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Thyroid Hormones and Red Cell Indices of HIV Subjects at Enugu

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Authors' contributions

This work was carried out in collaboration among all authors. Author NAM designed the study, wrote the protocol and wrote the first draft of the manuscript, performed the statistical analysis and managed the analyses of the study. Author EA managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Thyroid hormones act on nearly every cell in the body including red blood cells. Thyroid hormones are also important to proper development and differentiation of all cells of the human body. Human Immunodeficiency Virus (HIV) is a virus that destroys certain cells in the immune system. The aim of this study was to determine free triiodothyronine (FT3), free thyroxine (T4) and red cell indices level of HIV subjects attending clinic at Enugu State University of Science and Technology Teaching Hospital.
Study Design: Case control study.
Place and Duration of Study: Human Immunodeficiency Virus (HIV) clinic and Haematology Laboratory both of Enugu State University of Science and Technology Teaching Hospital, between August and October 2021.
Methodology: Sixty HIV subjects and thirty apparently healthy individuals within the age range of 30 - 60 years were recruited for this study. Free triiodothyronine (FT3), free thyroxine (FT4), hemoglobin (HGB), packed cell volume (PCV), red blood cell count (RBC), mean cell volume (MCV), mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC), red cell

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distribution width standard deviation (RDW-SD), red cell distribution width coefficient of variation (RDW-CV) were determined in HIV subjects and apparently healthy individuals.
Results: There was significant difference in MCV (*125.79+/- 7.57* vs *78.89+/- 5.71 fl*), MCH (*23.17+/- 2.10* vs*27.21+/- 3.68 pg*), MCHC (*25.08+/- 2.74* vs*30.09+/- 3.27 g/dl*), RDW-SD (*61.52+/- 7.55* vs*46.23+/- 5.87 fl*), RDW-CV (*23.06+/- 5.78* vs*43.87+/- 1.28 fl*) and PCV (*39.38+/- 3.06* vs*31.75+/- 2.44 %*) between patients on antiretroviral therapy (ART) and ART-naïve patients respectively. There was significant difference in T4 (8.*29+/- 1.29 vs 6.12 µg/dl*), MCV (*78.89+/- 5.71 vs 84.47 +/- 3.79 fl*), MCH (27.21+/- *3.68 vs 29.20 +/- 2.27 pg*), RDW-CV (*43.87+/- 1.28 vs 12.51 +/- 1.08 fl*) and PCV (*31.75+/-2.44vs 37.63+/-2.95 %*) on ART-naïve patients and apparently healthy subjects respectively. There was a positive correlation between FT3 and MCH in HIV patients on antiretroviral therapy (ART) (p= 0.016).
Conclusion: In people taking antiretroviral therapy, mean cell haemoglobin, mean cell hemoglobin concentration and red cell distribution width coefficient of variation significantly reduced, as well as raised mean cell volume and red cell distribution width standard deviation. This study also observed reduced mean cell haemoglobin, mean cell haemoglobin concentration and mean cell volume in ART- naïve subjects.

Keywords: Triiodothyronine; thyroxine; antiretroviral therapy; red cell distribution width.

1. INTRODUCTION

Thyroid hormones have great effects on numerous physiologic processes, including development, growth and metabolism. Countless effects of thyroid hormone have been described by study of excess and deficiency states. Thyroid hormones cause many metabolic activities in tissues, which leads to an increase in basal metabolic rate. One effect of this activity is to raise body heat production, which appears to occur, slightly in part, from raised oxygen consumption and rates of adenosine triphosphate hydrolysis [1]. Human immunodeficiency virus (HIV) infection is one of the most critical diseases globally, with about 940,000 deaths in 2017 [2]; which leads to decline in CD4 T lymphocytes cells, resulting in immune system failure, susceptibility to opportunistic infections and cancer development. HIV diagnosis has improved over the years because of antiretroviral regimens [3].Several disease conditions caused by HIV have been recently reported; such as anomalies of pancreas, endocrine and gonadal metabolisms [4,5]. Studies have also reported antiretroviral medications induce complications such as hypercholesterolaemia lipoatrophy and glucose intolerance [6]. In HIV patients, manifestations of thyroid problems which include functional disturbances and abnormal changes have been reported. Mechanism behind thyroid disease in HIV patients has been unclear. But some explanation such as opportunistic diseases induce reversible thyroid organ damage has been made [7]. Thyroid hormones are important for different metabolic activities in the body. Thyroid dysfunction can decrease the quality of life in HIV patients, hence there is need to carry out thyroid function screening test in HIV patients during treatment. Red blood cell (RBC) indices, such as the mean cell hemoglobin concentration (MCHC), mean cell volume (MCV) and mean cell hemoglobin (MCH),haemoglobin level and red blood cell count are indicators of systemic iron status [8, 9]. Exact measures of red blood cell size such as mean cell volume, which also depend on reduction-oxidation homeostasis and normal biosynthesis of red blood cell membrane lipids, may also show mitochondrial dysfunction [10,11]. In HIV infection, anemia has been reported in individuals with stunted viremia during highly active antiretroviral therapy, with or without macrocytosis [12, 13]. Therefore, the aim of this study was to determine free triiodothyronine (FT3), free thyroxine (T4) and red cell indices level of HIV subjects taking antiretroviral therapy (ART) treatment, not yet on ART and to correlate FT3, FT4 and red cell indices.

2. METHODOLOGY

2.1 Study Design

This is a case control study.

2.2 Study Location and Study Participants

The study was conducted at Enugu State University of Science and Technology Teaching Hospital from August to October 2021. Enugu

State University of Science and Technology Teaching Hospital (ESUTTH) is the second largest health care facility in Enugu State. Human Immunodeficiency Virus was one of the commonest causes of medical ward admissions in ESUTTH. Previous study at ESUTTH showed that out of 3,865 cases recorded that 503 (13.01%) were HIV with case fatality rate of 127/503 (25.2%) [14]. Subjects were selected by simple random sampling method.After obtaining informed consent, the subjects were recruited for both groups. Patients who were confirmed HIV for at least 6 months were included in this study. These patients were of either gender and between the ages of 30-60 years and antiretroviral therapy (ART) duration of 1-15 years. The subjects were grouped into three; Group one were HIV positive patients taking ART, group two were HIV positive patients not yet on ART and group three were apparently healthy individuals. Antiretroviral therapy treatment duration was grouped as less than 5 years, 6-10 years and more than 10 years. The drugs were Tenofovir, Lamivudine, Dolutegravir. Blood samples were collected via venepuncture. Free triiodothyronine and free thyroxine were determined by competitive solid-phase enzyme linked immunosorbent assay. Red cell indices were analyzed by automated haematology analyzer (Mindray/BC-5150). The data were evaluated in statistical programme SPSS version 21.0. Student's t-test and one-way ANOVA were applied with mean ± standard deviation. The association between FT3, FT4 and red cell indices was determined by Pearson correlation. P- Value ≤ 0.05 was considered as statistical significant.

3. RESULTS

Table 1 shows HIV subjects on ART have significantly decreased MCH (23.17 +/- 2.10 vs27.21+/- 3.68 pg), MCHC (25.08 +/- 2.74 vs30.09+/- 3.27 g/dl) and RDW-CV (23.06+/- 5.78 vs43.87+/- 1.28 %) compared with ART-naïve subjects (p=<0.001, <0.001 and <0.001 respectively). Again, HIV subjects on ART have significantly decreased MCH (23.17 +/- 2.10 vs29.20+/- 2.27 pg), MCHC (25.08 +/- 2.74 vs33.70+/- 2.39 g/dl) and significantly increased MCV (125.79 +/- 7.57 vs84.47+/- 3.79 fl), RDW-SD (61.52 +/- 7.55 vs44.23+/- 2.16 fl) and RDW-CV (23.06 +/- 5.78 vs12.51+/- 1.08 %) compared with control subjects (p=<0.001, <0.001, <0.001, <0.001 and <0.001 respectively). Antiretroviral therapy-naïve subjects have significantly decreased MCV (78.89 +/- 5.71 vs84.47+/- 3.79 fl), MCH (27.21 +/- 3.68 vs29.20 +/-2.27 pg), MCHC (30.09 +/- 3.27 vs33.70 +/- 2.39 g/dl), PCV (31.75 +/- 2.44 vs 37.63 +/- 2.95 %) and significantly increased RDW-CV (43.87 +/- 1.28 vs12.51 +/- 1.08 %), FT4 (8.29 +/- 1.93 vs6.12 +/- 1.51 µg/dl) compared with control subjects (p=<0.001, 0.04, <0.001, <0.001, <0.001 and 0.03 respectively).

Table 2 shows HIV patients that have taken ART treatment for more than 10 years had significantly increased MCV (132.40 +/- 2.30 vs122.05 +/- 7.67 fl) compared with those who were still less than 5 years (p=0.001). Packed cell volume of HIV patients who had taken ART for more than 10 years were significantly low (36.92 +/- 1.28 vs41.45 +/- 1.44 %) (p=<0.001) compared with those who were between 6-10 years.

Table 3 shows Mean cell hemoglobin significantly correlated with free triiodothyronine (p=0.016) in HIV subjects on ART.

Table 4 shows no significant correlation was found in red cell indices and thyroid hormones of HIV subjects not yet on ART.

4. DISCUSSION

This study investigated thyroid hormones and red blood cell indices of 60 HIV- positive adult on ART and ART-naïve. Thus, the commonest findings found in the current study were increased RDW-SD, RDW-CV and MCV in ART subjects. Also in ART- naïve subjects decreased MCV, MCH, MCHC and increased RDW-CV and free thyroxine were found. Red blood cell distribution width (RDW), as well as different types hereof (red cell distribution width standard deviation and red cell distribution width coefficient of variation), is a measure of the range of variation of RBC volume that is reported as part of a types standard complete blood count [15]. The average volume of red blood cells is 80-100 femtoliters, but in healthy human blood, individual cell volumes vary. Certain disease conditions, however, give rise to a significantly increased variation in cell size. Higher Red blood cell distribution width value shows greater variation in size [16]. Normal value of RDW-CV in RBC is 11.5-15.4% [17]. In anaemia patients, Red cell distribution width test results are often used together with MCV results to determine the possible causes of anaemia [18]. Folate and vitamin B_{12} deficiency anemia normally presents with high RDW and high MCV.

Table 1. Mean values of thyroid hormones and red cell indices of HIV subjects

	FT3 (ng/ml)	FT4(µg/dl)	HGB(g/dl)	PCV(%)	RBC(x10^{12}/l)	MCV(fl)	MCH(pg)	MCHC(g/dl)	RDW-SD(fl)	RDW-CV(%)
HA	1.23±	7.38±	12.82±	39.38±	4.22±	125.79±	23.17±	25.08±	61.52±	23.06±
N=30	0.44	1.89	0.82	3.06	0.54	7.57	2.10	2.74	7.55	5.78
AN	1.17±	8.29±	10.63±	31.75±	3.53±	78.89±	27.21±	30.09±	46.23±	43.87±
N=30	0.42	1.93	0.86	2.44	0.26	5.71	3.68	3.27	5.87	1.28
C	1.23±	6.12±	12.61±	37.63±	4.27±	84.47±	29.20±	33.70±	44.23±	12.51±
N=30	0.54	1.51	0.97	2.95	0.53	3.79	2.27	2.39	2.16	1.08
F (P)	0.18	3.52	56.27	59.74	24.03	567.07	36.79	70.66	83.91	81.79
value	(0.84)	(0.03)	(<0.001)	(<0.001)	(<0.001)	(<0.001)	(<0.001)	(<0.001)	(<0.001)	(<0.001)
HA vs AN	0.85	0.17	<0.001**	<0.001**	<0.001**	<0.001**	<0.001**	<0.001**	<0.001**	<0.001**
HA vs C	1.00	0.83	0.65	0.07	0.91	<0.001**	<0.001**	<0.001**	<0.001**	<0.001**
AN vs C	0.87	0.03*	<0.001**	<0.001**	<0.00!**	<0.001**	0.04*	<0.001**	0.20	<0.001**

Abbreviations: HA= HIV subjects on ART, AN= ART naïve subjects, C= control

Table 2. Mean values of thyroid hormones and red cell indices based on ART duration

	FT3(ng/ml)	FT4(µg/dl)	HGB(g/dl)	PCV(%)	RBC(x10^{12}/l)	MCV(fl)	MCH(pg)	MCHC(g/dl)	RDW-SD(fl)	RDW-CV(%)
<5yrs	1.17±	7.29±	12.98±	39.67±	4.18±	122.05±	23.22±	25.06±	59.99±	21.56±
N=14	0.56	2.50	0.92	3.21	0.59	7.67	2.25	2.89	10.14	3.15
6-10yrs	1.23±	7.29±	12.95±	41.45±	4.29±	127.55±	22.78±	24.99±	61.64±	23.58±
N=11	0.28	1.24	0.56	1.44	0.58	6.53	1.24	2.70	4.30	4.45
> 10yrs	1.38±	7.86±	12.10±	36.92±	4.15±	132.40±	23.88±	2.32±	65.60±	24.80±
N=5	0.38	1.20	0.75	1.28	0.41	2.30	3.27	2.97	1.82	4.02
F (P) value	0.40	0.18	2.54	5.99	0.16	5.08	0.46	0.02	1.02	1.66
<5yrs vs 6-10yrs	(0.67)	(0.84)	(0.09)	(0.01)	(0.85)	(0.01)	(0.64)	(0.98)	(0.37)	(0.21)
<5yrs vs >10yrs	0.94	0.17	0.99	0.18	0.88	0.15	0.81	0.10	0.85	0.43
6-10yrs vs	0.64	0.83	0.15	0.04*	0.99	0.001*	0.91	0.98	0.15	0.31
>10yrs	0.72	0.88	0.14	<0.001**	0.85	0.11	0.76	0.98	0.06	0.85

Table 3. Pearson correlation coefficient between red cell indices and thyroid hormones in HIV subjects on ART

	HGB (g/dl)	PCV (%)	RBC (x10^{12}/l)	MCV (fl)	MCH (pg)	MCHC (g/dl)	RDW-SD (fl)	RDW-CV (%)
FT3r	0.157	0.190	0.063	0.101	0.435	0.123	0.152	-0.162
p value	0.406	0.315	0.739	0.596	0.016*	0.516	0.424	0.392
FT4r	0.134	0.150	-0.019	0.107	0.350	0.053	0.201	0.026
P value	0.481	0.429	0.920	0.573	0.058	0.783	0.286	0.890

Table 4. Pearson correlation coefficient between red cell indices and thyroid hormones in ART- naïve subjects

–	HGB (g/dl)	PCV (%)	RBC (x10^{12}/l)	MCV (fl)	MCH (pg)	MCHC (g/dl)	RDW-SD (fl)	RDW-CV (%)
FT3 r	-0.097	- 0.078	- 0.090	-0.238	-0.133	-0.237	0.296	0.165
p value	0.609	0.681	0.638	0.204	0.484	0.207	0.112	0.383
FT4r	-0.188	- 0.181	-0.298	-0.246	-0.233	0.329	0.221	0.128
P value	0.319	0.337	0.110	0.190	0.215	0.076	0.241	0.501

Study had shown that micronutrient concentrations are lower among patients with HIV wasting syndrome [19]. Antiretroviral therapy is generally recommended for patients with HIV-related opportunistic infections or a CD4 count < 200 cells/μL. Antiretroviral therapy restores immunologic function [20], but does not put an end to weight loss and wasting [21, 22]. In this study increased levels of MCV, RDW-SD and RDW-CV were found in HIV patient on ART. This finding is consistent with the study done in North India which reported macrocytic anaemia in patients taking ART [23]. Mean cell haemoglobin (MCH) value refers to the average quantity of haemoglobin present in a single red blood cell. Mean cell haemoglobin value is connected to two other values, MCV and MCHC. At the same moment, MCH, MCV and MCHC are sometimes called red blood cell indices. Mean cell haemoglobin value calculated below 27.5 pg is considered low MCH. A low MCH value shows the presence of iron deficiency anaemia [24]. In this study decreased levels of MCH, MCHC and MCV were found in ART naïve subjects. This finding is consistent with the study done in Indonesia that found significantly lower MCH, HGB and PCV in subjects with CD4 ≤ 350mm^3 [25]. Thyroid dysfunction has been reported in HIV patients [26]. In the present study, free thyroxine significantly increased in ART-naive subjects and MCH significantly correlated with free triiodothyronine. This finding is similar with the study done in India that reported significant positive correlation between thyroid stimulating hormone and CD4 count [27]. The cause of thyroid dysfunction in HIV subjects are not yet clear, but hypotheses involve coexisting infections, autoimmune disease, damage by opportunistic infections, and drug reactions [28]. Thyroid dysfunctions are associated with disease progression, such as severe immunosuppression and increase viral load [29].

5. CONCLUSION

In people taking antiretroviral therapy, mean cell haemoglobin, mean cell hemoglobin concentration and red cell distribution width coefficient of variation significantly reduced, as well as raised mean cell volume and red cell distribution width standard deviation. This study also observed reduced mean cell haemoglobin, mean cell haemoglobin concentration and mean cell volume in ART- naïve subjects. We suggest further study that will involve larger study population and vitamin B12, folate and iron measurement in HIV patients taking antiretroviral therapy.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

Approval was given by the Research Ethics Committee of Enugu State University of Science and Technology Teaching Hospital (ESUTH) Enugu prior to the study.

COMPETING INTERESTS

Authors have declared that they have no known competing financial interests or non-financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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