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ASSESSMENT OF THE RISK FACTORS AND THE EFFECT OF VITAMIN SUPPLEMENTS IN HYPERLIPIDEMIC PATIENTS

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ABSTRACT

Objective: The aim of the study was to compare the effect of vitamin supplements on the lipid profile of the hyperlipidemic patients and to assess their Cardiovascular risk factors by estimating the lipid profile. **Study design and methodology:** A prospective observational study was carried out for a period of six months with 91 hyperlipidemic patients after obtaining the ethical clearance. They were divided into three groups i.e., Control, Group A and Group B.The control group consisted of patients at the risk of developing hyperlipidemia or the newly diagnosed hyperlipidemic patients. Group A and group B consisted of patients taking Atorvastatin 20 or 10 mg/day and patients taking Atorvastatin 20 or 10 mg/day along with vitamin supplements respectively. Then the baseline lipid levels were calculated. At the end of 6 months, the lipid profile was measured again as the endpoint and compared. Statistical analysis of the collected data was done using Graph Pad Instat version 3.10. **Results:** In this study, we observed that the serum total cholesterol, LDL and triglyceride levels significantly reduced in those who were supplemented with vitamins along with statins. However, HDL levels didn't show any significant improvement.Furthermore, male gender, old age (>50 years), social habits (unhealthy diet, smoking and alcohol consumption) or an underlying disease condition may also increase the CVD risk. **Conclusion:** The vitamin supplementation along with the statin therapy proves to be effective in lowering the increased lipid levels and further aid in reducing many of the cardiovascular diseases associated with high cholesterol levels.

KEYWORDS: Hyperlipidemia, Anti-hyperlipidemic drugs, Vitamin supplements, Lipid profile.

INTRODUCTION

Hyperlipidemia is a medical condition in which the concentration of lipids and lipoproteins are found to be elevated from the normal value. It is often a major risk factor in the development of most of the cardiac diseases all over the world.[1] It is also known as Hypercholesterolemia or hyperlipoproteinemia.[2] In this condition the various lipid parameters like the Chylomicrons, verylowdensity lipoprotein (VLDL), Low density lipoprotein (LDL), Intermediate density lipoprotein (IDL) gets elevated from the normal level.[3] The causes for hyperlipidemia include genetic factors, sedentary life style, autoimmune conditions and old age.[4] Generally, Hyperlipidemia has no noticeable symptomsand thus the condition can only be diagnosed by blood test. However, breathlessness, palpitation, chest pain, cramping of one or both calves when walking can be observed.[5]

Lipid Metabolism Pathway

Normally the lipid metabolism takes place in two pathways i.e, the exogeneous andendogenous Pathway. Lipid metabolism involves the synthesis and metabolism of lipids in the hepatic cells. The process begins from the exogeneous pathway in which the dietary cholesterol and fats are transported to the liver for breakdown, storage of fats and for synthesis of structural and functional lipids. Later, when required these substances are transported back to the bloodstream.

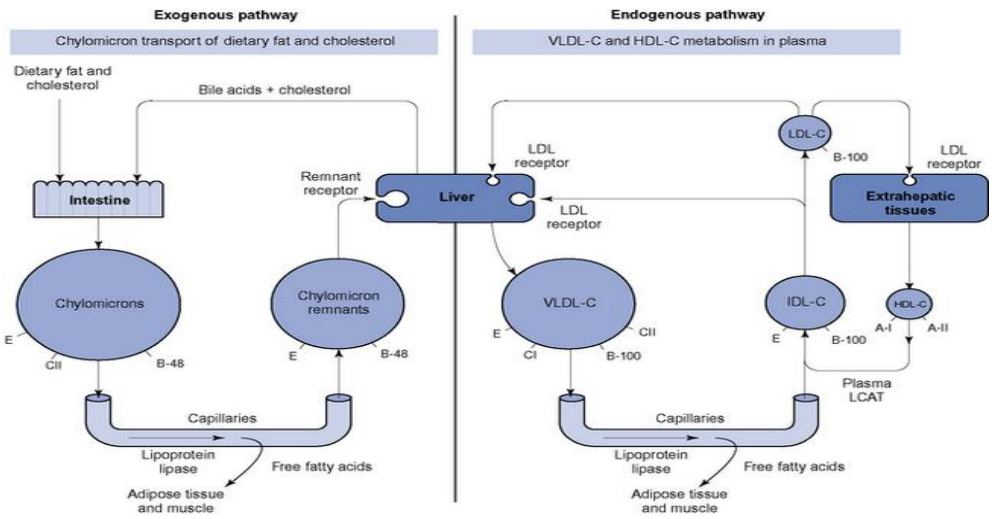

Figure 1: Lipid metabolic pathway.[6]

Consequences Associated With Co-Morbidities in Hyperlipidemia

Co-morbidity is the occurrence of multiple chronic disorders in a person and it could also develop due to one index disease condition. Multiple diseases together may adversely affect the quality of life of an individual. Common comorbidities found along with dyslipidemia are diabetes, hypertension, thyroid, renal failure, liver failure and obesity along with or as progressing to cardiovascular complications.[7]

Dyslipidemia interacts with high blood pressure and thus dyslipidemia and hypertension are established risk factors for CVDs as it will accelerate the process of atherosclerosis resulting in plaque formation and damage to the endothelium.[8,9] Alcoholic fatty liver disease (AFLD) and non-alcoholic fatty liver disease (NAFLD) are also a major cause of morbidity and mortality worldwide and it is influenced by numerous factors including alcohol abuse and high-fat diet. Recent studies have also shown that thyroid imbalance also negatively affects the lipid metabolism. Hyperlipidemia in hypothyroidism is mainly due to a reduction in low-density lipoprotein (LDL) receptor activity.[10] Obesity was associated with an increased prevalence of coronary heart disease (CHD), hypertension, osteoarthritis (OA), and high blood cholesterol among > 16000 volunteersaccording to The National Health and Nutrition Examination Study (NHANES) III.[11] Lipid imbalance in kidney patients is largely due to corticosteroids, cyclosporine, and sirolimus usage in CKD. Sirolimus cause both increased cholesterol and triglycerides by interfering with the catabolism of VLDL and LDL in the body.[12] Alcohol consumption and smoking canalso increase the risk for cardiovascular complications and are recognized as an independent risk factor for atherosclerosis. Increased age, genetics, weight gain and unhealthy lifestyle habits are addon factors for hyperlipidemia progression to cardiovascular disorders.[13]

The Impact of Vitamins on Lipid Metabolism

Vitamin supplementation has shown to improve health and reduce the risk of many chronic illness. Recent researches have shown that vitamins play an important role in reducing cardiovascular risk factors due to their anti-oxidant properties and involvement in the lipid metabolism. Significant reduction in the total triglycerides and VLDL-Cholesterol and improvement in the HDL-Cholesterol was seen in the hyperlipidemic patients who were administered with vitamin supplements.[14,15] Triglycerides was identified as a major biomarker to predict the development of Cardiovascular risk by the American Heart Association.[16]

In humans, generally 13 essential vitamins i.e, four fat soluble vitamins (Vitamin A, Vitamin D, Vitamin E and Vitamin K) and nine water soluble vitamins (Vitamin B_1, Vitamin B_2, Vitamin B_3, Vitamin B_5, Vitamin B_6, Vitamin B_7, Vitamin B_9, Vitamin B_{12} and Vitamin C) are found to be essential for the normal growth and development of the body. These vitamins individually have a specific role to play in the total physiological activity of our body.[17]

Mechanism of Vitamins in Lowering the Lipid Levels

Vitamin A in the form of retinyl esters taken in through diet enters the bloodstream via the lymph lipoprotein particles. During the circulation of these lipoprotein particles, triglycerides are removed by the enzymelipoproteinlipase.[18]

Vitamin B -12 deficiency may lead to the accumulation of MM – CoA (Methylmalonyl CoA). This is due to the fact that Vitamin B12 functions as a coenzyme in the conversion of methylmalonyl CoA to Succinyl –CoA. The above reaction could be blocked in the absence of vitamin B12. Gradually the accumulation of MM-CoA inhibits the rate limiting enzyme of fatty acid oxidation (CPTI – Carnitine Palmitoyl transferase) and result in lipogenesis.[19] Similarly, Folic acid and vitamin B6 deficiency could also increase the risk of cardiovascular events. Under normal metabolic activities Vitamin B6, B12 and folic acid break down homocysteine and convert it to other substances according to the bodily needs. Thus, only a few amounts of homocysteine is left in the bloodstream. When there is a deficiency in vitamin B6, B12 and Folic acid the above mechanism is interrupted which could gradually increase the levels of homocysteine in the body. Homocysteine activates the 3-hydroxy-3 methyl glutaryl coenzyme A reductase which is present in the endothelial cells and promote the synthesis of Cholesterol and can gradually increase the risk of macro-vascular diseases such as myocardial infarction, cerebral ischemia as well as increase the risk of coronary artery disease (CAD).[20]

Vitamin C aids in reducingthe monocyte adherence to the endothelium and improve the endothelium dependent nitric oxide production and vasodilation and reduce vascular smooth muscle cell apoptosis. This mechanism prevents the plaque instability in atherosclerosis.[21,22,23] The antioxidant property of Vitamin C prevents oxidative damage, majorly the oxidative modification of low-density lipoproteins and improve the cardiovascular functioning and help in the prevention of cardiovascular diseases.[24,25]

Vitamin D reduce serum PTHconcentration and regulate the calcium balance. This suppression further helps in the peripheral removal of triglycerides and eventually help to reduce the total serum triglycerides present in the body. Vitamin D receptor and 1-α-hydroxylase present in cardiovascular tissues convert vitamin D into hormonal 1,25-OH vitamin D.[26] A lack in VDR may promote in the formation of a fibrotic extracellular matrix leading to ventricular dilation and impaired electromechanical coupling. vitamin D is also a negative regulator of renin angiotensin aldosterone system (RAAS). Low levels of Vitamin D may promote RAAS activation and production of angiotensin eventually leading to arterial stiffening, exacerbation of atherogenesis and acceleration of arterial calcification leading to a hypertensive condition slowly progressing to cardiovascular disorders.[27]

Vitamin E increase the activity of nitric oxide synthase by trapping reactive nitrogen species molecules. This in turn produces vessel relaxing nitric oxide by trapping the reactive oxygen species and improve the endothelial function and help in reducing the cardiac risk factors and complications.[28,29]

Due to vitamin K-mediated γ-carboxylation, various Gla proteins can bind with the calcium ions and get activated. Carboxylated MGP (matrix Gla proteins) is an important inhibitor of vascular calcification. Correspondingly, uncarboxylated MGP (ucMGP) is an independent risk factor for arteriosclerosis. Vitamin K-dependent matrix Gla protein (cMGP) counteracts vascular calcification and age-related wear and tear on the arteries and protects the blood vessels from calcium overload and help in the protection of bone health and reduce cardiovascular complications.[30]

METHODOLOGY

This was a Prospective observational studyconducted in the Department of cardiology, Vivekanandha Medical Care Hospital, Tiruchengode, Tamilnaduduring the period of December 2019 – June 2020 after obtaining the Ethical clearance from theInstitutional Ethical Committee.

A total of 91 patients were included in the study as per the inclusion and exclusion criteria. Out of which 33 patients were enrolled ascontrol, 30 in Group-A (T. Atorvastatin therapy) and 28 patients in Group B (T.Atorvaststin + Vitamin) respectively. The datawere collected in a very particularly designed data entry form after obtaining the informed consent. The details of demographics such as name, age, gender, complaints on admission, past medical

and medication history, family history, allergies (food, drugs & others), social history (alcoholic, smoker) and anthropometric measurements such as weight, height, BMI were included. The laboratory parameters such as the lipid profile, serum creatinine levels and serum electrolytes were also collected.

Statistical analysis of the collected data was done using GraphPad Instat version 3.10. All values were expressed as mean ± standard deviation.The student t-test was used to compare the baseline and endpoint levels within each group and also to obtain the mean differences and the standard deviation between the groups. A P-value of less than 0.05 was considered to be statistically significant for a 95 % confidence interval.

RESULTS

A total study population of 91 patients was enrolled in the study. Out of which, 33 patients were included in the Control group, 30 patients were enrolled in Group A (Atorvastatin 20mg/Day) and 28 patients were included in Group B (Atorvastatin 20 mg/day + Multi vitamin Tablet).

Gender Distribution of the Study Population

Out of the total study population of 91 patients, 59 were male patients and 32 were females.

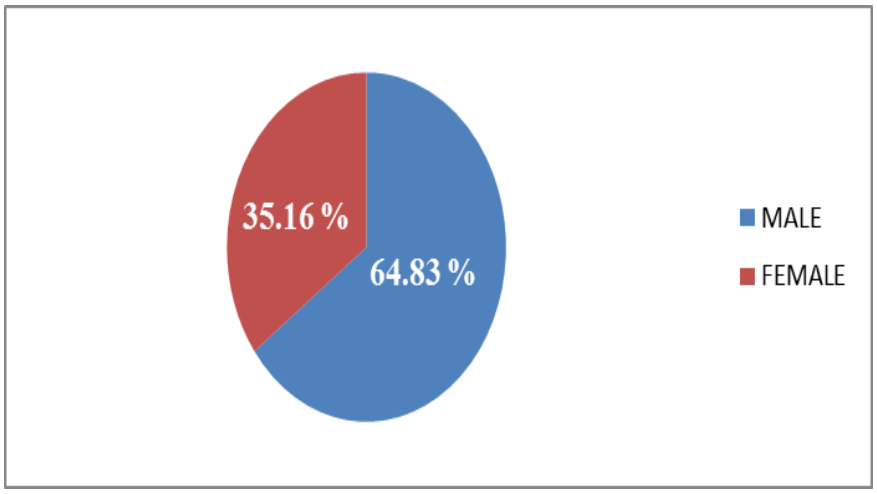

Figure 1: Gender Distribution of Study Population.

Age Group Distribution

Majority of the patients were within the age group of 51 - 60 years, male patients were predominant in the group.

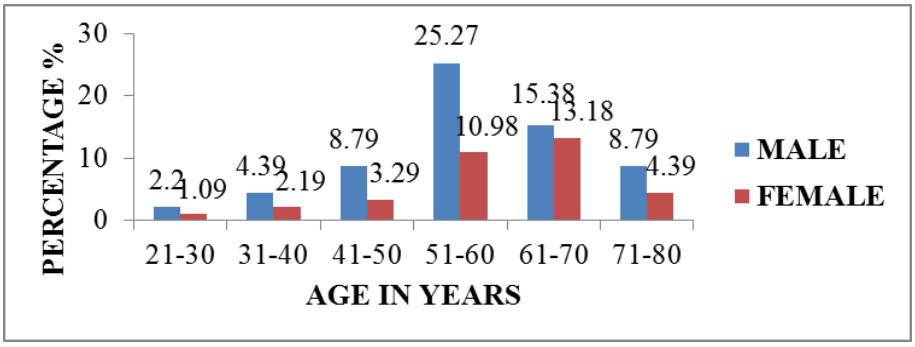

Figure 2: Age Group Distribution.

Distribution On The Basis Of Smoking Habit

48 male patients were found to be smokers, 11 males and 32 female patients were non-smokers.

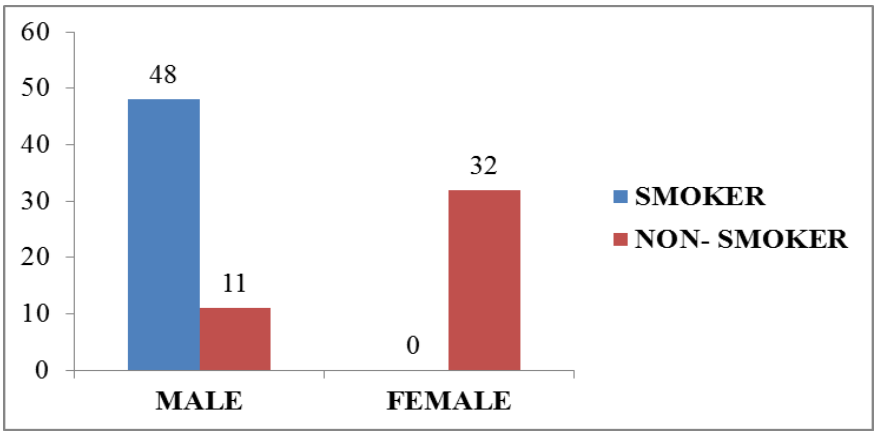

Figure 3: Distribution on the Basis of Smoking

Distribution On The Basis Of Alcohol Intake

It was observed that 50 male patients were alcoholic, 19 male and 32 female patients were non-alcoholic**.**

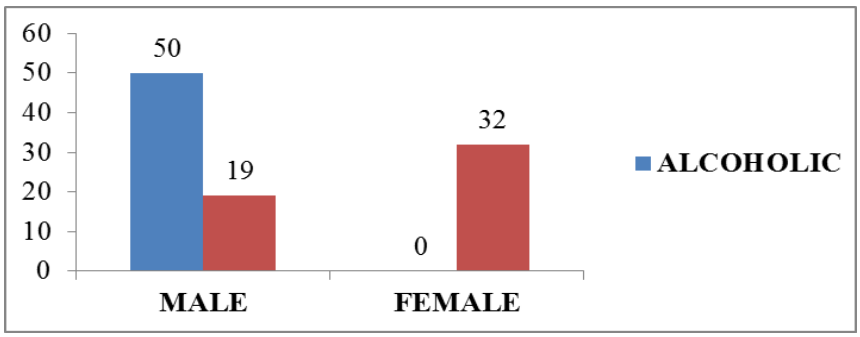

Figure 4: Distribution Based on Alcohol Intake.

Co-Morbidities of Hyperlipidemia

The most commonly prevalent co-morbidity was DM with HTN followed by HTN, DM, obesity and thyroid disorders.

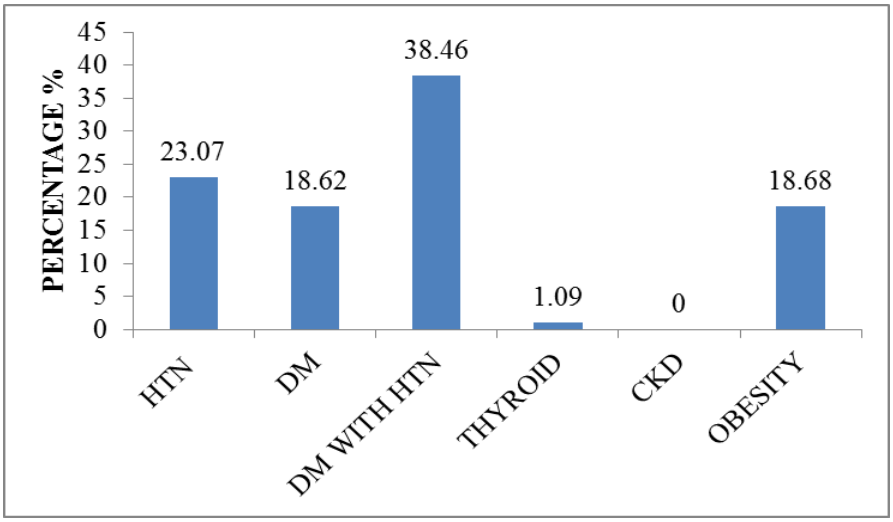

Figure 5 : Co-morbidities

Changes In Serum Total Cholesterol Levels

Figure 6 imply that the changes in serum total cholesterol levels in study groups were reduced significantly.

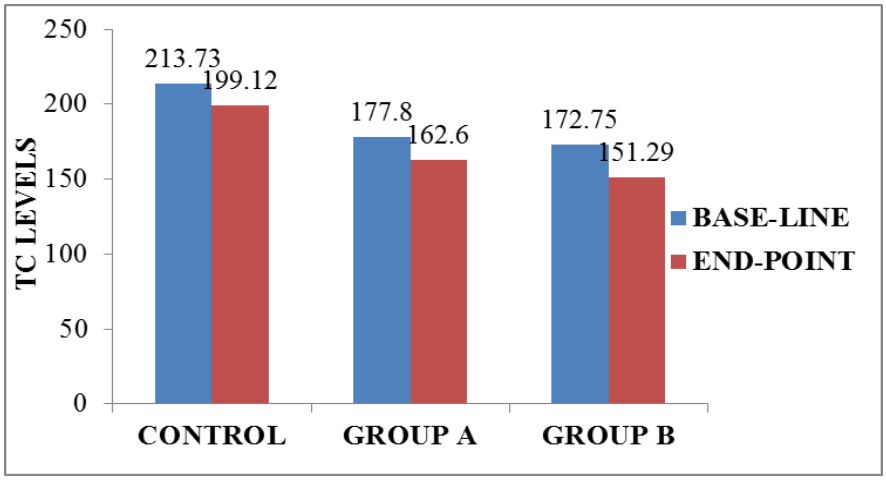

Figure 6: Serum Total Cholesterol Level.

Mean Difference In Serum Total Cholesterol Level

Figure 7 implies that the mean difference in serum total cholesterol levels in Group-B was found to be more significant when compared to Group-A followed by control.

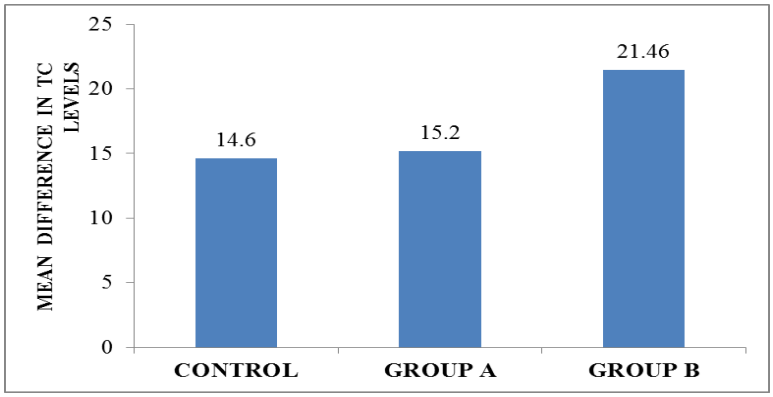

Figure 7: Mean Difference in Serum Total Cholesterol Level

Changes in Serum LDL Levels

The serum LDL levels of study groupsreduced significantly as represented in the figure 8.

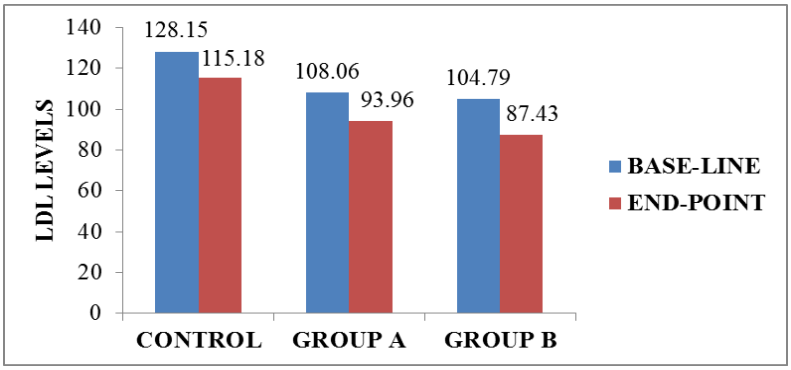

Figure 8: Serum LDL Levels.

Mean Difference in Serum LDL Levels

Figure 9 implies that the mean difference in serum LDL levels between control, Group-A and Group- B was significant.

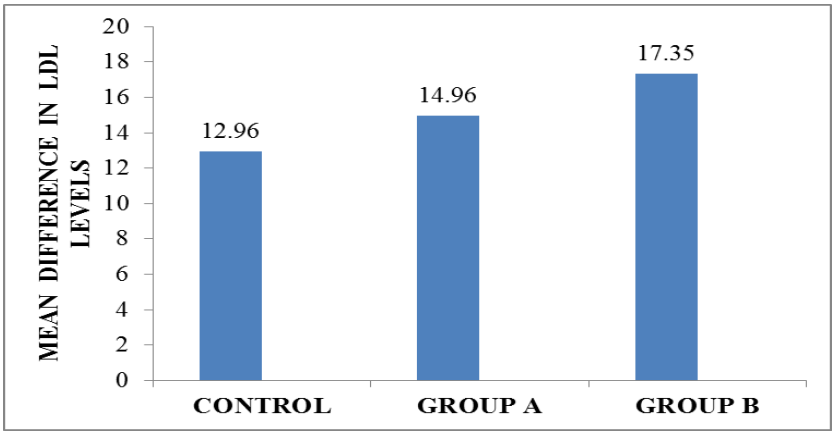

Figure 9: Mean Difference in Serum LDL Levels.

Changes in Serum Triglyceride Levels

Figure 10 imply that the serum triglyceride levels in the group B was significantly reduced when compared to the control group and group A.

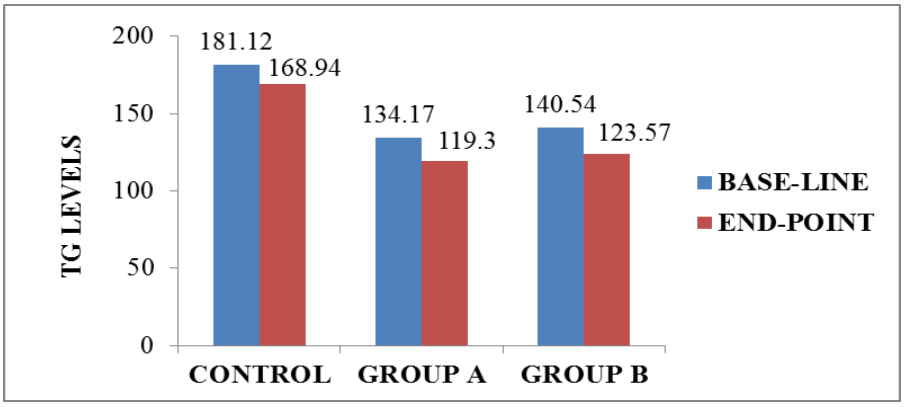

Figure 10: Changes in Serum Triglyceride Levels.

Mean Difference of Serum Triglyceride Levels

Figure 11 implies that the mean difference in serum TG levels of study groups were significantly reduced.

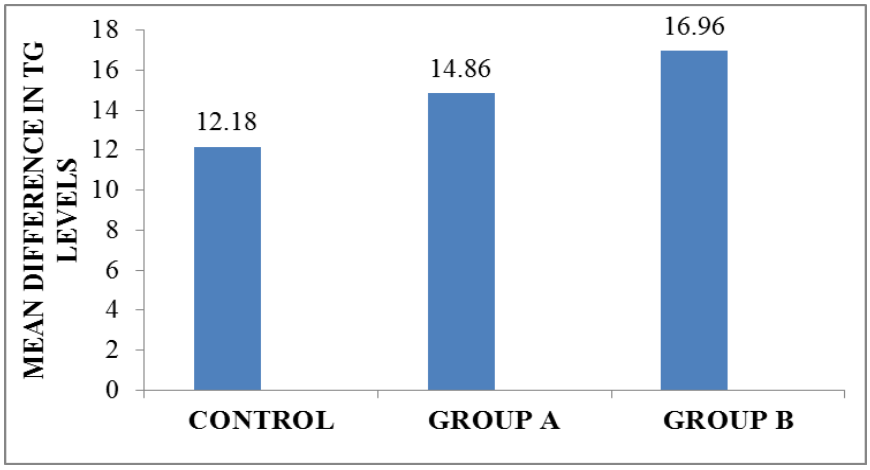

Figure 11: Mean Difference in Serum Triglyceride Levels.

Changes in Serum Hdl Levels

Figure 12 imply that the changes in serum HDL levels in control Group A, Group B was not statistically significant.

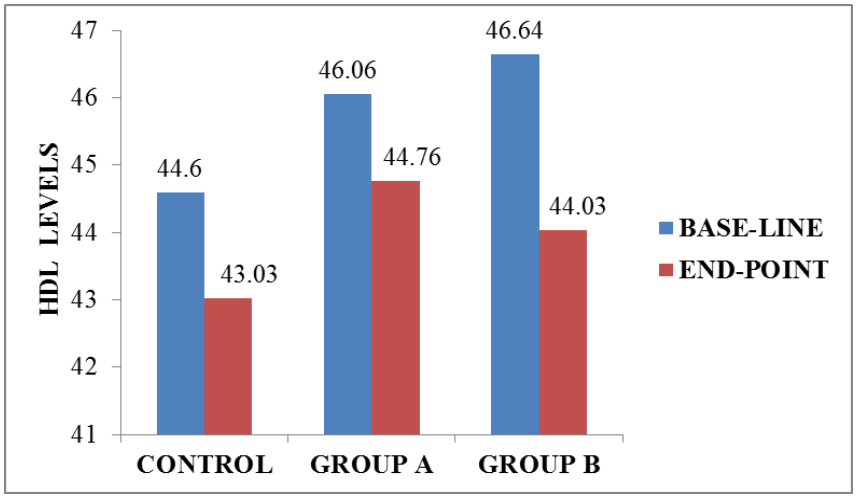

Figure 12: Changes in serum HDL level.

Mean Difference in Serum HDL Levels

Figure 13shows that the mean difference in serum HDL levels between Control, Group A and Group B was not significant.

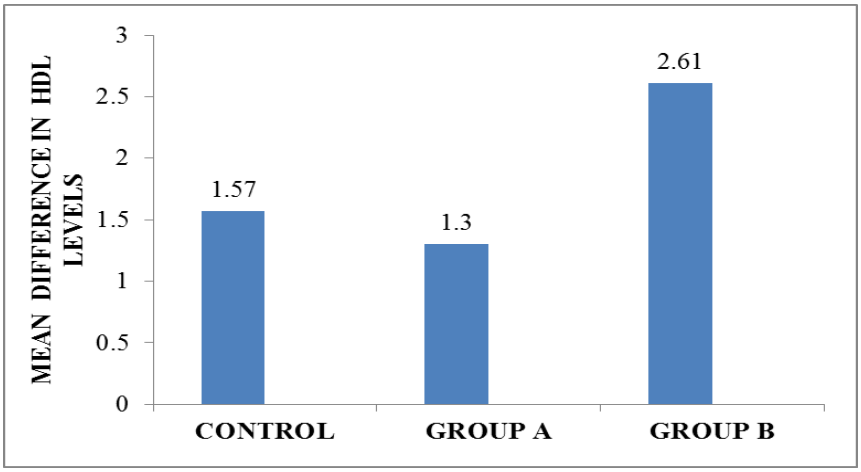

Figure 13: Mean difference in serum HDL level.

DISCUSSION

The study results indicate that there is a significant association between the vitamin levels and the lipid profiles of hyperlipidemic subjects. Vitamin deficiencies are associated with increased oxidative stress leading to an abnormality in the lipid metabolism. Study of Antonysunil et al., showed that Vitamin B12 deficient population was more prone to cardiovascular complications and adverse lipid profile.[20] Another study by Suzanne E. Judd et al., showed that vitamin D deficiency may lead to many cardiovascular risk factors like HTN,DM, dyslipidemia, obesity and other cardiovascular diseases.[31]

Among the 91 patients, 59 were males and 32 were females which indicate that males are more prone to hyperlipidemia when compared to females. Farshid Gheisaretal et al., reported that men under 55years have four times increased chance to develop MI than women. In women, the risk for coronary artery diseaseincreasegradually after menopause due to the changes in the estrogen levels.[32]

With increased age, the risk in the development of hyperlipidemia and its associated complications may also increase. In our study, the age distribution shows that the prevalence of hyperlipidemia increased after 50 years. In the age group of 51-60 years there was a 36.26% increase in the development of hyperlipidemia and for those between 61-70 years it was 28.57 % increase. Francisco J. Felix Redondo et al., in their study identified that hyperlipidemia is a major risk factor for the incidence of atherosclerotic diseases in the elderly.Hypercholesterolemia is prevalent in older population due to genetic factors, environmental factors and co-morbidity. Majority of the cardiac complications and death is also reported in thispatients.[33]

Smoking and alcohol consumption was also seen to increase the risk in the development of hyperlipidemia and its associated cardiovascular complications. Among the 59 males, 50 were alcoholics and 48 were smokers. Females were found to be non-smokers and non-alcoholics. Study results of Jana keto et al., showed smokers of age group 31-46 years who quit smoking later was observed to have a reduced CVD risk almost to the same as a non-smoker subject in the study.[34] Another study by Elizabeth Mostofsly et al., suggested that habitual moderate drinking of 1-2 glasses per day increased HDL, heart rate and endothelial functions.Whereas heavy drinking is associated with increased risk of HTN, diabetes,MI and mortality.[35]

The most common co-morbidity present along with hyperlipidemia in our study was DM with HTN followed by HTN, DM, obesity and thyroid disorders. Serum total cholesterol is one important factor to determine the abnormal lipid metabolism. Here the mean reduction in serum total cholesterol in the control, Group A and Group B was 14.60± 20.21 mg/dl ,15.2± 26.22mg/dl and 21.46± 24.92 mg/dl respectively. A significant reduction in the serum total cholesterol was seen in the patient population of GroupB which was in concordance with the study conducted by Joel C Exebio et al., which showed a significant decrease in total cholesterol and triglycerides in African American and Hispanic participants who were under Vitamin D supplementation for a period of 6 months.[36]

Similarly, triglycerides are an important marker to determine the risk of atherosclerosis and other cardiac complications. The mean reduction in triglycerides was 12.18 ± 35.13, 14.86 ± 26.19 mg/dl and 16.96 ±26.43 in the control, group A and group B respectively. It implies that the values are significant enough and showed that the consumption of vitamins along with drug was effective in lowering triglyceride levels. The mean reduction in LDL was 12.96 ± 26.56, 14.96 ± 17.75 and 17.36 ± 0.03 in the control, group A and group B respectively. These results are supported by the study conducted by Marc P McRac et al.[37]

The HDL values however did not show any significant improvement on the intake of vitamins. The mean reduction in the HDL was 1.57 ± 1.33, 1.3 ± 6.25 and 2.61 ± 0.84 in the control, group A and group B respectively. However, the HDL levels were within the normal range as evident from the study of G S Mannu et.al., which stated that hyperlipidemia with increased serum LDL, TC, TG and low HDL levels may increase CV risk.[38] All together when all the changes in the lipid profile were compared, it was observed that the lipid profile was improved in those who consumed vitamin supplements along with statins.

CONCLUSION

The results of the study illustrate a significant association between the intake of the vitamin supplements and the lipid levels in the body. Patients consuming vitamins along with Atorvastatin were presented with a better hyperlipidemic control when compared to the patients taking statins alone and to those on irregular hyperlipidemic treatment regimen. The vitamin supplementation along with the statin therapy was shown to be more effective in lowering the lipid levels. Further, we also observed that gender, old age (>50 years), social habits (smoking and alcohol consumption) or an underlying disease condition may also increase the CVD risk. In conclusion, vitamins play an important role in lipid metabolism and its deficiency may lead to an increase in the lipid levels which in turn increase the cardiovascular complications as hyperlipidemia itself is a major risk factor for the development of atherosclerosis.

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