# GENDER COMPARISON OF SOME APOLIPOPROTEIN AND LIPID PROFILES IN APPARENTLY HEALTHY ADULT MALE AND FEMALE SUBJECTS AT NNAMDI AZIKIWE UNIVERSITY TEACHING HOSPITAL, NNEWI, SOUTH-EASTERN NIGERIA.


## ABSTRACT:

Apolipoproteins are a group of proteins that are found on the surface of lipoprotein particles and are involved in lipid metabolism. Lipoproteins are complexes of lipids and proteins that transport lipids in the bloodstream, transport triglycerides to peripheral tissues, and reverse transport of cholesterol from peripheral tissues to the liver for excretion. They are important biomarkers of lipid metabolism and are known to be associated with an increased risk of CVD. This study aims to examine the gender-based comparison of mean serum apolipoproteins and lipoproteins at NnamdiAzikiwe University Teaching Hospital (NAUTH) Nnewi.A total of 51 adult female and 49 adult male subjects were randomly recruited at the Voluntary and counseling center NAUTH. The apolipoproteins such as Apo A-1, Apo A-2, Apo B, Apo C-2, Apo C-3, and Apo E, and the lipoproteins such as Total cholesterol (Chol), Low-Density Lipids (LDL), High-Density Lipids (HDL), and Triglycerides (TG) were analyzedusing routine laboratory analyses. The data were analyzed using Statistical Product and Service Solution (SPSS) version 21, independent Students'-test, and one-way analysis of variance (ANOVA) were used to compare means.The Apo A-1, Apo A-2, Apo B, Chol, HDL, and TG levels were significantly elevated in the male subjects compared to the female subjects with $p<0.05$. Conclusively, the male subjects studied were more prone to cardiovascular conditions.


**Comment [D1]:** SPSS: Statistical Package for the Social Sciences



## INTRODUCTION

Cardiovascular disease (CVD) is a significant health burden in Nigeria, with high morbidity and mortality rates[1]. Gender-based differences in the pathogenesis of CVD are well documented, with men at a higher risk of developing CVD than premenopausal women[2]. These differences are thought to be due to differences in sex hormones and their effects on lipid metabolism[3]. Apolipoproteins and lipoproteins are important biomarkers of lipid metabolism and are known to be associated with an increased risk of CVD[4].

Apolipoproteins(Apo-) are a group of proteins that are found on the surface of lipoprotein particles and are involved in lipid metabolism[5]. There are several types of apolipoproteins, ApoA-I is the main component of high-density lipoprotein (HDL), which is known as the "good" cholesterol[6]. ApoB is the main component of low-density lipoprotein (LDL), which is known as the "bad" cholesterol[7]. ApoE is involved in the uptake of LDL and very low-density lipoprotein (VLDL) by cells, and apoC-III is involved in the regulation of triglyceride metabolism[8]

Lipoproteins are complexes of lipids and proteins that transport lipids in the bloodstream, transport triglycerides to peripheral tissues, and reverse transport cholesterol from peripheral tissues to the liver for excretion[9]

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The study of gender differences in apolipoproteins and lipoproteins has significant implications in the field of medicine and healthcare. Lipoproteins and apolipoproteins play a critical role in cholesterol metabolism and are key indicators of cardiovascular disease risk. The study of gender differences in these biomarkers can help identify sex-specific risk factors and inform gender-specific diagnostic and treatment strategies.

Another important aspect of studying gender differences in lipoproteins and apolipoproteins is the impact of menopause on lipid metabolism. A study byAnagnostis et al. (2016) found that menopausal women had higher levels of total cholesterol, LDL-C, and apoB than premenopausal women[10]. This increase in cardiovascular disease risk factors highlights the importance of regular lipid monitoring and intervention strategies targeted at menopausal women.

Another important aspect to consider when studying gender differences in apolipoproteins and lipoproteins is their role in other diseases. A study by Hildrum et al. (2015) found that women had higher levels of high-density lipoprotein cholesterol (HDL-C) than men, which has been shown to have protective effects against cardiovascular disease. However, the same study also found that women had higher levels of HDL-C in conditions such as systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), where higher HDL-C levels have been linked to an increased risk of cardiovascular disease.[11] Moreover, research has also shown that gender differences in lipid metabolism may contribute to differences in the progression of neurological disorders such as Alzheimer's disease. A study by Kim et al. (2020) found that women with Alzheimer's disease had higher levels of total cholesterol and triglycerides than men with the same condition. The study suggests that gender-specific

**Comment [D3]:** Either “HDL” or “HDL-C”; “LDL” or “LDL-C”

differences in lipid metabolism may contribute to the differences in the progression and severity of Alzheimer's disease [12].

The study of gender differences in lipoproteins and apolipoproteins is crucial for understanding the sex-specific risk factors for cardiovascular disease. Hormonal factors, genetic variations, and lifestyle factors all contribute to differences in lipid metabolism between men and women. The identification of these differences can help inform the development of gender-specific diagnostic and treatment strategies to improve cardiovascular outcomes in both men and women. In this paper, we will examine the gender-based comparison of mean serum apolipoproteins and lipoproteins at NnamdiAzikiwe University Teaching Hospital Nnewi.

## METHODOLOGY

A total of 51 adult female and 49 adult male subjects aged 18-65 years were randomly recruited at the Voluntary and counseling center, NnamdiAzikiwe Teaching Hospital (NAUTH), Nnewi. The procedure of the study was explained to the subjects and their informed consent was obtainedverbally before proceeding with sample collection.

The observation of standard aseptic procedures and universal safety precautions in samples collected, stored, and processed was ensured [10]. Five milliliters (5 ml) of fasting blood sampleswere collected from each of the participants in the study. The samples were placed in different labeled plain sample tubes and were allowed to clot. They were further centrifuged, separated, and aspirated into plain sample tubes. They were further frozen until assay for lipoproteins (Chol, LDL, HDL, and TG) and apolipoproteins (Apo A-1, Apo A-2, Apo B, Apo C-2, Apo C,-3 and Apo E).

### ESTIMATION OF APOLIPOPROTEINS:

ApolipoproteinsA1, A2, B, C2, C3, and E were estimated using the principle of turbidimetry, the method of Tietz[13] and using kits from Spinreact Laboratories Limited, Spain.

### ESTIMATION OF LIPOPROTEINS

~~The lipoproteins were estimated as follows:~~

Total cholesterol was estimated using the enzymatic method as described by Allain et al. [14]For Triglycerides, enzymatic hydrolysis and oxidation by lipase method as described by

**Comment [D4]:** •Mention the study method/type.
•Mention both Inclusion and Exclusion criteria.
•Mention Statistical analyses plan in last paragraph of Methodology.

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Buccolo and David [15]. The HDL was estimated using Precipitating enzymatic method as described by Assmann et al. [16], While LDL was Calculated from a formula described by Kaplan et al. [17].

## RESULT

### APOLIPOPROTEIN PARAMETERS

A total of 100 adults (51 females and 49 males) aged between 18-65 years (32.52±5.50)participated in the study. The mean (±SD) Apo A-1 value in female participants was 1.24±0.05, while that of the male was 1.31±0.04. The Apo A-1 level was significantly higher in the male subjects than the female subjects ($p<0.05$). The mean (±SD) Apo A-2 value in female was 0.22±0.04, while that of the male subjects was 0.26±0.11. There was significant elevation in the Apo A-2 value in the male subjects compared to the female subjects ($p<0.05$).The mean (±SD) Apo B value in the female participants was 0.56±0.15, while in the male subject the mean (±SD) Apo B value was 0.80±0.39. Apo B was significantly elevated in the male subjects than the female subjects ($p<0.05$).

Although no significant elevation was observed in the Apo C-2 values of the subjects with $p>0.05$, the mean (±SD) Apo C-2 value in female was 0.05±0.02, while that of the male subjects was 0.05±0.01. The mean (±SD) Apo C-3 value in female was 0.03±0.02, while that of the male was 0.03±0.01. The Apo C-3 value of the female subjects were significantly not elevated than the male subjects ($p>0.05$). Although no significant difference was observed in the Apo E of the male and female subjects with $p>0.05$, the mean (±SD) Apo C-3 value in female was 0.05±0.02, while that of the male subject was 0.05±0.02.



| SEX | AGE | Apo A-1 g/L | Apo A-2 g/L | Apo B g/L | Apo C-2 g/L | Apo C-3 g/L | Apo E g |
|---|---|---|---|---|---|---|---|
| FEMALE (n=51) | 30.05 ± 6.54 | 1.24±0.05 | 0.22±0.04 | 0.56±0.15 | 0.05±0.02 | 0.03±0.02 | 0.05±0.02 |
| MALE | 34.98 ± 4.46 | 1.31±0.04 | 0.26±0.11 | 0.80±0.39 | 0.05±0.01 | 0.03±0.01 | 0.05±0.02 |

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| | | | | | | | |
|---|---|---|---|---|---|---|---|
| (n=49) | | | | | | | |
| P-value | <0.05 | <0.05 | <0.05 | <0.05 | >0.05 | >0.05 | >0.05 |
| F-value | 0.000 | .000 | .030 | .030 | .653 | .821 | .141 |

**TABLE 1: Gender-based comparison of the mean (±SD) levels of Apolipoproteins parameters studied among the participants.**

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ANOVA used when comparing groups are three or more. Post-Hoc test also required.



**LIPOPROTEIN PARAMETERS**

The mean (±SD)total cholesterol(Chol) value in female subjects was 4.56±0.25, while that of male subjects was 4.68±0.22. The Chol value was significantly elevated among the male subjects than the female subjects ($p<0.05$). The mean (±SD) Low Density Lipid (LDL) value in the female subjects was 2.32±0.12, while that of the male subjects was 2.33±0.14. There was no significant elevation in the LDL value of the male subjects compared to that of the female subjects ($p>0.05$). The mean (±SD) High Density Lipid (HDL) value in the female subjects was 1.35±0.06, while that of the male subjects was 1.40±0.05. The HDL in the male subjects was significantly elevated, compared to that of the female subjects ($p<0.05$). The mean (±SD) Triglycerides (TG) value in the female subjects was 1.43±0.05, while that of the male subjects was 1.45±0.05. TG value was significantly elevated in the male subjects compared to the female subjects ($p<0.05$).

**TABLE 2: Gender-based comparison of the mean (±SD) levels of Lipoproteins parameters studied among the participants.**

| SEX | AGE | CHOL mmol/L | LDL mmol/L | HDL mmol/L | TG mmol/L |
|---|---|---|---|---|---|
| FEMALE (n=51) | 30.05 ± 6.54 | 4.56±0.25 | 2.32±0.12 | 1.35±0.06 | 1.43±0.05 |
| MALE (n=49) | 34.98 ± 4.46 | 4.68±0.22 | 2.33±0.14 | 1.40±0.05 | 1.45±0.05 |
| P-value | <0.05 | <0.05 | >0.05 | <0.05 | <0.05 |
| F-value | 0.000 | .011 | .786 | .000 | .013 |

## DISCUSSION

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The study of gender differences in lipoproteins and apolipoproteins, important biomarkers of lipid metabolism known to be associated with an increased risk of CVD is crucial for understanding the sex-specific risk factors for cardiovascular disease. Hormonal factors, genetic variations, and lifestyle factors all contribute to differences in lipid metabolism between men and women.

A decrease in Apo A1 may compromise the structural composition of HDL, since it is the major apolipoprotein in HDL[20]. HDL particles must adhere to the ATP-binding cassette transporter (ABCA-1) on the cell surface in order for ApoA1 to function [21]. Lecithin cholesterol acyl transferase also needs the cofactor apoA1 [22,23]. Typically, there is a significant correlation between plasma ApoA1 concentration and HDL-C levels [24]. In this study, we observed a significant elevation in the Apo A-1 of the male subjects when compared to the female subjects. This finding is in contrary to that of Anagnostis et al where Apo A-1 was significantly higher in post-menopausal women than men [10]. Our finding also contradicted the findings of Nakhjavani*et al*, where there was a significant elevation in the Apo A-1 of the female subjects compared to the male subjects studied [18]. However, our finding concurs with that of Ezeugwunne*et al*[19] where Apo A-1 was significantly higher in HIV seropositive subjects studied.

The rate of hepatic and lipoprotein lipase activity has been found to rise in response to normal blood Apo A2, and this impact tends to promote plasma TG hydrolysis and subsequently reduce plasma TG. Elevated Apo A-2 level was observed among the male subjects than the female subjects in this study. While our finding was relatively comparable with the findings of Ogbodo et al[25], this finding concur with the findings of Ezeugwunne*et al*[19] who studied the Apo A-2 levels among HIV seronegative subjects.

Apo B is strongly associated with coronary heart diseases [26-29]. The liver produces apoB, which is then secreted together with VLDL. They are then transformed into intermediate-density lipoproteins (IDL) and then LDL in the peripheral circulation. Each lipoprotein particle contains one apoB molecule, hence apoB represents the overall amount of VLDL, IDL, and LDL particles and, consequently, the concentration of proatherogenic particles. Similarly, Apo B was found significantly elevated when compared with the Apo A-3 of the female subjects that participated in this study. The Apo B value of our male subjects was not

comparable to the values of the male subjects with Coronary Heart Disease in the study by Pischon*et al.* [31]

This study showed no significantly higher serum levels of Apo C-2, Apo C-3, and Apo Elevelsin the studied subjects. Increased blood Apo C2 levels have been associated with hypertriglyceridemia, hypercholesterolemia, and hyperchylomicronemia[32]. Intermediate lipoproteins (IDLs) and chylomicrons include the apo E protein, which is necessary for the transfer of cholesterol to neurons via apo E receptors and for the degradation of triglyceride-rich lipoprotein components[33].

There is evidence that Apo E prevents atherogenesis, hence the decreased value of Apo E seen as the length of therapy increased may suggest a cardio-protective role on the heart[34]. A relationship between Apo E and neurodegenerative diseases like multiple sclerosis and Alzheimer's disease has also been reported[35].

The serum total cholesterol studied in this study was significantly higher in the male subjects when compared to the female subjects. This finding is in line with that of Ezeugwunne*et al*[19], where total cholesterol level was elevated in both symptomatic not on ART and on ART, and asymptomatic seronegative HIV male subjects. On the contrary, this finding disagrees with that of Chinechelum et al who studied the lipid profiles in undergraduate students. [38]

While LDL- cholesterol levels were significantly increased in male than in female subjects studied in symptomatic HIV-positive subjects not on ART and in asymptomatic HIV seronegative, as reported by Ezeugwunne*et al*[19], this study observed no significant elevation in the LDL levels of the male subjects than the female subjects. This finding also contradicts that ofMagati*et al* where LDL was significantly higher in the male subjects studied. [39]

Our subjects had significantly higher HDL values than the female subjects. This finding is in contrary to similar study where males had lower HDL cholesterol than the female subjects[36] but agrees with the findings of Zhang et al where HDL was significant elevated in the female subjects studied.[40]

Cardiovascular disorders are strongly predicted by an elevated LDL level (Riddler*et al*, 2003). Cardiovascular illnesses have been linked to high levels of total cholesterol, triglycerides, and LDL (Ahaneku*et al.*, 2001; Kabiri*et al.*, 2010).Significantly, in our study, the male subjects had higher TG values than those of females, a finding concurring with that of similar studies, [36,37,39, 40]. However, this finding agrees with the findings of Ezeugwunne*et*

*al*, where TG values were significantly higher in the male seronegative subjects than the female subjects.[19] This finding suggests that the male subjects are more prone to cardiovascular conditions [41].

## CONCLUSION

Apolipoproteins and lipoproteins are important biomarkers of lipid metabolism and are known to be associated with an increased risk of CVD. Constant monitoring of these values will play a significant role in the prevention and control of many pathological conditions. This stud revealed significant Gender-based discrepancies in the Apolipoprotein and Lipid profiles. Additionally, this study revealed a significant elevation in the Apo A-1, Apo A-2, Apo B, Total Cholesterol, HDL and TG in the male subjects compared to the female subjects. Therefore, our study suggests that men have more chances of cardiovascular conditions than the female subjects.

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**Comment [D9]:** Need gross revision, write uniformly. Follow a specific guideline: either "APA" or "Vancouver" or "Journal guideline" strictly.

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