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Research Article

The Association between Cholesterol Ratio and Viral load Among HIV individuals on Antiretroviral Therapy at a Tertiary Hospital in Zambia

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Abstract:

Objective: To examine the association between cholesterol ratio and viral load among HIV positive individuals receiving antiretroviral therapy (cART)

Design and Methods: A retrospective cohort study was conducted at the Ndola Teaching Hospital in Zambia, focusing on individuals with HIV who were receiving care at the outpatient department. Through an in-depth secondary analysis of an existing database, we explored the relationship between cholesterol ratio and viral load in HIV-positive individuals undergoing antiretroviral therapy.

Using a quantitative-methods approach, we selected and processed data from the database to address our research question. The study records included patient subjects initiating and on cART within 12 months and were stratified into 3 groups namely: group A optimal normal (cholesterol ratio between 1 and 3.5), group B high normal (cholesterol ratio between 3.5 and 5) and group C, high cholesterol ratio (cholesterol ration above 5). STATA was used for statistical analysis.

Results: A total of 174 participants were included in the study analysis, with 61% (107) being female and 39% (67) male. Lipid profiles fell within normal ranges for both genders. The median cholesterol ratio was [3.16 (2.93, 3.40)] and total cholesterol was [3.86 (3.02, 4.62)]. The median HDL-c concentration was higher in males [1.4 (1.21, 1.55)] than females [1.33(1.13, 1.51)]. The median viral load in females was [355; (20, 6770)] and in males, [254 (23, 2694)] with a p=0.84. The study identified an inverse relation between cholesterol ratio and viral load, but this association did not reach statistical significance.

Conclusion: The study population predominantly exhibited normal cholesterol ratios, and although a potential inverse relationship with viral load was indicated, statistical significance was not established.

Key words: Cholesterol ratio, HIV, Viral load.

1.0 Introduction

1.1 Background to the problem

The sub-Saharan Africa region bears the brunt of the Human Immunodeficiency Virus (HIV) pandemic, with 25.7 million out of the global total of 37.7 million infected individuals [1]. In 2020, Zambia's estimated national HIV prevalence rate exceeded 1,070,000 people, and annually, 43,000 new infections are reported [2]. Substantial efforts have been dedicated to managing the HIV pandemic.

Ending the AIDS epidemic by 2030 is a target of the Sustainable Development Goals (SDGs). Accompanying this objective are the Joint United Nations Programme on HIV/AIDS (UNAIDS) goal of reducing the number of new HIV infections by 90% between 2010 and 2030, and its 95-95-95 target which proposes that by 2030, 95% of people living with HIV should be diagnosed, of whom 95% should be on treatment, of whom 95% should be virally suppressed [3].

Several studies have reported alterations in lipid profiles among HIV patients undergoing antiretroviral therapy [4, 5]. These changes may have implications for cardiovascular health, as dyslipidemia is a known risk factor for cardiovascular diseases [6]. However, the interplay between cholesterol levels and HIV viral load remains an area requiring further investigation.

The correlation between cholesterol levels and viral load in HIV patients is a subject of growing interest due to its potential implications for both HIV disease progression and cardiovascular health. Previous research has explored the complex relationship between HIV, antiretroviral therapy, and lipid metabolism, but a comprehensive understanding of how cholesterol levels correlate with viral load is yet to be fully elucidated.

There is a paucity of data on lipid profiles among HIV patients receiving cART in Zambia. While hypercholesterolemia and undernutrition are associated with complications that can lead to poor clinical outcomes as established in most non-communicable diseases, less research has been done to establish how cholesterol may impact HIV disease progression.

This study therefore seeks to address the knowledge gap by exploring the association between cholesterol ratio and viral load in HIV patients on antiretroviral therapy. By examining this relationship, our objective is to provide valuable insights into the complex interplay between HIV infection and dyslipidemia, specifically focusing on cholesterol ratio. This exploration may shed light on potential implications for the long-term health outcomes of individuals undergoing HIV management.

1.2 Literature Review

Malnutrition is the global problem potentially affecting all, but the most vulnerable groups are poverty-stricken people, young children, adolescents, older people and those with illness and have a compromised immune system. It is an important determinant of disease progression [7]. According to the World Health Organization (WHO), 462 million adults are underweight, while 1.9 billion adults are overweight and/or obese.

Malnutrition, involving both undernutrition and over nutrition, plays a significant role in shaping the trajectory of HIV disease progression. Undernutrition, characterized by insufficient intake of essential nutrients, compromises the immune system, impeding the body's ability to combat HIV and accelerating disease progression [8, 9]. Micronutrient deficiencies associated with undernutrition, such as vitamins and minerals, further contribute to immunosuppression and increased susceptibility to opportunistic infections among HIV-infected individuals [10].

On the other hand, over nutrition, often manifesting as obesity, has also been linked to adverse outcomes in HIV-positive individuals. Obesity is associated with chronic inflammation and immune dysregulation, potentially exacerbating HIV-related comorbidities and complications [9, 11].

Malnutrition and HIV are found to be interwoven in a vicious cycle [12]. People living with HIV are more vulnerable to developing undernutrition by different mechanisms. HIV is often accompanied by reduction in food intake due to: food insecurity, cognitive impairment or depression, medication-related nausea, and opportunistic infections (OIs) of mouth and esophagus, which bring about painful swallowing [13]. In addition, HIV increases the energy requirements of HIV-infected adults by 10% for asymptomatic, and by 20–30% for symptomatic patients [14]. Conversely, undernutrition weakens the immune system and increases the risk of early mortality and morbidities in people living with HIV [15]. Studies conducted across the globe have confirmed that low body mass index (BMI) at ART initiation hastened disease progression and increased the risk of OIs [16].

Limited information exists to relate cholesterol ratio and HIV viral load among HIV-infected patients in Africa. In a systematic review and meta-analysis in sub-Saharan Africa by Animut et al, (2017), it was found that undernutrition has significant effects on mortality and morbidity among adults living with HIV. As the degree of undernutrition becomes more severe, mortality rate also increased. Based on the findings, it was recommended that nutritional assessment among adults living with HIV be done regularly [17].

In a study conducted in Ugandan on children, it was demonstrated that those who were on cART, adherent and malnourished had virologic failure as a consequence of the effect of malnutrition on the bioavailability of the drugs [18].

In trying to compare the prevalence for dyslipidemia characterized by low-HDL among HIV-infected ART-naïve adults and their uninfected partners in Nairobi, Kenya by Njoroge et al (2017), it was demonstrated that a high prevalence of dyslipidemia characterized by low-HDL was associated with a high viral load and low CD4 cell count [19].

In Zambia, a study aimed at estimating the prevalence of low high-density lipoprotein cholesterol (HDL-c) was conducted. Low HDL-c was prevalent in adults living with HIV, especially among young adults. Low HDL-c among individuals taking ART was related to viral load, ART regimen, LDL-c, younger adult age, and sex. The study found that participants who had virological failure had lower HDL-c. The use of dolutegravir (INSTI) was associated with lower values of HDL-c, which could increase the risk for CVD. In young adults, prevalence of low HDL-c was significantly higher than in adults (63 vs. 38%, $p<0.001$). The conclusion was that Low HDL-c is highly prevalent among young adult with HIV in Sub-Sahara Africa independent of other risk factors for metabolic derangements [20].

2.0 Research design and Methods

The study adopted a retrospective cross-sectional approach, involving the analysis of secondary data from a pre-existing database derived from the primary study. The research was conducted at Ndola Teaching Hospital (NTH), serving as the study site for the investigation. The target population comprised individuals aged 18 and above who had been diagnosed with HIV and were enrolled at Ndola Teaching Hospital within a 12-month period after initiating combination antiretroviral therapy (cART). The determination of the sample size, set at 174 participants, was achieved using the Cochran formula. The formula, denoted as $n = z^2pq/d^2$, incorporated parameters such as the HIV prevalence for the Copper belt Province (13.2%), z-value (1.96), and a margin of error (d) of 0.05 at a 95% confidence interval.

A simple random sampling method was applied to select study participants during their routine visits to the HIV clinic at Ndola Teaching Hospital. The technique employed relies on applying a selection method that provides each participant with the same chance of being selected thereby preventing the potential for bias and making the sample more representative of the study population. The data collection team, comprised healthcare professionals, trained and certified in Good Clinical Practice/Good Clinical Laboratory Practice. Initial encounters involved pre-enrollment procedures, including study explanation and informed consent acquisition. Subsequent interactions included history taking, physical examination, and anthropometric measurements, with blood specimens collected for the assessment of plasma fat status, absolute CD4+ counts, and plasma viral load at baseline and on the follow-up visit.

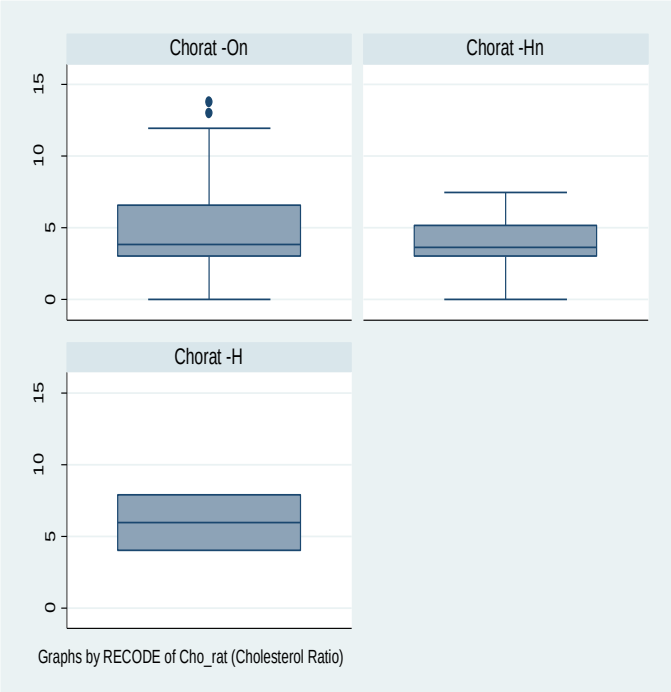
The baseline characteristics of participants by gender were

analyzed using Wilcoxon rank sum test for continuous variables and chi-square test for categorical variables. The main research question was addressed by establishing the association between cholesterol ratio and viral load adjusted for potential confounders using the multiple linear regression model. STATA version 12 was used to analyze the data. Ethical approval was sought and granted by the TDRC Research Ethics Committee in Ndola and the National Health Research Authority in Lusaka, Zambia.

3.0 Results

The study comprised a total of 174 participants for analysis, with 61% (107) being female and 39% (67) male. Lipid profiles were within normal ranges for both genders. The median cholesterol ratio was [3.16 (2.93, 3.40)], and total cholesterol was [3.86 (3.02, 4.62). Males exhibited a higher median HDL-c concentration [1.4 (1.21, 1.55) compared to females [1.33 (1.13, 1.51). The median viral load was 355 (20, 6770) in females and 254 (23, 2694) in males, with a p-value of 0.84. Although an inverse relationship between cholesterol ratio and viral load was observed, this association did not achieve statistical significance in the study. The outcome of the analysis suggesting the association between cholesterol ratio and viral load as categorized into optimal, high normal and high cholesterol ratio is depicted in the following box plots:

Figure 1: Cholesterol ratio vs viral load



On= Optimal normal, Hn =High normal and H=high.

Notably, the category with a high normal median cholesterol ratio appears to present the lowest viral load, followed by the optimal normal cholesterol ratio while the high median cholesterol ratio group reported a relatively higher viral load
The association as determined by the multiple linear regression outputs is as tabulated in the following overall and by gender models:

Table 1: Multiple linear regression taking viral load as the dependent variable on a log scale- Overall model

Independent Var.	Coef.	P-value	95%-CI
Cho_rat	-0.34	0.34	[0.35, 1.03]
Gender	0.98	0.19	[-0.51, 2.47]
Age_n	-0.04	0.20	[-0.10, 0.02]
BMI	-0.31	0.13	[-0.22, 0.03]
AlSt	2.27	0.01	[0.68, 3.86]
SmoSt	-0.95	0.41	[-3.23, 1.34]

Using multiple linear regression, Cholesterol ratio, adjusted for age, BMI, smoke status and alcohol status. Cho rat= Cholesterol Ratio, BMI=Body Mass Index (kg/m2), AISt=Alcohol status, Smost=Smoke status.

Table 2: Multiple linear regression taking viral load as the dependent variable on a log scale-by male gender

Independent Var.	Coef.	P-value	95%-CI
Cho_rat	-0.50	0.61	[-2.49, 1.49]
Age_n	0.02	0.67	[-0.08, 0.12]
BMI	-0.12	0.37	[-0.41, 0.16]
AlSt	1.38	0.23	[-0.92, 3.68]
SmoSt	-0.18	0.88	[-2.59, 2.23]

Using multiple linear regression, Cholesterol ratio, adjusted for age, BMI, smoke status and alcohol status. Cho rat= Cholesterol Ratio, BMI=Body Mass Index (kg/m2), AISt=Alcohol status, Smost=Smoke status.

Table 3: Multiple linear regression taking viral load as the dependent variable on a log scale-by female gender

Independent Var.	Coef.	P-value	95%-CI
Cho_rat	-0.21	0.61	[-1.05, 0.63]
Age_n	-0.06	0.17	[-0.14, 0.02]
BMI	-0.10	0.19	[-0.24, 0.50]
AlSt	3.10	0.02	[0.49, 5.71]
SmoSt	-1.98	0.46	[-7.30, 3.34]

Using multiple linear regression, Cholesterol ratio, adjusted for age, BMI, smoke status and alcohol status. Cho rat= Cholesterol Ratio, BMI=Body Mass Index (kg/m2), AISt=Alcohol status, Smost=Smoke status.
Notably, there is a consistent inverse correlation between cholesterol ratio and viral load demonstrated in the overall and by gender regression models, adjusted for potential confounders, though falling short of statistical significance

4.0 Discussion

4.1 Cholesterol ratio and viral load profiles

The study finding indicating a relatively normal median cholesterol ratio in the examined population, are consistent with analogous observations of the within-normal plasma fat profiles

in other analyses [21]. The median viral load profile corresponds with the findings of the primary study, where suboptimal suppression was reported both overall and by gender.

4.2 Cholesterol ratio correlation with viral load

The findings in this study suggesting a consistent inverse association between cholesterol ratio and viral load correspond with the outcome in other studies predicting a potential positive association between plasma fat and CD4+ count and an inverse relation between plasma fat and viral load [19, 21].

The study finding that a high normal median cholesterol ratio appears to present the lowest viral load, followed by the optimal normal cholesterol ratio while the higher than normal median cholesterol ratio group reported a relatively higher viral load seem to correspond with findings in other studies indicating that a high serum total cholesterol is associated with a lower HIV viral load [22, 23, 24]. However, in our study it is especially the optimal normal to high normal range of cholesterol ratio that is favorable for viral suppression than the higher than normal category. This is in contrast with other studies which have looked at total cholesterol and not the ratio in particular and regardless of the degree of normality.

For instance, in a study by Adal M, et al, (2013), gender and serum total cholesterol were found to be associated and independent predictors of HIV RNA load, and CD4+ cell count and/or WHO clinical stages. The study reported a significantly lower HIV RNA load and better CD4+ T cell count in women and those study participants with higher serum total cholesterol [22]. The findings in the study further underscore the role that gender can play in impacting viral load. The study states that the finding of a higher HIV RNA viral load in men than women was because women produce higher antibody and cell mediated immune responses following either infection or vaccination than men which avoids infection and/or inhibits replication of the pathogens in the host [25].

Regarding the role of HDL-c, a key component in the cholesterol ratio, a study has shown that the association between uncontrolled viremia and having lower HDL-c concentrations was stronger when patients had low CD4+ cell counts. Further, immunosuppression and viremia were each independently associated with higher atherogenic cholesterol concentrations among older HIV-infected patients than among younger patients [26]. Similar findings have been reported in another study where a high prevalence of dyslipidemia characterized by low-HDL-c and associated with a high viral load and low CD4+ cell count was found [19].

Some observed disparities among related studies may be attributed to variations in study design, participant demographics, and methodologies employed to measure cholesterol levels and viral load. Additionally, the complex interplay between antiretroviral therapy, immune response, and lipid metabolism necessitates a further understanding of these factors to interpret the diverse study outcomes accurately.

4.3 Regression with cholesterol ratio rather than total-cholesterol

The application of cholesterol ratio rather than total cholesterol is preferable when assessing the role of cholesterol in disease progression due to its ability to provide a more accurate picture of lipid profiles [27]. The cholesterol ratio, often expressed as the ratio of low-density lipoprotein (LDL) cholesterol to high-density lipoprotein (HDL) cholesterol, offers a more comprehensive view of the lipid balance in the body.

Additionally, gender-specific analysis, as mentioned in the earlier paragraphs, becomes more meaningful when using cholesterol ratio. It helps tailor risk assessments to the unique cholesterol profiles observed in men and women.

4.4 Future studies

In order to understand the true nature of the relationship between cholesterol ratio and viral load in HIV patients, future research should consider applying larger sample sizes, accounting for confounding variables, and employing standardized methodologies. Longitudinal studies that track changes in cholesterol profiles and viral loads over time will be crucial for establishing causality and informing potential therapeutic interventions.

5.0 Conclusion

Normal cholesterol ratios and suboptimal viral suppression were characteristic in the study population. While there was evidence supporting a consistent inverse association between cholesterol ratio and viral load among study participants, statistical significance was not established. The findings of our study highlight the significance of maintaining an optimal normal to high normal range of cholesterol ratio for achieving favorable viral suppression. This suggests that individuals with cholesterol levels within this specific range may experience enhanced outcomes in managing viral infections compared to those with higher-than-normal ratios. These insights contribute to our understanding of the relationship between cholesterol levels and viral suppression, emphasizing the importance of maintaining a balanced cholesterol profile in the context of overall health and immune response. Further research and exploration in this area may provide valuable insights for developing targeted interventions and strategies to optimize health outcomes in individuals facing viral infections.

6.0 Acknowledgements

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7.0 Conflict of Interest

The authors declare that there was no conflict of interest regarding the publication of the manuscript.

8.0 Financial Support

The authors declare that there was no financial support or benefits from commercial sources for the work reported in the manuscript.

9.0 Author contributions

The concept, design, analyses and interpretation of study findings were conducted by Nyirenda C and Kamozi P. All coauthors contributed towards the content, review and ultimate write-up of the manuscript

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