Original Article

Screening for antiretroviral drug resistance among treatment-naive human immunodeficiency virus type 1-infected individuals in Lebanon

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Abstract

Introduction: Antiretroviral therapy (ART) has been successful at decreasing the morbidity and mortality associated with human immunodeficiency virus type 1 (HIV-1) infection. HIV-1 drug resistance (HIVDR) among ART-naive patients has been documented to compromise the success of initial therapy. This study was conducted to determine the prevalence of HIVDR mutations among newly diagnosed drug-naive HIV-infected individuals in Lebanon.

Methodology: Plasma samples from 37 newly diagnosed participants at various stages of HIV-1 infection were used to determine HIV-1 RNA viral load, isolate viral RNA, and amplify DNA by RT-PCR. Purified PCR products were used to perform genotypic resistance tests.

Results: The prevalence of resistance mutations to nucleoside reverse transcriptase inhibitors (NRTI), non-nucleoside reverse transcriptase inhibitors (NNRT), and protease inhibitors (PI) were 5.4%, 10.8%, and 8%, respectively. The major mutations detected in the study participants conferred resistance to NRTIs and NNRTIs recommended for HIV-1 treatment. No significant relationship between HIV-1 viral load of participants and the mode of HIV-1 transmission or between the occurrence of HIVDR and the mode of transmission was found.

Conclusions: To our knowledge, this is the first study on HIVDR mutations among newly diagnosed HIV-infected persons in Lebanon. The overall prevalence of HIVDR mutations detected in our study was 16%. Our results are important for evaluating the utility of the standard first-line regimens in use, determining the feasibility of HIVDR testing before the initiation of ART, as well as minimizing the emergence and transmission of HIVDR.

Key words: HIV-1; ART; resistance mutations; NRTIs; NNRTIs; PIs

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Introduction

The use of antiretroviral therapy (ART) has significantly reduced the mortality and morbidity caused by human immunodeficiency virus type-1 (HIV-1) [1]. ART aims at suppressing HIV-1 replication and enhancing immune reconstitution assessed by increased $CD4^+$ T cell counts [2]. By the end of 2011, approximately eight million people living with HIV were receiving antiretroviral therapy in low- and middle-income countries. This represents a 20-fold increase in the number of people receiving therapy in developing countries between 2003 and 2011 [3,4]. There are up to 15 million people estimated to be currently eligible for ART, leading to a treatment gap of 7 million. Despite the increased access to therapy, reports show that the rate of virologic failure among ART recipients is associated with the rate of antiretroviral resistance [5]. Importantly, HIV-1 drug resistance (HIVDR) can be transmitted to ART-naive HIV-infected individuals [6,7]. The International AIDS Society USA guidelines for the use of ART in adults recommend testing for HIVDR prior to initiation of therapy in high-resources countries [8,9].

Resistance to ART is a survival strategy adopted by the virus and precedes the introduction of therapy. Knowledge of ART resistance is described as a predictor of immunologic, virologic, and clinical

outcomes of therapy [10]. Consequently, the identification of HIVDR in treatment-naive patients is critical to maximize the detection of transmitted drug resistance, guide the selection of treatment regimen to suppress HIV-1 replication, and ultimately prevent resistance-associated virologic failure [9,11,12]. The prevalence of HIVDR among ART-naive people in the United States and Europe has been estimated to be 10%-15% [11,13]. In sub-Saharan Africa, HIVDR was reported to be less than 5%, with growing evidence of increasing levels of resistance [14,15,16]. In a recent review by Paredes *et al*. [10], statistics show that the prevalence of primary or pre-existing resistance in high-income countries among treatment-naive HIV-patients is 8%-19% for any drug; 5%-12% for nucleoside reverse transcriptase inhibitors (NRTIs); 2%-8% for non-nucleoside reverse transcriptase inhibitors (NNRTIs); and 3%-7% for protease inhibitors (PIs). Despite the current low rates of HIVDR in resource-limited countries, the authors suggest that an increase is likely to be observed in the years to come, especially due to the high frequency of secondary resistance in many of the resource-limited countries.

The first case of AIDS diagnosed in Lebanon was in a homosexual man in 1984. The use of ART started in the country as early as 1988 with zidovudine monotherapy, followed by the introduction of didanosine in 1991. Towards the end of 1996, a combination of zidovudine, didanosine (later replaced by lamivudine), and indinavir was used. Stavudine was introduced in the late 1990s, and efavirenz was first used in 2000. HIV-infected individuals receive their treatment free of charge from the National AIDS Program (NAP) of the Lebanese Ministry of Public Health (MOPH). Until the end of November 2012, the number of HIV-1 cases reported by the NAP in Lebanon was 1,552 cases, with 540 HIV-infected persons receiving antiretroviral therapy regularly; the latter constituted 35% of HIV-infected persons in the country. The UNAIDS estimates 2,900 people living with HIV-1 in Lebanon with a prevalence rate of HIV/AIDS of 0.1% [17].

In Lebanon and similar resource-limited countries, the management and treatment of HIV-positive individuals are based on the revised WHO recommendations [18]. The treatment protocol followed in Lebanon consists of a NNRTI (efavirenz [EFV] or nevirapine [NVP]) with two NRTIs (lamivudine [3TC], zidovudine [AZT/ZDV], or tenofovir [TDF]) as first-line therapy, and two NRTIs plus one ritonavir-boosted protease inhibitor based regimen (PI) as second-line therapy. The currently available drugs in Lebanon are: five NRTIs (AZT/ZDV, 3TC, TDF, didanosine [ddI], and abacavir [ABC]); two NNRTIs (EFV and NVP); one PI (lopinavir/ritonavir [LPVr]); and one integrase inhibitor (raltegravir [RAL]). The current starting treatment regimen consists of TDF, 3TC, or emitricitabine and EFV. This is the same drug combination prescribed at the time of sample collection. Due to the frequent shortage of drugs, unscheduled treatment interruptions occur. These interruptions have been described to be associated with viral rebound, resulting in pretreatment viral load [19] as well as a possible increased risk of complications [20].

Limited data are available on the prevalence of HIVDR in the WHO Eastern Mediterranean region (EMR). Drug resistance mutations to NRTIs and PIs have been reported in untreated patients in Algeria [21]. Moreover, HIVDR to NRTIs, NNRTIs, and PIs were described in Morocco among ART-naive patients [22]. To our knowledge, there are no data on antiretroviral drug resistance among treatment-naive HIV-1-infected individuals in Lebanon. With increased access to antiretroviral therapy in Lebanon, it is relevant to assess the burden of HIVDR among untreated individuals. Moreover, knowledge of the prevalence of transmitted drug resistance and testing for it in newly presented HIV-infected individuals in Lebanon will help target better care and prevention strategies. The purpose of this study was to determine the prevalence of drug resistance mutations among newly infected ART-naive patients. The generated data will be important for future evaluations of the treatment failure or success following the intake of first-line regimen, and will demonstrate the importance of clinically monitoring resistance for better control of HIV-1.

Methodology

Study participants

Thirty-seven newly diagnosed participants at various stages of HIV-1 infection provided written informed consent upon enrolment in the study (between March 2006 and December 2007). Human subject approval for this study was obtained from the institutional review board of Rizk University Hospital. The study participants were recruited from the Rafic Hariri University Hospital and Rizk Hospital, affiliated with the Lebanese University and the Lebanese American University, respectively. Individuals presenting at the sites to test for recent

HIV-1 infection were approached, regardless of the stage of infection. ART-experienced individuals were excluded from the study. HIV-1 seropositivity was confirmed by two positive enzyme-linked immunosorbent assays (ELISAs) and/or a western blot with bands corresponding to at least two of the Gag, Pol, and Env proteins as previously described [23]. A data collection form was administered to volunteers to collect demographic information and data related to risk behavior information.

Clinical and virologic characteristics

Plasma samples were collected from the study participants and stored at -80°C. These samples were used to determine HIV-1 RNA viral load, which was determined via quantification of HIV-1 viral RNA using COBAS AMPLICOR HIV-1 MONITOR Test version 1.5 (Roche Molecular Diagnostics, Basel, Switzerland) [24,25].

HIV-1 drug resistance mutations

HIV-1 genotypic drug-resistance testing was performed at the Rafic Hariri University Hospital Research Laboratories using the FDA-approved ViroSeq HIV-1 genotyping system (Abbott Laboratories, Abbott Park, IL, USA), as per the manufacturer's instructions. Testing was performed on specimens with more than 1000 copies/mL. Briefly, virions from 500 µL of plasma were centrifuged and viral RNA was isolated using QIAamp viral RNA kit (Qiagen, Hilde, Germany) followed by DNA amplification by RT-PCR. PCR products were purified using QIAquick spin PCR purification kit (Qiagen, Hilden, Germany), analyzed by agarose gel electrophoresis, and followed by extension using the ViroSeq HIV-1 genotyping system [26]. Genotypic sequencing using this method generates sequences of the entire protease (codons 1 to 99) and reverse transcriptase (codons 1 to 335) genes. DNA sequencing was performed using ABI Prism 310 Genetic Analyzer (Applied Biosystems, Foster City, CA, USA). Drug resistance mutations were identified based on the published 2009 WHO list for surveillance of transmitted resistance [27,28,29] as well as the Stanford HIV Drug Resistance Database [30].

Statistical analysis

Descriptive statistics were used to examine the prevalence of HIVDR and the characteristics of the study sample. To examine the relationship between viral load and the mode of HIV transmission, the distribution of the viral load among study participants was first examined. The normality of the distribution was then tested using the Shapiro-Wilk test of normality. The modes of transmission among study participants were heterosexual intercourse (n = 23, 62%), homosexual intercourse (n = 9, 24%), and intravenous drug use (n = 1, 2.7%). Data on mode of transmission was not available for four (10.8%) participants. Given that only one subject had intravenous drug use as a mode of transmission, that category was excluded from the analyses. The null hypothesis that the distribution of the viral load is normal (Shapiro-Wilk test showed a statistic of 0.179

Table 1. Characteristics of participants and viral subtypes

Variable	Number (%)
Gender	
Male	32 (86.5)
Female	5 (13.5)
Age range in years (mean)	21-55 (33)
Viral load copies/ml (range, median)	1,300-111,000,000/66,900
HIV exposure category	
Heterosexual	23 (62)
MSM	9 (24)
IDU	1 (2.7)
Others, Unknown	4 (10.8)
Subtype	
A	4 (11)
CRF-02 AG	4 (11)
CRF-06 cpx	1 (2.7)
CRF-16 AD	1 (2.7)
B	12 (32.4)
C	1 (2.7)
F	1 (2.7)
G	1 (2.7)

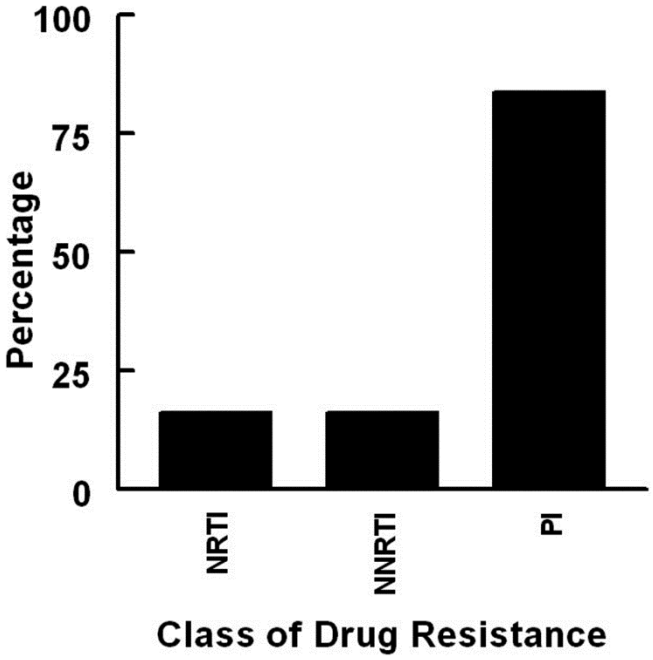
and SW significance of 0.000 or a p value < 0.05) was rejected. Consequently, the non-parametric Mann-Whitney test was used to compare viral load by mode of HIV transmission as well as to compare viral load of study participants with or without major NRTI, NNRTI, or PI resistance mutations. The chi-square test was used to examine the relationship between type of HIVDR mutation and mode of transmission. All analyses were conducted using SPSS version 17.0. $p < 0.05$ was used as the significance level.

Results

Characteristics of the study participants

A total of 37 HIV-1 infected patients were enrolled in the study. Table 1 summarizes the demographic, virologic, and immunological characteristics of the study participants. These participants were newly diagnosed and ART-naive. Overall, 86.5% (n = 32) were males and 13.5% (n = 5) were females. The average age was 33.5 for males and 32 years for females. Importantly, the majority of participants (78%) included in this study were ≥ 25 years of age. The modes of HIV-1 transmission among the study participants were heterosexual intercourse (n = 23, 62%), homosexual intercourse (n = 9, 24%), and intravenous drug use (n = 1, 2.7%). Data on the mode of transmission was not available for 10.8% (n = 4) of the participants. The date of infection of the study participants was not known. A total of 37.8% (14/37) of the study participants reported travelling to the Gulf, West Africa, and the United States, whereas 27% (10/37) reported no travel history. Fifty percent (n = 5) of those with no travel history were heterosexuals, 40% (n = 4) were homosexuals, and 10% (n = 1) were intravenous drug users. Twenty-seven percent of enrolled participants did not report travelling outside Lebanon. All participants reporting travel history were males, and 8% (3/37) were females with a partner travelling to West Africa. The participants were infected with the following subtypes: HIV-1A (n = 4, 11%), HIV-1B (n = 12, 32%), HIV-1C (n = 1, 2.7%), CRF02_AG (n = 4, 11%), and 4 patients separately infected with HIV-1F (2.7%), HIV-1G (2.7%), CRF-06cpx (2.7%), and CRF-16AD (2.7%). Thirty-two percent of ART-naive participants were not sub-typed. HIV-1B subtype was predominant among the study participants.

Figure 1. The distribution of drug class resistance among ART-naive subjects. HIV-1 genotypic drug resistance testing was performed on plasma samples from 37 treatment-naive HIV-1 infected subjects. The percentage of major and other NRTI, NNRTI, and PI resistance mutations are plotted. X-axis: class of drug resistance; Y-axis: percentage of patients with a class of a drug resistance.



Drug resistance mutations among the study participants

HIV drug resistance was evaluated on samples from 37 participants. Figure 1 shows the distribution of classes of mutations; PI resistance was the most frequently observed among ART-naive HIV-1 infected patients (83.7%, n = 31). NRTI and NNRTI mutations were each detected in 16% (n = 6) of the study participants. The reported mutations included major, minor, and other mutations (Table 2). Table 3 summarizes the major resistance mutations detected among the study participants as reported by the Stanford HIV Drug Resistance Database along with the level of resistance to corresponding drugs. The following NRTIs were detected in the respective number of study participants: G333D/E (n = 1), V179E (n = 1), V179I (n = 1), T69D (n = 1), Y115F (n = 1), V118I (n = 2), K219E (n = 2), V75M (n = 1), M184I (n = 1), T215S (n = 1), and A62V (n = 1). Among the thymidine analogues mutations (TAM) described in the literature [31,32], K219E was detected in two study participants. T69D, V75M, Y115F, M184I, T215S, and K219E have been reported by the updated list of drug resistance mutations [27] and are all known as major mutations, except for V75M (Table 3).

Table 2. The prevalence of NRTI, NNRTI, and PI resistance mutations among the study participants

Mutation	Number (%)
NRTI	
G33D/E	1 (0.03)
V179E	1 (0.03)
V179I	1 (0.03)
T69D	1 (0.03)
Y115F	1 (0.03)
V118I	2 (0.05)
K219E	2 (0.05)
V75M	1 (0.03)
M184I	1 (0.03)
T215S	1 (0.03)
A62V	1 (0.03)
NNRTI	
Y181I	2 (0.05)
V179E	1 (0.03)
Y188H	1 (0.03)
L100I	1 (0.03)
V108I	1 (0.03)
F227L	1 (0.03)
PI	
M36I	19 (51)
R41K	14 (38)
I13V	12 (32)
H69K	11 (30)
L89M	9 (24)
L63P	9 (24)
K20R	7 (19)
G16E	6 (16)
K20I	5 (14)
E35D	5 (14)
I62V	4 (11)
L10I	4 (11)
L10F	3 (8)
I15V	3 (8)
L89I	2 (5)
A71T	2 (5)
V77I	2 (5)
L10V	2 (5)
D60E	2 (5)
I50L	1 (3)
I15L	1 (3)
V321	1 (3)
L33V	1 (3)
I74V	1 (3)
L89K	1 (3)
M36L	1 (3)
L33F	1 (3)
L90M	1 (3)

T69D causes low level resistance to ddI and potential low-level resistance to stavudine (d4T) [33] and, according to Paredes *et al*. [10], it confers multi-NRTI resistance. M184I is also a signature mutation for 3TC and emtricitabine (FTC), with moderate impact on resistance to ABC and ddI [34]. It has also been reported to generate hypersensitivity to and synergy with ZDV, TDF, and d4T [10], and to decrease viral replication fitness [30]. Additional NRTI-selected mutations reported by the HIV drug resistance database [30] and detected in this study include V75M conferring resistance to ddI and d4T, and V118I, the latter being a minor mutation. T215S is associated with resistance to thymidine analogues and specifically to ZDV and d4T. Y115F is associated with high-level phenotypic or clinical resistance to ABC but moderate resistance level to TDF. Finally, K219E, also a thymidine analog mutation, confers moderate phenotypic and clinical resistance to ZDV and d4T. K103N, conferring resistance to NVP and EFV [35], was not detected in any of the ART-naive patients.

Y181I, Y188H, and L100I were major NNRTI mutations (Table 3) detected in two, one, and one patients, respectively. V179E (n = 1), V108I (n = 1), and F227L (n = 1) (Table 2) were also detected in this study and are on the surveillance list of drug resistance [27] but are not described as major mutations. K103N and Y181C, conferring cross-resistance to all NNRTIs, were not detected in the study group.

Among the detected PI resistance mutations, M36I was predominantly observed in 51% (n = 19) of the ART-naive participants, followed by R41K (n = 14, 38%), I13V (n = 12, 32%), H69K (n = 11, 30%), L89M (n = 9, 24%), L63P (n = 9, 24%), and K20R (n = 7, 19%). Other mutations were detected in ≤ 16% of participants (Table 2). M36I, L63P, K20R, and V77I are highly polymorphic compensatory mutations and were all detected in the study participants (Table 2) [27]. M36I, described as a polymorphic substitution in subtype F and other non-B HIV proteases, has been suggested to lead to early development of drug resistance in individuals infected with non-B subtypes of HIV. The study participants harboring the M36I mutation did not show a particular predominance of any HIV-1 subtype (subtype A, n = 4; subtype B, n = 3; subtype CRF-02AG, n = 4; subtype CRF-02AD, n = 1). R41K, H69K, L89M, and I15V were reported to be more frequent in subtype C [25,36]. In this study, one patient was infected with HIV-1C harboring R41K, H69K, and I15V. V32I, I50L, and L90M were each detected in one patient (Tables 2 and 3) and have been

Table 3. Major drug resistance mutations detected in ART-naive subjects

Sample ID	VL copies/ml	Major mutations	Resistance profile	
			High level	Moderate level
		NRTIs		
33	111,000,000	T69D	ABC, ddI, TDF, d4T, ZDV	3TC, FTC
		Y115F	ABC	TDF
		K219E		d4T, ZDV
34	283,000	V75M	ddI, d4T	
		M184I	3TC, FTC	ABC, ddI
		T215S		
		K219E		d4T, ZDV
		NNRTIs		
1	43,400	Y181I	NVP, ETR, RPV	
2	279,000	Y181I	NVP, ETR, RPV	
33	111,000,000	Y188H	NVP	EFV
34	283,000	L100I	EFV, ETR, RPV	NVP
		PIs		
16	4,660	V32I	FPV	ATVr, DRVr, IDVr, LPVr, TPVr
33	111,000,000	I50L	ATVr	
36	315,000	L90M	NFV	SQVr

This table includes a list of ART-naive study participants with detected major drug resistance mutations and the impact of these mutations on the resistance profile to the respective drugs. The HIV-1 viral load of these participants upon enrolment in the study ranged between 4,660 and 111,000,000 copies/mL of plasma.

Abbreviations. NRTIs: 3TC, lamiduvine; ABC, abacavir; ddI, didanosine; d4T, stavudine; FTC, emtricitabine; TDF, tenofovir; ZDV, zidovudine. **NNRTIs**: EFV, efavirenz; ETR, etravirine; NVP, nevirapine; RPV, rilpivirine. **PIs:** ATV, atazanavir; DRV, darunavir; FPV, fosamprenavir; IDV, indinavir; LPV, lopinavir; NFV, neflinavir; SQV, saquinavir; TPV, tipranavir; r, ritonavir-boosted

reported as major mutations by the Stanford HIV Drug Resistance Database and by the updated surveillance list of drug resistance mutations [27,30]. L90M, a signature mutation, induces significant phenotypic or clinical resistance to NFV and significantly contributes to saquinavir (SQVr, ritonavir-boosted) as well as decreased susceptibility to most other PIs, specifically NFV [10]. I50L has been reported to induce significant phenotypic or clinical resistance to ATVr, whereas V32I is known to contribute to high resistance to ATVr, DRVr, FPVr, IDVr, LPVr, and TPVr.

Other resistance mutations (L89I, L10I, and L10V) were detected in this study, though in less than 10% of the study participants. These minor PI resistance mutations are associated with resistance to most PIs when detected concurrently with other mutations [37,38]. Moreover, several other mutations in the protease gene were detected. These were either polymorphic or non-polymorphic with established resistance (*e.g.* F227L, V118I). Although these mutations may have limited effect on susceptibility to antiretroviral drugs, they have been associated with high viral fitness; in addition, it has been suggested that pre-existing accessory mutations lead to faster emergence of PI-resistant viruses [39]. The PI-selected accessory polymorphic mutations D60E, V77I, and I62V were also detected in addition to I13V, a non-polymorphic mutation (Table 2) [40].

Drug resistance mutations and relationship with HIV-1 transmission and viral load

Five out of the six participants harboring major drug resistance mutations (Table 3) were heterosexuals and one was homosexual. The latter did not report on travel outside Lebanon, whereas the former either reported travel (4/5) or had a partner who travelled to West Africa (1/5).

Dual- (NRTI, NNRTI) and triple-class resistance mutations (Table 3) were each detected in one participant. Among the participants, five (13.5%) ART-naive patients did not show any drug resistance mutations and had a lower average viral load as compared to those showing NRTI, NNRTI, or PI mutations. Viral load was high in most study participants, consistent with the lack of ART. No significant difference in the viral load of study participants with major NRTI, NNRTI, or PI drug resistance mutations was found as compared to those without them ($p = 0.099$, $p = -0.345$, and $p = 0.54$, respectively). When looking at the mode of transmission and the type of HIVDR detected (major or not), 8.7% with major NRTI mutations were heterosexuals versus 0% homosexuals; 13% of study participants with NNRTI major mutations were heterosexuals, whereas 11% were homosexuals. Finally, 13% with PI major mutations were heterosexuals and none were homosexuals. When comparing the viral load by mode of transmission, the data showed no significant difference between homosexuals and heterosexuals in the study group. Moreover, there was no significant difference in the occurrence of these mutations among heterosexuals and homosexuals.

Discussion

HIV-infected persons with evidence of HIVDR are known to begin ART with a higher risk of virologic failure, as well as an increased risk of developing resistance to drugs that could have been active [5,10]. These findings resulted in the new guidelines recommending the performance of genotypic resistance testing in therapy-naive patients before the initiation of first-line regimens [9]. The lack of laboratory monitoring of drug resistance in low-income countries is a serious challenge to the management of HIV-infected patients. To our knowledge, this is the first report investigating drug resistance among HIV-infected individuals in Lebanon. The current starting regimen of HIV-1 treatment in Lebanon consists of TDF, 3TC (or emitricitabine) and EFV. The major resistance mutations detected in our study participants are associated with a response failure to all the NRTIs available in Lebanon. NVP and EFV are the NNRTIs available in Lebanon. The NNRTIs resistance mutations detected in our study (albeit in four ART-naive persons) confer a low-level resistance to NVP and EFV (as is the case with Y181I and Y188H), whereas L100I leads to high level of phenotypic and clinical resistance to EFV and contributes to NVP resistance. Hence, first-line NNRTIs available in Lebanon will fail at controlling HIV-1 infection among these participants. M46I, known as a stable mutation hampering PI-based antiretroviral regimens [41], was not detected in any of our study participants; moreover, L90M, a frequently reported mutation, was detected in one patient. Our results indicate that the use of recommended treatment regimen will fail at controlling HIV-1 among the study participants as indicated by the type of detected HIVDR mutations.

The WHO classifies the prevalence of HIVDR among treatment-naive individuals into three classes: low, < 5%; moderate, 5%-15%; and high, > 15% [42]. Our study reveals an overall HIVDR prevalence of

16%. According to the WHO guidelines, this prevalence is classified as high. The prevalence of the NRTI, NNRT, and PI resistance mutations were 5.4%, 10.8%, and 8%, respectively. These results are comparable with the values reported in high-income countries [10]. Consequently, it is expected that therapy with any of the recommended and available drugs in Lebanon is doomed to failure. Reports show a tenfold increase in the number of people receiving ART in low- and middle-income countries [43]. With the scaling-up of antiretroviral therapy, the establishment of control strategies for surveillance and prevention of emergence of resistance is a high priority. In the absence of adequate monitoring, the increased access to ART might lead to spread of transmitted and acquired drug-resistant HIV-1, resulting in reduced effectiveness of these drugs. Drug-resistant viruses have been reported to become the major circulating virus populations in infected individuals, with subsequent failure of therapy in treatment-naive patients [12,44,45,46].

Even though the number of participants included in this study is small, it is worrisome to detect this high prevalence of resistance mutations, especially to the available treatment combination in Lebanon. An important limitation of this study is that we could not determine the stage of the disease nor draw any correlations between $CD4^+$ T cell count and drug resistance due to lack of access to clinical data of participants. Nevertheless, this alarmingly high resistance might have been the result of the transmission of drug-resistant viruses from partners infected with the resistant virus or selection as a result of undisclosed use of ART, especially among those cases with dual or triple resistance mutations. The prevention of the transmission of HIV drug resistance should be a national priority.

Conclusions

Our study reveals a high prevalence of resistance mutations among our study participants, conferring resistance to the recommended and available drugs in Lebanon. More studies are needed to further evaluate this reported rate of drug resistance and its impact on the failure of current drug regimens as well as transmission of drug-resistant strains in Lebanon. With the scaling-up of antiretroviral therapy, the establishment of control strategies for surveillance and prevention of resistance emergence is a high priority.

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