Original Article

Study of Lipid Profile in Iron Deficiency Anaemia

Archana Deshpande[1], Anuradha Kapoor[2]

ABSTRACT

Introduction : Both Iron Deficiency Anemia (IDA) and dyslipidemia are widely prevalent problems in the Indian population, irrespective of the socio-economic status of the people. Some link has been postulated between anemia and dyslipidemia both of which are potentially morbid, conditions however enough data in this regard was not found in the Indian published studies. The present study was undertaken to evaluate the relationship between Iron deficiency anemia and lipid levels in the adult Indian population.

Objectives : To find out the quantitative changes in each lipid sub fraction in anemic cases compared to healthy controls, and also to correlate changes in lipid sub fractions with respect to increasing severity of anemia.

Material and Method : It is a case control study conducted in a tertiary care hospital from September 2014 to September 2016. Total 100 cases and 100 age and sex matched controls were included in this study as per inclusion criteria. Patients underwent detailed clinical examination and laboratory assessment. Various parameters were compared between these two groups.

Results : The mean total cholesterol in cases and controls were 122.02 mg/dl and 178.91 mg/dl respectively, mean HDL in cases and controls were 30.5 mg/dl and 38.4 mg/dl respectively, mean LDL in cases and controls were 81.38 mg/dl and 116.53 mg/dl respectively and mean triglyceride in cases and controls were 108.9 mg/dl and 130.7 mg/dl respectively. All values were significantly decreased in cases compared to controls. There was a larger reduction in mean total cholesterol, HDL, LDL, and triglyceride levels, with increased severity of anemia.

Conclusion : Indian adults having IDA have abnormal serum lipid profile.Hyperlipidemia is recognised as a risk factor in the development of Coronary artery disease. In patients with severe anemia the lipid profile should be interpreted with caution,especially in those patients who have cardiovascular risk factors.

Key words : IDA - iron deficiency anemia; HDL - high density lipoprotein; LDL - low density lipoprotein; TC - total cholesterol; TG - triglyceride; VLDL - very low density lipoprotein; TS - transferrin saturation; TIBC - total iron binding capacity

Introduction :

Both Iron Deficiency Anemia (IDA) and dyslipidemia are widely prevalent problems in the Indian population, irrespective of the socio-economic status of thepeople[1]. Various studies show that lipid parameters in iron deficient patients are higher in value than those of healthy control patients, whereas others indicate that lipid parameters fall to lower levels in iron deficient patients, but improve to normal range following the rise of hemoglobin after iron replacement or transfusion.

Serum lipid levels are significantly correlated with the risk of atherosclerosis, which causes coronary artery disease, cerebrovascular disease and peripheral vascular disease, important causes for mortality and morbidity worldwide. The total cholesterol level is only a general guide to the risk of atherosclerosis. Levels of the components of total cholesterol - particularly LDL and HDL cholesterol are more important. A high level of LDL cholesterol increases the risk of atherosclerosis. A high level of HDL cholesterol decreases the risk of atherosclerosis. However, a low level of HDL cholesterol (defined as less than 40 mg/dl) increases the risk of atherosclerosis.

[1]Associate Professor, [2]Senior Resident,
Department of General Medicine, Govt. Medical College, Nagpur

Address for Correspondence -
Dr. Archana Deshpande
E-mail : arcsandeshpande@rediffmail.com
Received on 16th February 2018 Accepted on 15th May 2018

Objectives :

- To study the lipid profile in patients of Iron deficiency anemia and to compare it with age and sex matched controls.
- To correlate the changes of various lipid sub fractions with the severity of anaemia.

Methodology :

100 cases and 100 age and sex matched controls were included.

Inclusion Criteria :

1. All proven casesof iron deficiency anaemia with cut off value of Hb in male is < 13 gm%, and in Female < 12 gm%. Only subjects with Body Mass Index (BMI) between 18.5 kg/m2 to 24.99 kg/m2 were selected for the study.
2. Healthy age and sex matched controls with Body Mass Index (BMI) between 18.5 kg/m2 to 24.99 kg/m2 were selected for the study.

Exclusion Criteria :

1. Children below 12 years of age
2. Overweight,Obese and underweight
3. Hypertensive / Diabetics / Chronic kidney disease / Ischaemic heart disease / Cerebrovascular accident / HIV positive were excluded from the study.
4. Alcoholics / Smokers
5. History of recent blood loss
6. History of use of steroids, oral contraceptives, diuretics, beta-blockers

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.

Each patient was subjected to a detailed general physical examination and relevant blood investigations. The reference values of the haematological and the biochemical tests were based on the hospital laboratory reference data. Complete haemogram, peripheral smear for typing of anaemia, bloodsugar : fasting (after overnight fasting) and post prandial (2 hours after meal),thyroid function test, liver function test, kidney function test, iron profile, lipid profile : sample collected after overnight fasting was done in both groups. Bone marrow aspiration cytology was done in selected cases based onclinical assessment.

The diagnosis of IDA was confirmed when hemoglobin (Hb), serum iron and transferrin saturation levels were lower than the expected ranges for the selected group.

Normal reference range : Serum Iron - males-59-158 µg/dl, females-37-145 µg/dl; **TIBC -** males - 225-535 µg/dl, females - 215-535 µg/dl; **Serum Ferritin -** Males - 30-400 ng/ml, Females 13-150 ng/dl; **TC -** 150-200 mg/dl; **TG -** 25-160 mg/dl; **HDL -** Males - 30-65 mg/dl, Females - 35-80 mg/dl; and **LDL -** <130mg/dl.

Statistical Methods

Results were given as Mean ± SD. Haematological and lipid parameters were compared across different levels of haemoglobin values by performing **oneway ANOVA** for normalized data. **Kruskall - wallis ANOVA** was used for non-normalized data. Different levels of haemoglobin were correlated with levels of haematological parameters by performing **pearson's chi2 -** test. Pearson's correlation coefficient was calculated to assess nature and magnitude of correlation between lipid parameters and haematological parameters. $P < 0.05$ was considered as statistical significance.

Statistical software :

Statistical software STATA version was used for the analysis.

Results :

The cases and controls were matched for age. The mean age of iron deficiency anaemia cases was 30.79 ± 9.57 years and the mean age of control was 31.05 ± 9.71 years. Maximum number of patients belonged to age group between 31-40 years. The youngest case was 15 years old and eldest was 48 years old. Out of total 100 cases haemoglobin less than 6 gm/dl was present in 29% cases, haemoglobin between 6-9 gm/dl was present in 43% cases and haemoglobin more than 9 gm/dl was present in 28% cases. There was no significant difference in the age distribution of cases and controls since the controls were age group matched with cases. ***(Table 1)***

The cases and controls were matched for sex. Out of total 100 cases and controls 44% were males and 56% were females. Haemoglobin < 6gm/dl was present in 20 females (35.7%) and 9 males (20.4%), haemoglobin between 6-9gm/dl was present in 25 females (44.6%) and 18 males (40.9%), and

Table 1 : **Correlation of haemoglobin levels with age in cases**

Age group (in years)	Total no. of patients (n=100)	Haemoglobin (in gm/dl)		
		< 6.0	**6.0-9.0**	**> 9.0**
11-20	18	7 (38%)	6 (33%)	5 (27.7%)
21-30	29	9 (31%)	15 (51.7%)	5 (17.2%)
31-40	32	7 (21.8%)	15 (46.8%)	10 (31.2%)
41-50	21	6 (28.5%)	7 (33.3%)	8 (38%)
Total	100	29 (29%)	43 (43%)	28 (28%)

Table 2 : **Correlation of haemoglobin levels with sex in cases**

Sex	Number (n=100)	Haemoglobin (in gm/dl)		
		< 6.0	**6.0-9.0**	**> 9.0**
Male	44	9 (20.4%)	18 (40.9%)	17 (38.6%)
Female	56	20 (35.7%)	25 (44.6%)	11 (19.6%)
Total	100	29 (29%)	43 (43%)	28 (28%)

Table 3 : **Various Basic parameters in patients of iron deficiency anaemia and controls**

Parameters	Cases (n=100)	Controls (n=100)	p-value
Age (in years) Mean ± SD	30.79 ± 9.57	31.05 ± 9.71	> 0.05 (NS)
Gender			> 0.05(NS)
Male	44	44	
Female	56	56	
Dietary Pattern			> 0.05 (NS)
Veg	70	76	
Mixed	30	24	

NS : Not significant

haemoglobin > 9gm/dl was present in 11 females (19.6%) and 17 males (38.6%). There was no gender wise difference found. ***(Table 2)***

Out of total 100 cases 70% were vegetarians and 30% were on mixed diet.Out of total 100 controls 76% were vegetarians and 24% were on mixed diet.The relationship between anaemia and dietary practices was not statistically significant (p>0.05). ***(Table 3)***

The mean serum total cholesterol levels were significantly lower (P < 0.01) in cases (122.02 mg/dl) compared to controls (178.9 mg/dl). The effect of anemia on serum total cholesterol was very large. Mean serum HDL levels were significantly lower (P < 0.01) in cases (30.5 mg/dl) compared to controls (38.43 mg/dl). Mean serum LDL levels were significantly lower (P < 0.01) in cases (81.38 mg/dl) compared to controls (116.5 mg/dl). Mean serum triglyceride levels were significantly lower (P < 0.01) in cases (108.9 mg/dl) as compared to controls (130.7 mg/dl). The mean total cholesterol / HDL ratio was 4 in cases and 4.67 in controls (P value < 0.01).The mean LDL / HDL ratio was 2.66 in cases and 3.03 in controls. (P value < 0.01). Hematological parameters such as haemoglobin, serum iron, transferrin saturation and serum ferritin levels were found to besignificantly (< 0.001) decreased in IDA cases compared to controls. Total iron binding capacity level was significantly (<

Table 4 : **Baseline hematological and lipid parameters of iron deficiency anemia patients and controls**

Parameters	Cases (n=100)	Control (n=100)	p-value
Lipids			
Mean Total cholesterol	122.02 ± 27.47	178.91 ± 11.18	< 0.001
Mean HDL	30.5 ± 4.39	38.43 ± 3.59	< 0.001
Mean LDL	81.38 ± 19.33	116.53 ± 7.42	< 0.001
Mean TG	108.93 ± 19.95	130.74 ± 16.93	< 0.001
TC / HDL	4.00 ± 0.76	4.67 ± 0.34	< 0.001
LDL / HDL	2.66 ± 0.40	3.03 ± 0.30	< 0.001
Hematological			
Hb (gm/dl)	8.59 ± 1.42	13.27 ± 1.34	< 0.001
Sreum iron (ug/dl)	38.33 ± 6.22	95.14 ± 18.58	< 0.001
TIBC	389.01 ± 40.56	291.72 ± 25.02	< 0.001
TS (%)	10.33 ± 1.91	50.4 ± 30.33	< 0.001
Serum ferritin (ug/dl)	8.80 ± 3.4	51.4 ± 30.0	< 0.001

Table 5 : **Correlation of Lipid profile with severity of Anaemia**

Lipid parameters (in mg/dl)	Haemoglobin (in gm/dl)			p-value
Mean value	**< 6**	**6-9**	**> 9**	
TC	92.27 ± 12.61	123.97 ± 17.24	149.82 ± 19.56	< 0.001
HDL	26.10 ± 3.18	31.20 ± 3.17	33.96 ± 3.26	< 0.001
LDL	59.13 ± 11.10	86.13 ± 12.73	97.10 ± 12.88	< 0.001
TG	90.15 ± 21.86	114.79 ± 10.88	118.96 ± 16.09	< 0.001
TC / HDL	3.56 ± 0.58	4.03 ± 0.86	4.41 ± 0.46	< 0.001
LDL / HDL	2.26 ± 0.33	2.75 ± 0.30	2.86 ± 0.34	< 0.001

0.001) increased in IDA cases compared to controls. ***(Table 4)***

The mean serum total cholesterol levels were significantly lower (P < 0.01) in cases with Hb less than 6 gm/dl (92.27 mg/dl), as compared to cases with Hb more than 9 mg/dl (149.82 mg/dl). Mean serum HDL levels were significantly lower (P < 0.01) in cases with Hb < 6 gm/dl (26.10 mg/dl), as compared to cases with Hb > 9 mg/dl (33.96 mg/dl). The mean serum LDL levels were significantly lower (P < 0.01) in cases with Hb < 6 gm/dl (59.13 mg/dl), compared to cases with Hb > 9 mg/dl (97.10 mg/dl). Mean serum triglyceride levels were significantly lower (P < 0.01) in cases with Hb < 6 gm/dl (90.15 mg/dl), compared to cases with Hb > 9 mg/dl (118.96 mg/dl). ***(Table 5)***

Discussions :

Iron deficiency is the world's most widespread nutritional disorder regardless of age, gender and socioeconomic status, affecting both developed and developing countries. WHO has estimated that about a third of world population is suffering from anemia with Iron deficiency affecting over twice as many.

Dyslipidemia is a known modifiable risk factor for coronary artery disease, cerebrovascular disease and peripheral vascular disease. It is commonly found in Asian Indians where hypertriglyceridemia and low HDL cholesterol levels are widely prevalent as components of metabolic syndrome. A close relationship has been found between serum

lipoprotein abnormalities and the risk of atherosclerosis.

The relationship between iron states and atherosclerosis has long been a topic of debate in the literature. It has been suggested that iron plays an important role in the pathogenesis of atherosclerosis, primarily by acting as a catalyst in the formation of powerful free radicals which subsequently modify LDL cholesterol. Since oxidation of low-density lipoprotein (LDL) cholesterol is important in atherosclerosis, and oxidation is catalyzed by iron, it has been hypothesized that the lower iron stores in women reduce their risk of coronary heart disease through lessened lipid peroxide[2]. Though the lipid abnormalities and iron deficiency are commonly encountered health problems, the number of studies comparing the association of both these abnormalities are few in number and varied in the results and conclusions.

Lipids and red blood cells do not interact directly. It is proposed that in conditions of anemia, the ensuing erythropoiesis leads to increased cholesterol uptake by certain types of white blood cells. Anemia also leads to haemo-dilution thereby reducing the cholesterol concentrations (the increased volume of serum in anemia carrying the same totalload of cholesterol)[3,4,5]. It is also postulated that due to the reduced red cell mass there could be unused iron which may affect the liver cell function; thereby resulting in reduced levels of cholesterol as most of the cholesterol is produced by the liver cells[6].

Other possibilities are increased utilization of cholesterol by proliferating cells, decreased endogenous synthesis of cholesterol by the liver due to decreased liver oxygenation, elevated levels of granulocyte - macrophage colony stimulating factor and enhanced receptor mediated removal of LDL in the bone marrow[7,8]. However the cause and effect relationship of these two conditions is only speculative and the exact mechanism is not yet confirmed.

In our study,100 cases and 100 age and sex matched controls were taken. The mean total cholesterol in cases and controls were 122.02 mg/dl and 178.91 mg/dl respectively, mean HDL in cases and controls were 30.5 mg/dl and 38.4 mg/dl respectively, mean LDL in cases and controls were 81.38 mg/dl and 116.53 mg/dl respectively and mean triglyceride in cases and controls were 108.9 mg/dl and 130.7 mg/dl respectively. All values were significantly decreased in cases compared to controls. There was a larger reduction in mean total cholesterol, HDL, LDL, and triglyceride levels, with increased severity of anemia. In a study carried out by **Sandeep N. et al**[9] in 2014, 100 cases and 200 age and sex matched controls in age group of 18 to 40 years were included. Out of total 100 cases 49 were males and 51 were females. Out of total 200 controls 96 were males and 104 were females. There was no gender wise difference found. The mean total cholesterol (129.1 vs 171.4), HDL (30.6 vs 36.6), LDL (77.6 vs 115.3), VLDL (20.3 vs 26.7) and triglyceride (106.1 vs 124.6) levels, were significantly decreased in cases compared to controls. There was a larger reduction in mean total cholesterol, HDL, LDL, VLDL and triglyceride levels, with increased severity of anemia. In a study carried out by **Sivapriya A. et al**[10] found that mean serum cholesterol level was significantly ($p < 0.001$) reduced in study group (144.975 mg/dl) as compared with control group (171.925 mg/dl). In a study carried out in premenopausal women by **Ozdemir et al**[4] found that the mean levels of total and LDL cholesterol of anemic women were lower than those of non anemic controls (173.6 ± 39.3 vs 205.7 ± 36.0, $P = 0.001$, 105.3 ± 32.7 vs 135.6 ± 31.3 mg/dL, $P < 0.001$, respectively). In a study carried out by **Dhungat M. P. et al**[6] in 2014 total 50 cases and 50 age and sex match controls were included. Maximumnumbers of patients were in the age group of 26 to 45 years. Out of total 50 cases 26 were males and 24 were females and out of 50 controls 28 were males and 22 were females. There was no gender wise significant difference ($p > 0.05$).The serum total cholesterol (T.Chol), serum triglycerides (TG) and low density lipoprotein cholesterol (LDL-C) levels were significantly lower in patients with IDA as compared to matched controls with normal hemoglobin levels ($p < 0.001$). The high density lipoprotein cholesterol (HDL-C) values did not

show any statistically significant difference in the two groups (p = 0.982). Thus our results are consistent with the results of previously published studies. Our study differs from the studies by**Antappanavar V. B. et al[1], Verma U. et al[5], Merono T. et al[11]** in Turkish children in that the levels of TC, TG, LDL, VLDL were significantly raised in patients suffering from IDA compared to the age and sex matched control patients.

Conclusion :

Our study as well as the other studies concludes that there is a definite correlation between anaemia and lipid abnormalities. **Framingham heart study** states that both increase and decrease in level of serum cholesterol increases the risk for coronary heart disease and the desirable range is 160-199 mg/dl. It is hypothesized that low hemoglobin exert an additional protective effect against atherosclerotic heart disease by lowering lipid levels. But anemia can cause severe life threatening conditions like angina, cardiac failure etc. So to maintain low blood cholesterol level, anemia is not a healthy way to obtain this result and the desirable cholesterol level can be maintained by diet, exercise and other lifestyle modifications. So in patients with anemia the lipid levels should be interpreted with caution. Both reductions in hemoglobin and blood cholesterol level can lead to various medical problems. To maintain low blood cholesterol level anemia cannot be promoted[4].

References :

1. 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.
2. B. de Valk, J. J. M. Marx. Iron, Atherosclerosis, and Ischemic Heart Disease. Arch Intern Med. 1999;159:1542-1548.
3. Nnodim JK, Opara AU, Nwanjo HU, et al. Plasma lipid profile in sickle cell disease patients in Owerri ,Nigeria. Pakistan Journal of nutrition 2012;11: 64-5.
4. Ozdemir A, Sevinç C, Selamet U, Türkmen F. The relationship between iron deficiency anemia and lipid metabolism in premenopausal women. Am J Med Sci. 2007 ;334(5):331-3.
5. Verma U, Shankar N, Madhu SV. Relationship between iron deficiency anaemia and serum lipid levels in Indian adults. J Indian Med Assoc. 2010;108(9):555-8,562.
6. Dhungat MP, Dhungat PP, Bhoge D. Relationship between iron deficiency anaemia and serum lipid levels in Indian rural population. Transworld Medical Journal. 2014;2(3):160-164.
7. Zorca S, Freeman L, Hildesheim M, Allen D, Remaley AT, Taylor JG 6th, Kato GJ. Lipid levels in sickle-cell disease associated with hemolytic severity, vascular dysfunction and pulmonary hypertension .Br J Haematol. 2010; 149(3): 436-45.
8. Cabrera MA, de Andrade SM, Dip RM. Lipids and all-cause mortality among older adults: a 12-year follow-up study. The Scientific World Journal. 2012 May 1;2012.
9. Sandeep N, Rao VD, Hanumaiah A, Rampure D. Lipid Profile Changes in Anemia. TransworldMedical Journal. 2014;2(1):29-32.
10. Sivapriya. A, Santhanalashmi. L. Effect of Anaemia on Serum Cholesterol Level in Middle Aged Women. International Journal of Advanced Research, ISSN 2320-5407, Volume 3, Issue 11, 2015 pp 1462-1465.
11. Tanzer F, H_zel S, Çetinkaya Ö, Sekreter E. Serum free carnitine and total triglycerid levels in children with iron deficiency anemia. International journal for vitamin and nutrition research. 2001 Jan 1;71(1):66-9.