

Influence of Antiretroviral Therapy on Lipid Profile in HIV Patients

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Received: 21 June 2026
Accepted: 29 June 2026
Published Online: 30 June 2026

Published by:
Gopalganj Medical College, Gopalganj,
Bangladesh

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DOI: 10.5281/zenodo.21073779

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ABSTRACT

Background: As dyslipidemia is associated with an elevated risk of cardiovascular disease, it represents significant health issues for HIV-positive patients receiving antiretroviral therapy (ART). There is limited information regarding ART treatment and its influence on lipid profiles manifest in HIV infected persons in Bangladesh. To determine the pattern and characteristic of lipid profile among HIV patients on WHO recommended firstline antiretroviral therapy, the study was performed. **Methods & Materials:** A total 51 HIV patients receiving ART for >1 year (group A) and 51 treatment naïve patients (group B) were enrolled in this study. Written informed consent was obtained from all subjects. Each patient was subjected to a full clinical examination, history-taking and lipid profile determination. After collection of the required data, analysis was performed in SPSS 27.0. **Results:** The mean age was 35.52 ± 11.55 (SD) years among total study population and more than two third (77.5%) patients were male altogether. Majority of HIV infected patients had history of unprotected sex (89.2%) and 17.7% had history of transmission of HIV from partner. Mean values of serum lipid profile was found significantly higher among treatment receiver groups (TC= 176.7 ± 37.1 , HDL= 36.7 ± 6.7 , LDL= 104.46 ± 32.9 , TG= 196.86 ± 88.91) compared to treatment naïve patients (TC= 151.9 ± 35.6 , HDL= 31.9 ± 10.6 , LDL= 87.8 ± 25 , TG= 158.7 ± 67.4). Being on ART for three or more years was associated with higher levels of TC and LDL-c ($p < 0.05$). **Conclusion:** The present study findings have suggested an association between antiretroviral therapy (ART) and lipid abnormalities. However, further large multi-centre study is recommended.

Keywords: HIV, Antiretroviral Therapy, Lipid Profile, Dyslipidemia, Cardiovascular Disease Risk

(The Insight 2026; 9(2): 494-498)

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INTRODUCTION

As seen from above, HIV remains a significant public health problem worldwide as it continues to affect millions of people. The populations at risk in Bangladesh have continued to rise over the years. Nonetheless, the stigma against HIV and poor health provider and facility makes the disease difficult to manage. However, ART being the only known life-saving therapy has worked well to contain the disease by lowering the viral up to a standstill. ART is a combination therapy that blocks the viral replication table 1 slowing the advancement of the disease. ART has been proven to be active in the improvement of the PLHIV lifespan; however, it affects several body physiologic processes. One of the major side cautions is the development of dyslipidemia, which is a metabolic disorder that affects lipid, which affects three independent aspects of metabolic abnormality that are injurious to the cardiovascular system. Dyslipidemia may be expressed as elevations of specifically are high total cholesterol, high low-density lipoprotein cholesterol, high triglyceride and low high-density lipoprotein Cholesterol, and several demographic factors may influence cholesterol metabolism [1,2]. ART

influences lipid metabolism; cholesterol levels differ depending on diet and demographic characteristic; thus, it influences infection such as in cerebrovascular accident. According to available data, there is extensive global literature on ART-related lipid abnormalities. Despite this fact, there is an existing gap in the literature because populations from low- and middle-income countries, particularly in Asia, have been given minimal study since they are a minority. Additionally, information on HIV in Bangladesh is scanty, and only a few studies have been conducted to investigate ART's long-term effects, including its alteration of lipid metabolism [3]. Nonetheless, the pattern of lipid profile disruptions most likely associated with ART was established in the country. Some specific country factors, such as ART duration, sociodemographic parameters, and comorbidities, among other possibly meaningful factors established to influence lipid profile by other studies, remained unidentified. However, these factors are essential for enabling practitioners to do their best to care for patients, including identifying the patient category at the highest risk and allowing them to provide people with preventive measures against cardiovascular

diseases. It is likely that ART-induced dyslipidemia has more than one cause, but the critical ones are an increase in fat redistribution, particularly when the reason for it is the exhibit of insulin resistance, and whether or not are ART drugs altering lipid metabolism [4]. The burden of ART-induced dyslipidemia has been extensively reported in Western countries. However, the available data concerning the causes behind ART-related induced dyslipidemia and the prevalence of lipid abnormalities in ART-treated HIV patients is relatively low in Bangladesh [5]. For example, one study by Islam et al. investigated the existence of lipid abnormalities among ART-users in Dhaka regardless of being symptomatic. Nevertheless, no study was done on the association between the different ART regimens used and their duration of usage, if any. This calls for more in-depth studies most specific to Bangladeshi to assess the risk of ART-induced dyslipidemia. Additionally, the challenge is exacerbated by the increased utilization of the first-line ART regimens recommended by WHO. This newer therapy, namely tenofovir/lamivudine/dolutegravir, appears to have fewer lipid-altering effects compared to the older ART regimens and is still effective in viral suppression [6]. Meanwhile, the long-term effects on patients exposed to TLD in Bangladesh are yet to be known. Ultimately, the lipid profile in patients on ART, particularly with newer regimen, should be screened to counter the effect of ART on cardiovascular health and overall well-being.

METHODS & MATERIAL

This study was a cross-sectional design conducted to compare the lipid profiles of HIV patients who are currently on treatment with others who were treatment-naive. ART Centre of Bangladesh Medical University hospital, Dhaka, Bangladesh from September 2019 to December 2022. A total of 102 HIV patients were enrolled, with 51 patients in each group. Group A consisted of individuals who had been receiving ART for over one year, while Group B consisted of treatment-naive individuals.

Inclusion criteria

- Aged ≥ 18 years.
- Provided informed written consent.
- Was able to attend at the selected health center on the day of data collection.
- $BMI \leq 24.9$ kg/m².
- HIV patients administered WHO preferred first line antiretroviral therapy (EFV+3TC/ FTC+TDF) for more than one year.
- HIV patients without treatment.

Exclusion criteria

- Below 18 years.
- Pregnant woman or breast-feeding mother.

- Known case of Diabetes Mellitus, Nephrotic syndrome, Chronic kidney disease, Chronic liver disease, Hypothyroidism, PCOS.
- Having other drugs which cause dyslipidemia (eg: β -blockers, OCP, steroid, antidepressants, thiazide diuretics etc).

Data Collection Procedure

Data collection was performed in two consecutive steps. A structured questionnaire was prepared to obtain participant's demographic and clinical data referring to socio-economic state of the participants, HIV transmission way, history of ART initiation and its duration. Then, each participant was subjected to clinical examination with measurements of body weight, height, and blood pressure. A fasting blood samples were drawn from each participant for lipid profile measurement. Lipid profile included total cholesterol and high-density lipoprotein, low-density lipoprotein and triglycerides. The blood samples were centrifuged, treated, and processed in the laboratory of the hospital, and lipid levels were obtained enzymatically.

Statistical Analysis

The data was entered and analyzed on SPSS version 27.0 IBM Corp, Armonk, NY. All continuous and categorical data were organized using descriptive statistics. Categorical variables were reported as frequency and percentage, whereas continuous variables including age, lipid profile test results, and body mass index were presented as means and standard deviations. Continuous and categorical variables of the two groups (Group A Vs Group B) were compared by independent sample t-test and chi-square test respectively; further, comparison of lipid profile was performed for sub-category recipient groups of ART regime based on duration i.e., those who had been on ART regimen for ≥ 3 years, in order to see effect of duration since the beginning with baseline lipid profile. A p-value < 0.05 was considered statistically significant.

Ethical considerations

The study protocol was approved from the Institutional Review Board/Ethical Clearance Committee of Bangladesh Medical University, Dhaka, Bangladesh before commencement of this study (Memo no: BMU/2019/9827). All patients gave a written informed consent before recruitment.

RESULTS

The study population included 102 HIV patients, with the number of 51 per patient under Group A and the remaining 51 per Group B.

Table I: Socio-demographic characteristics of treatment naive HIV patients and those under antiretroviral therapy (ART) (n=102).

Variables	Group A n (%)	Group B n (%)	Total n (%)
Age Group			
<40 years	28 (54.9)	42 (82.4)	70 (68.6)
>40 years	23 (45.1)	9 (17.6)	32 (31.4)
Sex			
Male	40 (78.4)	39 (76.5)	79 (77.5)
Female	11 (21.6)	12 (23.5)	23 (22.5)
Education			
Illiterate	1 (2.0)	1 (2.0)	2 (2.0)
Primary	21 (41.2)	9 (17.6)	30 (29.4)
Secondary	16 (31.4)	14 (27.5)	30 (29.4)
Higher secondary	10 (19.6)	16 (31.4)	26 (25.5)
Tertiary (Graduation or Above)	3 (5.9)	11 (21.6)	14 (13.7)
Occupation			
Service	14 (27.5)	14 (27.5)	28 (27.5)
Business	5 (9.8)	4 (7.8)	9 (8.8)
Farmer	1 (2.0)	0	1 (1.0)
Student	3 (5.9)	8 (15.7)	11 (10.8)
Others	15 (29.4)	19 (37.3)	34 (33.3)
Retired	2 (3.9)	0	2 (2.0)
Unemployed	11 (21.6)	6 (11.8)	17 (16.7)
Monthly income			
<10,000 bdt	19 (37.3)	9 (17.6)	28 (27.5)
10,000-30,000 bdt	31 (60.8)	38 (74.6)	69 (67.6)
>30,000 bdt	1 (2.00)	4 (7.8)	5 (4.9)

The mean total population age of the study was 35.52 years 11.55 with a male predominance in both groups of 77.5% and 22.5%, respectively. Regarding age, our participants' population, 68.6%, was airing below the age of 40 years. Group A had a larger percentage of participants who had attained higher education, while the representation of individuals with higher tertiary level education in Group B. A relatively high

proportion of those in Group A were engaged in the service and business sectors, which was the opposite of Group B. More participants in Group B were jobless. Concerning monthly earnings, more participants in Group A earned about 10,000-30,000 BDT' while in Group B, more significantly lower income levels of less than 10,000 BDT were recorded (*Table I*).

Table II: Distribution of HIV infected treatment receiver and treatment naive patients by transmission mode /risks (n=102).

Variables	Group A n (%)	Group B n (%)	Total n (%)
H/O getting from partner	7 (13.7)	11 (21.6)	18 (17.65)
Blood transfusion	3 (5.9)	8 (15.7)	11 (10.78)
H/O Surgery	8 (15.7)	9 (17.6)	17 (16.67)
IV drug abuser	9 (17.6)	3 (5.9)	12 (11.76)
H/O unprotected sex	40 (78.4)	51 (100.0)	91 (89.22)

The leading mode of HIV transmission in the study comprised unprotected sex, with 89.2% of the population. A total of 78.4% in Group A also indicated unprotected sex as a mode of

transmission, while in Group B, the mode of transmission was unprotected among all the individual (100%) (*Table II*).

Table III: Clinical parameters between groups in the study (n=102).

Variables	Group A Mean±SD / n (%)	Group B Mean±SD / n (%)	P value
Weight (Kg)	57.90±4.94	58.15±6.84	0.830
Height (m)	5.45±0.28	5.46±0.26	0.846
BMI (Kgm-2)	21.11±1.66	20.83±1.66	0.399
Pulse (bpm)	80.94±9.96	79.61±5.87	0.412
SBP (mmHg)	109.80±13.34	106.08±17.33	0.227
DBP (mmHg)	69.96±8.34	67.84±6.73	0.161
Anaemia	11 (21.6)	12 (23.5)	0.813
Edema	0	1 (2.0)	0.315

Weight P=0.830, height P=0.846, BMI P=0.399 are not statistically significant different, pulse rate P=0.412, systolic blood pressure P=0.227 and diastolic blood pressure P=0.161, but a few individuals in the borderland and tabata groups

showed signs of anemia and edema, although these differences were not significant at P=0.813 and P=0.315, respectively (*Table III*).

Table IV: Distribution of study population according to mean lipid profile of treatment receiver and naive patients in the study (n=102).

Lipid profile	Group A (n=51)	Group B (n=51)	P value
	Mean±SD	Mean±SD	
TC (mg/dl)	176.67±37.09	151.88±35.60	0.001
HDL (mg/dl)	36.73±6.74	31.86±10.58	0.007
LDL (mg/dl)	104.46±32.94	87.77±24.99	0.005
TG (mg/dl)	196.86±88.91	158.68±67.45	0.035

Indicating a significantly higher level of TC, HDL, LDL, and TG in patients receiving ART in Group A than in treatment-naive patients in Group B. Specifically, the values of TC in Group A were 176.7 ± 37.1 mg/dL and 151.9 ± 35.6 mg/dL in Group B that was statistically significant; HDL levels in Group A-36.7 ±

6.7 and Group B-31.9 ± 10.6, p=0.007; LDL in Group A – 104.46 ± 32.9 and Group B – 87.8 ± 25.0, p=0.005; TG in Group A – 196.86 ± 88.91 and Group B – 158.7 ± 67.4, p=0.035 (Table IV).

Table V: Distribution of the study patients by Dyslipidemia Status (n=102).

Lipid Profile	Group A (n=51)	Group B (n=51)	Total (n=102)	P value
TC (mg/dl)				
Normal (<200)	37 (72.5%)	47 (92.2%)	84 (82.4%)	0.009
Dyslipidemia (≥200)	14 (27.5%)	4 (7.8%)	18 (17.6%)	
HDL (mg/dl)				
Normal (≥40)	17 (33.3%)	9 (17.6%)	26 (25.5%)	0.069
Dyslipidemia (<40)	34 (66.7%)	42 (82.4%)	76 (74.5%)	
LDL (mg/dl)				
Normal (<130)	41 (80.4%)	49 (96.1%)	90 (88.2%)	0.013
Dyslipidemia (≥130)	10 (19.6%)	2 (3.9%)	12 (11.8%)	
TG (mg/dl)				
Normal (<150)	16 (31.4%)	29 (56.9%)	45 (44.1%)	0.010
Dyslipidemia (≥150)	35 (68.6%)	22 (43.1%)	57 (55.9%)	

The prevalence of dyslipidemia was significantly higher in Group A than Group B. For total cholesterol, 27.5% of group A had TC≥200mg/dl, while that level of hypercholesterolemia was, however, 7.8% of group B, p=0.009. For HDL; the majority of group A showed HDL<40mg/dl as shown in figure 2 with non-statistical 82.4% of group B not was significantly p= 0.069.

Regarding the LDL, only 19.6% of group A had LDL ≥130 mg/dl, while it was that level of dyslipidemia 3.9% of Group B, p=0.013. For Triglyceride; 68.6% of group A had TRG ≥150 mg/dl compared to 43.1% of group B which was p=0.010 (Table V).

Table VI: Changes of mean values of lipid profile among treatment naive patients with different durations of treatment receivers (n=102).

Lipid profile	Treatment Naive	Treatment receivers		
		<2 years of treatment	2-3 years of treatment	>3 years of treatment
TC	151.88±35.60	167.2±33.60	173.73±23.64	183.64±43.17*
HDL	31.86±10.57	35.40±6.33	36.36±4.69	37.68±7.74
LDL	87.76±24.98	97.85±16.33	95.85±25.61	112.21±41.33*
TG	158.68±67.44	182.67±87.47	207.91±72.93	200.52±57.94

While the duration of the use of ART has grown, a tendency of the augment of the level of total cholesterol and LDL, and triglycerides has been stored. Thus, patients who took ART for over 3 years developed a significantly higher TC of 183.64 ± 43.17 mg/dL and LDL levels of 112.21 ± 41.33 mg/dL compared to administration within less than 3 years. Mind that levels of triglycerides also experienced a marked increase in patients who had been using therapy over 3 years of 200.52 ± 57.94 mg/dL compared to those who took ART less than 2 years 182.67 ± 87.47 mg/dL and 2-3 years 207.91 ± 72.93 mg/dL (Table VI).

DISCUSSION

The present study aims to assess the impact of ART on lipid profile and associated factors among ART naive HIV-infected patients in Bangladesh. Patients treated with ART had significantly higher TC, LDL-C, and TG levels than ART-naive patients. HDL-C levels were also nominally higher in ART users, although most of them still had suboptimal HDL-C

concentrations. In addition, it was noted that longer ART duration correlated positively with TC and LDL-C levels, indicating an accumulating influence of long-term therapy on abnormal cholesterol metabolism. The mean age of the study population was 35.52 ± 11.55 years, and most were male (77.5%), which is in keeping with other studies from Bangladesh and other Asian countries. For instance, Islam et al and Hossain et al observed that the preponderance of males among HIV-positive individuals was associated with local transmission patterns and occupational migration [3,5]. This high proportion of sexual route of transmission (89.2%) as the principal means of infection in this study was similarly reflected in national reporting, confirming sex without condom continues to be the highest mode of HIV transmission in Bangladesh [3]. In this study, there were significantly increased levels of TC, LDL-C and TG with a relatively higher level of HDL-C among ART users compared to ART-naive participants. Mean TC and LDL-C were 176.7 ± 37.1 mg/dL

and 104.46 ± 32.9 mg/dL respectively in ART group as compared to mean TC of 151.9 ± 35.6 mg/dL and LDL-C: 87.8 ± 25 mg/dL in the naive group ($p < 0.05$). These findings are similar to those published by Hulgan et al. and Carr et al who also observed these increases in lipids on ART among HIV-infected [1,7]. Islam et al found that the average values for TC and TG among those treated with ART were substantially higher when compared with those who had not received treatment, establishing the trend observed in their research [5]. Globally, Boulware et al and Zanni et al indicated that ART, particularly PI-based treatment, stimulates marked increases in TC, LDL-C and TG levels through hepatic lipogenesis (lipid synthesis within the liver) and peripheral fat redistribution [8,9]. The small increase of HDL-C in the ART group was not surprising, as this is also found by Barter et al who previously found that ART could yield a modest improvement in HDL-C associated with immune restoration and viral suppression [10], but the functionality of HDL may be impaired resulting in suboptimal clinical effects on cardiovascular disease prevention [11,12].

Dyslipidemia was more common in ART users than in treatment-naive patients. TC ≥ 200 mg/dL was identified in 27.5% of ART users vs 7.8% naive ($p = 0.009$) and hypertriglyceridemia (TG ≥ 150 mg/dL) affected 68.6% ART users vs 43.1% untreated patients ($p = 0.010$). These prevalence rates also closely correspond to the findings of Hossain et al who indicated 70% dyslipidemia in ART patients in Bangladesh [3], and Hernandez et al recorded equivalent values in African populations [13]. Western studies have also reported prevalence's higher than ours, reaching 80% among PI-based regimen treated patients, indicating in addition that lipid response depends on both regimen and genetic background [14]. In these subjects, 19.6% and 8.3% had high levels of LDL-C (≥ 130 mg/dL) and TC (≥ 200 mg/dL), respectively, similar to Western rates reported between 18 and 25% by Grinspoon and Carr [2]. Although the ART group had slightly higher levels of HDL-C (36.7 ± 6.7 mg/dL) than naive participants (31.9 ± 10.6 mg/dL), over two-thirds were below optimal levels and these results add to our understanding that low-HDL-C continues to be a prevalent risk factor despite treatment for HIV populations [10,15]. There was a gradual rise in TC, LDL-C and TG levels as ART duration became longer especially among those who were treated for over three years. Participants who had received ART for more than 3 years had the highest levels of TC (183.64 ± 43.17 mg/dL) and LDL-C (112.21 ± 41.33 mg/dL), showing a sense of accumulation with prolongation of drug exposure time; continually semester term was not considered in this study. These results are consistent with those reported by Zanni et al and Smit et al have also noted that long-term ART causes persistent metabolic dysregulation and increased cardiovascular risk [9,16]. Also found that lipid disturbances continued to deteriorate, independent of stabilized viral replication [17]. This experience suggests that repeated lipid profiles should be obtained and cardiovascular risk assessed in patients with long-term ART.

CONCLUSION

The present study findings have suggested an association between antiretroviral therapy (ART) and lipid abnormalities and long term exposure to ART treatment is one of the factors to cause increase in total cholesterol and LDL cholesterol in patients living with HIV. Therefore, fasting plasma lipid profile should be assessed in all HIV-infected persons before starting ART with periodic measurements of lipid profile after administering ART in HIV patients, since significant increases

in plasma TG, TC and LDL concentrations have been found in HIV patients on ART. But further studies are required to identify the possible association between specific antiretroviral drugs and the development of lipid abnormalities in HIV-infected patients.

FUNDING

No funding source

CONFLICT OF INTEREST

None declared

ETHICAL CONSIDERATION

The study was approved by ethical review committee.

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