A STUDY OF LIPID PROFILE IN ANEMIA PATIENTS- CASE-CONTROL STUDY IN INDIAN PATIENTS DONE IN THANJAVUR MEDICAL COLLEGE, TAMIL NADU

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ABSTRACT

BACKGROUND

Anaemia is a chronic nutritional health problem in India. Though there are plenty of causes for anaemia, iron deficiency anaemia is the most common cause of anaemia. As we all know, elevated serum lipids have a significant correlation with the risk of atherosclerosis, which in turn causes coronary artery disease, cerebrovascular disease and peripheral vascular disease, thus increasing morbidity and mortality worldwide. But, in the same way, low level of lipids in serum also cause some serious illness like depression, cancers, haemorrhagic stroke, aortic dissection and other metabolic abnormalities. Anaemia, irrespective of its cause produce decrease in serum lipid levels through various mechanisms. This study is conducted to assess the lipid profiles in various types of anaemia.

The aim of the study is to study lipid profile of anaemic patients as compared with age and sex matched controls. To correlate, if type of anaemia has any effect on lipid profile and to study if severity of anaemia is associated with changes in various lipid subfractions.

MATERIALS AND METHODS

This is a case-control study, which has been carried out in the Department of Internal Medicine, TMCH, Thanjavur, from January 2017 to June 2017.

RESULTS

Cases younger than 50 years were found to be more likely to have severe anaemia. Fatigue and pallor were the most common clinical features. Clinical features were more common among cases with severe anaemia. The mean serum total cholesterol levels were significantly lower ($P<0.01$) in cases (130.2 mg/dL) as compared to controls (172.4 mg/dL). The effect of anaemia on the total cholesterol levels was very large. The mean serum HDL levels were significantly lower ($P<0.01$) in cases (30.0 mg/dL) as compared to controls (38.9 mg/dL). The effect of anaemia on the HDL levels was large. The mean serum LDL levels were significantly lower ($P<0.01$) in cases (78.7 mg/dL) as compared to controls (111.1 mg/dL). The effect of anaemia on the LDL levels was very large. The mean serum VLDL levels were significantly lower ($P<0.01$) in cases (20.6 mg/dL) as compared to controls (24.0 mg/dL). The effect of anaemia on the VLDL levels was mild. The mean serum triglyceride levels were significantly lower ($P<0.01$) in cases (109.1 mg/dL) as compared to controls (123.5 mg/dL). The effect of anaemia on the triglyceride levels was mild. The mean total cholesterol/HDL ratio was significantly lower ($P<0.05$) in cases (4.34) as compared to controls (4.43). The effect of anaemia on TC/HDL ratio was mild. The mean LDL/HDL ratio was significantly lower ($P<0.01$) in cases (2.6) as compared to controls (2.85). The effect of anaemia on LDL/HDL ratio was mild. There was a larger reduction in mean total cholesterol, HDL, LDL, VLDL and triglyceride levels alone with TC/HDL and LDL/HDL ratios with increased severity of anaemia ($P<0.05$). Type of anaemia did not have a significant effect on lipid levels ($P>0.05$).

CONCLUSION

Younger cases were more likely to have more severe anaemia. There was no relation between sex and severity of anaemia. Dimorphic anaemia was the most commonly seen type of anaemia. Most cases had mild-to-moderate anaemia. The most common presenting symptom was fatigue. Patients with severe anaemia were more likely to be symptomatic. Vegetarians were more likely to have more severe anaemia. Pallor was the most common finding on general physical examination. Cases with more severe anaemia were more likely to have findings on general physical examination. The mean pulse rate was higher in cases. The mean pulse rate was higher in cases with severe anaemia. The mean blood pressure and BMI were lower in cases with severe anaemia. The most common findings on systemic examination were venous hum and flow murmurs. Features suggestive of hyperdynamic state of circulation and congestive cardiac failure were only seen in cases with severe anaemia. The mean total cholesterol, HDL, LDL, VLDL and triglyceride levels along with TC/HDL and LDL/HDL ratios were significantly decreased in cases compared to controls. There was a larger reduction in mean total cholesterol, HDL, LDL, VLDL and triglyceride levels along with TC/HDL and LDL/HDL ratios with increased severity of anaemia. The type of anaemia did not have a significant effect on the mean lipid levels.

KEYWORDS

Lipid Profile in Anaemia, Dyslipidaemia, Iron Deficiency Anaemia.

HOW TO CITE THIS ARTICLE: Vetrivel S, Ganesan C, Kannan VP. A study of lipid profile in anemia patients- Case-control study in Indian patients done in Thanjavur Medical College, Tamil Nadu. J. Evid. Based Med. Healthc. 2017; 4(67), 3989-4000. DOI: 10.18410/jebmh/2017/798

Financial or Other, Competing Interest: None.
Submission 17-07-2017, Peer Review 24-07-2017,
Acceptance 16-08-2017, Published 18-08-2017.
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DOI: 10.18410/jebmh/2017/798

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BACKGROUND

Research studies have generated considerable novel information about the effect of serum lipids on heart disease and vascular disease. Elevated serum lipids have a significant correlation with the risk of atherosclerosis, which in turn causes coronary artery disease, cerebrovascular disease and peripheral vascular disease, thus increasing morbidity and mortality worldwide. The most common nutritional disorder encountered in India is iron deficiency anaemia, although there are plenty of reasons attributable to anaemia. There are studies reporting the beneficial effect of anaemia on lipid profile. Type of anaemia does not influence the lowering of lipid levels. Decreased serum cholesterol levels is not due to specific lowering of any particular lipoprotein family, instead it is observed that there occurs a proportionate decrease in all major lipoprotein families. It's interesting that this fall in serum lipids in anaemic patients may decrease the risk of coronary artery disease - a disease which kills number of Indians every year. The mechanism by which anaemia causes a fall in serum lipid level is still a grey area. It might be due to dilution effect, increased cholesterol utilisation by actively dividing cells, decreased liver oxygenation leading to reduced endogenous cholesterol synthesis, increased levels GM-CSM and finally in the bone marrow-enhanced receptor mediated uptake of LDL. Once anaemia is corrected, lipid profile is normalised.

Objectives- To evaluate demography and clinical features in anaemia cases. To study lipid profile of anaemic patients as compared with age and sex matched controls. To correlate if type of anaemia has any effect on lipid profile. To study if severity of anaemia is associated with changes in various lipid subfractions.

MATERIALS AND METHODS

This is a study which has been carried out in the Department of Internal Medicine, Thanjavur Medical College and Hospital, Thanjavur.

Source of Data- The data for this study was collected from patients who presented to Thanjavur Medical College and Hospital, Thanjavur, either on inpatient or outpatient basis.

Inclusion Criteria- All proven cases of anaemia. Men- Hb<13 g%; women- Hb<12 g%.

Exclusion Criteria

1. Children below 14 years.
2. Obesity/overweight- BMI >25 kg/m2.
3. Malnutrition- BMI <19 kg/m2 or serum total protein <6 g/dL or serum albumin <3.5/dL.
4. Known case of diabetes mellitus or RBS >200 mg/dL or FBS >126 mg/dL or PPBS >200 mg/dL.
5. Known hypertensive or blood pressure persistently more than 140/90 mm of Hg on three consecutive readings taken on different days.
6. Alcoholics.
7. Smokers.
8. Known case of AIDS.
9. Known case of ischaemic heart disease/cerebrovascular accident.
10. History of recent blood loss.
11. History of use of steroids, oral contraceptives, diuretics, beta-blockers.
12. Urine albumin ≥+.
13. Blood urea >40 mg% or serum creatinine >1.4 mg%.
14. SGOT >40 U/L or SGPT >40 U/L or serum alkaline phosphatase >250 U/L.
15. TSH >7.0 µU/mL or TSH <0.3 µU/mL.

Clinical Evaluation- A detailed history was obtained from the subjects of the study with special emphasis on age, sex and occupation; nonspecific symptoms of anaemia like fatigability, dyspnoea, giddiness, palpitations and angina; symptoms suggestive of a specific cause for anaemia like pica, dysphagia, abdominal pain, bony pain, fever, loss of appetite, weight loss, jaundice, bleeding, melaena, haemoglobinuria, menorrhagia, pregnancy and postmenopausal bleeding. Past history of disorders associated with dyslipidaemia or anaemia was obtained, including diabetes mellitus, hypertension, ischaemic heart disease,[1,2] cerebrovascular accident, AIDS, recent blood loss and gallstones. Dietary habits[3] and habits like alcoholism and tobacco smoking was ascertained. History of intake of drugs affecting lipid levels, such as oral contraceptives, beta blockers, diuretics, steroids and NSAIDs was obtained. Family history of anaemia, jaundice and gallstones was also obtained. Each patient was subjected to a detailed general physical examination with special emphasis on pallor, koilonychias, icterus, pedal oedema, lymphadenopathy, glossitis, angular stomatitis, petechiae, haemolytic facies, ankle ulcers, perioral pigmentation and knuckle pigmentation. Pulse, blood pressure, weight, height and body mass index was measured. Thorough systematic examination was made of the cardiovascular system to look for the presence of elevated JVP, venous hum, cardiomegaly, S3 and flow murmur. The respiratory system

was examined to look for evidence of pulmonary congestion. Abdomen was examined to look for organomegaly. The central nervous system was examined for confusion, muscular weakness, deep tendon reflexes, vibration sense, position sense and Romberg's sign.

Investigations- Venous blood was drawn for investigations like complete haemogram, random blood sugar, blood urea, serum creatinine, liver function tests and thyroid stimulating hormone levels. A urine sample was obtained for urine analysis, including albumin, sugar and microscopy. Fasting venous blood sample (>12 hours) was obtained for estimation of lipid profile. T3 and T4 levels, fasting and postprandial (two hours after an oral dose of 75 g of glucose) blood sugar levels and bone marrow aspiration cytology was done in selected cases based on clinical assessment. Complete haemogram was performed using the Sysmex automated analyser. Haemoglobin levels were confirmed by the colorimetric method. Differential count and peripheral smear was done manually using Leishman's stain by a qualified pathologist. Urine albumin and sugar was estimated by dipstick method. Urine microscopy was done manually by a qualified pathologist. Biochemical analyses were done using the fully automated Technicon RA-XT system by Bayer. TSH, T4 and T3 were estimated using the chemiluminescence method on the fully automated ADVIA Centaur System by Bayer. Estimation of total cholesterol, HDL and triglycerides was done with the commercially available AUTOPAK cholesterol kit on Technicon RA-XT system.

VLDL was calculated using the formula, VLDL=triglyceride/5. LDL cholesterol was calculated using the Friedewald's equation. LDL=Total cholesterol-((triglycerides/5) + HDL) mg/dL.

Controls- Fifty non-anaemic age and sex matched subjects were selected and screened for compliance with the exclusion criteria. Complete haemogram, lipid profile and other investigations were performed on them.

Statistical Methods[4,5]

Student's t-test has been used to test the homogeneity of age between case and control. Chi-square test has been used to find the homogeneity of sex between case and control. Student's t-test has been used to find the significance of lipid profiles between case and controls. Analysis of variance has been used to find the significance of mean lipid profiles when there are more than 2 groups. Mann-Whitney U test has been carried to find the significance between case and control for TC/HDL and LDL/HDL ratio. Kruskal-Wallis test has been used to find significance of TC/HDL and LDL/HDL ratio when there are more than 2 groups. Effect size due to Cohen's D has been computed to find the extent of effect of anaemia on lipid profiles; 0 <d <0.20 no effect, 0.20 <d <0.50 mild effect, 0.50 <d <0.80 moderate effect, 0.80 <d <1.20 large effect and d>1.20 very large effect.

Statistical Software- The statistical software used for the analysis of the data was SPSS 11.0 and Systat 8.0. Microsoft Word and Excel have been used to generate figures and tables.

RESULTS

Study Design- A case-control study consisting of 50 anaemic cases and 50 normal subjects was undertaken to study the clinical presentation of anaemic cases and also to investigate the relationship between anaemia and lipid profile.

Age- The cases and controls were matched for age. Majority of the cases were middle aged (30-60). The youngest case was 14 years old. The oldest was 75 years old.

Age in Years	Case Haemoglobin levels (in gm/dl) n=80				Control (n=50)
	< 6 (n=9)	6-9 (n=19)	> 9 (n=22)	Total (n= 50)	
≤20	1 (11.17)	1 (5.3)	2 (9.1)	4	4
21-30	2 (22.2)	5 (26.3)	3 (13.4)	10	10
31-40	2 (22.2)	5 (26.3)	4 (18.2)	11	11
41-50	1 (11.1)	3 (15.7)	2 (9.1)	6	6
51-60	1 (11.1)	2 (10.5)	7 (31.8)	10	10
61-70	1 (11.1)	2 (10.5)	3 (13.6)	6	6
>70	1 (11.1)	1 (2.3)	1 (4.5)	3	3

Table 1. Age Distribution with Haemoglobin Levels in Cases and Controls

Inference- Samples are age matched (p>0.05) anaemic cases <50 years of are 2.42 times more to have Hb levels <6 g/dL (p=0.107) and anaemic cases >50 years of age are 4.31 times more likely to have >9 Hb g/dL (p<0.01) (Table 1).

Sex- The cases and controls were matched for sex. The cases consisted of 22 males and 28 females. Sex was not associated with haemoglobin levels.

Sex	Case Haemoglobin levels (in gm/dl)				Control (n=50)
	<6 (n=9)	6-9 (n=19)	>9 (n=22)	Total (n=100)	
Male	3 33.3	9 47.4	10 95.5	22	22
Female	6 66.7	10 52.6	12 54.5	28	28

Table 2. Sex Distribution between Case and Controls

Inference- Samples are sex matched (P>0.05) sex is not statistically associated with haemoglobin levels (P>0.05) (Table 2) (Figure 1).

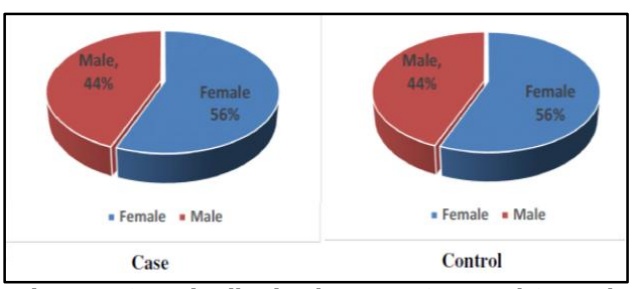

Figure 1. Sex Distribution between Case and Controls

Distribution of Cases According to Type and Severity of Anaemia[6]

A total of 50 cases were included in this study. 20 cases had Dimorphic Anaemia (DM) according to peripheral smear, 12 cases had microcytic hypochromic (MH) anaemia, 9 cases had Normocytic Hypochromic (NH) anaemia and 5 cases had a Normocytic Normochromic (NN) blood picture. Out of the 4 cases grouped together as 'others' for the purpose of analysis, 3 cases had megaloblastic anaemia, 2 cases had pancytopenia and one case each had chronic myeloid leukaemia and leukoerythroblastic blood picture. A total of 9 cases had haemoglobin less than 6 g/dL, 19 cases had haemoglobin between 6 and 9 g/dL and 22 cases had haemoglobin more than 9 g/dL (Table 3).

Hb (in gm/dl)	**Type of Anaemia**					
	DM	**MH**	**NH**	**NN**	**Others**	**Total**
<6	7	3	-	-	2	12
6-9	10	7	1	-	2	20
>9	3	2	8	5	0	18
Total	**20**	**12**	**9**	**5**	**4**	**50**

Table 3. Distribution of Cases According to Type and Severity of Anemias

Symptoms- The most common presenting symptom was easy fatigability, which was present in 25 cases. The next common symptoms were dyspnoea (15 cases), palpitations (16 cases) and giddiness (12 cases). Other symptoms were loss of appetite (4 cases), fever (2 cases), weight loss (2 cases), angina[7] (2 cases), dysphagia, jaundice and menorrhagia (3 cases each), bony pain and bleeding (1 case) each. Not seen in the study group were pica, abdominal pain, melaena, haemoglobinuria and pregnancy (Figure 2).

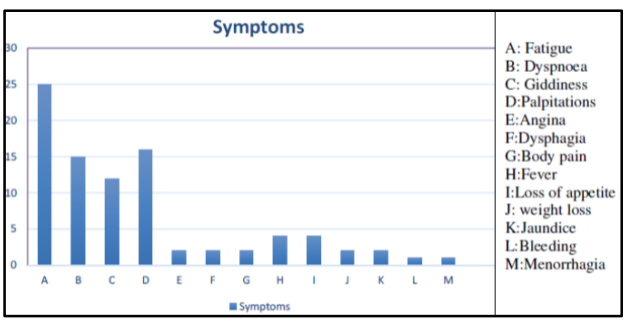

Figure 2. Symptoms of Anaemia

Presenting illness	Haemoglobin levels in cases (in gm/dl)			
	Total (n=50)	<6 (n=9)	6-9 (n=19)	>9 (n=22)
Fatigue	25	8 (88.9)	73.7 (14)	3 (13.6)
Dyspnoea	15	7 (77.8)	31.2	2 (9.09)
Giddiness	12	6 (66.7)	5 (26.3)	1 (4.5)
Palpitation	16	8 (88.9)	5 (26.3)	3 (13.6)
Angina	2	2 (22.2)	-	-
Pica	-	-	-	-
Dysphagia	2	2 (22.2)	-	-
Abd pain	1	1 (11.1)	-	-
Bony pain	2	-	-	2 (9.0)
Fever	4	1 (11.1)	1 (5.3)	2 (9.0)
Loss of appetite	4	2 (22.2)	1 (5.3)	1 (4.5)
Wt loss	3	2 (22.2)	1 (5.3)	-
Jaundice	2	1 (11.1)	1 (5.3)	-
Bleeding	1	1 (11.1)	-	1 (2.7)
Malaena	-	-	-	-
Haemoglobinuria	-	-	-	-
Menorrhagia	2	2 (22.2)	1 (5.3)	-
Pregnancy	-	-	-	-
Post menopausal bleed	1	1 (11.1)	-	-

Table 4. Symptoms and Severity of Anaemia

Symptoms and Severity of Anaemia- Cases with more severe anaemia were found to be more likely to have symptoms. All cases with haemoglobin less than 6 g/dL had at least one symptom, while out of 22 cases with haemoglobin more than 9 g/dL, only 8 cases (36.4%) had at least one symptom. Most symptoms were found more frequently in cases with more severe anaemia. 88.9% of cases with haemoglobin less than 6 g/dL complained of fatigue compared to just 13.6% of cases with haemoglobin more than 9 g/dL. Fever, bony pain and bleeding were the only symptoms, which were found more frequently in cases with less severe anaemia. Cases with severe anaemia also had more number of symptoms. Cases with haemoglobin

less than 6 g/dL had an average of 3.7 symptoms compared to cases with haemoglobin more than 9 g/dL who had only an average of 0.6 symptoms (Table 4).

Symptoms and Type of Anaemia- Nonspecific symptoms such as fatigue, dyspnoea, giddiness, palpitations, fever, loss of appetite and loss of weight were equally frequent in the different types of anaemia except normocytic hypochromic anaemia and cases with normocytic normochromic blood picture. This is possibly due to the fact that these cases had less severe anaemia. Symptoms like angina, dysphagia and menorrhagia were seen only in patients with dimorphic anaemia and microcytic hypochromic anaemia. Bony pain and bleeding was seen only in one patient with chronic myeloid leukaemia.[8,]

Personal History- 8 cases were vegetarian. 44.5% (4 cases out of 9) of all cases with haemoglobin less than 6 g/dL were vegetarian compared to 27.38% (6 cases out of 22) of all cases with haemoglobin more than 9 g/dL. Vegetarians were more likely to have dimorphic anaemia (55.6%) compared to the other types of anaemia (5.6% to 22.2%). None of the cases had a history of alcohol use or tobacco smoking.

Drug History- None of the cases had a history of intake of oral contraceptives, beta blockers, diuretics, steroids or nonsteroidal anti-inflammatory drugs.

Family History- Four cases had a family history of anaemia, out of whom, 3 had microcytic hypochromic anaemia. Five cases had a family history of jaundice, out of whom, 4 had dimorphic anaemia.

General Physical Examination- The most common finding on general physical examination was pallor, which was present in 30 cases. Also, seen were glossitis (10 cases), koilonychias (7 cases), angular stomatitis (5 cases), knuckle pigmentation (3 cases), pedal oedema (4 cases), icterus (1 cases), lymphadenopathy (1 case) and perioral pigmentation (1 case). None of the cases had petechiae, haemolytic facies or ankle ulcers.

GPE	Haemoglobin levels in cases (in gm/dl)			
	Total (n=50)	<6 (n=9)	6-9 (n=19)	>9 (n=23)
Pallor	30	9 (100.0)	17 (89.5)	4 (18.2)
Kollonyehia	10	8 (88.9)	2 (10.5)	-
Leterus	2	1 (11.1)	1 (5.3)	-
Pedal oedema	4	3 (38.3)	1 (5.3)	-
Lymphadenopathy	1	-	1 (5.3)	-
Glossitis	10	6 (66.7)	4 (21.1)	-
Angular stomatitis	5	4 (44.4)	1 (5.3)	-
Peterchiae	0	0	0	-
Haemolytis facies	0	0	0	-
Ankle ulcers	0	0	0	-
Peri oral Pigmentation	1	1 (11.1)	0	-
Knuckle Pigmentation	3	2 (22.2)	1	-

Table 5. GPE and Severity of Anaemia

General Physical Examination and Severity of Anaemia- Cases with more severe anaemia were found to be more likely to have findings on general physical examination. All cases with haemoglobin less than 6 g/dL had at least one sign, while out of 2, 2 cases with haemoglobin more than 9 g/dL, only 6 cases (21.6%) had at least one sign. All signs were found more frequently in cases with more severe anaemia. 100% of cases with haemoglobin less than 6 g/dL had pallor and 66.7% had glossitis compared to just 21.1% and 0% in cases with haemoglobin more than 9 g/dL. Cases with severe anaemia also had more number of signs on general physical examination. Cases with haemoglobin less than 6 g/dL had an average of 2.8 signs compared to cases with haemoglobin more than 9 g/dL who had only an average of 0.2 signs (Table 6).

General Physical Examination and Type of Anaemia
Pallor was equally frequent in the different types of anaemia except normocytic hypochromic anaemia and cases with normocytic normochromic blood picture. This is possibly due to the fact that these cases had less severe anaemia. Koilonychia, lymphadenopathy, glossitis and angular stomatitis were seen only in cases with dimorphic anaemia and microcytic hypochromic anaemia. Knuckle pigmentation and perioral pigmentation was seen only in cases with megaloblastic anaemia and dimorphic anaemia (Table 7).

Symptoms		Types of Anaemia				
		DM (n=20)	MH (n=12)	NH (n=9)	NN (n=5)	Others 4
Pallor	30	18 (90.0)	10 (83.3)	3 (33.3)	-	4 (100)
Koilonychia	10	6 (30.5)	4 (33.3)	-	-	-
Ictercs	2	1 (5.0)	1 (8.3)	-	-	0 (14.3)
Pedal oedema	4	3 (15.0)	1 (8.3)	-	-	0 (28.6)
Lymphadenopathy	1		1 (8.3)	-	-	-
Glossitis	10	6 (30.0)	4 (33.3)	-	-	-
Angulaer stomatitis	5	3 (15.0)	2 (16.7)	-	-	-
Petechiae	0	-	-	-	-	-
Haemolytis facies	0	-	-	-	-	-
Ankle ulcers	0	-	-	-	-	-
Peri Oral Pigmentation	1	5.0	-	-	-	0 (14.3)
Knuckle Pigmentation	3	2 (10.05)	-	-	-	1 (25.0)

Table 6. GPE and Type of Anaemia

Pulse Rate- The mean pulse rate was 85.4/minute in cases and 83.7/minute in controls. The mean pulse rate was significantly increased (89.3/minute) in cases with haemoglobin less than 6 g/dL. There was no difference in mean pulse rate between the different types of anaemia except in the 'others' group, in whom it was significantly raised (96.3/minute).

Blood Pressure- The mean blood pressure was 121.2/76.3 mm of Hg in cases and 122.1/76.5 mm of Hg in controls. It was less in cases with haemoglobin, less than 6 g/dL (118.7/75.2 mm of Hg) compared to cases with haemoglobin more than 9 g/dL (122.7/77.3 mm of Hg). There was no significant difference in mean blood pressure in the different types of anaemia.

Body Mass Index- The mean body mass index was 21.5 kg/m2 in cases and 21.6 kg/m2 in controls. It was significantly decreased (20.9 kg/m2) in cases with haemoglobin less than 6 g/dL. There was no significant difference of mean BMI among the various types of anaemia.

	Case Haemoglobin levels (in gm/dl)				Control (n=50)
	< 6 (n=9)	6-9 (n=19)	>9 (n=22)	Total (n=50)	
Mean pulse rate	89.3 ± 12.8	83.6 ± 9.8	84.9 ± 7.5	85.4 ± 10.0	83.7± 16.9
Mean systolic blood pressure	118.7 ± 9.7	121.3 ±8.5	122.7 ± 10.4	121.2 ± 9.6	122.1 ± 15.2
Mean diastolic blood pressure	75.2 ± 7.9	76.1 ± 7.7	77.3 ± 9.0	76.3 ± 8.2	76.5 ± 8.4
Mean BMI	20.9 ± 1.5	22.0 ± 1.7	21.4 ± 1.6	21.5 ± 1.7	21.6 ± 1.6

Table 7. Pulse Rate, Blood Pressure and BMI with Severity of Anaemia

Inference- Increased mean pulse rate (p=0.082) as well as significantly decreased mean BMI (P<0.01), m is seen in cases with Hb <6 g/mL. Mean systolic and diastolic blood pressure are not significantly different (p>0.05) (Table 8) (Figure 3,4,5).

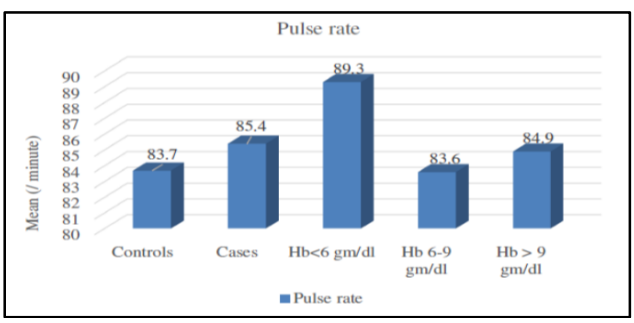

Figure 3. Pulse Rate with Severity of Anaemia

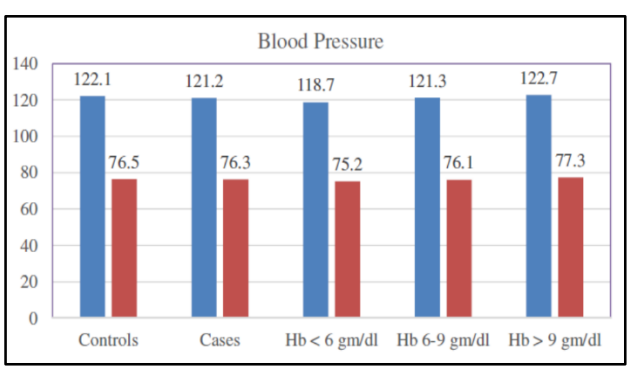

Figure 4. BP and Severity of Anaemia

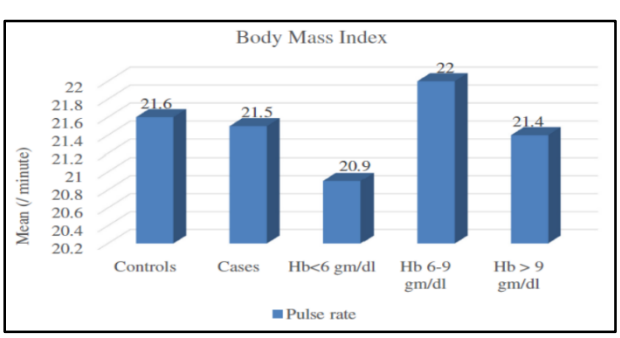

Figure 5. BMI and Severity of Anaemia

	Types of Anaemia				
	DM (n=40)	MH (n=25)	NH (n=18)	NN (n=10)	Others (n=7)
Mean pulse rate	85.0 ± 8.5	82.3 ±12.0	87.0 ± 7.5	84.1 ± 5.2	96.3 ± 14.9
Mean systolic	120.1 ± 9.8	122.3 ± 8.9	118.9 ± 8.3	126 ± 11.7	122.9 ± 9.5
Mean diastolic blood pressure	75.1 ± 6.7	75.6 ± 10.0	77.2 ± 8.3	79.0 ± 8.8	80.0 ± 8.2
Mean BMI	21.5 ± 1.7	21.4 ± 1.7	21.6 ± 1.8	21.4 ± 1.4	21.8 ± 1.9

Table 8. Pulse Rate, Blood Pressure and BMI with Type of Anaemia

Inference- Mean pulse rate significantly higher in the other group (P<0.05). Mean systolic and diastolic blood pressures are not significantly different (P>0.05). Mean BMI is not significantly different (P>0.05) (Table 9) (Figure 6).

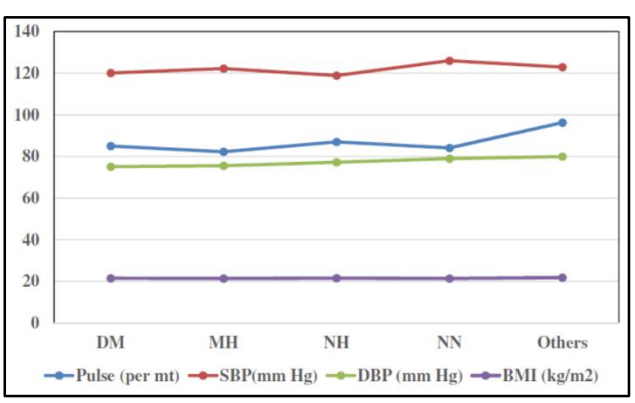

Figure 6. Pulse Rate, Blood Pressure and BMI with Type of Anaemia

Systemic Examination- The most common findings on systemic examination were venous hum and flow murmurs (4 cases each). Abdominal examination revealed 3 cases with splenomegaly and 2 cases with hepatomegaly. CNS findings were impairment of vibration sense (2 cases) and joint position sense (1 case) suggestive of peripheral neuropathy. Elevated JVP, cardiomegaly and basal crepitation's were seen in 2 cases each (Figure 7).

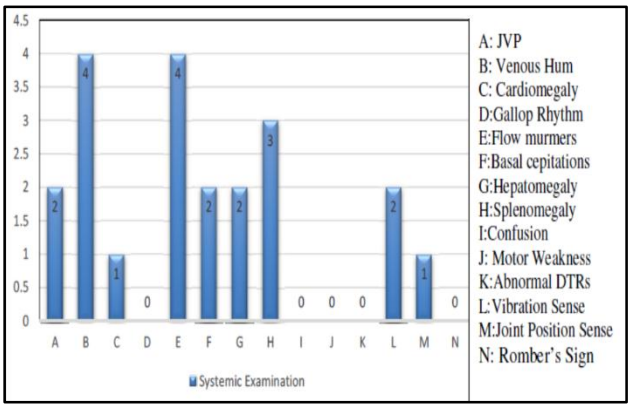

Figure 7. Systemic Examination

Systemic Examination and Severity of Anaemia

Cardiovascular and respiratory findings such as elevated JVP, venous hum, cardiomegaly, flow murmurs and basal crepitations were found only in cases with haemoglobin less than 6 g/dL with the exception of one case with haemoglobin between 6 and 9 g/dL who had a flow murmur. Impairment of vibration and joint position sense were also found only in cases with severe anaemia. Hepatomegaly and splenomegaly were found in all groups of cases equally (Table 10).

Systemic Examination	Haemoglobin levels in cases (in gm/dl)			
	Total (n=50)	<6 (n=9)	6-9 N=19	>9 22
CVS				
JVP	2	1 (11.1)	1 (5.3)	
Venous hum	4	3 (33.3)	1 (5.3)	
Cardiomegaly	1	1 (11.1)	-	
Gallop rhythm	-	-	-	
Flow murmur	4	3 (33.3)	1 (5.3)	
RS: Basal crepts	2	2 (22.2)	-	
P/A				
Hepatomegaly	2	1 (11.1)	1 (5.3)	0
Splennomegaly	3	2 (22.2)	1 (5.3)	0
CNS				
Confusion	-	-	-	-
Power	-	-	-	-
DTRs	-	-	-	-
Vibration		2 (22.2)	-	-
Position	2	1 (11.1)	-	-
Romberg's	1	-	-	-

Table 9. Systemic Examination and Severity of Anaemia

Systemic Examination and Type of Anaemia- Elevated JVP, venous hum, cardiomegaly, flow murmurs and basal crepitations were not found in cases with normocytic hypochromic anaemia and normocytic normochromic blood picture. This is possibly due to the fact that these cases had less severe anaemia. Hepatomegaly and splenomegaly was seen in all types of anaemia except cases with normocytic normochromic blood picture. Impairment of vibration and joint position sense was seen only in cases with dimorphic anaemia and megaloblastic anaemia (Table 11).

Symptoms		Types of Anaemia				
		DM (n=20)	MH (n=10)	NH (n=9)	NN (n=5)	Others (n=4)
CVS						
JVP	2	2 (10.0)	-	-	-	0 (28.6)
Venous hum	4	3 (15.3)	1 (8.3)	-	-	1 (26.0)
Cardiomegaly	1	1 (5.0)	-	-	-	0 (28.6)
Flow murmur	4	2 (10.0)	1 (8.3)	-	-	1 (50.0)
RS- Basal crepts	2	2 (10.0)	-	-	-	2 28.6
P/A						
Hepatomegaly	2	1 (5.0)	1 (8.3)	1 (5.6)	-	1
Splenomegaly	3	1 (5.0)	1 (8.3)	0	-	25.0
CNS						
Vibration	2	2 (10.0)	-	-	-	-
Position	1	1 (5.0)	-	-	-	-

Table 10. Systemic Examination and Type of Anaemia

Anaemia and Lipid Profile[9]

The mean serum total cholesterol levels were significantly lower (P<0.01) in cases (130.2 mg/dL) as compared to controls (172.4 mg/dL). The effect of anaemia on the total cholesterol levels was very large. The mean serum HDL levels were significantly lower (P<0.01) in cases (30.0 mg/dL) as compared to controls (38.9 mg/dL). The effect of anaemia on the HDL levels was large. The mean serum LDL levels were significantly lower (P<0.01) in cases (78.7 mg/dL) as compared to controls (111.1 mg/dL). The effect of anaemia on the LDL levels was very large. The mean serum VLDL levels were significantly lower (P<0.01) in cases (20.6 mg/dL) as compared to controls (24.0 mg/dL). The effect of anaemia on the VLDL levels was mild. The mean serum triglyceride[10] levels were significantly lower (P<0.01) in cases (109.1 mg/dL) as compared to controls (123.5 mg/dL). The effect of anaemia on the triglyceride levels was mild. The mean total cholesterol/HDL ratio was significantly lower (P<0.05) in cases (4.34) as compared to controls (4.43). The effect of anaemia on TC/HDL ratio was mild. The mean LDL/HDL ratio was significantly lower (P<0.01) in cases (2.6) as compared to controls (2.85). The effect of anaemia on LDL/HDL ratio was mild (Table 12) (Figure 8).

Lipid profile (mean ± SD)	Cases (n=50)	Controls (n= 50)	Significance by student t	Effect size (d)
Total Cholesterol	130.2 ± 28.0	172.4 ± 20.4	P <0.01**	1.64 (V. Large)
HDL	30.0 ± 6.3	38.2 ± 7.0	P <0.01**	1.12 (Large)
LDL	78.7 ± 24.0	111.1 ±16.5	P<0.01**	1.43 (V. Large)
VLDL	20.6 ±6.2	24.0 ± 6.2	P<0.01**	0.46 (Mild)
Triglycerides	102. 1± 31.4	123.5 ± 30.8	P<0.01**	0.46 (Mild)
TC/HDL ratio	4.34 ± 0.5	4.43 ± 0.7	P<0.05*M	0.27 (Mild)
LDL / HDL ratio	2.6 ± 0.7	2.85 ± 0.6	P<0.01*M	0.45 (Mild)

*Significant at 5% **Significant at 1% M-Mean Whitney U test

Table 11. Anaemia and Lipid Profile

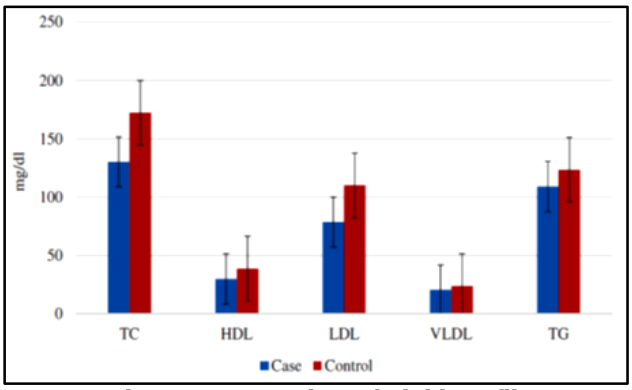

Figure 8. Anaemia and Lipid Profile

Severity of Anaemia and Lipid Profile

The mean serum total cholesterol levels were significantly lower (P<0.01) in cases with haemoglobin less than 6 g/dL (105.0 mg/dL), as compared to cases with haemoglobin more than 9 g/dL (154.7 mg/dL). The mean serum HDL levels were significantly lower (P<0.01) in cases with haemoglobin less than 6 g/dL (25.3 mg/dL) as compared to cases with haemoglobin more than 9 g/dL (35.5 mg/dL). The mean serum LDL levels were significantly lower (P<0.01) in cases with haemoglobin less than 6 g/dL (62.0 mg/dL) as compared to cases with haemoglobin more than 9 g/dL (96.8 mg/dL). The mean serum VLDL levels were significantly lower (P<0.01) in cases with haemoglobin less than 6 g/dL (18.0 mg/dL) as compared to cases with haemoglobin more than 9 g/dL (23.4 mg/dL). The mean serum triglyceride levels were significantly lower (P<0.01) in cases with haemoglobin less than 6 g/dL (94.4 mg/dL) as compared to cases with haemoglobin more than 9 g/dL (116.6 mg/dL). The mean serum total cholesterol/HDL ratio was significantly lower (P<0.05) in cases with Hb less than 6 g/dL (4.15) as compared to cases with Hb more than 9 g/dL (4.35). The mean serum LDL/HDL ratio was significantly lower (P<0.01) in cases with Hb less than 6 g/dL (2.45) as compared to cases with Hb more than 9 g/dL (2.72) (Table 13) (Figure 9).

Liqid profile (mean ± SD)	Hb < 6 gm/dl (n=9)	HB 6-9 gm/dl (n=19)	Hb > 9 gm/dl (n=22)	P value (ANOVA)
TC	105.0 ± 21.3	128.5 ± 22.6	154.7 ± 23.6	P <0.01**
HDL	25.3 ± 6.2	30.5 ± 6.4	35.5 ± 5.2	P <0.01**
LDL	62.0 ± 19.3	75.0 ± 21.5	96.8 ± 22.0	P <0.01**
VLDL	18.0 ± 7.4	21.8 ± 5.5	23.4 ± 5.9	P <0.01**
TG	94.5 ± 36.7	102.1 ± 27.9	116.6 ± 28.8	P <0.01**
TC/HDL	4.15 ± 0.7	4.21 ± 0.09	4.35 ± 0.7	P <0.05*K
LDL/HDL	2.45 ± 0.7	2.45 ± 0.7	2.72 ± 0.7	P <0.01*K

*Significant at 5% **Significant at 1% K- Kruskal Wallies test

Table 12. Severity of Anaemia and Lipid Profile

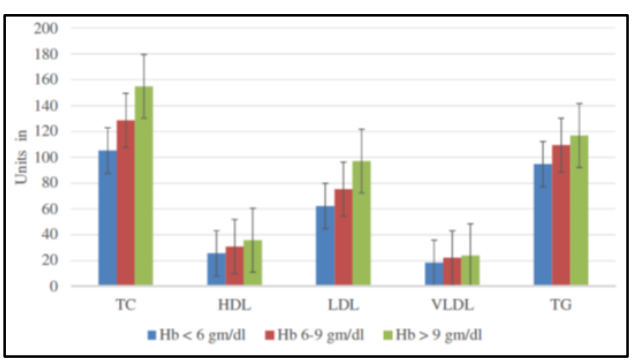

Figure 9. Severity of Anaemia and Lipid Profile

Type of Anaemia and Lipid Profile

Since the severity of anaemia was found to have a significant effect on the lipid profile, analysis of the effect of type of anaemia on lipid profile was done by further subdividing the types of anaemia on the basis of severity and comparing the lipid profile in groups having varying types of anaemia with similar severity. There was no significant difference (P>0.05) in the mean total cholesterol levels in different types of anaemia with similar levels of haemoglobin. There was no significant difference (P>0.05) in the mean HDL levels in different types of anaemia with similar levels of haemoglobin. There was no significant difference (P>0.05) in the mean LDL levels in different types of anaemia with

similar levels of haemoglobin. There was no significant difference (P>0.05) in the mean VLDL levels in different types of anaemia with similar levels of haemoglobin. There was no significant difference (P>0.05) in the mean triglyceride levels in different types of anaemia with similar levels of haemoglobin. There was no significant difference in the mean total cholesterol/HDL ratio (P>0.05) and mean LDL/HDL ratio (P>0.05) in different types of anaemia with similar levels of haemoglobin.

Inference- There is no statistically significant difference in lipid fractions between different types of anaemia (P>0.05) (Table 14).

Lipid Profile (mean ± SD)	Hb (in gm/dl)	Type of Anaemia					P Value (ANOVA)
		DM	MH	NH	NN	OTHERS	
TC In Mg/dl	<6	108.4 ± 19.3	106.6± 23.6	-	-	93.3 ± 25.9	P > 0.05
	6-9	125.8 ± 20.9	132.6 ± 26.2	113.0 ± 18.3	-	118.5 ± 2.1	P > 0.05
	>9	158.6 ± 22.5	143.6 ± 31.2	151.8 ± 23.6	163.6 ± 13.0	107.0± 0	P > 0.05
HDL (in mg/dl)	<6	21.6 ± 6.6	25.6 ± 3.6	-	-	248± 7.4	P > 0.05
	6.9	30.3 ± 6.1	28.2 ± 7.2	31.0 ± 0	-	30.0 ±9.9	P > 0.05
	>9	36.4 ± 4.2	32.8 ± 4.0	32.4 ± 4.9	36.4 ± 4.1	24. 0 ± 0[8]	P > 0.05
LDL (in mg/dl)	>6	65.7 ± 16.0	64.4 ± 22.5	-	-	44.5 ±22.4	P > 0.05
	6-9	74.3 ± 17.7	78.4 ±27.2	58.0 ±14.1	-	75.5 ±12.0	P > 0.05
	>9	79.3 ± 18.7	40.6 ± 32.3	93.0 ±23.0	104.4± 12.4	60.0 ± 0[8]	P > 0.05
VLDL (in mg/dl)	<6	18.6 ± 7.3	17.6 ± 5.3	-	-	25.0 ± 8.4	P > 0.05
	6-9	21.2 ± 5.5	23.1 ± 5.8	25.0 ± 4.2	-	21.0 ±0	P > 0.05
	>9	24.0 ± 5.0	20.2 ± 4.4	25.4 ±6.7	21.8 ±5.2	23.0 ± 0[8]	P > 0.05
TG(in mg/dl)	<6	81.6 ± 36.3	89.0 ± 27.3	-	-	124.8 ±41.1`	P > 0.05
	6-9	102.5 ± 27.8	115.7 ± 29.3	125.0 ± 21.2	-	103.5 ± 0.7	P > 0.05
	>9	113.2 ± 26.4	101.4 ± 23.4	126.6 ±32.4	109.5 ±25.7	114.0 ± o[8]	P > 0.05
TC /HDL	<6	5.0 ± 0.007	2.2± 1.0	-	-	3.8 ± 0.4	P > 0.05[K]
	6-9	4.1 ±0.08	4.3 ± 0.9	-	-	4.0 1.5	P > 0.05[K]
	>9	4.4 ± 0.7	4.4 ± 1.1	3.8 ±0.06	4.5 ± 0.5	4.5 0[8]	P > 0.05[K]
LDL HDL	<6	3.0 ± 0.6	2.8 ± 1.0	4.7 ± 0.8	-	1.8 ±0.6	P > 0.05[K]
	6-9	2.5 ± 0.06	4.7 ± 0.7	0.5	-	2.6 ± 1.2	P > 0.05[K]
	>9	2.1 ± 0.6	1.23 ± 1.1	2.9 ± 0.7	2.9 ± 0.5	2.5 ± 0[#]	P > 0.05[K]

Table 13. Type of Anaemia and Lipid Profile

DISCUSSION

The observations made in 50 cases of anaemia and 50 non-anaemic controls who presented to Department of Medicine, Thanjavur Medical College, Thanjavur, from January 2017 to June 2017 is discussed here and results have been compared with other similar studies.

Age- All cases in this study were between 14 and 75 years. Majority of the cases were middle aged (30-60 years). Anaemic cases younger than 50 years were more likely to have more severe anaemia as compared to cases older than 50 years, who were more likely to have less severe anaemia. This is probably due to younger individuals having a higher risk of worm infestations and also the onset of menopause with cessation of menstrual blood loss after the age of 50 years.

Sex- The cases consisted of 22 males and 28 females. There was no correlation between sex and severity of anaemia.[11]

Type and Severity of Anaemia

Dimorphic anaemia was the most commonly seen type of anaemia in this study. Microcytic hypochromic anaemia was the second most common followed by normocytic hypochromic anaemia and those with normocytic normochromic blood picture. Only a few cases of megaloblastic anaemia and pancytopenia and one case of chronic myeloid leukaemia were seen. This is consistent with

standard textbooks of medicine, which describe nutritional deficiencies, especially iron deficiency to be the most common cause for anaemia.[12,13] Most cases had mild-to-moderate anaemia as defined by haemoglobin level above 6 g/dL. None of the cases with normocytic hypochromic anaemia or normocytic normochromic blood picture had severe anaemia.

Symptoms- Cases commonly presented with nonspecific symptoms of anaemia such as fatigue, dyspnoea, palpitations and giddiness. Symptoms suggestive of a specific cause for anaemia were rarely seen. Cases with more severe anaemia were more likely to have symptoms and had more number of symptoms. Patients with haemoglobin[14] more than 10 g/dL were usually asymptomatic and incidentally detected to have anaemia on routine evaluation. This is consistent with standard textbooks of medicine, which state that mild anaemias of insidious onset are usually asymptomatic. Nonspecific symptoms such as fatigue, dyspnoea, giddiness, palpitations, fever, loss of appetite and loss of weight were equally frequent in different types of anaemia, except normocytic hypochromic anaemia and cases with normocytic normochromic blood picture. This is possibly due to the fact that these cases had less severe anaemia.

Personal History- 8 cases were vegetarians. Vegetarians were more likely to have more severe anaemia and to have dimorphic anaemia. Vegetarians are likely to have more severe anaemia as dietary iron of plant origin has less bioavailability.

General Physical Examination- Pallor was the most common finding on general physical examination. Cases with more severe anaemia were found to be more likely to have findings on general physical examination. Signs were usually not seen in cases with haemoglobin less than 10 g/dL. Koilonychia, lymphadenopathy, glossitis and angular stomatitis were seen only in cases with dimorphic anaemia and microcytic hypochromic anaemia. Knuckle pigmentation and perioral pigmentation was seen only in cases with megaloblastic anaemia and dimorphic anaemia. This is consistent with descriptions given in standard textbooks of medicine.[15]

Pulse Rate- The mean pulse rate was higher in anaemic cases when compared to non-anaemic controls. The mean pulse rate was higher in cases with more severe anaemia. The pulse rate has been described to be higher in case of anaemia in standard textbooks of medicine. This is part of a compensatory mechanism to raise cardiac output and maintain tissue oxygenation.[16]

Ickx, Rigolet and Linden[17] in 2000 demonstrated that anaemia causes a rise in pulse rate and stroke volume in patients whose haemoglobin was lowered from 13 g/dL to 8 g/dL.

Blood Pressure- The mean blood pressure was comparable in cases and controls. It was lower in cases with more severe anaemia. This is due to peripheral vasodilatation, another compensatory mechanism to raise cardiac output and maintain tissue oxygenation. Duke and Abelmann[18] in 1969 demonstrated that redistribution of blood volume and vasodilatation played a dominant role in the hyperkinetic circulatory response to chronic anaemia.

Body Mass Index- The mean body mass index was comparable in cases and controls. It was lower in cases with more severe anaemia.

Systemic Examination- The most common findings on systemic examination were venous hum and flow murmurs. Features suggestive of hyperdynamic state of circulation and congestive cardiac failure were only seen in cases with severe anaemia. Features suggestive of peripheral neuropathy were seen only in cases with megaloblastic anaemia and dimorphic anaemia. This was consistent with a study done by Graettinger, Parsons and Campbell[19] in 1983, which demonstrated that anaemia leads to significant haemodynamic changes only when it is severe.

Anaemia and Lipid Profile- The results of this study confirm the findings of previous investigators that the mean serum total cholesterol, HDL, LDL, VLDL and triglyceride levels are decreased in anaemia. The mean total cholesterol was found to be lower in anaemic cases when compared to controls. The decrease in mean serum cholesterol was not due to a specific lowering of any of the serum lipoprotein families; hypocholesterolaemia was caused by a reduction in all the major lipoprotein families, including mean HDL, LDL, VLDL and triglycerides. There was a very large decrease in mean total cholesterol and LDL levels and a large decrease in mean HDL levels, resulting in a mild fall in mean TC/HDL and LDL/HDL ratios. There was a mild decrease in mean VLDL and triglyceride levels. Rifkind and Gale[20,21] in 1967 showed that anaemia was associated with hypocholesterolaemia and the decrease in serum cholesterol was not due to a specific lowering of any of the serum lipoprotein families and that hypocholesterolaemia was caused by a proportional reduction in all the major lipoprotein families. Elwood and Mahler[22] in 1970 conducted a study in 4,070 women and demonstrated a significant difference in cholesterol between women with haemoglobin levels above and below 10.5 g/dL.

Severity of Anaemia and Lipid Profile- Patients with more severe anaemia were found to have a larger fall in mean total cholesterol and all the lipid subfractions. This suggests that the severity of anaemia is responsible for the hypocholesterolaemia seen in anaemia. A study conducted by Choi et al[23] in 2001 showed that lipid levels in patients with iron deficiency anaemia were directly related to the haemoglobin levels.

Type of Anaemia and Lipid Profile- The type of anaemia did not have a significant effect on the mean lipid levels. This suggests that it is anaemia per se and not the type of anaemia that is responsible for the lowering of lipid levels in anaemia. A study by Westerman[24] in 1975 examined the relationship between hypocholesterolaemia and various types of anaemia including megaloblastic anaemia, hereditary spherocytosis,[25] homozygous sickle cell disease,[26,27] aplastic anaemia and liver associated anaemia. The study showed that the plasma cholesterol level is closely related to haematocrit levels, both initially and throughout the course of the anaemias associated with hypocholesterolaemia. This association was maintained regardless of the cause of changes in haematocrit levels. The authors concluded that low haematocrit, not the type of anaemia, is the cause of low cholesterol levels. Seip and Skrede[28] in 1967 found an association between serum cholesterol and haemoglobin in all cases regardless of cause of anaemia.

CONCLUSION

This study was done on 50 anaemic cases and 50 non-anaemic controls to study the clinical presentation and effect on lipid profile of anaemia. Younger individuals are more likely to have severe anaemia. Cases with severe anaemia have more symptoms. They have higher mean pulse rate, lower mean blood pressure and mean BMI. Vegetarians are more likely to have severe anaemia. Cases with severe anaemia also have more signs on examination. Anaemia is associated with significant hypocholesterolaemia[29] with lowering in all lipid subfractions. The extent of hypocholesterolaemia is proportional to the severity of anaemia. The type of anaemia has no effect on the hypocholesterolaemia seen in anaemia. Further studies are required to study the long-term effect of anaemia on the risk of developing atherosclerosis and to study the long-term effect of treatment of anaemia on lipid levels and cardiovascular morbidity and mortality.[30]

REFERENCES

[1] Consensus conference. Lowering blood cholesterol to prevent heart disease. JAMA 1985;253(14):2080-2086.

[2] Fuster V, Alexander RW, O'Rourke RA. Hurst's the heart. 11th edn. New York: McGraw-Hill 2004:1123-1139.

[3] Gotto AM. Cholesterol intake and serum cholesterol level. N Engl J Med 1991;324(13):912-913.

[4] Rosner B. Fundamentals of biostatistics. 5th edn. Duxbury 2000.

[5] Reddy MV. Statistics for mental health care research. NIMHANS 2002.

[6] DeMaeyer E, Adiels-Tegman M. The prevalence of anaemia in the world. World Health Stat Q 1985;38(3):302-316.

[7] McCord JM. Is iron sufficiency a risk factor in ischemic heart disease? Circulation 1991;83(3):1112-1114.

[8] Gilbert HS, Ginsberg H, Fagerstrom R, et al. Characterization of hypocholesterolemia in myeloproliferative disease. Relation to disease manifestations and activity. Am J Med 1981;71(4):595-602.

[9] Hashima JA, Afroz N. Hypolipidemia in anemia. Am Heart J 1968;78(6):840.

[10] Tanzer F, Hizel S, Cetinkaya O, et al. Serum free carnitine and total triglyceride levels in children with iron deficiency anemia. Int J Vitam Nutr Res 2001;71(1):66-69.

[11] Sullivan JL. Iron and the sex difference in heart disease risk. Lancet 1981;1(8233):1293-1294.Greer JP, Foerster J, Lukens JN, et al. Wintrobe's clinical hematology. 11th edn. Vol. 1. Philadelphia: Lippincott Williams & Wilkins 2004:947-1486.

[12] Warrel Da, Cox TM, Firth JD, et al. Oxford textbook of medicine. 4th edn. Oxford: Oxford University Press 2003:639-648.

[13] Allen JB, Allen FB. The minimum acceptable level of haemoglobin. Int Anesthesiol Clin 1982;20(4):1-22.

[14] Hoffman R, Benz EJ, Shattil SJ, et al. Hematology: basic principles and practice. 4th edn. Philadelphia: Elsevier Churchill Livingstone 2005:514-556.

[15] Varat MA, Adolph RJ, Fowler NO. Cardiovascular effects of anemia. Am Heart J 1972;83(3):415-426.

[16] Ickx BE, Rigolet M, Van Der Linden PJ. Cardiovascular and metabolic response to acute normovolemic anemia. Effects of anesthesia. Anesthesiology 2000;93(4):1011-1016.

[17] Duke M, Abelmann WH. The hemodynamic response to chronic anemia. Circulation 1969;39(4):503-515.

[18] Graettinger JS, Parsons RL, Campbell JA. A correlation of clinical and hemodynamic studies in patients with mild and severe anemia with and without congestive failure. Ann Intern Med 1963;58:617-626.

[19] Rifkind BM, Gale M. Hypolipidaemia in anaemia. Implications for the epidemiology of ischaemic heart-disease. Lancet 1967;2(7517):640-642.

[20] Rifkind B, Gale M. Hypolipidemia in anemia. Am Heart J 1968;76(6):849-850.

[21] Elwood PC, Sweetnam P Welsby E, et al. Association between circulating haemoglobin level, serum cholesterol and blood-pressure. Lancet 1970;1(7647):589-590.

[22] Choi JW, Kim SK, Pai SH. Changes in serum lipid concentrations during iron depletion and after iron supplementation. Ann Clin Lab Sci 2001;31(2):151-156.

[23] Westerman MP. Hypocholesterolemia and anemia. Br J Hematol 1975;31(1):87-94.

[24] Tse WT, Lux SE. Red blood cell membrane disorders. Br J Haematol 1999;104(1):2-13.

[25] Bunn HF. Pathogenesis and treatment of sickle cell disease. N Engl J Med 1997;337(11):762-769.

[26] el-Hazmi MA, Jabbar FA, Warsy AS. Cholesterol and triglyceride levels in patients with sickle cell anemia. Scan J Clin Lab Invest 1987;47(4):351-354.
[27] Seip M, Skrede S. Serum Cholesterol and triglycerides in children with anemia. Scan J Hematol 1977;19(5):503-508.
[28] Evans JG, Prior IAM. Hypolipidemia in anaemia. Lancet 1967;2:1362-1363.
[29] Atac B, Brahaj D, Frishman WH, et al. Anemia and hypocholesterolemia. Heart Dis 2003;5(1):65-71.