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Comparative Study of Triglyceride Level in Ischemic Heart Disease Patients in different age groups of Patients in south east Rajasthan

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ABSTRACT

Backgrounds: Elevated body triglycerides have been implicated as a risk factor of ischemic heart disease (IHD).
Objectives: To study the association of serum triglyceride with ischemic heart disease and to assess the relationship of serum triglyceride with other established conventional risk factors.
Methods: A cross sectional case-control study of 75 cases of IHD and 75 controls without having any evidence of IHD/CHD between age group 30-70 years. Serum triglyceride levels were estimated by using Colorimetric Method and other risk factors by enzymatic methods.
Results: Mean serum triglyceride (263.674 ± 89.029mg/dl) was significantly higher in cases than controls (98.833 ± 62.682mg/dl). Amongst the patients of IHD, significantly higher level of Serum triglyceride was found in diabetics (340.63±90.78mg/dl) than non-diabetics (225.19±58.30mg/dl), male elderly (>60years of age) smokers (304.20±88.60mg/dl) compared to non smoker (206.37±48.88mg/dl), elderly male with high (>150mg/dl) LDL (323.48±86.73mg/dl) compared to patients with normal (<150mg/dl) LDL (249.33±66.12 mg/dl). Similarly male patients of IHD with high (>40mg/dl) VLDL had significantly higher serum triglyceride (326.49±77.95mg/dl) compared to male patients with normal (<40mg/dl) VLDL (257.18±85.46mg/dl).
Conclusion: High serum triglyceride level (>200mg/dl) may provide a cost effective tool for predicting an impending ischemic heart disease especially in diabetic patients, male elderly smokers, elderly males with high LDL, male patients of ischemic heart disease with high VLDL level.

Keywords: Ischemic heart disease (IHD), conventional risk factors, Serum triglyceride.

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1. Introduction

Although in most epidemiological studies a positive relationship has been found between TG level and the risk of IHD, the usefulness of measuring TG in general screening strategies has been questioned because multivariate analysis control for HDL-C usually eliminates or substantially diminishes the role of TG as a predictor of IHD (1). IHD is one of the most common causes of morbidity and mortality in the industrialized world and is becoming increasingly common in India as well. The mortality rate in acute myocardial infarction is approximately 30% within first month of which 50% of these deaths are attributed to sudden cardiac death and affects people in most productive period of life (2).

Atherosclerosis is the primary cause of heart disease and stroke. Death arising as a complication of atherosclerosis claims the lives of millions of people each year in the Western world, and also rapidly increasing in developing countries (3).

However, the interpretation of multivariate models that include TG and HDL-C is complex and associated with several problems. TG and HDL-C are closely associated both distinct roles of TG and HDL-C in IHD in standard multivariate analysis. In addition, in comparison with HDL-C, the distribution of TG levels is markedly skewed, requiring logarithmic transformation for distribution-dependent analyses such as standard regression analysis, a statistical manoeuvre that may not provide an appropriate representation of underlying biological processes (1). Finally, adding to the

complexity, some individuals with very high TG levels, such as those with lipoprotein phenotype I or V, appear to have no increased risk of IHD (4). With these problems kept in mind, the purpose of the present study was to present an analysis of data from the CMS to determine the effect of TG versus that of HDL-C on the risk of IHD.

Individual epidemiologic studies have differed regarding the strength of association between hypertriglyceridemia and CHD, specifically after adjusting for the presence of associated risk factors such as insulin resistance and HDL-C levels, and are further complicated when considering the skewed distribution and high variability of TG levels (5). Therefore, meta analysis has been crucial to distinguish TG as an independent risk factor from a risk marker of associated conditions such as those in the metabolic syndrome.

In 2007, Sarwar et al (6) performed a large meta-analysis of 29 prospective studies from Western populations and reported an odds ratio of 1.7 (95% CI, 1.6–1.9) comparing the risk of CHD for those in the upper to lower tertiles of the TG distribution after adjusting for other risk factors. Interestingly, in contrast to an earlier study by Hokanson and Austin (7), this study found no difference between men and women in the strength of association. A similar odds ratio was reported in a meta-analysis that included data from 26 prospective studies in Asian and Pacific populations(8).

In contrast, the Emerging Risk Factors Collaboration study (9) collected data from 68 prospective studies and found that the strong stepwise association observed between elevated TG levels and CVD and stroke lost significance once HDL-C and non-HDL-C levels were included in multiple variable models, concluding that TG measurement provided no additional information about vascular risk.

Recent case-control studies (10, 11) investigating the relative contributions of TGs and HDL-C to CHD have found that the residual risk after reduction of LDL-C to guide line recommended levels in patients with atherogenic dyslipidemia is strongly associated with both high TG levels and low HDL-C and the combination is at least additive to the odds ratio, and possibly synergistic. The high residual risk associated with TGs in the setting of optimal LDL-C levels might be related to a greater concentration of apo C-III containing lipoprotein (10). These findings contribute to the rationale for considering high TG and low HDL-C levels, especially when they occur together, in quantifying the risk level to select the type and intensity of treatment.

Studies of secondary prevention of CHD (10, 12, 13) found that a TG level below 150 mg/ dL was independently associated with a lower risk of CHD events in patients receiving highintensity statin treatment, which produced especially low LDL-C concentrations. Specifically, data from the PROVE IT-TIMI 22 trial comparing standard and high-intensity statin therapy after acute coronary syndrome (ACS) observed a 1.6% lower risk of the composite end point (death, myocardial infarction, and recurrent ACS) for each 10-mg/dL decline in on-treatment TG after adjusting for LDL-C and other covariates (13).

Before these recent epidemiological studies were published, and before compelling mechanistic information from basic science on atherogenicity of TRLs became available, the assignment of TG level as an independent risk factor and a causal factor in promoting CVD remained debatable. Therefore, the NCEP ATP III, published in 2001 and remaining the current US guidelines, determined that there was insufficient evidence to regard TG as an independent coronary risk factor in Western populations (14). However, more recent data add confidence to the conclusion that TG levels appear to provide unique information as a biomarker of risk.

The main objective of our study was to study the relationship of serum triglyceride with ischemic heart disease in analysis and to assess the relationship of increased serum triglyceride with classical risk factors like diabetes mellitus, smoking, alcohol intake, body mass index, other lipid profile and hypertension.

2. Materials and Methods

This was a cross sectional case-control study of 75 cases of Ischemic heart disease (IHD) admitted in medicine emergency/ general wards from January 2017 to December 2017 in Jhalawar Medical college & hospital, Jhalawar, and 75 controls without having any evidence of IHD/CHD. Individuals varied from 30-70years and different age groups were made accordingly viz. 30-40years, 40-50 years, 50-60 years and 60-70 years of age.

2.1. Inclusion criteria of cases

The diagnosis of IHD was based on fulfilling any two of the following criteria.

- Typical history of chest pain radiating to the neck or arms.
- ECG changes of ST elevation >2mm in two or more chest leads or >1mm in two or more limb leads or ST- T change.
- Rise in serum cardiac enzymes concentration (Troponin T or I) more than twice the upper limit of normal.
- Presumably, new onset left bundle-branch block.

2.2 Exclusion criteria of cases

- Men who at baseline had a history of acute myocardial infarction, angina pectoris, stroke, or intermittent claudication were excluded from the follow-up study.
- For all who reported admission to hospital because of acute myocardial infarction before the start of the study, hospital records were checked.
- Liver disease.
- Iron therapy.
- Aceruloplasminemia.
- Anaemia – haemolytic anaemia, sideroblastic anaemia, iron deficiency anaemia.

2.3 Controls

Age and sex matched controls were selected for each case irrespective of presence of risk factors (hypertension,

diabetes mellitus, dyslipidemia, smoking and alcohol intake) from subjects attending the outpatient department of the hospital for minor ailments or routine medical check-ups, subjects accompanying patients or amongst office working staff from various departments of this institution without having IHD (in the past or present) or any evidence of coronary heart disease (assessed by symptoms, clinical examination and normal electrocardiogram).

All the subjects were assessed by clinical examination, ECG, serum creatinine kinase-MB (CK-MB). Height and weight were recorded. Body mass index was calculated by formula, weight in kg/height^2 in meter. Body mass index > 25 was considered as a risk factor for IHD. Cases and controls were investigated for conventional risk factors (BMI, blood sugar and lipid profile). History of smoking and alcohol consumption were noted in details. Estimation of lipids was done by enzymatic method using autoanalyser while glucose oxidase and peroxidase (GOD-POD) method was used for measurement of blood sugar.

2.4 Statistical Evaluation

Data for all groups was expressed as mean ± SD. Students t-test (two tailed, independent) had been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square test had been used to find the significance of study parameters on categorical scale between two groups. The p value ≤ 0.05 was considered significant.

3. Results and discussion

A total of 75 cases and an equal number of controls were studied. Both the groups were age and sex matched. The mean age was 54.79 ± 11.15 years in patients with ischemic heart disease and 52.77 ± 11.18 years in control subjects. Mean hemoglobin in cases (12.94g %) and controls (12.77g %) was statistically matched, this was important because serum triglyceride level varies directly with hemoglobin. The mean value of serum triglyceride (mg/dl) in controls and cases were found to be 98.833 ± 62.682mg/dl and 263.674 ± 89.029mg/dl respectively (p <0.05). High serum triglyceride levels (> 200mg/dl) was significantly associated with ischemic heart disease (χ^2=37.167, OR = 9.25, 95% CI=4.34-19.73, p< 0.05). Correspondingly, more patients with IHD (68%) compared to control subjects (18.66%) had concentrations above the cut-off of 200mg/dl (Table 1). The mean value of controls and cases for cholesterol (mg/dl) 86.73±22.59 and 186.16±46.49, LDL cholesterol (mg/dl) 88.40 ± 34.75 and 117.29 ± 3 9.56, VLDL cholesterol (mg/dl) 27.84 ± 09.68 and 33.96 ± 15.25, tr, HDL cholesterol (mg/dl) 44.86 ± 06.61 and 38.68 ± 06.15 respectively (Table 2). There was no significant difference of mean serum triglyceride level in males and females.

The mean serum triglyceride level in different age group cases (i.e. 30-40 years, 40-50 years etc.) was significantly higher compared to their respective controls. As the age increases, mean value of the serum triglyceride also increases, but not statistically significant. While in case of 61-70years of age group female cases, mean serum triglyceride was (298.32±78.94mg/dl) significantly higher compared to 30-40years of age group (173.96± 21.06mg/dl) cases (t=2.611, p=0.028).

In univariate analysis, classical risk factors like DM, hypertension, BMI >25kg/m^2, high-density lipoprotein (HDL) < 35, LDL >150mg/dl and smoking were found to be significantly associated with IHD (Table 3).

We also assessed the relationship of serum triglyceride with other risk factors. Mean serum triglyceride level was statistically high in patients of IHD with diabetes mellitus (340.63±90.78mg/dl) compared to patients of IHD without diabetes mellitus (225.19±58.30mg/dl) (Figure 1). Male smoker patients >60years of age had (304.20 ±88.60mg/dl) statistically higher serum triglyceride level compared to non smoker of similar age group (206.37±48.88mg/dl) (Figure 2).

Similarly, male elderly (>50years of age) patients having high (>150mg/dl) LDL had (323.48±86.73mg/dl) higher serum triglyceride level compared to patients having normal (<150mg/dl) LDL level (249.33± 66.12mg/dl) (Figure 3). This study also stabilized that, high (>40mg/dl) serum VLDL in male patients of all age groups was associated with high serum triglyceride level (326.49±77.95mg/dl) compared to patients having normal (<40mg/dl) VLDL level (257.18±85.46) and thus, these patients may be at a higher risk of developing IHD (Figure 4).

Table1 Association of ischemic heart disease with high serum triglyceride

Serum Triglyceride	Cases (%) (n=75)	Controls (%) (n=75)	Total (%) (n=150)	p-value
≥ 200mg/dl	51(68%)	14(18.66%)	65(43.33%)	χ^2=37.167 OR=9.258 95%CI=4.34-19.73 p < 0.05*
< 200mg/dl	24(32%)	61(81.33%)	85(56.66%)	--

*Statistically significant. CI: confidence interval, OR: odds ratio.

Table 2 Characteristics of cases and control groups

Parameters	Cases (n=75) Mean ± SD	Control (n=75) Mean ± SD	p- value (by t test)
Hemoglobin (g%)	12.94 ± 0.87	12.77 ± 0.69	0.187
Mean age (years)	54.79 ± 11.15	52.77 ± 11.18	0.187
Triglyceride (mg/dl)	263.674 ± 89.029	98.833 ± 62.682	0.001
Cholesterol (mg/dl)	186.16±46.49	86.73±22.59	0.0001
HDL Cholesterol (mg/dl)	38.68±06.15	44.86±06.61	0.0001
LDL Cholesterol (mg/dl)	117.29±39.56	88.40±34.75	0.0001
VLDL Cholesterol (mg/dl)	33.96±15.25	27.84±09.68	0.0001

Table 3 Comparison of other conventional risk factors for ischemic heart disease in cases and controls (univariate analysis)

Risk factor	Cases (%) (n=75)	Control (%) (n=75)	Total (%) (n=150)	p-value
Diabetes mellitus Present Absent	 25(33.33) 50(66.66)	 8(10.66) 67(89.33)	 33 117	χ^2=11.227 Odds ratio=4.18 CI=1.74-10.05 p=0.0008(SIG.)
Hypertension Present Absent	 21(28) 54(76)	 10(13.33) 65(86.66)	 31 119	χ^2=6 Odds ratio=2.52 CI=1.20-6.73 P=0.014(SIG.)
Smoking Present Absent	 35(46.66) 40(53.33)	 22(29.33) 53(70.33)	 57 93	χ^2=5.50 Odds ratio=2.108 CI=1.07-4.13 p=0.029(SIG.)
BMI >25 <25	 27(36) 48(64)	 16(21.33) 59(78.66)	 43 107	χ^2=4.761 Odds ratio=2.07 CI=1.003-4.288 p=0.049(SIG.)
Alcoholic Present Absent	 29(38.66) 46(61.33)	 18(24) 57(76)	 47 103	χ^2=3.749 Odds ratio=1.99 CI=0.986-4.039 p=0.0528(N.SIG.)
Serum Cholesterol >200 <200	 26(34.66) 49(65.33)	 15(20) 60(80)	 41 109	χ^2=3.36 Odds ratio=2.12 CI=1.013-4.44 p=0.066(N.SIG.)
HDL <35 >35	 18(24) 57(76)	 6(8) 69(92)	 24 126	χ^2=7.142 Odds ratio=3.631 CI=1.351-9.756 p=0.0075(SIG.)
LDL >150 <150	 20(26.66) 55(73.33)	 8(10.66) 67(89.33)	 28 122	χ^2=5.310 Odds ratio=3.045 CI=1.24-7.445 p=0.0212(SIG.)
VLDL >40 <40	 20(26.66) 55(73.33)	 11(14.66) 64(85.33)	 31 119	χ^2=2.600 Odds ratio=1.97 CI=0.932-4.800 p=0.106(N.SIG.)

*SIG.=Significant, *N.SIG.=Non Significant

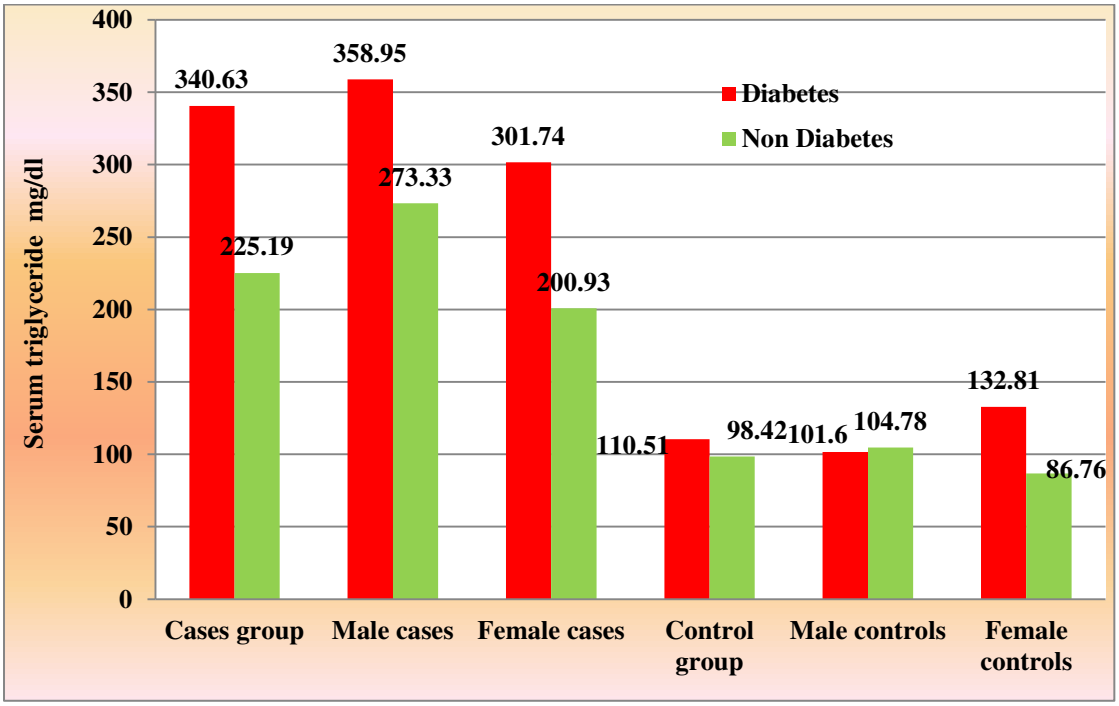

Figure 1. Cases and controls

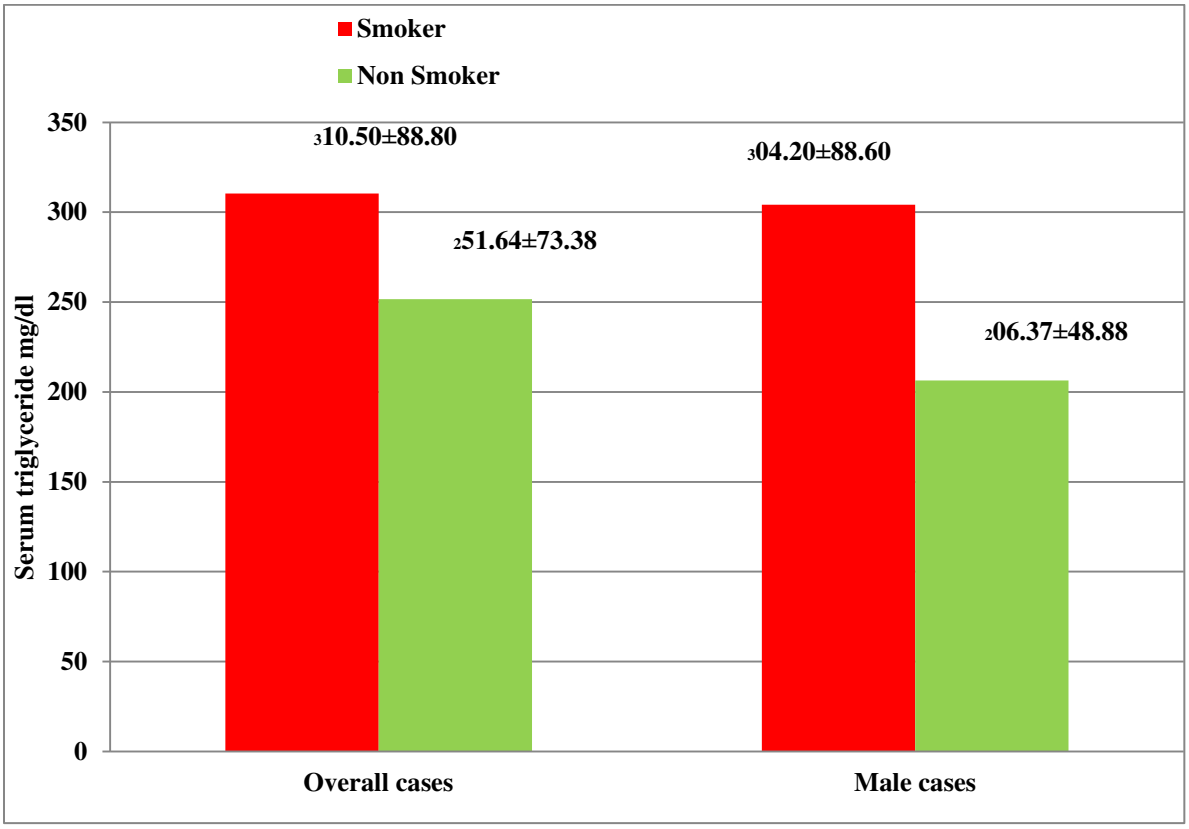

Figure 2. Graphical comparison of mean serum triglyceride (mg/dl) in smoker and non smoker 61-70years of age group cases

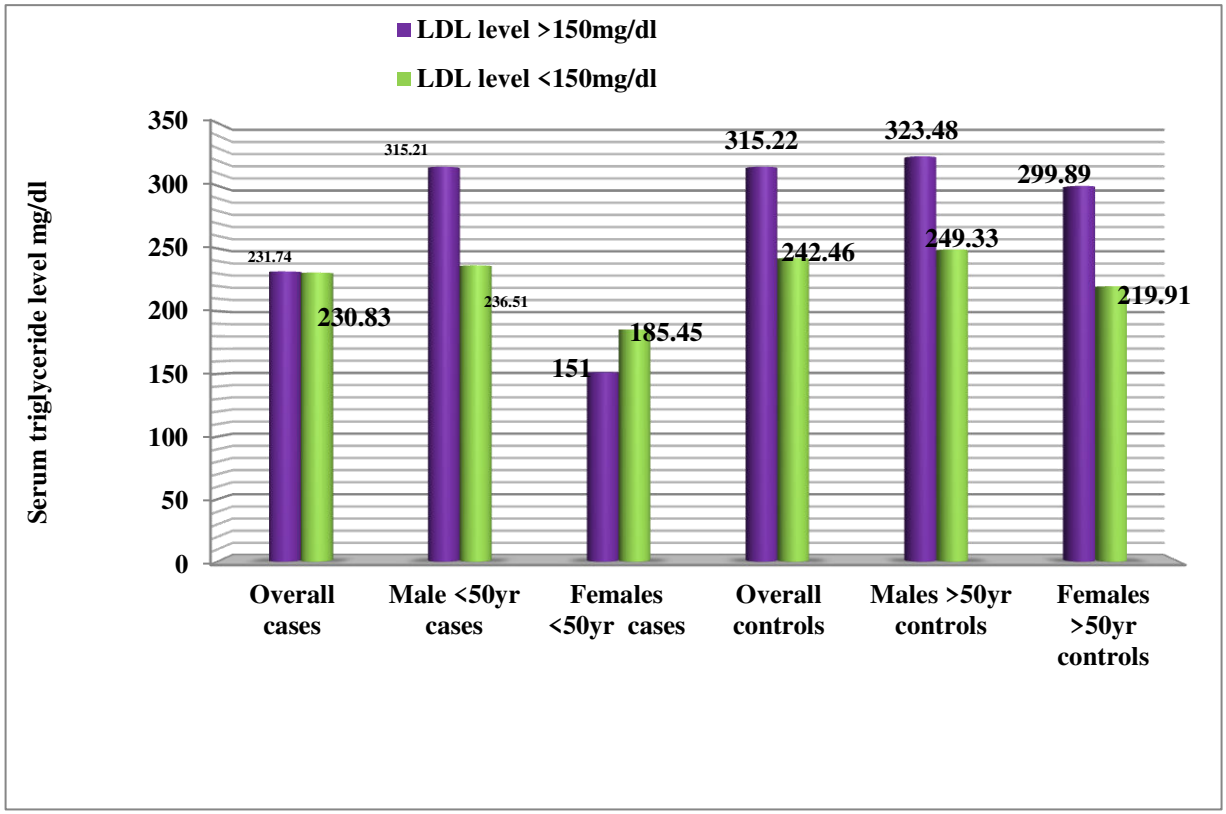

Figure 3. Graphical comparison of mean serum triglyceride (mg/dl) in relation to serum LDL level in cases

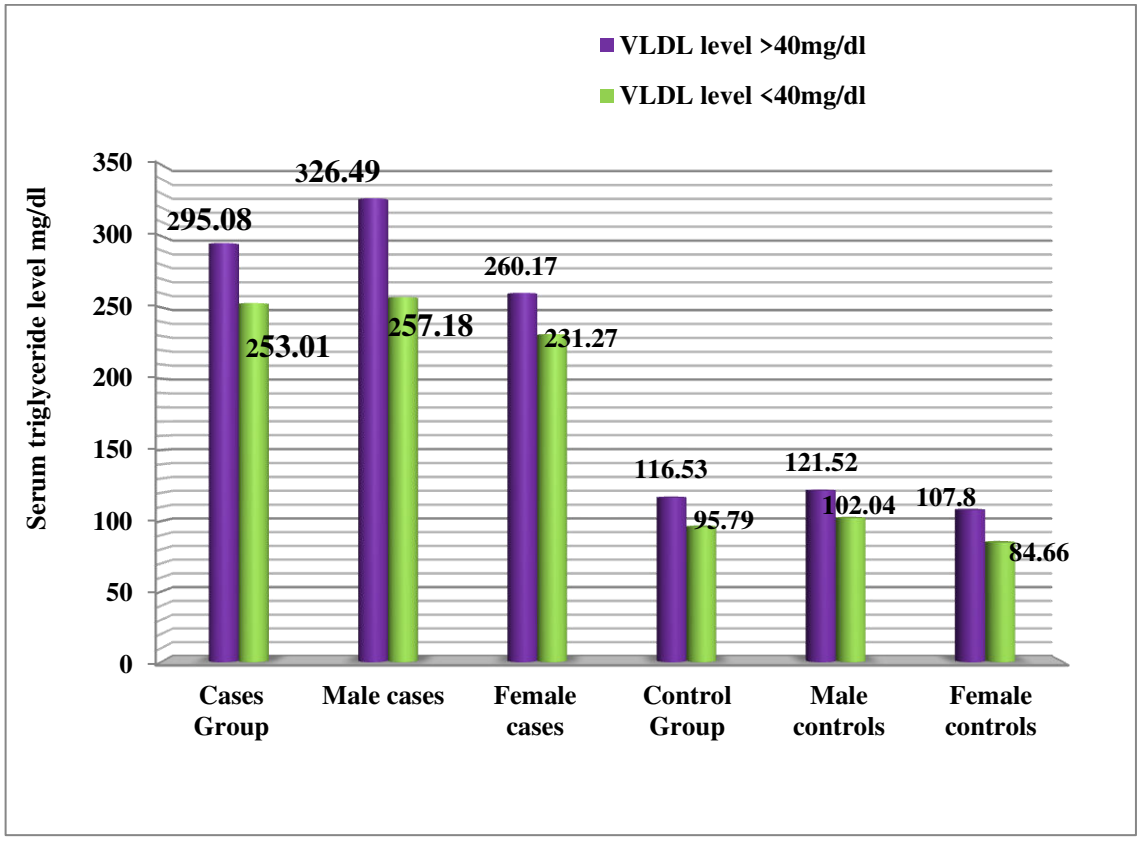

Figure 4. Comparison of mean serum triglyceride (mg/dl) in relation to serum VLDL level in cases and controls

This study including 150 (75 cases and 75 controls) subjects showed that elevated serum triglyceride concentration was associated with increased risk of ischemic heart disease. Epidemiological studies have found a positive relationship between body triglyceride and CAD.

As discussed by **Austin** (15) and Garber and **Avins** (16), the role of the TG level as a risk factor of IHD has long been controversial. However, it also is well recognized that the statistical characteristics of the distribution of TG levels, variability of TG measurements, and statistical and metabolic relations between TG and other risk factors (in particular, HDL-C) may reduce the ability to detect an association between TG and risk of IHD in standard multivariate analysis.1 To compensate for the problems described above, we used categorical transformation and divided the study population into subgroups stratifying TG levels by HDL-C levels, and in this context it should be remembered that in accordance with most1 but not all previous 25–27 studies, we could not identify fasting hypertriglyceridemia as a risk factor of IHD after adjustment for HDL-C in our conventional multivariate analysis. By working with categorically transformed TG data in relatively large subgroups, the effect of the large variability in TG measurements was smoothed out, and the effect was minimized of the apparent paradox that the highest TG levels are not necessarily associated with the highest risk of IHD. This may explain why in the present study, we were able to identify fasting hypertriglyceridemia as a strong independent risk factor of IHD. On the basis of our categorically transformed data and adjustments for HDL-C, subjects with TG levels of '2.0 mmol/L had a .100% increase in risk of IHD compared with subjects with TG levels of '1.0 mmol/L, a substantially higher value than the 14% increase in risk found in a recent meta-analysis study of TG, HDL-C, and risk of IHD with a 1.0 mmol/L increase in TG level.28 In addition, because in our analysis we stratified for HDL-C levels, it was possible to demonstrate a clear effect of TG on the risk of IHD distinct from that of HDL-C.

In this study, mean serum triglyceride level in patients of IHD in the presence of dyslipidemia likely elderly male (>50years of age) patients with high (>150mg/dl) LDL compared to patients with normal (<150mg/dl) LDL, all male patients of IHD with high (>40mg/dl) VLDL compared to patients with normal (<40mg/dl) VLDL had significantly high serum triglyceride level ($p<0.05$). However larger case-control studies would be required to stabilize the facts.

We observed that the elevated serum triglyceride concentrations to be associated with increased risk of ischemic heart disease.

4. Conclusion

According to this study, serum triglyceride may provide an important, simple, effortless and cost effective tool for predicting an impending ischemic heart disease especially in diabetic patients, male elderly smokers, elderly males with high LDL, males with high VLDL level. In middle-aged and elderly men, a high level of fasting triglycerides is a strong risk factor of IHD independent of other major risk factors, including HDL cholesterol.

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Conflict of interest

The authors declare that there are no conflicts of interest.

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