects, using the enzymatic method (auto analyser, Beckman 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 reinvestigated after 3 months. The controls were also followed up after 3 months. The statistical analysis (using 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 from their previous parameters. Correlations between various parameters/changes in parameters were determined with the help of the Pearson method. Results were given as means ± standard deviation (SD). The statistical significance level was accepted at p-value less than 0.05.

Observations and Results

The study group comprised 100 confirmed IDA adults (28 males and 72 females) in the age group of 18-35 years (mean 28.9 ± 6.82 years). Fifty healthy sex matched adults (14 males and 36 females) within the same age group (mean 27.9 ± 3.66 years) were enrolled as the control group. After iron therapy for 3 months, all patients were followed up.

Table 1: Age Distribution

Age Range (Years)	Cases	Controls	P value
18 – 25	56	26	NS
26 – 30	30	19	NS
31 – 35	14	5	NS

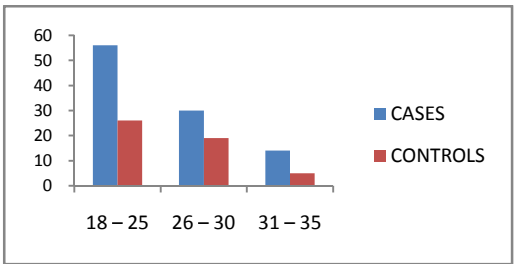


Figure 1: Age Distribution

Table 2: Sex Distribution

	Cases	Controls	P value
Males	18	8	Ns
Females	72	42	Ns

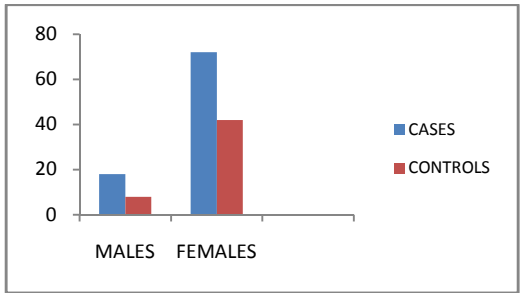


Figure 2: Sex Distribution

Table 3: Marital Status(Percentage)

	Cases (percentage)	Controls (Percentage)
Unmarried	32 (32)	19 (38)
Married	68 (68)	31 (62)

Table 4: Religion Distribution

	Cases	Controls
Hindus	33	17
Tribals	35	18
Muslims	21	10
Christians	12	05

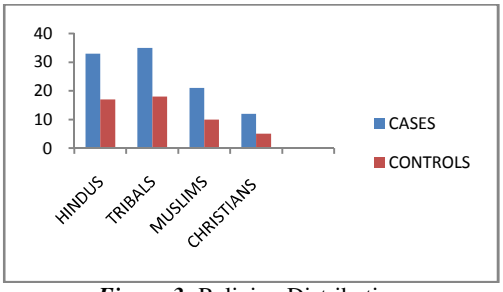


Figure 3: Religion Distribution

Table 5: Urban Rural Distribution

	Study group	**Control group**
Urban	42 (42%)	28 (56%)
Rural	58 (58%)	22 (44%)

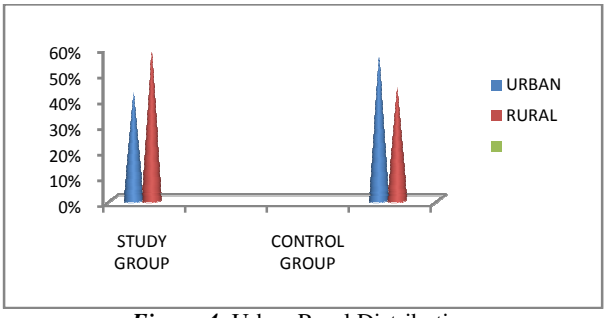


Figure 4: Urban Rural Distribution

Table 6: Dietary Preferences

	Cases	**Controls**	**P value**
Vegetarian	54 (54%)	23 (46%)	Ns
Non-vegetarian	46 (46%)	27 (54%)	Ns

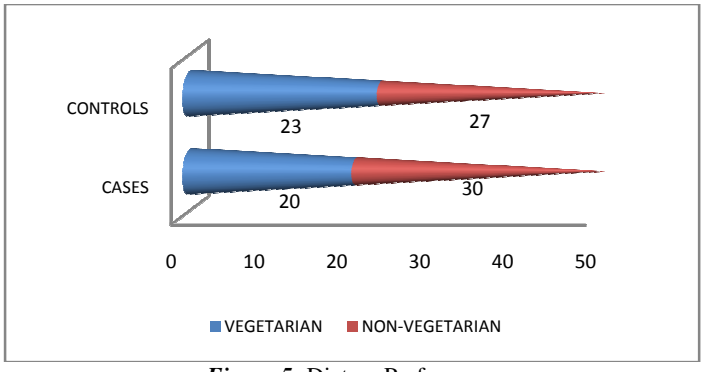


Figure 5: Dietary Preferences

Table 7: Presenting Complaints (Symptoms)

Complaints	**No of cases**
Easy fatigability	54
Headache	42
Neck pain	18
Generalised bodyache	28
Shortness of breath	26

Swelling of feet	10
Syncopal attacks	4
Asymptomatic	12

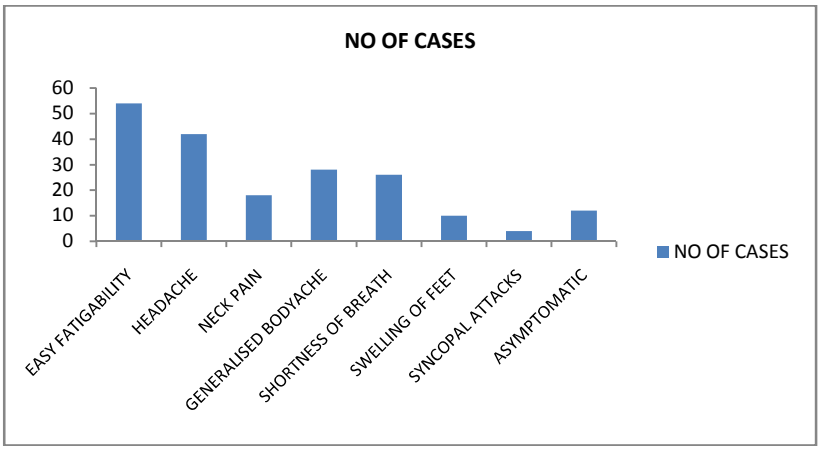


Figure 6: Presenting Complaints (Symptoms)

On presentation 54 cases had easy fatigability, 42 had headache, 18 had neck pain, 28 had generalized body ache, 26 had shortness of breath, 10 had swelling of feet and 4case had syncopal attackwhile 12 cases were asymptomatic.

Table 8: Signs on Presentation

Signs	No of cases
Pallor	100
Platynychia	44
Koilonychia	21
Cheilosis	11
Glossitis	36
Hemic murmer / cardiomegaly	21

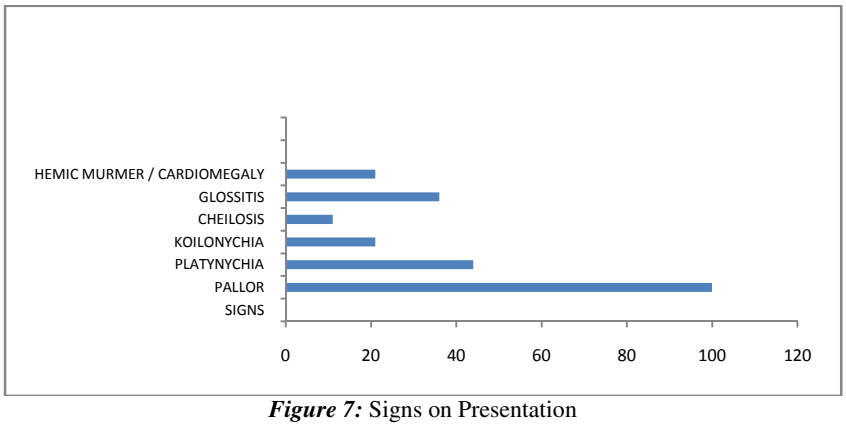


Figure 7: Signs on Presentation

Comparison of Lipid and Hematological Parameters

The baseline haematological parameters of the IDA patientswere found to be significantly different from controls (Table 15). The IDA subjects had significantly lower mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) values as compared to the control group. The comparison of serum lipid profile between the IDA and the control group is also summarized in Table.9.

Table 9: Baseline Haematological and Lipid Parameters of IDA Patients and Controls

Parameters	IDA Cases (n=100)	Controls (n=50)	P value
Haematological:			
Hb(g/dl)	6.24 ± 1.0	13.3 ± 0.61	<0.001, S
Serum iron(mcg/dl)	37.84 ± 7.07	103.2 ± 15.47	<0.001, S
TIBC(mcg/dl)	457.44 ± 23.69	304.24 ± 29.87	<0.001, S
TS(%)	8.28 ± 1.52	34.03 ± 4.53	<0.001, S

Serum ferritin(mcg/dl)	9.22 ± 1.81	55.58 ± 9.72	<0.001, S
Lipids:			
TC(mg/dl)	165.9 ± 11.49	149.04 ± 11.24	<0.001, S
LDL(mg/dl)	93.53 ± 10.65	80.02 ± 13.71	<0.001, S
Parameters	IDA Cases (n=100)	Controls (n=50)	P value

s- Significant (p<0.001)

Plus .minus values are means ± SD. IDA denotes iron deficiency anaemia group, Hb haemoglobin 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

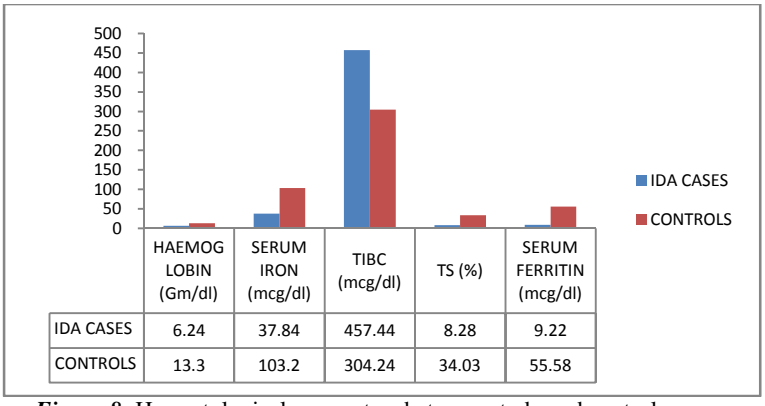


***Figure 8*:** Haematological parameters between study and control groups

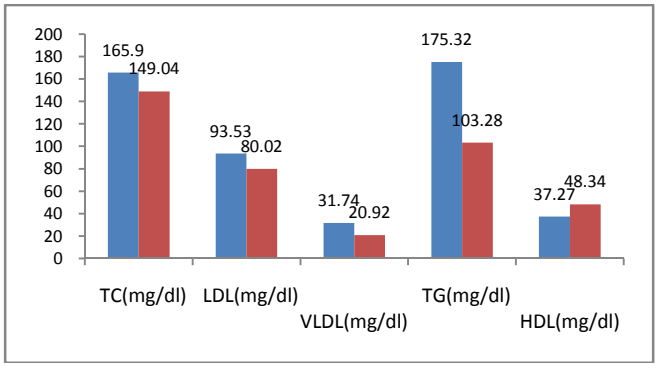


***Figure 9*:** Lipid parameters between study and control groups

Hematological parameters Haemoglobin, Serum iron, Transferrin saturation and Serum ferritin levels were found to be significantly (<0.001) elevated in IDA cases compared to controls. Total iron binding capacity level was significantly (<0.001) decreased in IDA cases compared to CONTROLS

Table 10: Effects of Iron Therapy on the Haematological and Lipid Parameters after 3 Months

Parameters	**Pretherapy IDA (n=50)**	**Post-therapy IDA (n=50)**	**P value**
Haematological:			
Hb (g/dl)	6.24 ± 1.0	12.88 ± 0.97	<0.001, S
Serum iron (mcg/dl)	37.84 ± 7.07	121.46 ± 10.94	<0.001, S
TIBC (mcg/dl)	457.44 ± 23.69	294.4 ± 16.77	<0.001, S
TS (%)	8.28 ± 1.52	41.21 ± 2.0	<0.001, S
Serum ferritin (mcg/dl)	9.22 ± 1.81	60.75 ± 7.79	<0.001, S
Parameters	Pretherapy IDA (n=50)	Post-therapy IDA (n=50)	P value

S: Significant (p<0.001)

§ Plus .minus values are means ± SD

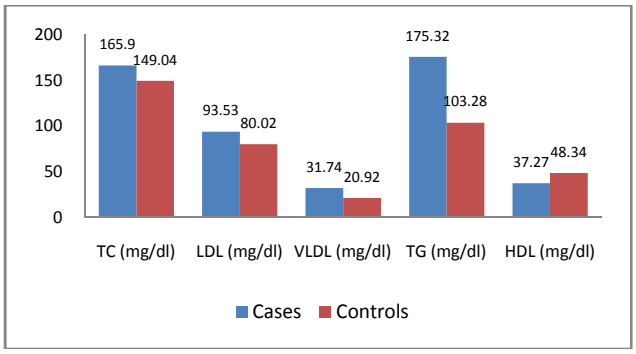
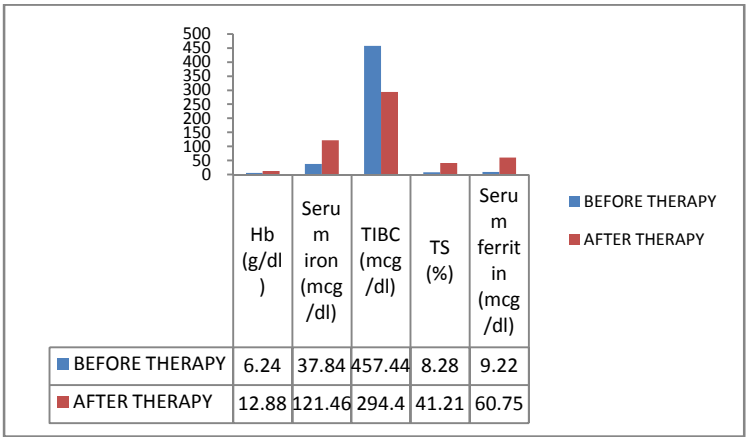


Figure 10: Comparison of Lipid parameters between IDA Cases and Controls

Lipid parameters Total cholesterol, Low density lipoprotein, Very low density lipoprotein and Triglyceride levels were found to be significantly (<0.001) elevated in IDA cases compared to controls. High density lipoprotein level was significantly (<0.001) decreased in IDA cases compared to controls. Pre-therapy IDA denotes iron deficiency anaemia group before treatment whereas, post-therapy IDA is the same group after 3 months of oral iron therapy, Hb haemoglobin 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 the use of Student.s .t. test



	Hb (g/dl)	Serum iron (mcg/dl)	TIBC (mcg/dl)	TS (%)	Serum ferritin (mcg/dl)
BEFORE THERAPY	6.24	37.84	457.44	8.28	9.22
AFTER THERAPY	12.88	121.46	294.4	41.21	60.75

Figure 11: Comparison of Haematological parameters between Pretherapy IDA group and Post-therapy IDA group

After 3 months of oral Iron therapy Hematological parameters Haemoglobin, Serum iron, Transferrin saturation and Serum ferritin levels were found to be SIGNIFICANTLY (<0.001) elevated in subjects POST-THERAPY compared to PRETHERAPY levels. Total iron binding capacity level was significantly (<0.001) decreased in subjects POST-THERAPY compared PRETHERAPY.

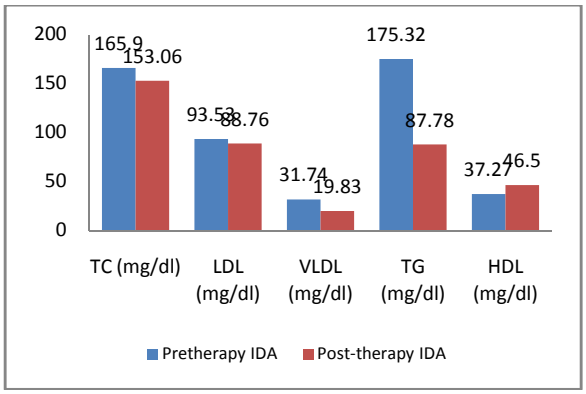


Figure-12: Comparison of Lipid parameters between Pre-therapy IDA group and Post-therapy IDA group

LIPID parameters Very low density lipoprotein and Triglyceride levels were found to be SIGNIFICANTLY (<0.001) decreased in subjects POST-THERAPY compared to PRETHERAPY levels. High density lipoprotein level was significantly (<0.001) decreased in subjects POST-THERAPY compared to PRE-THERAPY levels. Total cholesterol and Low density lipoprotein levels were found to be decreased but were not statistically significant.

Discussion

IDA is the world's most widespread nutritional disorder and also the commonest cause of anaemia occurring regardless of age, gender and socioeconomic status, affecting both industrialized and developing countries. It is the most common cause of anaemia. On a worldwide basis WHO has estimated that about a third of the population is suffering from anaemia with IDA affecting over twice as many. IDA is an important public health problem because of its complications[20]. Overcoming micronutrient malnutrition is a precondition for ensuring a rapid and high overall development of the country and its people[21]. In addition to altered glucose utilization, significant changes in lipid homeostasis have been reported, though mechanistic studies investigating the utilization, uptake, and storage of lipids in ID animals have offered mixed results [22,23,24] . In developing countries like India, anaemia is highly prevalent with most cases being those of IDA. WHO reports on IDA, using anaemia prevalence as an indirect indicator of IDA, estimated the prevalence of IDA 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 India are anaemic[25]. The present study, besides collecting the complete data from 100 adult subjects with IDA, excluded nearly three times this number with either ID without anaemia or with IDA under the various exclusion criteria. Dyslipidaemia is one of the major risk factor in the development of CAD. Various studies [26,27] have reported elevated plasma levels of TG, VLDL, LDL and low HDL cholesterol levels as risk factors in emergence of CAD. Hypertriglyceridemia and low plasma HDL cholesterol levels are widely prevalent problems even in the normal Indian population[4, 5]. The authors of the present study couldn't find any significant data about the cardiological or cerebro-vascular incidences in the present study. 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*[8] in Turkish children. Animal studies, reporting elevated TG levels, were performed by Guthrie *et al* [28] in offspring of ID(Iron deficient) rats and by Lewis and Iammarino[10] in ID rodents. However a study on ID Korean girls (14-19 years) found reduced levels of TG in severe IDA[19], while another study [9] 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 group. 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 Iammarino[10] observed reduction in the levels of TG after iron therapy in ID rats. However, Choi *et al* [19] found increase of TG levels over their pre-treatment values in young ID Korean girls. They also reported significant positive correlation between bloodhaemoglobin concentration with the total cholesterol and the triglycerides levels in severely anaemic (Hb< 8g/dl) subjects.

This study results can be compared to a recent Indian study Udit Varma et al[29] in 2010 in New Delhi, comparison is given below:

Table 11: Comparison of Data With Earlier Studies

	TG before therapy	TG after therapy	VLDL before therapy	VLDL after therapy	HDL before therapy	HDL after therapy
Udit verma et al	154.70 ± 53.89	111.56 ± 26.87	30.93 ± 10.84	22.30 ± 5.36	38.56 ± 9.57	38.70 ± 13.25
Present study	175.32 ± 27.8	87.78 ± 5.75	31.74 ± 2.96	19.83 ± 1.95	37.27 ± 3.07	46.5 ± 3.58

In Udit Verma et al study TG and VLDL decrease after 3 months of Iron therapy but there is not much change in HDL, but in my study even HDL improves with Iron therapy along with decrease in TG and VLDL levels. The present study observed increased levels of LDL cholesterol in the IDA group as compared to controls, but even after iron therapy there was not much (Statistically 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 show significant alteration in the IDA group while previous studies have reported variable results in relation to TC, with some studies reporting it as normal[10,30], while others reporting low levels[8,9]. Various studies have been performed to define the related mechanisms underlying dyslipidaemias in IDA. High TG levels have been explained on the basis of impaired carnitine biosynthesis together with increased TG synthesisand decreased TG degradation[8,10,31] in IDA while lower serum cholesterol has been related to be due

to decreased hepatic synthesis[6] or dilutional effects of serum[6,10,31,32]. The exact mechanism by which iron regulates or functions in lipid metabolism has not yet been established. The significance of the results obtained by this study is, at present, unclear, perhaps due to small data. We feel that in future a larger randomized controlled trial with iron can be planned, by adopting more vigilant screening for anaemia and motivating those suspected of the condition (who could even be asymptomatic) to follow up in the hospital, where relevant cardiovascular and biochemical investigations could be performed on them.

Conclusions

This study indicates that

1. Indian adults having Iron deficiency anaemia have abnormal serum lipid profile.
2. It responds significantly to iron therapy.
3. Since hyperlipidaemia is recognised as a risk factor in the development of CAD, all nutritional influences on the serum lipid concentrations assume considerable importance and warrant further study to enable us to more clearly understand the aetiology of this association though none of our patient had any cardiovascular or cerebro-vascular incidents.
4. 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 aetiology of cardiovasculardisease in humans.

5. 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.

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