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Research article

Prevalence and predictors of dyslipidemia among HAART treated and HAART naive HIV positive clients attending Debre Tabor Hospital, Debre Tabor, Ethiopia

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ABSTRACT

Background: Highly active anti-retroviral therapy has been reported to be associated with a number of side effects in human immunodeficiency virus patients among which dyslipidemia isa common metabolic disorder.
Methods: A Hospital based comparative cross-sectional study among 228 HIV positive patients was conducted from July to August 2020. Socio-demographic and clinical data were collected using structured questionnaires. Fasting venous blood sample was collected and analyzed for Lipid profiles. EDTA sample was analyzed for CD4+ T cell determination. Anthropometric measurement was done. Data were analyzed using SPSS version 22. Independent t-test was done. Logistic and binary regression was done.
Result: A total of 228 HIV patients were enrolled in the study. Prevalence of dyslipidemia in HAART naive and HAART treated patients was 61 (53.5%) and 84 (73.7%), respectively. The prevalence of Total Cholesterol ≥200 mg/dl was 50% and 30%; High density lipoprotein cholesterol <40 mg/dl was 43.8% and 36%; Low density lipoprotein cholesterol ≥130 mg/dl was 48.3% and 28.1%; and Triglyceride ≥ 150 mg/dl 59.6% and 39% among HAART treated and HAART naive, respectively. Age greater than 40 years (AOR = 3.27, 95% C.I: 1.47–7.25), blood pressure ≥140/90 (AOR = 16.13, 95% C.I: 5.81–44.75), being on HAART (AOR = 2.73, 95% C.I: 1.35–5.53) and body mass index >25 kg/m^2 (AOR = 1.92, 95% C.I: 1.20–4.81) were identified as determinants of dyslipidemia.
Conclusion: The mean value of lipid profile was significantly higher among HAART treated as compared to those HAART naive HIV positive clients.

1. Introduction

Acquired Immune Deficiency Syndrome (AIDS) has become a global public health concern [1]. The different HAART regimens being used by many countries include a combination of at least three drugs such as protease inhibitors (PI), non-nucleoside reverse transcriptase inhibitors (NRTI) and nucleoside reverse transcriptase inhibitors (NRTI) [1]. The introduction and extensive utilization of HAART in the treatment of HIV infection has led to significant reduction in AIDS-related morbidity and mortality [2].

Nowadays the World Health Organization (WHO) recommends the combination of two NRTI with a NNRTI [3]. PIs have become compulsory component of second-line treatment subsequent to failure of first-line regimens in which a change from Tenofovir/Lamivudine/Efavirenz

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(TDF/3TC/EFV) preferred first line combination to Tenofovir/Lamivudine/Lopinavir/r (TDF/3TC/LPV/r) second line combination [3]. Despite the pivotal role of HAART in the treatment of HIV infection, the use of HAART is reported to be associated with a series of side effects in HIV/AIDS infected clients [4]. The use of HAART is associated with abnormal changes in lipid profile in PLHIV [5]. Some of the lipid abnormalities include; elevated level of total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-c), triglyceride (TG) and decreased level of high-density lipoprotein-cholesterol (HDL-c) [3]. Use of stavudine (d4T) and PIs have been reported to cause an elevation of the blood levels of TC, LDL-c, and TGs with variable effects on levels of HDL-c [6]. Use of Nevirapine has been associated with increased LDL-c, whereas use of long term use of efavirenz for long period of time has been associated with increase TC and TG (7).

Mechanism for the development of lipid abnormality is still unclear and proposed to be multi factorial [7]. The individual contributions of HIV infection, specific ARV agents, host genetics and changes in body composition all should be considered for the development of lipid abnormality among PLHIV(9). These high levels of lipids increase the likelihood of developing blood clots, heart disease and heart attack, stroke and pancreatitis [1].

Most deaths among HIV positive clients are from liver disease, kidney disease and cardiovascular complications with factors related to the virus, the host and ART factors [8]. All HIV patients with dyslipidemia may not require lipid lowering therapy. The goal of lipid lowering therapy is to minimize an individual's cardiovascular risk. So, treatment of HIV-associated dyslipidemia should be a component of an attempt to improve cardiovascular health. Continuous monitoring and advice on diet and exercise, smoking cessation, management of hypertension and diabetes if present and use of anti-platelet agents are crucial measures in managing HIV associated dyslipidemia [9].

Although WHO ART guidelines do not include lipid monitoring in HIV treatment, lipid monitoring should be included in patients receiving HAART [4]. The prevalence of dyslipidemia on HAART individuals in resource-limited settings also has not been well characterized [10]. This study was aimed at identifying risk factors of dyslipidemia in HIV patients and determining whether HIV patients on HAART have high level of dyslipidemia compared to HAART naïve HIV positive clients [11].

2. Methodology

2.1. Study area and period

A facility based cross-sectional study was conducted from July to August 2020 in Debre Tabor referral hospital, which is found 665 km from Addis Ababa (the capital city of Ethiopia). The hospital is the largest in South Gondar zone, which was established in 1953 and serves more than 2.5 million population in its catchment area. It has more than 33 specialists in various areas of medical specialization and 230 other health professionals constituting the health care team with a total capacity of 160 inpatient beds in five major departments. The chronic follow up department is one of the main departments, which provides follow up services for chronic diseases like HIV/AIDS.

2.2. Sample size and study subjects

The sample size was determined using two population proportion formula by considering the following assumptions: proportion of HIV positive individuals on HAART with LDL-c ≥130 (40.8%) [3] and proportion of HIV positive individuals naive for HAART with LDL-c ≥130 (21%) [9]. Level of significance (α/2) = 5%; power (1 − β) = 90%; r = (Ratio of exposed: none exposed) = 1:1. By adding 10% non-response rate the final sample size was 228 (114 on HAART and 114 HAART naïve HIV positive clients).

All HIV positive individuals (age ≥18 years) who were available during the study period were included. HIV patients with known DM, renal failure and on anti TB drugs were excluded from the study. HIV positive individuals on HAART who change their regimen in less than a year and who took HAART for less than a year were excluded from the study.

2.3. Data collection techniques and instruments

Sociodemographic data including anthropometric measurements were collected using structured questionnaires by trained nurses.

2.3.1. Anthropometric measurements

The weight of the study participants was measured using a standard balance, and the height was measured by using a height-measuring device attached to the balance. Then, BMI was calculated by dividing weight (kg) by height (m^2). six categories of BMI can be identified as follows: underweight, <18.5 kg/m^2; normal, 18.5–24.9 kg/m^2; pre-obesity, >25.0–29.9 kg/m^2; and obesity class I, 30–34.9 kg/m^2 obesity class II – 35–39.9 kg/m^2, obesity class III >40 kg/m^2 [12].

2.4. Blood sample processing and analysis

A 5ml fasting venous blood sample was drawn for lipid profile and CD4 cell determination in separate test tube using vacutainer blood collection system. EDTA anti-coagulated venous blood was processed for CD4 count using BD FACSCount™ (BD USA). FACSCount employs a direct two-color immunofluorescence method for enumerating absolute lymphocyte counts. Whole blood of the following mature human lymphocyte subsets: T lymphocytes (CD3+), T-helper/inducer lymphocytes (CD3+CD4+), and T suppressor/cytotoxic lymphocytes (CD3+CD8+). These data provide important information for staging and monitoring patients infected with HIV(15). Lipid profile was assessed through enzymatic Methods using Clinical chemistry Analyzer (HumStar80, Canada).

According to the US National Cholesterol Education Program, Adult Treatment Panel III (NCEP-ATP III) guidelines, abnormal lipid profile was defined as TC ≥ 200 mg/dl, HDL-c <40 mg/dl, LDL-c ≥ 130 mg/dl, TG ≥ 150 mg/dl, TC/HDL-c ratio ≥5 (16). An elevation of any one of the lipid parameters above these limits was considered as dyslipidemia [13].

2.5. Statistical analysis

Data were coded and entered using Epi-Info version 3.5.6 and then exported to SPSS version 22 for analysis. Descriptive statistics using frequency distribution was done for socio-demographic and clinical characteristics of study participants. Binary and multivariate logistic regression. AP value <0.05 were considered as statistically significant.

2.6. Data quality assurance

Blood samples for lipid profiling and $CD4^+$ counts, were collected and processed by adherence with standard operation procedures (SOP). The questionnaire was developed in English and translated into the Amharic language, then back to English to check consistency. Weight measurement was done using a digital scale to the nearest 0.1 kg. A fixed base calibrated height scale was used for height measurement to the nearest 0.1 cm. Measurements were done twice and the mean values were used to compute BMI. All reagents were checked for expiry date.

3. Results

3.1. Socio-demographic andclinical characteristics of study participants

A total of 228 HIV positive (114 on HAART and 114 HAART naive) individuals were enrolled in this study from whom, majority, 125 (54.82 %) were females. The mean age of study participants was 35.31 (±7.20). The majority of patients can read and write. Majority (61.4%) of the

patients are urban residents. 29 (12.8%) of the participants had smoking history (Table 1).

31 of the HAART treated patients (27.2%) and 18 (15.8%) of HAART naive patients were obese. 53 (46.5%) of HAART treated patients and 46 (40.3%) of HAART untreated patients were hypertensive. 19 (16.6%) of HAART treated patients and 49 (42.9 %) of HAART naive patients have a CD4 count of <350 cells/mm^3.

3.2. Lipid profile of study participants

84 (73.7%) of HAART treated patients and 61 (53.5%) of HAART naive patients have dyslipidemia. 57 (50 %) of HAART treated patients and 34 (29.8%) of HAART naive patients have a total cholesterol of ≥200 mg/dl 50 (43.9%) of HAART treated and 41 (36%) of HAART naive have HDL-c level of <40 mg/dl 55 (48.2%) of HAART treated and 32 (28.1%) of HAART untreated patients have LDL-c level of >130 mg/dl 68 (59.6%) of HAART treated and 44 (38.6) of HAART naive patients have TG level of >150 mg/dl (Table 2).

3.3. Associated risk factors of dyslipidemia

Among the study participants involved, 84 (73.68%) of HAART treated and 61 (53.51%) of HAART naive patients had at least one lipid abnormality. The prevalence of dyslipidemia in HAART treated patients for TC, LDL-c & TG was greater than that of HAART naive which was significantly different (p-value < 0.001). The Mean value of TC, LDL-c and TG were higher among HAART treated patients than in HAART naive whereas the mean value of HDL-c was higher among HAART naive than that of HAART treated patients (Table 3).

Multivariable logistic regression analysis was done for variables having p <0.25 in binary logistic regression analysis (age, CD4 count, BMI, blood pressure, and HAART status) (Table 4).

After controlling potential confounding factors in multiple logistic regression analysis; age greater than 40 years old (AOR = 3.27, 95% C.I: 1.47–7.25), blood pressure ≥140/90 (AOR = 16.13, 95% C.I: 5.81–44.75), being on HAART (AOR = 2.73, 95% C.I: 1.35–5.53) and body mass index >25 kg/m^2 (AOR = 1.92, 95% C.I: 1.20–4.81)were identified as determinants of Dyslipidemia (Table 5).

4. Discussion

The prevalence of dyslipidemia in this study was 145 (63.60%), of them 84 (73.68%) were HAART treated and 61 (53.51%) were HAART naive HIV positive clients. The mean value of TC, LDL-c and TG were higher in HAART treated than those of HAART naive. The mean value of HDL-c was higher among HAART naive HIV clients than those of HAART treated. This might be due to the effect of HAART regimen on the lipid metabolism of HIV patients [9]. In this study the mean value of CD4 cell count on HAART treated group was significantly different from HAART naive HIV positive clients. But, CD4 cell count was not significantly associated with dyslipidemia and lipid profile level. This might be due to HAART effect on improving immunological status of HIV clients [12].

In this study the mean value of each lipid profile was significantly higher among HIV clients on HAART than HAART naïve HIV clients which was similar with a study conducted in Sao Paulo, Brazil [14]. In this study we found that the proportions of raised TC, LDL-c, TG and TC/HDL-c ratio were significantly higher among HIV clients on HAART when compared to HAART naive HIV clients. This might be due to the atherogenic effect of HAART for the development of cardiovascular diseases [15]. The association between HAART and adverse lipid profile has been largely described for regimens when hypothetically switching patients from first-line to second-line treatment [16].

HIV patients on HAART with TC ≥ 200 mg/dl (50%) was higher than the findings reported from; Cameron (37.7%), Hawassa-Ethiopia (43.4%) & Jimma-Ethiopia (6.4%) [3]. This variation might be due to the sampling technique and the difference in the duration of HAART treatment [17].

The prevalence of HDL-c < 40 mg/dl among HIV clients on HAART was 43.8%. This is comparable with the prevalence reported from Hawassa-Ethiopia which is 43.4% [3]. However, the prevalence of HDL-c

Table 1. Socio-demographic characteristics among HAART treated and HAART naive HIV patients in Debre Tabor referral hospital, Debre Tabor, Ethiopia, 2020.

Variable	Categories	HAART No (%)	HAART naïve
Sex	Male	53 (46.49)	50 (43.86)
	Female	61 (53.51)	64 (6.14)
Age	18–30	24 (21.04)	32 (28.07)
	31–40	67 (58.77)	62 (54.39)
	>40	31 (27.2)	20 (17.54)
Educational status	Illiterate	15	19
	Read and write	69	70
	Diploma &above	30	25
Residence	Rural	46	42
	Urban	68	72
Smoking habit	Yes	17	12
	No	97	102
Physical exercise	Yes	39	42
	No	75	72

HAART- Highly active anti-retroviral therapy.

Table 2. Serum lipid profile of study participants by HAART status in Debre Tabor referral Hospital, Debre Tabor-Ethiopia.

Variable	Categories	HAART treated No (%)	HAART untreated No (%)
Total dyslipidemia	Absent	30 (26.3)	53 (46.5)
	Present	84 (73.7)	61 (53.5)
TC	<200 mg/dl	57 (50)	80 (70.2)
	≥200 mg/dl	57 (50)	34 (29.8)
HDL-c	<40 mg/dl	50 (43.85)	41 (36)
	≥40 mg/dl	64 (56.15)	73 (64)
LDL-c	<130 mg/dl	59 (51.75)	82 (71.9)
	≥130 mg/dl	55 (48.25)	32 (28.1)
TG	<150 mg/dl	46 (40.4)	70 (61.4)
	≥150 mg/dl	68 (59.6)	44 (38.6)

TC – total cholesterol TG – triglyceride LDL-c – low density lipoprotein cholesterol HDL-c – High density lipoprotein cholesterol.

Table 3. Comparison of the mean of variables by HAART status in Debre Tabor Hospital, Debre Tabor -Ethiopia.

Variable	Group	Mean (SD)	T (95% CI)	P-value
TC > 200 mg/dl	HAART naïve	186 (24.09)		
	HAART treated	202 (23.98)	4.9 (9.41, 21.88)	<0.001
HDL <40 mg/dl	HAART naive	43.85 (7.91)		
	HAART naive	40.52 (6.09)	-3.5 (-5.2, -1.5)	<0.001
LDL ≥130 mg/dl	HAART naive	111.35 (24.79)		
	HAART treated	126 (22.86)	4.6 (8.8, 19.8)	<0.001
TG ≥ 150 mg/dl	HAART naive	155 (23.34)		
	HAART treated	175 (36.81)	5.1 (11.9, 28.2)	<0.001
CD4 Cells/mm^3	HAART naive	339 (75.88)		
	HAART treated	500 (157.25)	9.9 (128.5, 193)	<0.001
BMI in Kg/M^2	HAART naive	22.11 (2.63)		
	HAART treated	23.33 (2.72)	3.4 (0.54, 1.92)	0.862

BMI – body mass index.

Table 4. Associations of variables with dyslipidemia among HAART treated and untreated HIV patients in Debre Tabor Hospital, Debre Tabor-Ethiopia.

		Outcome variable in Mg/dl (95% CI)			
Explanatory Variable		TC ≥ 200	HDL-c < 40	LDL-c ≥ 130	TG ≥ 150
Male	COR	1.01 (0.58–1.72)	1.6 (0.57–1.63)	1.10 (0.65–1.92)	1.23 (0.71–2.01)
	P-value	0.990	0.880	0.720	0 .510
Age > 40 years	COR	4.88 (2.05–11.61)	4.32 (1.12–16.54)	4.05 (1.77–9.27)	9.20 (2.39–35.49)
	P-value	0 .001	0.030	0.001	<0.001
CD4 < 350 cells/mm^3	COR	3.31 (1.50–7.28)	2.06 (0.96–4.44)	4.00 (1.80–8.87)	3.39 (1.52–7.58)
	P-value	0 .003	0.062	0 .001	0.003
BMI > 25 kg/m^2	COR	2.01 (1.34–6.15)	5.22 (2.63–10.72)	3.20 (1.71–7.55)	10.83 (1.38–84.37)
	P-value	<0.011	<0.001	<0.001	<0.001

COR – Crude odds ratio.

Table 5. Determinant factors of Dyslipidemia and lipid profile level among HIV positive patients, adjusted for the potential confounding factors of study participants in Debre Tabor Hospital, Debre Tabor-Ethiopia.

			Lipid profile level in mg/dl (95% CI)			
Explanatory variable		Dyslipidemia	TC ≥ 200	HDL-c < 40	LDL-c ≥ 130	TG ≥ 150
Age > 40 years	AOR	3.27 (1.47–7.25)				2.44 (1.06–5.64)
	p-Value	0.004				0.037
BMI > 25 kg/m^2	AOR	1.92 (1.20–4.81)	2.31 (1.04–7.66)		3.20 (1.71–7.55)	10.83 (1.38–84.37)
	p- value	0.044	0.025		<0.001	<0.001
On HAART	AOR	2.73 (1.35–5.53)	3.15 (1.49–6.68)		3.02 (1.42–4.23)	2.87 (1.51–5.45)
	p-Value	0.005	0 .003			0.001
BP ≥ 140/90 MmHg	AOR	16.13 (5.81–44.75)	28.59 (13.39–61.04)	5.24 (2.69–10.22	18.44 (9.10–37.41	7.08 (3.45–14.53)
	p-Value	<0.001	<0.001	<0.001	<0.001	<0.001

AOR-adjusted odds ratio.

< 40 mg/dl among HIV clients on HAART is higher than the prevalence reported from Jimma-Ethiopia (32.6%) [9]. This variation might be due to the difference in the sample size and the duration of HAART treatment [18]. The prevalence of LDL-c ≥ 150 mg/dl in HAART treated group was 48.3% which is comparable with the prevalence reported from Cameron (46.4%) [16]. The prevalence of raised TG on HAART group was 59.6%, which is comparable with the report from Hawassa-Ethiopia (55.8%) But was higher than studies done in; India, Cameron, Jimma-Ethiopia reported 32%, 39%, 18.2%, respectively [3, 9]. This variation might be due to the difference in the study setting and life style of the study participants [14].

We found that older age was significantly associated with poor lipid profiles (Dyslipidemia and TG), and this was consistent with findings of previous study conducted in north Shewa of Ethiopia [19].

We found that BMI > 25 kg/m^2 was associated with an elevation in the plasma levels of TG, LDL-c and Tc. This finding was in line with the findings reported from [12, 19, 20].

In this study we have found that being on HAART was significantly associated with poor lipid profile (dyslipidemia, increased Tc and TG). This finding was in agreement with studies done in South Africa, Nigeria and North Shewa of Ethiopia [7, 19, 20]

We have investigated that being hypertensive was significantly associated with poor lipid profile of the study participants in this study. This finding was in line with reports from Nigeria, South Africa and Malawi [4, 7, 9].

5. Conclusion and recommendation

The initiation of highly active anti-retroviral therapy has led to an increment in the serum levels of TC, LDL-c and TG. Old age, raised BP, being on HAART and increased in body mass index were determinant factors of dyslipidemia among HIV clients.

So, further studies with long term follow-up are vital to explain more on the causes of dyslipidemia and the pattern of lipid profile changes with HAART in HIV clients in resource limited countries.

Declarations

Author contribution statement

Anemut Tilahun Mulu; Endeshaw Chekol; Awgchew Behaile Teklemaryam; Melaku Mekonnen Agidew; Zelalem Tilahun Muche; Fitalew Tadele Admassu; Nega Dagnaw; Misganaw Asmamaw Mengstie; Alebachew Amsalu Abebe; Enyew Fenta Mengistu; Yibeltal Akelew; Tadesse Asmamaw Dejenie; Berihun Bantie: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Data availability statement

Data will be made available on request.

Declaration of interest's statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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