Research Square

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Thyroid Hormones and Lipid Levels in People living with HIV on Antiretroviral Therapy in Kisumu County, Western Kenya

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Abstract

Background

ART has reduced HIV mortality, but dyslipidaemia and thyroid dysfunction are increasingly observed; effects in Kisumu County remain unclear.

Methodology

Serum lipids (TC, TG, HDL, LDL) and thyroid hormones (TSH, T4, T3) were assessed in 84 ART-treated and 20 ART-naïve subjects using colorimetric and immunofluorescence methods. Mann–Whitney U and Spearman's correlation tests were used.

Results

ART-treated subjects had higher TSH [1.72 (1.71) vs 0.87 (1.07) nmo/L, *P* = 0.001]. T4, HDL, TC, TG, and LDL did not differ significantly. T4 positively correlated with LDL (*P* = 0.014).

Conclusion

ART is linked to elevated TSH; routine lipid and thyroid monitoring is advised.

INTRODUCTION

The introduction of highly active antiretroviral therapy (ART) has greatly reduced HIV-related morbidity and mortality, particularly in sub-Saharan Africa, where HIV remains common [1]. However, ART use in people living with HIV (PLWH) has been linked with metabolic complications, including dyslipidaemia and thyroid dysfunction, which may increase cardiovascular disease risk [2]. Thyroid dysfunction, especially subclinical hypothyroidism, has been reported among ART users, although its cause remains unclear [3]. Subclinical hypothyroidism is defined by elevated thyroid-stimulating hormone (TSH) with normal free thyroxine (T4), not by low T4 [4]. Previous studies have reported altered TSH, triiodothyronine (T3) and T4 levels in ART-treated and ART-naive patients [4–6]. Reduced thyroid hormone levels during HIV infection may represent an adaptive response that conserves energy during chronic illness [7].

Dyslipidaemia has also been described in ART-treated and ART-naive patients [8]. ART-associated dyslipidaemia is usually characterised by increased total cholesterol (TC), triglycerides (TG) and low-density lipoprotein (LDL), together with reduced high-density lipoprotein (HDL) [9]. ART may impair hydrolysis of triglyceride-rich lipoproteins and disrupt free fatty acid and lipoprotein catabolism [10]. Thyroid hormones regulate metabolic pathways, including lipid metabolism [11,12], and associations between thyroid hormones and lipid profiles have been reported [13]. This study determined serum lipid levels, including TC, TG, HDL and LDL, and thyroid hormones, including TSH, T4 and T3, among ART-treated and ART-naive patients attending Jaramogi Oginga Odinga Teaching and Referral Hospital

(JOOTRH), Kisumu County. It also assessed correlations between thyroid hormone levels and lipid profiles.

METHODOLOGY

This study was premised at the Comprehensive Care Centre (CCC) at Jaramogi Oginga Odinga Teaching and Referral Hospital (JOOTRH) located in Kisumu County, Western Kenya. The hospital serves both rural and urban population from the expansive western Kenya where HIV prevalence remains high at 11.7% compared to the national prevalence at 3.03% [14]. Kisumu County neighbors Siaya County to the West, Vihiga County to the North, Nandi County to the North East, Kericho County to the East, to the South is Nyamira County and Homa Bay County is to the South West. The facility acts as the regional referral center to most of these counties. Likelihood of ease of access of the participants with desired characteristics was considered high hence the choice of the study area. ART-treated patients who had received treatment for at least six months were recruited as cases. Newly diagnosed HIV-1-infected patients who had not started ART were recruited as ART-naive controls.

Eligible participants were HIV-infected adults aged 18 years and above who provided written informed consent. Exclusion criteria were pregnancy, lactation, known thyroid, liver, kidney or cardiovascular disease, current use of anabolic steroids, corticosteroids, immune-modulating therapy, lipid-lowering medication or thyroid medication, excessive alcohol intake, cigarette smoking, inability to consent, and inability or unwillingness to keep study appointments. These factors were excluded because they could confound metabolic outcomes.

The minimum sample size was 94, calculated using Epi Info based on a national HIV prevalence of 6.5%, a 95% confidence interval and one cluster. Participants were recruited through systematic random sampling. Questionnaires with unique identifiers collected age, sex and ART regimen. Weight was measured using a calibrated medical weighing scale, and height using a height metre. Body mass index (BMI) was calculated as weight in kilograms divided by height in metres squared since BMI has been shown to be associated with plasma lipid levels [15].

Participants returned in a fasting state for venous blood collection. Approximately 3 mL of blood was collected into red-top vacutainers by a qualified laboratory technologist. Serum was obtained by centrifugation and stored before analysis. Serum TC, TG and HDL were measured using a FujiFilm FujiDry-Chem NX500i clinical chemistry analyser. LDL was calculated using the Friedewald formula, LDL = TC - HDL - TG/5, for measurements in mg/dL [15]. Serum TSH, T3 and T4 were measured using the i-CHROMA reader according to the manufacturer's protocol.

Ethical approval was obtained from the Maseno University Ethics Review Committee, and written informed consent was obtained before enrolment. Categorical variables were compared using chi-square analysis. Serum lipid and thyroid hormone levels were compared using the Mann-Whitney U test.

Associations between thyroid hormones and lipid profiles were assessed using Spearman's correlation. Statistical significance was set at $P \leq 0.05$.

RESULTS

The results are A total of 104 participants were enrolled: 84 ART-treated patients and 20 ART-naive patients. As shown in Table 1, sex distribution, age and BMI did not differ between the two study groups. Only TSH levels significantly differed between the groups. Further, there were no difference in serum levels. The measured lipid levels were all within the stated reference ranges in both groups. Among ART-treated participants, the commonest regimen was TDF/3TC/EFV (51.7%), followed by TDF/3TC/NVP (20.2%), AZT/3TC/NVP (15.5%) and TDF/3TC/DTG (13.1%). All regimens contained 3TC. Using Spearman correlation, a significant positive correlation between T4 and LDL ($\rho = 0.240$, $P = 0.014$) was shown. No significant correlations were found between T4 and TC, TG or HDL; between T3 and any lipid parameter; or between TSH and any lipid parameter, Table 2.

Table 1
General Demographic and laboratory characteristics of the ART-treated and ART-naive HIV patients

Variables	**ART-treated (n = 84)**	**ART-naïve (n = 20)**	***P***
Gender			
Male/Female n (%)	31/53	9/11	0.504[a]
Age (Median, IQR)			
Age, (years)	41.0 (32.0–47.0)	43.0 (29.2–49.1)	0.061[b]
Body Mass Index (Median, IQR)			
BMI, (kg/m^2)	22.3 (19.9–25.0)	24.2 (21.0 -26.10	0.198[b]
Hormone Levels (Median, IQR)			
TSH, (nmol/L)	1.72 (1.20–2.81	0.87 (0.41–2.93)	**0.010** [b]
T3, (nmol/L)	2.43 (1.89–3.70)	3.10 (2.21–3.79)	0.147 [b]
T4, (nmol/L)	144.39 (54.91-156.23)	136.90 (126.22-143.72)	0.426 [b]
Serum Lipid Levels			
TC, (mg/dL)	186.00 (78.92–179.0)	149.50 (70.30)	0.092 [b]
TG, (mg/dL)	82.00 (59.21–109.80)	94.50 (51.80-98.91)	0.504 [b]
HDL, (mg/dL)	52.50 (24.00)	44.00 (32.81–57.10)	0.280 [b]
LDL, (mg/dL)	138.00 (78.19–143.30)	117.00 (98.71-189.46)	0.476 [b]

Data is presented as n (%) of the participants within the study groups unless stated otherwise. The study participants were categorized into ART-treated (n = 84) and ART-naïve (n = 20). *P*- Values were considered significant at $P \leq 0.05$. Abbreviations; IQR: Inter Quartile range, BMI: Body Mass Index, TSH: Thyroid Stimulating Hormone, T3: Triiodothyronine, T4: Thyroxine, TC: Total Cholesterol, TG: Triglycerides, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein. [a]Statistical significance determined using chi-square tests. [b]Data presented as median (interquartile ranges) and statistical test performed using Man Whiteney U tests., Hormone levels were measured in nanomoles per litter. Serum lipid levels were measured in milligrams per decilitre (mg/dL)

Table 2
Relationship between lipid profiles and thyroid hormones levels among ART-treated and ART-naïve patients

Characteristics	Spearman's rho (ρ)	*P*- value
TSH		
TC	0.013	0.897
TG	0.085	0.392
HDL	-0.126	0.201
LDL	-0.016	0.871
T3		
TC	0.019	0.849
TG	-0.094	0.342
HDL	0.074	0.458
LDL	0.037	0.706
T4		
TC	0.145	0.143
TG	-0.039	0.693
HDL	0.134	0.174
LDL	0.240	**0.014**

The correlations were determined using spearman correlation test. *P*- Values and spearman correlation coefficients **(ρ)** were considered significant at $P \leq 0.05$. *P*- Values in bold are statistically significant. TC: Total Cholesterol, TG: Triglycerides, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein.

DISCUSSION

The study found significantly higher TSH levels among ART-treated participants than ART-naive participants, although values remained within the reference range. This may reflect changes in the pituitary-thyroid axis after immune recovery on ART, including immune reconstitution-related thyroid effects [16]. Lower TSH among ART-naive participants may be linked to untreated HIV infection and higher viral activity [10]. Because TSH is the accepted first-line screening test for suspected thyroid dysfunction, monitoring remains relevant in HIV care.

T3 levels were lower among ART-treated participants, but the difference was not significant and values remained within the reference range. HIV infection may reduce extra-thyroidal conversion of T4 to T3

through altered deiodinase activity [17]. However, normal T3 despite higher TSH suggests preserved peripheral conversion and does not show overt thyroid disease. T4 was slightly higher among ART-treated participants, but the difference was not significant. This finding is consistent with the results and does not support overt hypothyroidism in either group. Instead, the pattern shows biochemical variation within normal thyroid function ranges.

Lipid findings showed non-significantly higher TC, HDL and LDL among ART-treated participants, while TG was lower in the ART-treated group. These findings suggest less favourable cholesterol-related parameters, particularly TC and LDL, among ART-treated patients, but the differences were not statistically significant. The higher HDL level may be protective, although median HDL remained below the level often considered strongly cardioprotective. The lower TG level among ART-treated participants differs from studies reporting ART-associated hypertriglyceridaemia [5]. This difference may relate to regimen composition, as the participants were not reported to be on protease inhibitor-based therapy, which is more strongly associated with raised TG.

The significant positive correlation between T4 and LDL suggests a relationship between thyroid hormone activity and LDL metabolism in this population. Thyroid hormones influence LDL receptor activity, sterol regulatory element binding proteins and hepatic cholesterol synthesis [18,19]. However, no significant correlations were found between TSH or T3 and lipid parameters. Therefore, the findings do not support a broad thyroid-lipid association in this sample. The cross-sectional design, unequal group sizes and lack of viral load, CD4 count and regimen-duration analysis limit causal interpretation. These factors are important because immune recovery, viraemia and drug exposure may modify thyroid function and lipid metabolism. Nevertheless, the findings support routine metabolic and thyroid monitoring in HIV care.

CONCLUSION

ART-treated participants had significantly higher TSH than ART-naive participants. T4 showed a significant positive correlation with LDL, indicating a possible thyroid-lipid interaction in HIV-infected patients. Longitudinal studies with matched groups, viral load, CD4 count and regimen-duration data are required to clarify the effects of ART on thyroid function and lipid metabolism. Routine metabolic monitoring should include thyroid assessment alongside lipid profiling, in patients receiving long-term antiretroviral treatment.

LIST OF ABBREVIATIONS

3TC Lamivudine

ABC Abacavir

AIDS Acquired Immunodeficiency Syndrome

ApoAV Apolipoprotein AV

ATP Adenosine Triphosphate

AZT Zidovudine

BMI Body Mass Index

cAMP Cyclic Adenosine Monophosphate

CCC Comprehensive Care Centre

CCR5 Chemokine receptor 5

CD4 Cluster of Differentiation

CETP Cholesteryl ester transfer protein

CVD Cardiovascular diseases

CYP3A4 Cytochrome P450 3A4

d4T Stavudine

DNA Deoxyribonucleic acid

DTG Dolutegravir

FFAs Free fatty acids

fT3 free T3

fT4 free T4

FTC Emtricitabine

ART Antiretroviral Therapy

HDL High-density lipoprotein

HDLC High Density Lipoprotein Cholesterol

HIV-1 Human Immunodeficiency Virus -1

HL Hepatic lipase

HMG-CoA Hydroxy-3-methyl-glutaryl-CoA reductase

IHD Ischemic heart disease

INSTIs Integrase strand transfer inhibitors

JOOTRH Jaramogi Oginga Teaching and Referral Hospital

KNH Kenyatta National Hospital

LDL Low-density lipoprotein

LDLR low density lipoprotein receptor

LPL Lipoprotein lipase

LPV/r Lopinavir/Ritonavir

LRP1 LDL-receptor-related protein type 1

MCT8 Monocarboxylate transporter 8

MI Myocardial infarction

MUERC Maseno University Ethics Review Committee

NNRTI Non-Nucleoside reverse transcriptase inhibitors

NRTIs Nucleoside reverse transcriptase inhibitors

NTI non-thyroidal illness

NVP Nevirapine

PI Protease Inhibitor

PLWH People Living with HIV

rT3 reverse triiodothyronine

RXR- PPARγ Retinoid X receptor-peroxisome proliferator-activated receptor γ

SCH Subclinical hypothyroidism

SREBP-2 Sterol regulatory element-binding protein-2

T3 Triiodothyronine

T4 Thyroxine

TBG Thyroid binding globulin

TC Total cholesterol

TDF Tenofovir disoproxil fumarate

TFT Thyroid Function Test

TG Triglycerides

TH Thyroid Hormone

TNF Tumor Necrosis Factor

TRH Thyroid Releasing Hormone

TSH Thyroid Stimulating Hormone

VDLD Very low-density lipoprotein

VLDL Very low-density lipoprotein

WHO World Health Organization

DECLARATIONS

COMPETING INTEREST

Authors declare no competing interest in this study.

ACKNOWLEDGEMENTS

We acknowledge participants at the JOOTRH, Kisumu County, Kenya.

AUTHORS' CONTRIBUTIONS

OAJ: Developed the concept, generated data, data analysis and developed the manuscript; MEO: Analysed the data and wrote the manuscript GNM and MGO; Proofread the manuscript and guided data analysis

ETHICS AND APPROVAL

Ethical clearance was obtained from the Maseno University Ethics Review Committee (MUERC).

CONSENT

Informed consent was sought from all eligible study participants

AVAILABILITY OF DATA AND MATERIALS

Data for this manuscript is available on request from the corresponding author through Maseno University Ethical Review Committee

FUNDING

The work did not receive funding from any organisation.

Data Availability

Restrictions apply to the availability of these data, which were used under licence for the current study and so are not publicly available. The data are, however, available upon request and with the permission of Maseno University Ethical Review Committee

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