Impact of gender on the lipid profile of patients with coronary artery disease: a Bayesian analytical approach

Accepted version

Impact of gender on the Lipid Profile of Patients with Coronary Artery Disease: A Bayesian Analytical Approach

Vivek Verma[1], Ashwani Kumar Mishra[2], Anita Verma[3], Hafiz T.A. Khan[4], Dilip C. Nath[5], Rajiv Narang[6]

[1] Department of Neurology, All India Institute of Medical Sciences (AIIMS), New Delhi. 110029, India Email: viv_verma456@yahoo.com

[2] National Drug Dependence Treatment Centre (NDDTC), All India Institute of Medical Sciences (AIIMS), New Delhi, 110029, India Email: ashwaniiop@gmail.com

[3] Department of Neurology, All India Institute of Medical Sciences(AIIMS), New Delhi. 110029, India Email: anii121514@gmail.com

[4] Health Promotion and Public Health**,** College of Nursing, Midwifery and Healthcare, University of West London, Paragon House, Boston Manor Road, Brentford TW8 9GB United Kingdom, Email: hafiz.khan@uwl.ac.uk. Also an associate professorial fellow at the Oxford Institute of Population Ageing, University of Oxford, UK.

[5] Assam University, Silchar, Assam, 788011, India Email: dilipc.nath@gmail.com

[6] Department of Cardiology, All India Institute of Medical Sciences (AIIMS), New Delhi. 110029, India Email: r_narang@yahoo.com

Abstract

Background: The variation of the lipid profile by sex in patients with coronary artery disease (CAD) is well known. However, when the sample size is small, it is difficult to establish this association.

Objectives: The present study uses the Bayesian paradigm to understand the association between sex and lipid profile in patients with coronary artery disease and compares the results with classical approaches.

Methods: The study is based on a secondary analysis of CAD patients' data (n = 1045) from NHANES (2015-2016), older than 50 years for which lipid profile measurements were available. The clinical diagnosis of CAD was positive in 91 individuals and negative in 945. The comparison of differences in lipid profiles by sex was performed under the classical paradigm (independent sample t-test and Wilcoxon Rank Sum Test) and Bayesian.

Results: CAD-positive men were younger (54-80 years) than women (57-80 years). Lipid parameters (total cholesterol, LDL, direct HDL, non-HDL) differed significantly according to sex, under both classical and Bayesian paradigms; except triglycerides and two proportions (TC: HDL, LDL: HDL). However, the Bayesian paradigm has suggested differences even for triglycerides and two sex ratios.

Conclusions: The present study demonstrates the application of Bayesian t test in the case of a small sample size. This clearly suggests that even when the sample size is small, the Bayesian paradigm closely approximates our prior knowledge of the lipid profile as a risk factor for the development of CAD. The Bayesian paradigm revealed the importance of clinical parameters (triglycerides, TC: HDL and LDL: HDL), which remained hidden under the classical t-test and the non-parametric Wilcoxon Rank Sum Test.

Key Words: Bayes factor; posterior distribution; Triglyceride; Ratio of TC:HDL; Ratio of

LDL:HDL.

1. Introduction

Cardiovascular diseases are grouped into diseases based on problems of the heart and blood vessels[1], including coronary artery disease, acute coronary syndrome, and coronary artery disease (CAD). CAD occurs when the heart has not received adequate amounts of oxygen and blood due to plaque buildup within the coronary arteries, and coronary artery disease is the most common type of heart disease. The deposition of cholesterol (known as atherosclerosis) and other materials (called plaque) within the coronary arteries causes the arteries to narrow and harden, which affects the blood supply to the heart. If such deposition continues, then it will lead to heart failure. According to the World Health Organization (WHO, 2015), worldwide, CAD is one of the leading causes of morbidity and mortality and is also the leading cause of death.

According to the American Heart Association, among several risk factors for coronary heart disease, the components of the lipid profile, namely triglycerides, low-density lipoprotein cholesterol (LDL-C), direct high-density lipoprotein cholesterol (HDL-C), and total cholesterol are very common. According to the Center for Disease Control and Prevention (CDC), CAD is the leading cause of death in the United States for both men and women. The burden of the disease associated can be visualized by the fact that CAD alone is responsible for more than 4.5 million deaths worldwide[2].

Risk factors associated with CAD include lifestyle, environment, and genetic factors[3]. Previous CAD studies have documented the association of the lipid profile; in this sense, intensive lifestyle changes can also stop or reverse its progression without the use of lipid-

lowering drugs[4]. According to the American Heart Association, the recommended normal range prescribed for lipid profile is: total cholesterol<200 mg /dl, triglycerides<200 mg/dl, HDL-C> 40 mg/dl, and LDL-C<130 mg/dl. The lipid profile acts as a diagnostic tool for the detection and clinical management of cases of coronary artery disease. For example, in dyslipidemia, patients with CAD, LDL cholesterol, total cholesterol and triglycerides, will be higher, and HDL-C cholesterol will lower down[5]. It is also well known that in patients with CAD, triglycerides[6], total cholesterol, and LDL-C are significantly higher, and HDL-C is significantly lowered[7-10].

The influence of gender on the components of the lipid profile is also studied in various situations. Total cholesterol levels in women are significantly reduced in the 25–49 year age group and are higher in 50–64 age-groups than in men[11]. Total cholesterol, LDL-C, and the ratio of total cholesterol to HDL-C levels are significantly higher in older women (> 50 years) than in younger women (30-46 years), but in men, these levels do not change dramatically with age[12]. The impact of gender on triglycerides turns out to be significantly different[13-15].

It had shown that 13.3% of the populations older than 55 years were affected by CAD and, among them; the percentage of men was higher than that of women[6]. The appearance of CAD is associated with changes in the lipid profile, which is influenced by several factors, and among them, the sex of an individual is also an important factor. Therefore, the objective of the present study is to examine the impact of sex on the lipid profile in patients with CAD. For this study, the data set from the National Health and Nutrition Survey (NHANES), 2015-2016 was used. The study population is made up of people 50 years of age or older. To compare the differences in the lipid profile between the sexes when the sample size is comparatively small, both a classic two-tailed Student test and a non-parametric Wilcoxon rank sum test, as well as

the Bayesian t test were adopted. Statistical significance was measured using p-values in the context of the Student's t test and the Wilcoxon rank sum test, while the Bayes factor was used for the Bayesian t test.

2. Methods

For the evaluation of the health and nutrition component of the non-institutionalized population in the United States, since the early 1960s, CDC has conducted the National Health and Nutrition Survey (NHANES). The NHANES program was initiated to assess the level of health and nutritional status in the United States, collecting information on various characteristics-household, physical and medical examinations of sampled children and adults. In this study, we used NHANES 2015-2016, which was launched with 15,327 people. The NHANES (2015-16) database was considered, which included 9971 individuals, who completed the interview.

Study population: Participants aged less than 50 (n = 8635) and lipid profiles were not observed or declared (n = 291), are excluded. There were 1,045 participants, aged 50 years or older, and among them, 91 were clinically diagnosed with CAD and the remaining 945 did not have CAD (non-CAD), and their lipid profiles were observed and reported (Figure 1 in the appendix).

Laboratory Methods: Information on laboratory parameters, including lipid profiles, including triglycerides (mg/dL), LDL cholesterol (mg/dL), direct HDL cholesterol (mg/dL), and total cholesterol. (mg/dL), were obtained from the participants, who were recommended too fast for at least 9 hours before physical examination at the mobile examination center (MEC) for blood collection.

The criteria of the lipid standardization program of CDC were used to standardize the parameters of the serum lipid profile due to changes in laboratory methods during years of research to ensure accuracy and comparability of measurements between studies.

3. Statistical Analysis

For the comparison of the descriptive statistics among gender, the results were expressed as Mean (μ) ± Standard Deviation (s) and percentage (%). Under the assumption that the variation among the components of lipid profile and other continuous differences based on sex (for male (μ_M, s_M); female (μ_F, s_F)) are fixed quantities, to test the hypothesis

$$H_0: \mu_M = \mu_F \text{vs } H_1: \mu_M \neq \mu_F \qquad (1)$$

the classical two tail Student's t-test and Wilcoxon Rank Sum Test under parametric and non-parametric setup, respectively, were appropriately used and discussed and statistical significances were measured using their p-values. For testing the hypothesis of equation (1), the test statistic takes the following form under the classical paradigm:

$$t = \frac{\bar{x}_M - \bar{x}_F}{\left(\frac{(n_M - 1)s_M^2 + (n_F - 2)s_F^2}{n_M + n_F - 2}\right)^{1/2} \Big/ \sqrt{n_\theta}} \qquad (2)$$

where, $n_\theta = \left(\frac{1}{n_M} + \frac{1}{n_F}\right)^{-1}$, the degree of freedom are $\tau = n_M + n_F - 2$, $\bar{x}_i$ and μ_i respectively, denotes the sample and population mean corresponding to each the continuous quantity of the i^{th} gender, $\{i = Male(M), Female\ (F)\}$.

In real sense the exact characterization of the randomness inherent in the quantitative

measurement is ignored. Under such situation, the comparison of any continuous quantities and their assessments under traditional test of significance becomes a serious concern. Therefore, the present work emphasizes another promising paradigm of statistical framework that can address such situation by considering the formulation under Bayesian t-test. In this analytical procedure, a reasonable and useful prior has suggested to obtain a closed form of Bayes factor for emphasizing the statistical significance. To test the hypothesis under two-sided alternatives, the Bayesian version of the two-sample *t* statistic under the null and alternative hypotheses was adopted and the decision was made using the value of Bayes factor (B). In the present study, common variance, say σ^2, has assumed in both sex corresponding to each quantity. In order to work with Bayesian paradigm, we need to specify the prior distribution of the effect size (difference) that needs to be tested. Under the suggested hypothesis of a non-zero difference, the standardized difference $\frac{|\mu_M - \mu_F|}{\sigma}$ has prior mean, say θ, and prior variance, say $\sigma_\theta{}^2$. The Bayes Factor for testing H_0 against H_1 of equation (1) is:

$$B(\boldsymbol{x}) = \frac{T_\tau(t|0,1)}{T_\tau(t|\ \theta\sqrt{n_\theta}, 1 + n_\theta\ \sigma_\theta{}^2)} \qquad (3)$$

where $T_\tau(t|\alpha,\beta)$ denotes the value that results from plugging t into non-central t distribution probability density function with f degree of freedom and parameters α for location and $\beta^{1/2}$ for scale[16]. The Rule of thumb[17-18] followed for inference is as follows, if $log_{10}(B(\boldsymbol{x}))$ varies between 0 and 0.5, the evidence against null hypothesis H_0 will be poor, if $log_{10}(B(\boldsymbol{x}))$ lies between 0.5 and 1, it is substantial, if it is between 1 and 2, it is strong, and if it is above 2 it

is decisive. The results are simulated by following the Gibbs sampling, with 100,000 iterations, by using R-software version 3.6.2 and data processing is done using SAS University edition.

4. Results

4.1 Descriptive characteristics

Table 1 show the comparison of patients with CAD and non-CAD, which includes the age at which CAD occurred, its duration, ever doctor said about obesity, to reduce salt and fat/calories intake. A total of 91 CAD and 954 non-CAD participants [males (CAD=55; non-CAD=450) and females (CAD=36; non-CAD=504)] were included in this study. The overall mean age $\pm$ general standard deviation of the participants was 69.8 ± 7.5 years in CAD (54-80 years) and 64.5 ± 9.2 in non-CAD (50-80) years. The mean age of presentation to seek treatment for CAD in men (57.2 years) was earlier than in women (60.4 years). The duration of CAD in men (12.2 years) was longer than in women (10.1 years). Most of the patients with CAD were obese (51.7%) and it was recommended to reduce their salt intake (52.8%) and diet control (57.8%). Among non-CAD participants, the percentage distribution of obese people prescribed to reduce salt intake and diet control is almost the same.

4.2 Clinical features

A comprehensive gender comparison between the lipid profile parameters as well as some of the derived parameters, namely triglycerides (mg/dL), LDL cholesterol (mg/dL), direct HDL cholesterol (mg/dL) and total cholesterol (mg/dL), non-HDL cholesterol, TC: HDL and LDL: HDL ratio were listed in Table 2-4. The gender association between the various components of the lipid profile and their derived proportions has been measured under the classical (both parametric and non-parametric) and Bayesian paradigms. Furthermore, the empirical gender-

wise distribution pattern of each of the lipid parameters and their means are shown in Figure 2-4 of participants (n = 1045) [regardless of CAD and absence of CAD], participants without CAD (n = 945) and CAD participants (n = 91), respectively in the Appendix section. In Table 2, it was hypothesized (null hypothesis) that there is no gender difference in the lipid profile of the participants (independent of CAD and absence of CAD). The classical t-test and nonparametric Wilcoxon Rank Sum test based on participants (n = 1045) suggested a significant difference between the sexes (P <0.05) for triglycerides, LDL cholesterol, direct HDL cholesterol, total cholesterol, and non-cholesterol. HDL, TC: HDL ratio and LDL: HDL ratio of the lipid profile. The similar significant gender difference in lipid profiles was also captured by Bayesian t tests and revealed that Bayes factor (Log (B)) is greater than 2 as triglycerides (Log (B) = 8.58), LDL cholesterol (Log (B) = 2.76), direct HDL cholesterol (Log (B) = 16.96), total cholesterol (Log (B) = 14.03) and non-HDL cholesterol (Log (B) = 5.11), TC: HDL ratio (Log (B) = 2.73) and LDL: HDL ratio (Log (B) = 2.29).

The classical t-test and non-parametric Wilcoxon Rank Sum test based on no-CAD participants (n=945) is presented in **Table 3,** which was also suggesting a significant (P<0.05) gender-wise difference among Triglyceride, LDL-cholesterol, Direct HDL-Cholesterol, Total Cholesterol and non–HDL cholesterol, TC: HDL ratio and LDL: HDL ratio of lipid profile. Significant difference among lipid profiles of males and females were also captured by Bayesian t tests with Bayes factor (Log(B)) greater 2 i.e., Triglyceride (Log(B) = 4.76), LDL-cholesterol (Log(B) = 2.45), Direct HDL-Cholesterol (Log(B) = 32.62), Total Cholesterol (Log(B) = 22.79) and non–HDL cholesterol (Log(B) = 3.51), TC: HDL ratio (Log(B) = 4.54) and LDL: HDL ratio (Log(B) = 4.06).

The classical t-test and non-parametric Wilcoxon Rank Sum test based on CAD participants

(n=91) is presented in **Table 4,** which suggested a significant gender-wise differences only among LDL-cholesterol, Direct HDL-Cholesterol, Total Cholesterol and non–HDL cholesterol, of lipid profile. On the other hand, Bayesian t tests suggested a significant gender-wise differences among all lipid profile parameters with Bayes factor (Log(B)) greater 2 i.e., Triglyceride (Log(B)=7.21), LDL-cholesterol (Log(B) = 2.52), Direct HDL-Cholesterol (Log(B) = 3.36), Total Cholesterol (Log(B) = 3.38) and non–HDL cholesterol (Log(B) = 4.55), TC: HDL ratio (Log(B) = 4.55) and LDL: HDL ratio (Log(B) = 3.76).

5. Discussion

Table 1 show that the mean age of participants with CAD is higher than that of non-CAD participants. The mean age of onset of coronary artery disease in men was lower than that of women; therefore, the mean duration of the coronary artery disease period was longer in men than in women. The age factor is an important predictor for CAD. The majority of the CAD prevalence's occurred between the ages of 50 and 70, approximately four times the prevalence in people older than 70 years. Among patients with CAD compared to non-CAD, more than 50% of the individuals corresponding to each of the risk factors of being overweight, high salt intake, and fat / calorie intake were prescribed to reduce the intake and food control. This suggests the need to focus on the daily routine of the participants.

Non-significant results obtained in the both of classic non-parametric Wilcoxon Rank Sum t tests for some of the important lipid parameters, namely triglycerides, TC: HDL ratio and LDL: HDL ratio, which is considered a good predictor of CAD, and was found significantly different in Tables 2 and 3, which suggests that the null hypothesis is contrary to the theory of the difference between the sexes, and is also observed in the empirical densities shown in Figure 2-3 of Appendix.

Previous studies that focused on the impact of triglycerides, the TC: HDL ratio, and the LDL: HDL ratio on CAD have shown that elevated triglyceride levels increase the risk of prevalence of coronary heart disease and is lowered through clinical management in addition to diet control, regular exercise and pharmacotherapy[19]. This is of great importance for public health since such a suggestion can have positive reinforcement among patients towards adopting a healthy dietary pattern in their daily routine. The higher value of the LDL: HDL ratio shows a positive association with the prevalence of hypertension and hypercholesterolemia in men and women[20] and the higher TC: HDL ratio was considered an independent indicator of extensive coronary disease.[21] As with the classic t-test and nonparametric Wilcoxon rank-sum paradigms, some of the important lipid parameters, namely triglycerides, the TC: HDL ratio, and the LDL: HDL ratio were not found to differ significantly across gender, which were found to be different in earlier studies. Based on the results obtained, data-based estimates for lipid profile parameters were found to be consistent with clinical characteristics and were also found to be effective in demonstrating statistical significance with clinical significance. Therefore, the quality of the data was not questioned regarding the insensitivity to distinguish the theory from the null hypothesis. However, to clinically link the data to theory, apart from certain lipid parameters, namely LDL cholesterol, direct HDL cholesterol, total cholesterol, and non-HDL cholesterol, these were found to be non-significant in the classical tests, Bayesian technique was adopted in Table 4. The Bayesian t-test suggested evidence of differences in the lipid profile across gender and was also observed in the empirical densities shown in Figure 4 of the Appendix. The significant difference in elevated levels of lipid parameters, namely triglycerides, LDL cholesterol, direct HDL cholesterol, and total cholesterol in women with CAD as compared to men, has also been discussed in several other studies[22-26] which has also been observed

under the Bayesian test paradigm.

The lipid parameters of LDL cholesterol, direct total HDL cholesterol, and non-HDL cholesterol that were significantly different between sexes according to the classical test paradigms also corresponded to the Bayesian paradigms. On the other hand, the reverse is not true, as triglycerides, TC: HDL ratio, and LDL: HDL ratio also differed significantly across gender in Bayesian t tests and were discussed in previous studies, but they were not captured in the conventional classical tests, possibly due to small sample size.

6. Conclusion

In the study Bayesian inferential procedure is presented, where the sample size is comparatively smaller, with emphasis on the possible differences in the parameters of the lipid profile of patients with CAD between men and women. Assuming that the differences in parameters due to gender are fixed, the classical t-test and the nonparametric Wilcoxon rank sum test were not fully compatible to capture significant changes in lipid parameters due to gender. On the other hand, even with small sample size, the results obtained on the basis of Bayesian t-tests turned out to be more reliable for concordance of clinical practices on the sex difference in the association of lipid profile in patients. Patients with coronary artery disease whose results were not fully recognized in the conventional t-tests and Wilcoxon Rank Sum non-parametric tests, viz. Triglycerides (p-value = 0.7613 (0.8806), log (B) = 7.21), TC: HDL ratio (p-value = 0.8110 (0.5976), log (B) = 6, 14) and LDL: HDL ratio (p-value = 0.9893 (0.9418), log (B) = 3.76).

References:

[1] Sanchis-Gomar, F., Perez-Quilis, C., Leischik, R., & Lucia, A. Epidemiology of coronary heart disease and acute coronary syndrome. *Annals of translational medicine*, *4*(13), 2016.

[2] Okrainec, K., Banerjee, D. K., & Eisenberg, M. J. Coronary artery disease in the developing world. *American heart journal*, *148*(1), 7-15, 2004

[3] Musa, H. H., Tyrab, E. M., Hamid, M. M., Elbashir, E. A., Yahia, L. M., & Salih, N. M. Characterization of lipid profile in coronary heart disease patients in Sudan. *Indian heart journal*, *65*(2), 232–233, 2013. doi:10.1016/j.ihj.2013.03.007

[4] Ornish, D., Scherwitz, L. W., Billings, J. H., Gould, K. L., Merritt, T. A., Sparler, S., ... & Brand, R. J. Intensive lifestyle changes for reversal of coronary heart disease. *Jama*, *280*(23), 2001-2007, 1998.

[5] Haque, A. E., Yusoff, F. B. M., Ariffin, M. H. S. B., Fadhli, M., Ab Hamid, B., Hashim, S. R. B., & Haque, M. Lipid Profile of the Coronary Heart Disease (CHD) Patients Admitted in a Hospital in Malaysia. *Journal of Applied Pharmaceutical Science*, *6*(05), 137-142, 2016.

[6] Kumar, L., & Das, A. L. Assessment of serum lipid profile in patients of coronary artery disease: a case-control study. *International Journal of Contemporary Medical Research*, *5*(5), 59-62, 2018.

[7] Haddad, F. H., Omari, A. A., Shamailah, Q. M., Malkawi, O. M., Shehab, A. I., Mudabber, H. K., &Shubaki, M. K.. Lipid profile in patients with coronary artery disease. *Saudi medical journal*, *23*(9), 1054-1058, 2002.

[8] Bestehorn, K., Jannowitz, C., Karmann, B., Pittrow, D., &Kirch, W. Characteristics, management and attainment of lipid target levels in diabetic and cardiac patients enrolled in Disease Management Program versus those in routine care: LUTZ registry. *BMC Public Health*, *9*(1), 280, 2009.

[9] Abraham, G. Evaluation of variation in the lipid profile and risk for coronary artery disease in healthy male individuals with respect to age. *Int J Res Med Sci*, *2*(2), 551-556, 2014.

[10] Sun, X., & Du, T. Trends in cardiovascular risk factors among US men and women with and without diabetes, 1988–2014. *BMC public health*, *17*(1), 893, 2017.

[11] Gostynski, M., Gutzwiller, F., Kuulasmaa, K., Döring, A., Ferrario, M., Grafnetter, D., &Pajak, A. Analysis of the relationship between total cholesterol, age, body mass index among males and females in the WHO MONICA Project. *International journal of obesity*, *28*(8), 1082, 2004.

[12] Goh, V. H., Tong, T. Y., Mok, H. P., & Said, B. Differential impact of aging and gender on lipid and lipoprotein profiles in a cohort of healthy Chinese Singaporeans. *Asian journal of andrology*, *9*(6), 787-794, 2007.

[13] Rosenkranz, S. K.. Lifestyle influences on airway health in children and young adults (Doctoral dissertation, Kansas State University), 2010.

[14] Carroll, M. D., Kit, B. K., &Lacher, D. A. *Trends in elevated triglyceride in adults: United States, 2001-2012* (No . 2015). US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics, 2015.

[15] Alzahrani, S. H., Baig, M., Aashi, M. M., Al-shaibi, F. K., Alqarni, D. A., &Bakhamees, W. H. Association between glycated hemoglobin (HbA1c) and the lipid profile in patients with type 2 diabetes mellitus at a tertiary care hospital: a retrospective study. *Diabetes, metabolic syndrome and obesity: targets and therapy*, *12*, 1639, 2019.

[16] Gronau, Q. F., Ly, A., &Wagenmakers, E. J. Informed Bayesian t-tests. *The American Statistician*, 1-14, 2019.

[17] Kass, R. E., & Raftery, A. E. Bayes Factors. *Journal of the American Statistical Association*. 90 (430). 773, 1995.

[18] Verma V, Mishra AK, Narang R. Application of Bayesian analysis in medical diagnosis. *J Pract Cardiovasc Sci*;5:136-41, 2019.

[19] Coughlan, B. J., & Sorrentino , M. J. Does hypertriglyceridemia increase risk for CAD? Growing evidence suggests it plays a role. *Postgraduate medicine*, *108*(7), 77, 2000.

[20] Chen, Q. J., Lai, H. M., Chen, B. D., Li, X. M., Zhai, H., He, C. H., ... & Ma, Y. T. Appropriate LDL-C-to-HDL-C ratio cutoffs for categorization of cardiovascular disease risk factors among Uygur adults in Xinjiang, China. *International journal of environmental research and public health*, *13*(2), 235.0, 2016.

[21] Luz, P. L. D., Favarato, D., Faria-Neto Junior, J. R., Lemos, P., & Chagas, A. C. P. High ratio of triglycerides to HDL-cholesterol predicts extensive coronary disease. *Clinics*, *63*(4), 427-432, 2008.

[22] Schildkraut, J. M., Myers, R. H., Cupples, L. A., Kiely, D. K., &Kannel, W. B. Coronary risk associated with age and sex of parental heart disease in the Framingham Study. *The American journal of cardiology*, *64*(10), 555-559, 1989.

[23] Brown, S. A., Morrisett, J. D., Boerwinkle, E., Hutchinson, R., &Patsch, W. The relation of lipoprotein [a] concentrations and apolipoprotein [a] phenotypes with asymptomatic atherosclerosis in subjects of the Atherosclerosis Risk in Communities (ARIC) Study. *Arteriosclerosis and thrombosis: a journal of vascular biology*, *13*(11), 1558-1566, 1993.

[24] Bostom, A. G., Gagnon, D. R., Cupples, L. A., Wilson, P. W., Jenner, J. L., Ordovas, J. M., ... & Castelli, W. P. A prospective investigation of elevated lipoprotein (a) detected by electrophoresis and cardiovascular disease in women. The Framingham Heart Study. *Circulation*, *90*(4), 1688-1695, 1994.

[25] Roeters van Lennep, J. E., Westerveld, H. T., Erkelens, D. W., & van der Wall, E. E. Risk factors for coronary heart disease: implications of gender. *Cardiovascular research*, *53*(3), 538-549, 2002.

[26] Hossain, A., & Khan, H. T. Risk factors of coronary heart disease. *Indian heart journal*, *59*(2), 147-151, 2007.

Table 1. Demographic and Clinical Characteristics of the Patients with **CAD** versus **no CAD**

Characteristics& Categories		**CAD (n=91) (Mean± SD/ Percentage) (Range)**	**No CAD (n=954) (Mean± SD/ Percentage) (Range)**
Age (in years) (Mean± SD) (range)	**Male**	69.3±7.2 (54-80)	64.5±8.9 (50-80)
	Female	70.6±7.9 (57-80)	64.5±9.4 (50-80)
	All	69.8±7.5 (54-80)	64.5±9.2 (50-80)
CAD Occurrence Age (in years) (Mean± SD)	**Male**	57.2± 9.8	NA
	Female	60.4± 10.5	NA
	All	58.5±10.2	NA
Duration of period of CAD	**Male**	12.2±8.1	NA
	Female	10.1±8.9	NA
	All	11.4±8.4	NA
"Doctor ever said you were overweight" [#]	Yes	47 (51.7)	370(38.8)
"Doctor told to reduce salt in diet"* [#]	Yes	48 (52.8)	350(36.7)
"Doctor told to reduce fat/calories" [#]	Yes	47 (57.7)	371(38.9)

[#] from the questionnaire used in the study.

Table 2. Classical and Bayesian evaluation of gender differences in association of lipid profile among total patients (large sample size)

Parameter	**Gender (n=1045)**		**Parametric test for difference in mean**		**Non-parametric Wilcoxon Rank Sum Test**	**Bayes factor (Log(B))**
	Male (n_M=505) Mean± SD	**Female(n_F=540) Mean± SD**	**t-value**	**p-value**	**p-value**	
Total Cholesterol (mg/dL)	178.80±39.91	200.30±40.97	-8.56	**<.0001**	**<.0001**	**14.03**
LDL-cholesterol (mg/dL)	105.90±36.25	115.80±36.54	-4.39	**<.0001**	**<.0001**	**2.76**
Direct HDL-Cholesterol (mg/dL)	53.02±16.73	63.41±18.93	-9.37	**<.0001**	**<.0001**	**16.96**
Non–HDL cholesterol	125.80±38.28	136.80±39.68	-4.57	**<.0001**	**<.0001**	**5.11**
Triglyceride (mg/dL)	99.21±46.07	105.00±46.66	-2.00	**0.0457**	**0.0347**	**8.58**
TC:HDL ratio	3.60±1.11	3.36±1.03	3.69	**0.0002**	**<.0001**	**2.73**
LDL:HDL ratio	2.17±0.94	1.98±0.85	3.40	**0.0007**	**0.0005**	**2.29**

Table 3. Classical and Bayesian evaluation of gender differences in association of lipid profile among patients with **no CAD** (large sample size)

Parameter	**Gender (n=954)**		**Parametric test for difference in mean**		**Non-parametric Wilcoxon Rank Sum Test**	**Bayes factor (Log(B))**
	Male (n_M=450) Mean± SD	**Female(n_F=504) Mean± SD**	**t-value**	**p-value**	**p-value**	
Total Cholesterol (mg/dL)	182.20±39.67	201.10±40.29	-7.28	**<.0001**	**<0.0001**	**22.79**
LDL-cholesterol (mg/dL)	109.00±36.14	116.60±36.26	-3.23	**0.0013**	**0.0006**	**2.45**
Direct HDL-Cholesterol (mg/dL)	53.76±16.62	63.72±18.84	-8.61	**<.0001**	**<0.0001**	**32.62**
Non–HDL cholesterol	128.50±38.04	137.40±39.51	-3.55	**0.0004**	**0.0003**	**3.51**
Triglyceride (mg/dL)	97.12±42.47	103.80±44.28	-2.38	**0.0176**	**0.0193**	**4.76**
TC:HDL ratio	3.61±1.10	3.35±1.02	3.81	**0.0001**	**<0.0001**	**4.54**
LDL:HDL ratio	2.20±0.94	2.00±0.86	3.68	**0.0003**	**0.0001**	**4.06**

Table 4. Classical and Bayesian evaluation of gender differences in association of lipid profile among patients with **CAD** (small sample size)

Parameter	**Gender (n=91)**		**Parametric test for difference in mean**		**Non-parametric Wilcoxon Rank Sum Test**	**Bayes factor (Log(B))**
	Male (n_M=55) Mean± SD	**Female(n_F=36) Mean± SD**	**t-value**	**p-value**	**p-value**	
Total Cholesterol (mg/dL)	151.02±29.92	188.58±48.37	-4.15	**<.0001**	**0.0004**	**3.38**
LDL-cholesterol (mg/dL)	80.80±26.14	105.28±39.24	-3.29	**0.0017**	**0.0039**	**2.52**
Direct HDL-Cholesterol (mg/dL)	46.96±16.60	59.14±19.88	-3.16	**0.0021**	**0.0007**	**3.36**
Non–HDL cholesterol	104.10±95.08	129.40±115.30	-3.21	**0.0018**	**0.0054**	**4.55**
Triglyceride (mg/dL)	116.29±66.93	120.8±71.31	-0.30	0.7613	0.8806	**7.21**
TC:HDL ratio	3.50±1.17	3.43±1.15	0.24	0.8110	0.5976	**6.14**
LDL:HDL ratio	1.91±0.90	1.91±0.79	-0.01	0.9893	0.9418	**3.76**

Appendix

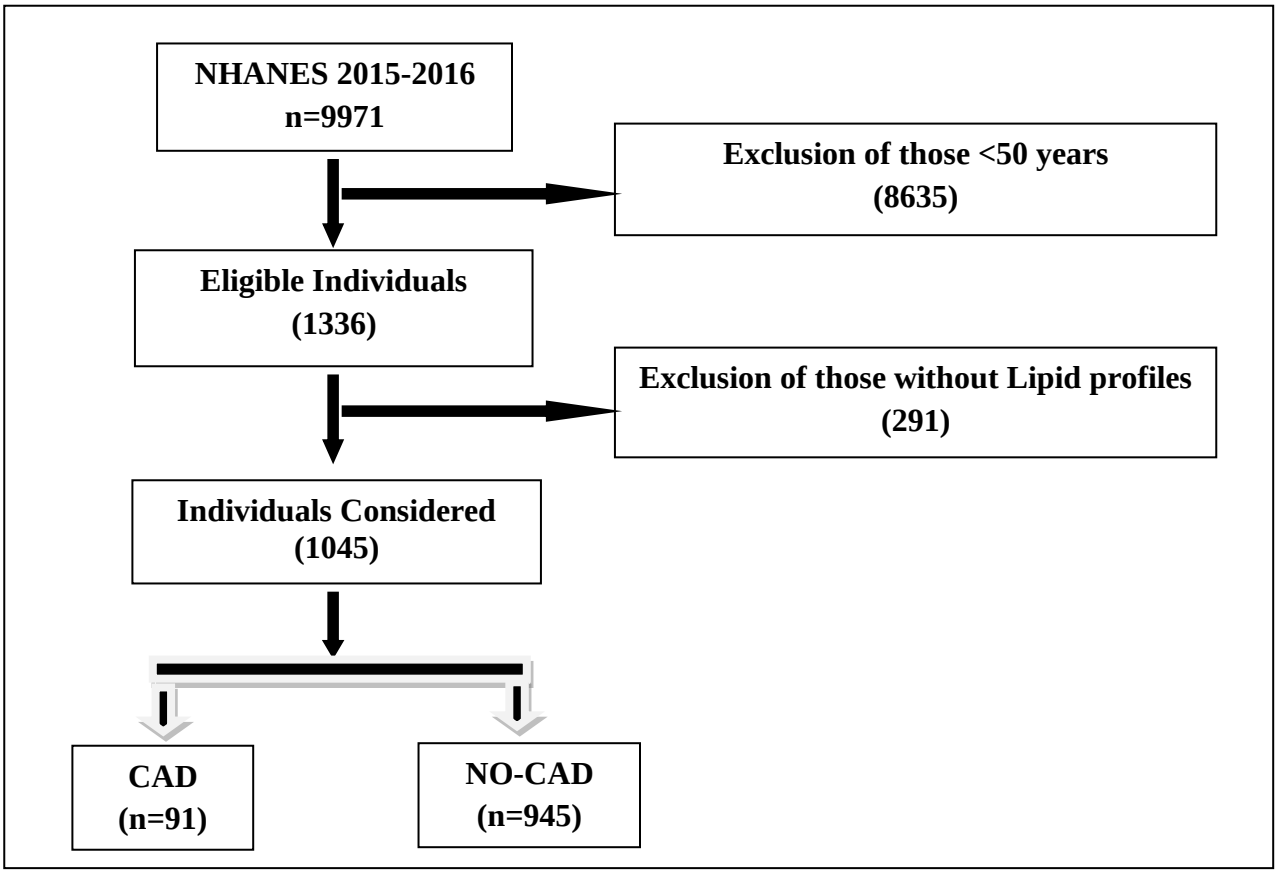

Figure 1: Procedure of Sampling from the NHNES 2015-16.

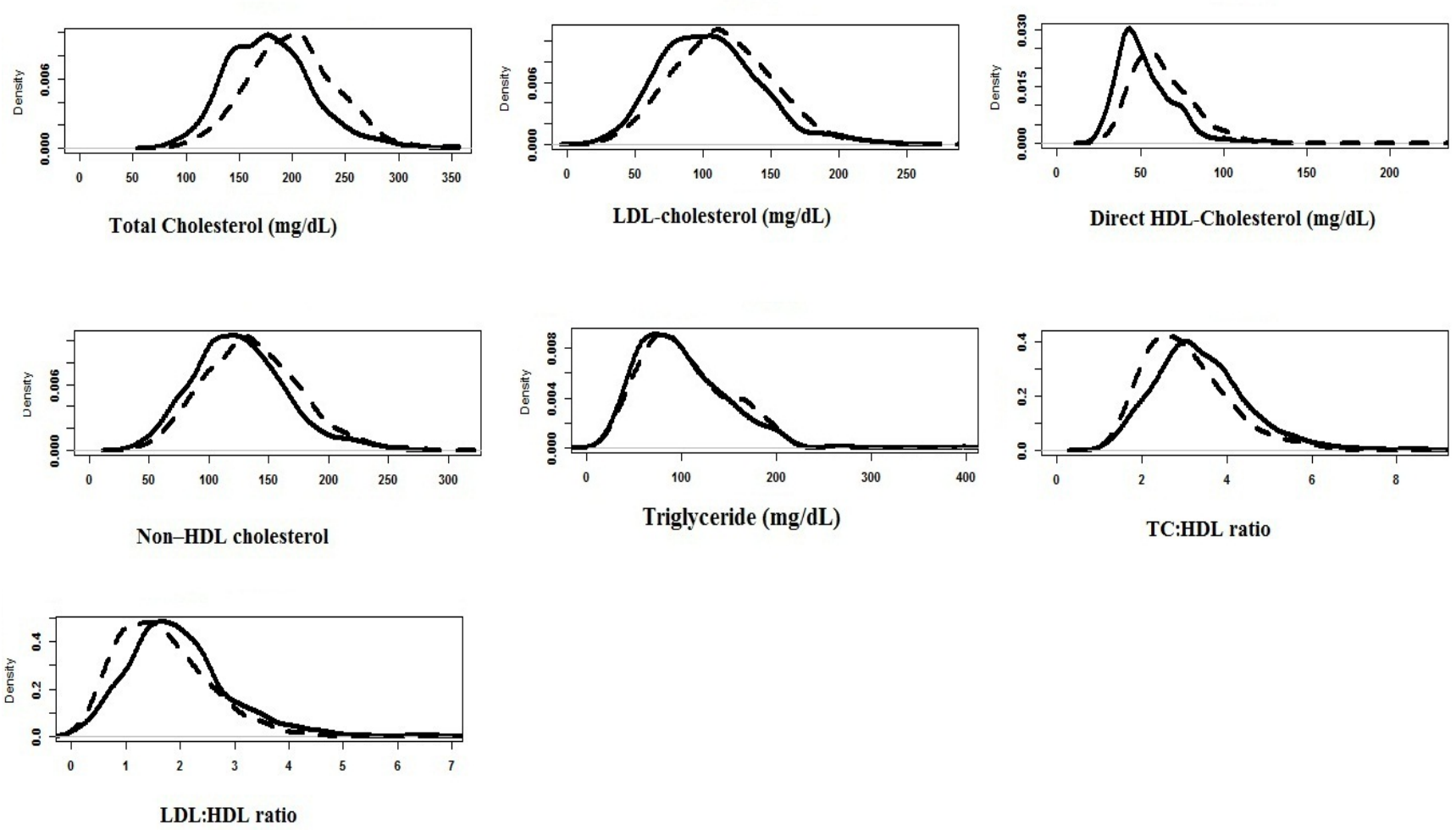

Figure 2: Gender wise empirical distributional patterns of lipid parameters pattern of all participants (**Male =505; Female=540)**, black denotes male and dashed denotes female.

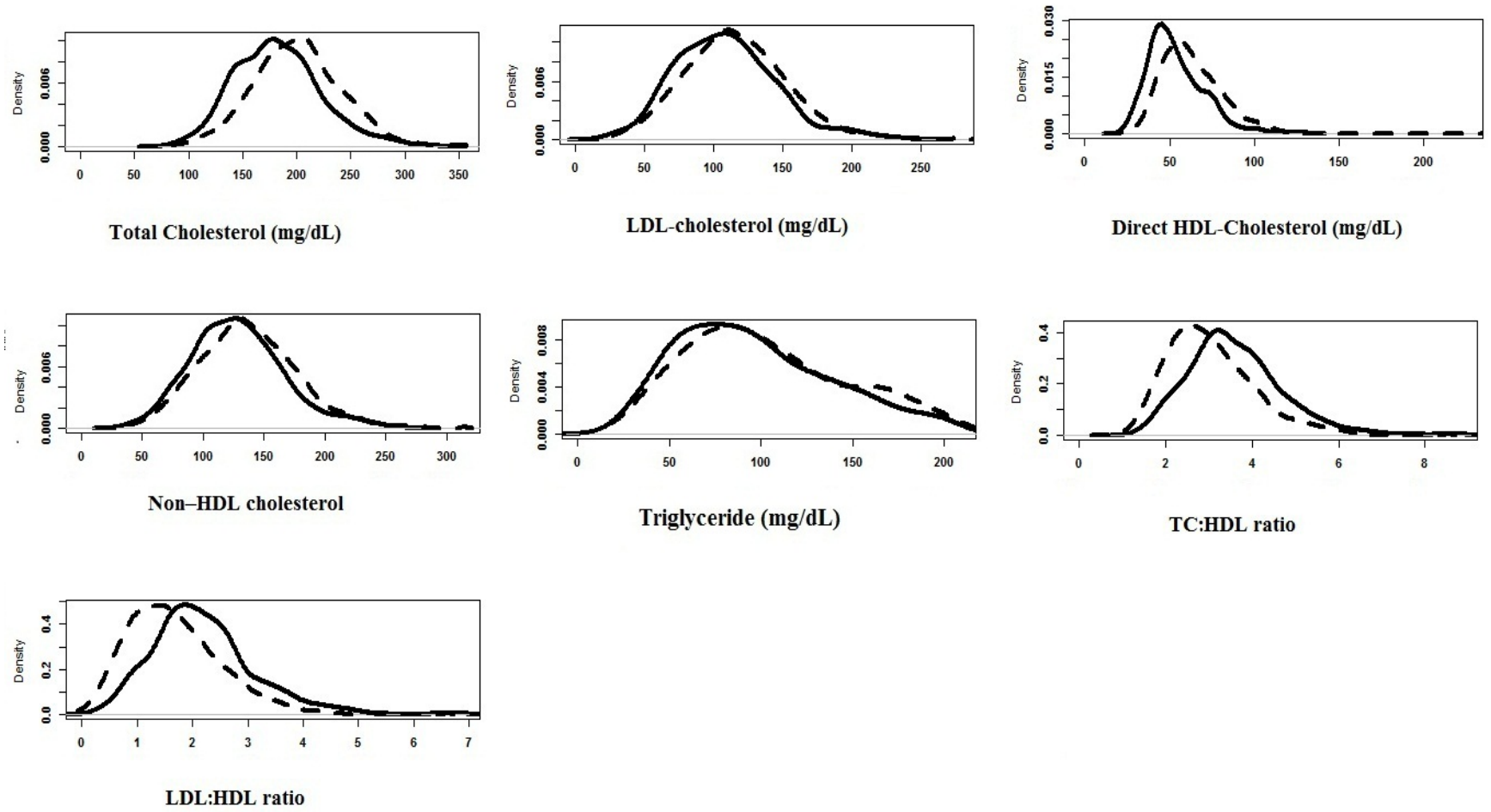

Figure 3: Gender wise empirical distributional patterns of lipid parameters pattern of no CAD participants (**Male =450; Female=504)**, black denotes male and dashed denotes female.

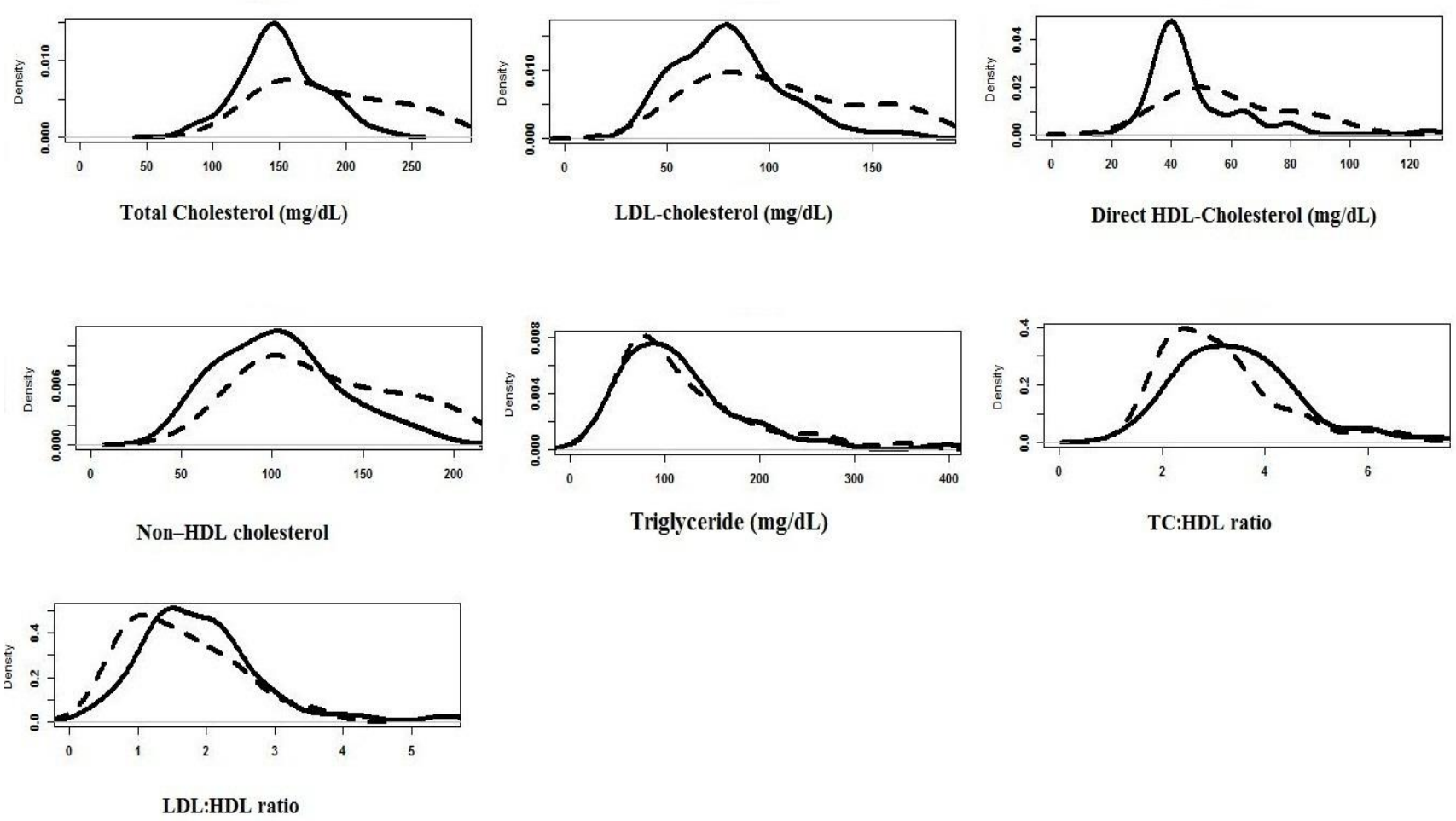

Figure 4: Gender wise empirical distributional patterns of lipid parameters pattern of CAD participants (**Male =55; Female=36)**, black denotes male and dashed denotes female.