Baseline HIV Genotyping in Saudi Arabian population - a multicenter, cross-sectional study

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INTRODUCTION AND BACKGROUND

Human immunodeficiency virus (HIV) infection remains a major global public health issue. A recent report by the World Health Organization (WHO) indicates that approximately 39 million people were living with HIV at the end of 2022 worldwide.[1] The estimated total number of people living with HIV (PLWH) in Saudi Arabia is around 20,539 person according to the literature.[2]

Baseline genotyping studies are lacking in the region. The one that did assess the baseline genotyping was limited to a single-center with very low sample size, limited age range of patients and geographical distribution in the kingdom.[3]

In this study we attempted to investigate the baseline genotyping of PLWH in Saudi Arabia.

METHODOLOGY

This was a multi-centre, retrospective cross-sectional study was conducted over three centres from two distinct regions of Saudi Arabia. Adults (≥ 18 years old) who were anti-retroviral treatment-naïve were included regardless of gender, ethnicity, co-morbidities or pregnancy status, while those who were paediatrics (<18 years old), treatment-experienced, PrEP users or elite controllers were excluded. PLWH who had missing data or had partial genotyping due to technical issues were also excluded. Genotyping was conducted in several reference labs using the same exact method while genotyping reports using other methods were excluded. IRB approval was obtained from all three centres involved in this study.

Although estimated significant sample size needed was around 385, all possible PLWH were included. Data were collected through a unified electronic data sheet form separately for each centre and combined later for data analysis using Microsoft Excel after coding and anonymization. Mutation interpretations were done using the Sanford HIV Database.

RESULTS

We included a total of 614 PLWH who were anti-retroviral treatment-naïve, with the majority being male from the western region of Saudi Arabia (Figure 1). The median of ages at diagnosis of HIV ranged between 29 to 34 years across gender and 32 to 40 years across centres, while majority of patients were younger than 50 years of age (Table 1).

The median HIV-1 RNA Viral Load was 146,040 copies (IQR= 35,538 - 816,164 copies) while median CD4 was 360 cell/mm^3 (IQR= 196 - 590 cell/mm^3). The most commonly detected clade/subtype was C followed CRF02_AG and G (Figure 2). There were multiple mutations detected in most of the PLWH but were not contributing to drug resistance like R211A/E/G/K/N/Q/R/S/T in 429 PLWH (69.9%). The top three frequent drug resistance mutation (DRM) in the NRTI, NNRTI, PI and INSTI classes are summarized in (Table 2).

There were some APOBEC mutations detected in one patient indicating a possible PCR errors or G-to-A hypermutation during the sequence.

CONCLUSION

This study concurs with the previous reports of the most common subtype in Saudi Arabia but differ in the distribution of the other subtypes. While the majority of detected DRMs are known to cause resistance to some antiretrovirals, none did significantly affect the first-line regimens used currently (INSTI-based regimen). Some mutations are selected by the prior use of certain antiretrovirals in the index case, which indicate possible local transmission among persons who were either not compliant to their medications or experiencing virological failure of therapy.

REFERENCES

1.WHO 2023, HIV and AIDS, Fact sheets. 2. Al-Mozaini M, *et al*, J Infect Public Health. 2023 Sep;16(9):1500-1509. 3. Zaki EA, *et al*, Medicine (Baltimore). 2020 Dec 4;99(49):e23274.

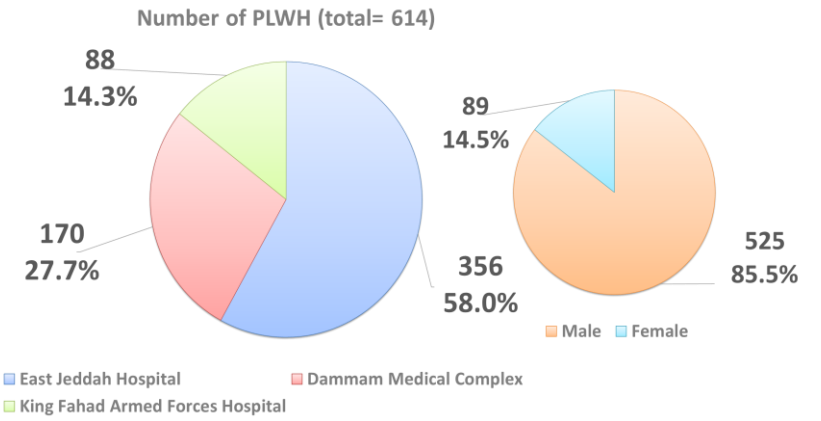

Figure 1. Numbers of patients across the involved centres and gender distribution.

	Male	Female	Total
Median (IQR)	34 (29-42)	29 (27-42)	34 (28-42)
>50 years (%)	66 (12.6%)	10 (11.2%)	76 (12.4%)
<50 years (%)	459 (87.4%)	79 (88.8%)	538 (87.6%)
	East Jeddah Hospital	King Fahad Armed Forces Hospital	Dammam Medical Complex
Median (IQR)	34 (28-42)	40 (30-50)	32 (28-38)
>50 years (%)	36 (10.1%)	22 (25.0%)	18 (10.6%)
<50 years (%)	320 (89.9%)	66 (75.0%)	152 (89.4%)

Table 1. Age distribution across gender and involved centres.

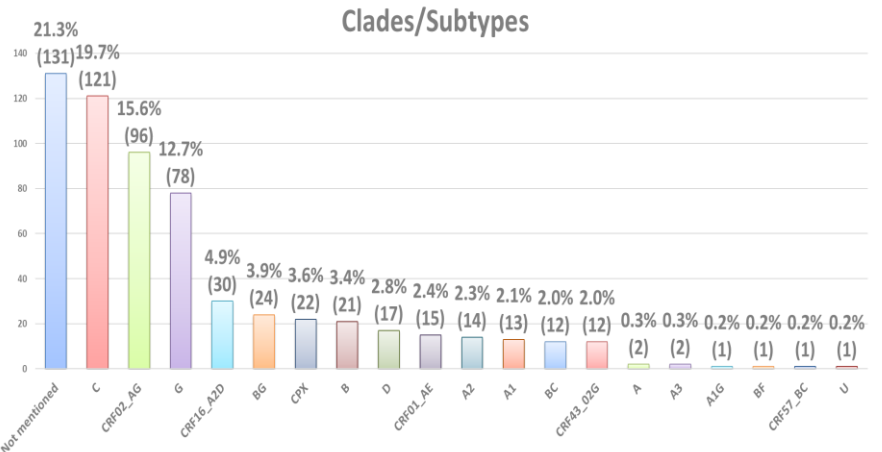

Figure 2. Distribution of the most commonly detected clades/subtypes.

Class	Mutation	Frequency (%)
NRTI	S68G/N/S	59 (9.6%)
	M184I/M/V	10 (1.6%)
	V75I	5 (0.8%)
NNRTI	V179A/D/E/I/T/V	85 (13.8%)
	A98A/G/R/S	59 (9.6%)
	E138A/E/S/T	43 (7.0%)
PI	**Major Mutations:**	
	V81I/F/L/V	147 (23.9%)
	M46I/L/M	16 (2.6%)
	I50L	1 (0.2%)
	Accessory Mutations:	
	L89I/L/M/V	493 (80.3%)
	L10F/I/K/L/M/N/V	166 (27.0%)
	L33F/I/L/V	9 (1.5%)
INSTI	**Major Mutations:**	
	E138D/E/K	7 (1.1%)
	G140A	2 (0.3%)
	Q148R	2 (0.3%)
	Accessory Mutations:	
	L74I/L/M/V	65 (10.6%)
	G163A/D/E/G/M/N/Q/R/S/V	50 (8.1%)
	E157D/E/I/K/Q	10 (1.6%)

Table 2. Top three mutations across different classes of antiretroviral therapies.