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Trends & predictors of non-AIDS comorbidities among people living with HIV and receiving antiretroviral therapy in Lebanon

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Abstract

Combined antiretroviral therapy (cART) increased the life expectancy of people living with Human Immunodeficiency Virus (HIV) (PLHIV) and remarkably reduced the morbidity and mortality associated with HIV infection. Consequently, PLHIV are experiencing non-acquired immunodeficiency syndrome (AIDS) associated comorbid conditions including diabetes, hyperlipidemia, hypertension, and cardiovascular disease. The aim of this study is to determine the frequency of non-AIDS associated comorbid conditions among a cohort of PLHIV on cART in Lebanon.

Data were collected between November 2018 and December 2019 from 105 voluntary participants. A standardized questionnaire was used to collect demographic and behavioral data including lifestyle, smoking, physical activity, substance use and abuse in addition to co-infections and family history of non-communicable diseases. Moreover, data on occurrence and treatment of cardiovascular disease, hypertension, diabetes, lipid and metabolic disorders as well as mental health were collected. Blood samples were used to assess the levels of fasting blood sugar (FBS), glycosylated hemoglobin (HbA1C), triglycerides (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), total cholesterol, and serum creatinine.

Hypertension (29.5%) and hyperlipidemia (29.5%) followed by diabetes (23.7%) and cardiovascular disease (9.7%) were mainly reported among study participants. Higher rate of comorbid conditions was observed among participants >40 years of age than those ≤40 years with both hypertension and hyperlipidemia most commonly reported. Older age (odds ratio [OR] 7.6; 95% CI: 1.83-31.98; $P = .005$) is associated with higher odds of having hyperlipidemia. Moreover, participants on cART for ≥10 years are 5 times more likely to have hyperlipidemia (OR 5; 95% CI: 1.08-22.73; $P = .039$). Our results also showed that study participants did not experience anxiety, depression or somatic symptoms and that there was no association between these mental disorders and older age or comorbidities.

Our results provide important information on HIV trends and associated comorbidities in Lebanon and can be used to improve the management of non-communicable diseases among PLHIV.

Abbreviations: AIDS = acquired immunodeficiency syndrome, cART = combined antiretroviral therapy, CVD = cardiovascular disease, FBS = fasting blood sugar, FET = Fisher exact test, HbA1C = glycosylated hemoglobin, HDL = high density lipoprotein, HIV = Human Immunodeficiency Virus, LDL = low density lipoprotein, OR = odds ratio, PLHIV = people living with HIV, TG = triglycerides.

Keywords: aging, comorbidity, HAART, HIV, Lebanon

1. Introduction

The use of combined antiretroviral therapy (cART) significantly reduced the morbidity and mortality associated with Human Immunodeficiency Virus (HIV) infection.[1] The former contributed to an increase in the life expectancy of people living with HIV (PLHIV) approaching that of HIV-negative individuals.[2–4] Globally, the proportion of people aging with HIV is increasing and is estimated to reach 21% by 2020.[5] While new cases of

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PLHIV above 50 years of age are declining, the Centers for Disease Control and Prevention recently reported 1 in 6 HIV diagnoses in this group; moreover, almost 50% of PLHIV are 50 years of age and older.[6] The age of the majority of PLHIV globally is projected to be under the age of 55 years in 2050 compared to <35 years in 2010.[7] Specifically, the number of adolescent and young people living with HIV (15-24 years) is projected to decline by 61% between 2010 and 2050.[7] These data suggest a dramatic demographic shift among PLHIV.

With the success of cART, the rate of non-acquired immunodeficiency syndrome (AIDS) comorbidities are increasing in treated PLHIV leading to an increased number of deaths exceeding those of AIDS-related deaths.[8] These comorbidities include cardiovascular disease (CVD),[9,10] liver disease,[11,12] renal disease,[10] diabetes,[9,13] neurocognitive abnormalities,[14,15] as well as non-AIDS defining malignancies.[16,17] While biological aging among HIV-infected individuals is believed to start earlier compared to healthy subjects (55 vs 65 years, respectively),[18] the impact of aging with HIV infection and subsequent pathways leading to disease manifestation is not fully understood. A number of parallels have been advanced to explain the relationship between HIV and aging. HIV-associated immune activation, host-genetic factors, behavioral factors (i.e., diet, exercise, and smoking) and drug-to-drug interactions in combination with cART have been suggested to cause these metabolic perturbations.[19,20]

The HIV and Aging Consensus Project recommended screening HIV-infected individuals for diabetes, kidney functions, hypertension as well as cognitive impairment and depressive disorders. In addition, assessment of the Framigham Risk Score was also recommended along with cholesterol and blood pressure.[21] A projected increased life-expectancy coupled with an expected increase in burden of non-communicable diseases would impact HIV management, treatment and control. With the absence of a chronic care model especially in limited resource countries, these non-AIDS morbidities pose a major risk on treated HIV-infected people progressing into an older population.

Globally, the number of PLHIV is at 38 million with 67% on antiretroviral therapy.[22] The majority of new HIV infections reported in 2019 were among key populations (men having sex with men, sex workers, people who inject drugs, prisoners, transgenders) and their sexual partners.[23] By the end of 2019, the UNAIDS estimated a cumulative number of 2700 PLHIV in Lebanon (2300 males and <500 females) with 63% on antiretroviral therapy. While Lebanon is considered a low HIV prevalence country (less than 0.1% of the total population), the rate of HIV infection is increasing yearly by an average of 100 new cases. Recent evidence clearly defines pockets of concentrated HIV epidemic and a high epidemic potential in Lebanon.[24] The majority of PLHIV in Lebanon are ≥30 years old with more than 46% being 30 to 49 years old in 2017 compared to 31% in 2012.[25] The paucity of data on PLHIV in Lebanon, especially among key populations, is a major challenge that hinders the comprehensive understanding of HIV trends and associated comorbidities. Currently, data are limited on the comorbidity profiles associated with people living and aging with HIV in the developing world in general, the Eastern Mediterranean region and Lebanon specifically. The aim of this study is to determine the trends and predictors of non-AIDS comorbid conditions among treated people living and aging with HIV in Lebanon and to assess the association between these predictors and comorbid conditions.

2. Methods

2.1. Study design, population, and data collection

Human subject approval was obtained for this cross-sectional study from the institutional review board (IRB) of the American University of Beirut (AUB) and the Lebanese American University (LAU). All voluntary participants provided a written informed consent. A standardized questionnaire was administered to a total of 105 treated adult HIV-infected individuals between November 2018 and December 2019. Demographic and behavioral data including lifestyle, smoking, physical activity, substance use and abuse, co-infections, chronic diseases (cardiovascular disease, hypertension, diabetes, lipid and metabolic disorders, cancer, mental health and others), first-degree family history (i.e. parents or siblings) of chronic diseases, co-medication data and mental health data were collected. Physical activity was classified as vigorous-intensity (carrying or lifting heavy loads, running, playing football and others) or moderate-intensity (swimming, playing volleyball and others) activity for at least 10 minutes continuously.

A one time blood draw was collected from 104 voluntary participants to measure the following clinical parameters: fasting blood sugar (FBS), glycosylated hemoglobin (HbA1C), cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides (TG) and creatinine.

2.2. Measurement of anxiety, depression, and clinical parameters

We used the 9 item Patient Health Questionnaire (PHQ-9) to assess depression among our study participants as previously described.[26–30] The response was rated as "0" (not at all), "1" (several days), "2" (more than half the days) or "3" (nearly every day). The severity of depressive symptoms was determined based on the summation of the scores ranging between 0 and 27.[31] Scores of 5 to 9 points indicate mild levels of depressive symptoms, 10 to 14 points indicate moderate levels of depressive symptoms, 15 to 19 points indicate moderately severe levels of depressive symptoms, and 20 to 27 points indicate severe levels of depressive symptoms. 15 item Patient Health Questionnaire (PHQ-15), the somatic symptom module of 9 item Patient Health Questionnaire, was rated as "0" (not bothered at all), "1" (bothered a little), or "2" (bothered a lot). Similarly, the severity of somatization symptoms was determined based on the summation of the scores (0-30).[32,33] Scores of 0 to 4, 5 to 9, 10 to 14 and ≥15 points indicate no somatization disorder, mild levels of somatization, moderate levels of somatization and severe levels of somatization, respectively. Similarly, the Generalized Anxiety Disorder-7 (GAD-7) item Assessment was used to measure symptoms of generalized anxiety.[34] Briefly, the scale of GAD-7 item Assessment was rated from "0" (not at all) to "3" (nearly every day). The severity of anxiety was determined based on the summation of the scores (0 to 21). Scores of 0 to 4, 5 to 9, 10 to 14 and ≥14 points indicate no anxiety, mild anxiety, moderate anxiety, and severe anxiety, respectively.

The guidelines of the American Diabetes Association[35] were used to classify the tested levels of FBS and HbA1C. The

reference range of clinical parameters were as follows: normal FBS level, <100 mg/dl; prediabetes FBS level, ≥100-<126 mg/dl; diabetes FBS level, ≥126 mg/dl; HbA1C levels <5.7%, between 5.7% and 6.4% and ≥6.5% were defined as normal, prediabetic and diabetic, respectively. Moreover, we followed the guidelines of the Centers for Disease Control and Prevention to report on total cholesterol, LDL, HDL and triglycerides (TG) with normal values of: <200 mg/dl, <100 mg/dl, ≥60 mg/dl, and <150 mg/dl, respectively.[36] Furthermore, normal serum creatinine levels were defined as 0.6 to 1.1 mg/dl in women and 0.7 to 1.3 mg/dl in men.

2.3. Statistical analysis

Data were summarized descriptively using counts and frequencies for categorical variables and mean, standard deviation and range for continuous variables. We examined the relationship between age, sex and risk factors of interest and non-AIDS associated comorbid conditions using χ^2 and Fisher exact test (FET). When appropriate, we used the *t* test to compare the levels of the clinical parameters among the study participants. Variables with *P* values less than .2 using the univariate regression model were eligible for entering analysis using the multivariate regression model. Diabetes and CVD were considered rare events since they constitute less than 20% of our sample size. Consequently, we used exact logistic regression for rare events to test for any association between the participants' risk factors and the aforementioned outcomes. These analyses were performed using STATA SE 13.0 (StataCorp LP, TX, USA).

3. Results

3.1. Sociodemographic, life style, behavioral, and clinical characteristics of the study participants

The majority of the study participants were >40 years old (68.5%) (mean age 48.14 ± 10.83 years), males (83%), and employed (59%). More than 50% of our cohort were heterosexuals and 33% were men having sex with men (Table 1). Our data showed that more than 57% of participants were smokers (cigarettes hookah, and/or e-cigarettes); we did not detect any significant difference between males and females (Table 1). Albeit less common than smoking, alcohol use was significantly higher among males (*P* = .046); moreover the use of recreational drugs (e.g., ecstasy, amphetamines, marijuana, cocaine heroin, and others) was reported by only males (*P* = .039). Marijuana/weed and cocaine were the most commonly used drugs (77% vs 47%); only 2 participants were injecting drug users (data not shown).

Table 1

Demographic and clinical characteristics of study participants.

	Males n (%)	Females n (%)	Total n (%)	*P* value[†]
Age in years (N = 105)				.041
≤40	31 (35.6)	2 (11.1)	33 (31.4)	
>40	56 (64.4)	16 (88.9)	72 (68.6)	
Sexual history (N = 101)				
Heterosexual	37 (44)	17 (100)	54 (53.4)	<.001
MSM	33 (39.3)	0 (0)	33 (32.7)	.001
Bisexual	14 (16.7)	0 (0)	14 (13.9)	.062
Tobacco use[*] (N = 105)	50 (57.5)	10 (55.6)	60 (57.1)	.881
Alcohol use (N = 104)	18 (20.7)	2 (11.1)	20 (19.2)	.046
Recreational drug use (N = 104)	18 (20.7)	0 (0)	18 (17.3)	.039
Body weight consideration (N = 105)				.551
Underweight	10 (11.5)	1 (5.6)	11 (10.4)	
Normal/healthy weight	57 (65.5)	11 (61.1)	68 (64.8)	
Overweight	20 (23)	6 (33.3)	26 (24.8)	
Vitamins/supplements intake (N = 104)	31 (35.6)	10 (58.8)	41 (39.4)	.074
HIV route of transmission (N = 105)				.456
Unprotected sex	59 (67.8)	13 (72.2)	72 (68.6)	
Shared needle/syringe	7 (8.1)	0 (0)	7 (6.7)	
Others	21 (24.1)	5 (27.8)	26 (24.7)	
Duration of HIV infection (N = 103)				.232
<5 yrs ago	9 (10.6)	0 (0)	9 (8.7)	
5-10 yrs ago	34 (40)	6 (33.3)	40 (38.8)	
>10 yrs ago	42 (49.4)	12 (66.7)	54 (52.5)	
Duration of cART (N = 105)				.592
<5 yrs ago	14 (16.1)	2 (11.1)	16 (15.2)	
5-10 yrs ago	36 (41.4)	6 (33.3)	42 (40)	
>10 yrs ago	37 (42.5)	10 (55.6)	47 (44.8)	
cART regimen (N = 102)				.775
NRTI + NNRTI	40 (47.1)	7 (41.2)	47 (46.1)	
NRTI + INSTI	39 (45.9)	8 (47.1)	47 (46.1)	
Others (PI + NRTI and/or NNRTI)	6 (7)	2 (11.8)	8 (7.8)	
Adherent to cART (N = 105)	86 (98.8)	18 (100)	104 (99.1)	.648

cART = combined antiretroviral therapy, INSTI = integrase inhibitors, MSM = men who exclusively have sex with men, NRTI = nucleoside/nucleotide reverse-transcriptase inhibitor, NNRTI = non-nucleoside reverse-transcriptase inhibitor, PI = protease inhibitor.

[*] Tobacco use includes participants who smoke cigarettes, e-cigarettes and/or hookah; Vitamins/supplements include vitamin B, C, D, folic acid, omega 3, calcium, magnesium, and glucosamine.

[†] Pearson chi[2] test.

When asked about diet, type and diversity (fruits, vegetables, and type of fatty acids) as well as frequency of meals (breakfast, lunch, and dinner), our study participants reported balanced and healthy diets with no significant difference between males and females (data not shown). Interestingly, participants were generally not physically active.

Unprotected sex was the main mode of HIV transmission in our group with no significant difference between males and females. Importantly, more than 50% contracted HIV more than 10 years ago. Similarly, the majority of participants (45%) were on cART for more than 10 years. All participants were adherent to cART (i.e., never stopped taking ART). The most frequently used cART regimens among participants were a combination of nucleoside/nucleotide reverse-transcriptase inhibitors (NRTIs) and non-nucleoside reverse-transcriptase inhibitors (NNRTIs) or a combination of NRTIs and integrase inhibitors (INSTIs). Only 8 participants were using other cART combinations, half of them were on a drug regimen containing a protease inhibitor (PI). The vast majority of participants (87%) received cART free of charge through the Lebanese National AIDS Program (data not shown). Our data reveal that co-infections, specifically sexually transmitted infections, were most prevalent among men having sex with men (data not shown).

3.2. Frequency of non-AIDS comorbidities among study participants

We measured the levels of FBS, HbA1C, lipid profile (cholesterol, LDL, HDL, and TG) and creatinine and compared these levels between participants ≤40 years and those >40 years (data not shown). While this was a cross-sectional assessment, these clinical parameters are important risk factors of high blood pressure, diabetes, and hyperlipidemia.[35,36] The mean levels of FBS, cholesterol, LDL, and TG were above normal in our cohort. The mean levels of FBS and TG were specifically higher among participants aged >40 compared to those ≤40 years old (not significant). HbA1C mean level was in the prediabetic range among individuals >40 years. We did not detect a significant difference between males and females.

Importantly, 42% of participants reported to have at least 1 comorbid condition (hyperlipidemia, hypertension, diabetes and/or CVD); 51% of these participants were >40 years whereas 21% were ≤40 years (FET, $P = .005$). Our data showed that the frequency of comorbid conditions was significantly higher among males >40 years than males ≤40 years (FET, $P = .038$) (data not shown). Moreover, being on cART for more than 10 years was significantly associated with the frequency of these comorbid conditions among both males (FET, $P = .008$) and females (FET, $P = .01$) (data not shown). Hypertension (29.5%) and hyperlipidemia (29.5%) followed by diabetes (23.7%) and CVD (9.7%) were mainly reported among our study participants with no significant difference between males and females (Table 2). Following the above trend, anti-hypertensives and lipid-lowering agents were the most commonly used non-cART medications. When we compared the relationship between family history and having diabetes, hypertension, hyperlipidemia or CVD among all participants, we did not detect any significant difference (Table 2). However, when we compared the association between family history and the conditions above among PLHIV suffering from these conditions, we only detected a significant difference among those with hypertension (FET, $P = .015$) (data not shown).

Nineteen percent of our participants >40 years old reported 1 or 2 comorbid conditions each followed by approximately 10% and 3% suffering from 3 and 4, respectively. As expected, PLHIV less than 40 years old suffered from less disease conditions whereby 15% suffered from 1 comorbidity with 3% living with 2 and 3 comorbid conditions, each (FET, $P = .03$) (Fig. 1). Collectively, our results showed that the frequency of comorbid conditions increases with age among PLHIV; with hyperlipidemia and hypertension being most commonly observed among our cohort. When we grouped our participants into 3 age groups: 25 to 44 (n = 42), 45 to 59 (n = 44) and ≥60 (n = 19) years, we found that the majority of participants in the 25 to 44 age group (14.3%) and 45 to 59 age group (22.7%) have 1 comorbidity. On the other hand, 36.8% of participants in the ≥60 age group have 2 comorbid conditions (FET, $P = .006$) (data not shown).

We then sought to determine the relationship between hyperlipidemia and hypertension and age while adjusting for confounders specifically family history of comorbid conditions and smoking. Our results showed that the odds ratio (OR) of

Table 2

Non-AIDS comorbidities and treatment.

	Males n (%)	Females n (%)	Total n (%)	*P* value*
Comorbidities				
Hypertension	23 (26.4)	8 (44.4)	31 (29.5)	.283
Hyperlipidemia	22 (25.3)	9 (50)	31 (29.5)	.069
Diabetes	8 (9.2)	1 (5.6)	9 (8.6)	.209
CVD	7 (8.1)	3 (16.7)	10 (9.5)	.571
Family history				
Hypertension	42 (48.3)	6 (33.3)	48 (45.7)	.304
Hyperlipidemia	5 (5.6)	3 (16.7)	8 (7.6)	.302
Diabetes	26 (29.9)	6 (33.3)	32 (30.5)	.783
CVD	41 (47.1)	6 (33.3)	47 (44.8)	.426
Non-cART medications				
Anti-hypertensives	23 (26.4)	8 (44.4)	31 (29.5)	.158
Lipid-lowering agents	22 (25.3)	9 (50)	31 (29.5)	.048
Hypoglycemic agents	9 (100)	0 (0)	9 (8.6)	.1

cART = combined antiretroviral therapy, CVD = cardiovascular disease.

* Fisher exact test.

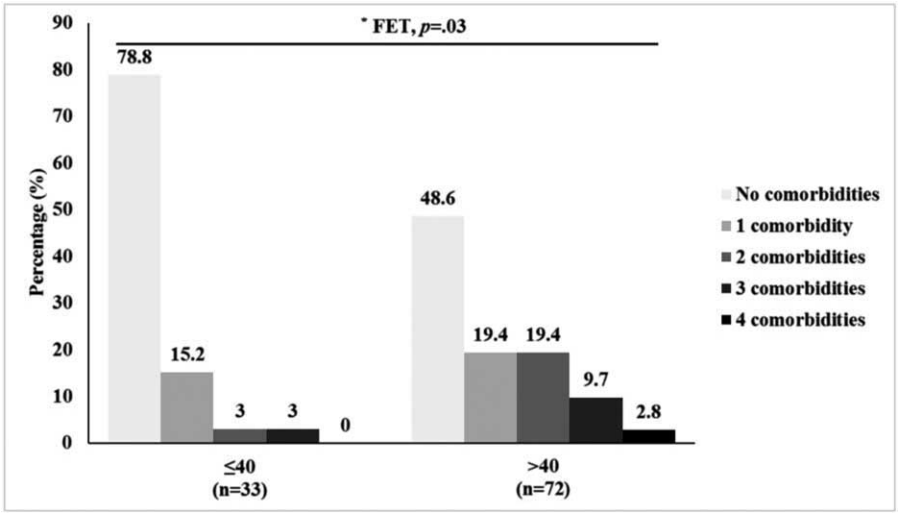

Figure 1. Frequency of comorbidities by age among PLHIV. The figure presents the percentages of participants ≤40 and >40 yrs old with no comorbidity, a single comorbidity or multimorbidity. *P* value <.05 was considered statistically significant. FET = Fisher exact test, PLHIV= people living with Human Immunodeficiency Virus.

having hyperlipidemia among participants aged >40 years was significantly higher than those ≤40 years. We then determined the relationship between these comorbidities (hyperlipidemia and hypertension) and duration of HIV infection and cART treatment while adjusting for age, family history of the comorbid condition and smoking. Our results showed that participants who have been on cART for more than 10 years were 5 times more likely to have hyperlipidemia (OR 5; 95% CI: 1.08-22.7; *P*=.039) and hypertension (OR 5.2; 95% CI: 0.98-28.15; *P*=.052) (Table 3). Multivariate analyses, while adjusting for family history of diabetes, smoking and alcohol use, revealed a significantly increased odd of diabetes with longer duration of treatment (OR 5; 95% CI: 1.07-47.93; *P*=.0374) (data not shown). When we added age as a confounding factor, the OR decreased to 2.3 with no significant difference observed between diabetes and prolonged duration of cART treatment (OR 2.3; 95% CI: 0.61-23.57; *P*=.248) (data not shown). These results suggest that people aging with HIV are more likely to develop hyperlipidemia. Our results also suggest that prolonged duration of cART (i.e., >10 years) is associated with hyperlipidemia and hypertension. Our results are to be cautiously interpreted due to the small sample size.

3.3. The prevalence of anxiety, depression, and somatization among study participants

PLHIV are 2 to 3 times more likely to experience mental health disorders such as depression and anxiety compared to HIV-naïve individuals.[31,37,38] Interestingly, our data showed that more than 80% of our participants did not experience anxiety, depression or somatic symptoms. These results were similar among those less than 40 and older as well as among males and females. Moreover, we did not detect any association between anxiety (*P*=.891), depression (*P*=.113) or somatic symptoms

Table 3

Odds ratio of comorbidities with respect to age, sex, duration of HIV infection, and duration of cART treatment.

	Hyperlipidemia		Hypertension	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
≤40 yrs (*Reference*)*				
>40 yrs	7.6 (1.83-31.98)	**.005**	2.2 (0.59-7.86)	.242
Female (*Reference*)†				
Male	0.4 (0.11-1.63)	.212	0.3 (0.07-1.43)	.137
Duration of HIV infection†				
<5 yrs ago (reference)				
5-10 yrs ago	1.05 (0.09-12.82)	.965	1.3 (0.08-18.39)	.859
>10 yrs ago	8.13 (0.82-80.22)	.073	5.2 (0.37-72.55)	.218
Duration of cART treatment†				
<5 yrs ago (*Reference*)				
5-10 yrs ago	0.9 (0.18-5.03)	.958	1.3 (0.22-7.15)	.794
>10 yrs ago	5 (1.08-22.73)	**.039**	5.3 (0.98-28.15)	.052

Variables with *P* values less than .2 using the univariate regression model were eligible for entering analysis using the multivariate regression model.

95% CI = 95% confidence interval, cART=combined antiretroviral therapy, HIV = Human Immunodeficiency Virus, OR = odds ratio.

* Adjusted for family history of comorbid condition and smoking.

† Adjusted for age, family history of comorbid condition, and smoking.

($P = .068$) and having non-AIDS associated comorbid condition (data not shown).

4. Discussion

We assessed the trends and predictors of non-AIDS comorbidity among treated PLHIV in Lebanon. Our data showed that 42% suffered from 1-to-4 comorbid conditions with 29.5% suffering from hypertension and hyperlipidemia each, and 9.5% and 8.6% suffering from CVD and diabetes, respectively. Previous studies detected an association between duration of cART treatment and development of non-AIDS associated comorbidities (CVD, Hypertension, Diabetes, Bone Fractures, and Renal Failure).[39,40] Our results showed an association between prolonged cART treatment and having hyperlipidemia. However, there was no significant association between cART duration and having hypertension, diabetes or CVD in our cohort. This is probably due to our small sample size.

There is scarcity of data on comorbidities among PLHIV in the Middle East and North Africa (MENA) region. Moreover, to our knowledge, this study is the first in Lebanon to assess trends and predictors of non-AIDS associated comorbidities among PLHIV. We have previously reported on the health status of 100 people living and aging with HIV in Lebanon[41]. Preliminary data from this exploratory study showed that both hyperlipidemia and hypertension were the most common comorbidities (31% vs 20%, respectively) followed by diabetes (12%) and CVD (11%). Moreover, the duration of HIV infection was associated with CVD. This is in contrast to the results of this study whereby no association between duration of infection and any comorbid condition was detected. Recently, an association between being a male, older age, prolonged duration of HIV infection, higher body mass index and higher prevalence of hyperglycemia was reported in Tehran.[42]

A large number of studies have been published during the past 5 years worldwide on the effect of aging with HIV on non-AIDS associated comorbidities.[43–47] Data from the United States (US) showed that the prevalence of multimorbidities (≥ 2) among a cohort of more than 22,900 of PLHIV increased from 8% to 22% during a 9-year period of follow-up.[48] Hypertension and hypercholesterolemia were the most common co-occurred comorbidities. Similarly, the prevalence of multimorbidities increased by more than 3-folds in a cohort of PLHIV in Brazil followed for 10 years; older age, low nadir $CD4^+$ cell count as well as being a female were significantly associated with higher risk of multimorbidities.[44] Other studies in Europe also demonstrated an association between older age (≥ 40 years) and nadir $CD4^+$ cell count (<350 cells/mm^3) with metabolic syndrome among HIV-infected individuals.[49] Moreover, diabetes, hypertension, hyperlipidemia, and coronary artery disease were more prevalent among PLHIV aged ≥ 50 years compared to those 40 to 49 years old in Taiwan.[50] Consistent with these data, our results showed that the frequency of comorbidities, specifically hyperlipidemia, increases with age. We were unable to test the association between nadir $CD4^+$ cell count and comorbidities among our study participants as data on the former were inaccessible. Similar to what has been observed previously among treated HIV-infected patients (age ≥ 45 years),[44,48,50] our data revealed a significantly higher frequency of multimorbidity among individuals older than 40 years of age.

Importantly, as PLHIV age, the number of co-medications (i.e., in addition to cART) to treat comorbid conditions increases. This leads to drug-to-drug interaction (DDI), adverse drug effects (ADEs), increased hospitalization due to DDI and ADEs and lower adherence to cART.[19,51] Consistent with previously reported data,[50–52] our results showed a complete adherence to cART along with a significantly higher frequency of non-cART medication use among our study participants >40 years old compared to those ≤ 40 years with anti-hypertensives and lipid-lowering agents being the most commonly reported medications. The long-term impact of comedications among PLHIV requires further investigation in Lebanon and the region as well as longitudinal follow-up for improved HIV care.

Several studies reported higher prevalence of smoking and recreational drug use among PLHIV compared to the general population.[53,54] Moreover, alcohol use among PLHIV was associated with risky behaviors including unprotected sex.[55] Higher frequency of mental health disorders including generalized anxiety, depression and somatization symptoms was also reported among PLHIV compared to healthy controls.[37,38,56] More than 50% and less than 20% of our enrolled participants were smokers and reported drug and alcohol use, respectively. In contrast to the previously published data, our study did not suggest any association between age and comorbidities and mental health disorders. Our results are to be cautiously interpreted due to the small sample size and the lack of a healthy HIV-naïve control group along with data on risk factors associated with metabolic disorders.

Our study has several limitations. Our study lacks a control group of HIV-negative individuals; thus, we were unable to compare the frequencies of comorbid conditions between our cohort and HIV-naïve individuals. However, limited data exist on the prevalence of metabolic disorders in Lebanon. Recently, hypertension was reported at 31% in a cross-sectional study; moreover, the prevalence of hypertension increased with increasing age and body mass index, and in the presence of previous CVD.[57] A national study also reported the prevalence of type I diabetes mellitus was estimated at 0.1%, or almost 1% of all detected cases of diabetes mellitus in Lebanon.[58] Our study is a cross-sectional study without historic clinical and medical data to assess the evolution of comorbid conditions and pertinent risk factors across time. Moreover, data on nadir $CD4^+$ count were lacking which hampered our ability to assess the association between the latter and the risk of developing a comorbid condition in our cohort. The results of this study were collected during a single visit; consequently, neither temporality nor causality could be determined between age and comorbid conditions.

5. Conclusion

Further studies are needed to investigate the impact of aging on the prevalence of non-AIDS related comorbid conditions in PLHIV. These studies are important for the proper management and care of comorbid conditions among PLHIV in Lebanon. The integration of HIV programs with non-communicable diseases programs is necessary to reduce the burden of multi-morbidities among people living and aging with HIV.

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