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The prevalence of comorbidities among adult people diagnosed with HIV infection in a tertiary care hospital in western Saudi Arabia

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ABSTRACT

Background: The life expectancy of people living with HIV is markedly increasing with the introduction of effective antiretroviral medications. However, these patients face an increased risk of developing multi-morbidities-especially with advanced age. This study was conducted to assess the prevalence of and risk factors associated with the occurrence of chronic comorbidities among patients diagnosed with HIV infection.

Methods: A retrospective chart review was conducted on the medical records of patients with HIV diagnoses from 2000 to 2018. Data were collected on age, sex, date of diagnosis, associated co-morbidities, antiretroviral medications (ART) and status at time of data collection (alive or deceased). Only adult patients 18 years or above were studied.

Results: A total of 130 confirmed HIV cases were included. Patient ages ranged from 23 to 86 years old (mean ± SD 50.1 ± 12.6). Almost half of the patients (48.5%) had at least one associated comorbidity. The most common chronic comorbidity was diabetes mellitus (15.4%), followed by dyslipidemia (10.8%), hypertension (10.8%) and lymphoma (10.0%). Comorbidity proportions increased with advanced patient age ($p = 0.047$). Three or more comorbidities were reported in 40.7% of patients aged 60 years old or above. Using logistic regression analysis, only patients aged 50 years old or above were more likely to have at least one comorbidity (OR = 7.59, 95%CI = 2.25, 25.61).

Conclusions: The burden of chronic comorbidities among people diagnosed with HIV is high, especially among older age individuals, with an increasing number of comorbidities per patient. Proper counseling for HIV patients is highly recommended-not only for prevention of other infectious diseases (e.g., vaccination) but also for lifestyle modification and self-management for those with chronic conditions.

Introduction

The mortality of patients with HIV infection has significantly dropped with the use of antiretroviral therapy (ART) [1]. With earlier diagnosis and initiation of effective medications, HIV hospitalization rates are declining [2]. Moreover, the life expectancy of HIV-positive individuals who are on optimal treatments is markedly increasing [3–5], and chronic conditions are more likely to occur associated with normal aging [6,7]. However, several studies have been carried out to explore the direct and indirect impact of

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HIV infection [8,9], antiretroviral medications [10] and other independent risk factors [11]. A cross-sectional study that compared HIV-positive and HIV-negative patients found that HIV-positive patients are considerably more susceptible to higher incidences of diabetes mellitus, hypertension, myocardial infarction, and renal failure [12]. Moreover, elderly patients with HIV infection have a higher risk of chronic conditions (e.g., hypertension, hypertriglyceridemia, low bone mineral density, and lipodystrophy) than non-infected elderly people [13], although such comorbidities occur almost a decade earlier in life among the infected people [10,14]. Number of people living with HIV is increasing both in developed and developing countries [15,16]. Immunological and virological response among elderly people living with HIV compared to younger uninfected population showed controversial results [17–20]. Medical insurance companies reported that 22% of HIV-positive patients aged 50 years and older present with one medical condition along with HIV, 36% present with two to three comorbidities, 50% present with four to five comorbidities, and 10% present with more than five comorbidities [21]. The increasing prevalence of comorbidities impacts the clinical, neurocognitive and socioeconomic burden of HIV infection [6,22]. Such burden will reflect on the health care system, which should be well-equipped to maintain optimal clinical, psychological and social care for HIV-infected individuals [23]. Data are very lacking in Saudi Arabia on HIV infection and associated co-morbidities. The current study was carried out to assess the prevalence of chronic co-morbidities and related risk factors among HIV infected patients in western Saudi Arabia.

Methods

A retrospective chart review was conducted to analyze data on confirmed HIV cases at King Abdulaziz Medical City-Jeddah (KAMC-J) over an eighteen-year period from 2000 to 2018. King Abdulaziz Medical City-Jeddah (KAMC-J) is a governmental tertiary care hospital with a 750-bed capacity. KAMC-J has an outpatient department and five affiliated primary healthcare centers (PHCs) in western Saudi Arabia. The medical city and PHCs provide care to the National Guard military personnel, employees, and their families. The Infection Prevention and Control Department at KAMC-J is responsible for reporting all communicable diseases, including HIV, to the Ministry of Health. In the current study, HIV patients' medical records were identified through the Infection Prevention and Control Department where all confirmed HIV cases are immediately reported through the medical laboratory and blood bank for Ministry of Health notification, patient counseling and referral to infectious diseases' specialist for case management, and to perform contact screening.

Patient data were obtained from the medical records and included information on patients' age, sex, date of diagnosis, associated co-morbidities, antiretroviral medications (ART) and status at the time of data collection (alive or deceased). Only adult patients 18 years and above were studied.

Comorbidities were considered based on physician documentation at the time of HIV diagnosis or on other follow-up visits. Body Mass Index (BMI) measurements at the last follow up visit were included.

This study was approved by the Institutional Review Board (IRB) of King Abdullah International Medical Research Center (KAIMRC). The study was conducted in accordance with the Code of Ethics of the World Medical Association, and in line with the Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals. However, no informed consent was required because of the retrospective collection of data. All collected patients' data were anonymous and confidentiality was maintained throughout the study.

Table 1
Demographic and clinical characteristics of the studied patients (n = 130).

Variable	n (%)
Age in years,	
Mean (SD)	50.1 (12.6)
Range	(23–86)
Gender,	
Male	93 (71.5)
Female	37 (28.5)
BMI,	
Below 18.5 (underweight)	12 (13.3)
18.5–24.9 (Normal)	33 (36.7)
25.0–29.9 (Overweight)	21 (23.3)
30.0 and above (Obese)	24 (26.7)
Number of associated comorbidities,	
None	67 (51.5)
One	23 (17.7)
Two	18 (13.8)
Three or more	22 (16.9)
Status at time of data collection,	
Alive	115 (88.5)
Died	15 (11.5)
Type of prescribed antiretrovirals,	
Nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs)	121 (93.1)
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	55 (42.3)
Integrase inhibitors	34 (26.2)
Protease inhibitors (PI)	37 (28.5)

Statistical analysis

Descriptive statistics were applied using mean, standard deviation (SD), number and percentage (%) to describe the demographic characteristics. The Chi-square test (or Fisher's exact test), as appropriate was performed to compare association of comorbidities according to age categories. Multivariate logistic regression analysis and 95% confidence intervals (95% CI) were performed to determine predictors of comorbidity occurrence. The level of significance was determined at p-value <0.05. All statistical analyses were conducted using IBM SPSS version 25.

Results

A total of 130 confirmed HIV cases were included in the study. Ages ranged from 23–86 years old (mean ± SD 50.1 ± 12.6). All patients were Saudi, and the majority were male (71.5%). More than one-third (36.7%) had a normal BMI, although 50.0% were overweight or obese. Median duration of HIV infection was 6 years (Interquartile range was 7 years). Almost half (48.5%) had at least one associated comorbidity. At the time of data collection, 88.5% were alive. Overall, the most commonly used antiretroviral class was nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) (93.1%) (Table 1).

Most patients received a Tenofovir disoproxil fumarate/Emtricitabine combination (52.3%), followed by Efavirenz, a non-nucleoside reverse transcriptase inhibitors (NNRTI) (41.5%) (Table 2).

The most common chronic comorbidity was diabetes mellitus (15.4%), followed by dyslipidemia (10.8%), hypertension (10.8%) and lymphoma (10.0%) (Table 3). There were one Hodgkin's lymphoma and 12 non-Hodgkin's lymphoma cases (seven Burkitt's lymphoma and five diffuse large B-cell lymphoma). Six out of the 13 lymphoma cases (46.2%) were diagnosed at the same time of the diagnosis of HIV infection.

Fig. 1 shows the proportions of multimorbidities among the studied patients. The proportions of comorbidities increased with advanced patient age (p = 0.047). Three or more comorbidities have

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Table 2
Proportions of specific antiretroviral medication regimens used.

Antiretroviral medication class	n (%)
Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs)	
• Tenofovir disoproxil fumarate/Emtricitabine	68 (52.3)
• Zidovudine/lamivudine	18 (13.8)
• Zidovudine	9 (6.9)
• Lamivudine	9 (6.9)
• Stavudine	1 (0.8)
• Tenofovir disoproxil fumarate	1 (0.8)
NNRTIs (Non-nucleotide reverse transcriptase inhibitors)	
• Efavirenz	54 (41.5)
• Etravirine	1 (0.8)
Integrase inhibitors	
• Raltegravir	15 (11.5)
• Dolutegravir	3 (2.3)
• Elvitegravir	1 (0.8)
Protease inhibitors (PI)	
• Lopinavir/Ritonavir	22 (16.9)
• Indinavir	8 (6.2)
• Ritonavir	3 (2.3)
• Atazanavir	2 (1.5)
• Darunavir	2 (1.5)
Integrase inhibitor/NRTI combination	
• Elvitegravir/Cobicistat/Tenofovir disoproxil fumarate/Emtricitabine	14 (10.8)
• Elvitegravir/Cobicistat/Tenofovir alafenamide/Emtricitabine	1 (0.8)

Table 3
Number and percentage of individual chronic comorbidities.

Comorbidity	n (%)
Diabetes Mellitus	20 (15.4)
Dyslipidemia	14 (10.8)
Hypertension	14 (10.8)
Lymphoma[a]	13 (10.0)
Ischemic heart disease	8 (6.2)
Hepatitis B	8 (6.2)
Chronic kidney disease	7 (5.4)
Depression	7 (5.4)
Osteoarthritis	5 (3.8)
Bronchial asthma	4 (3.1)
Peripheral vascular disease	3 (2.3)
Cardiomyopathy	3 (2.3)
COPD	3 (2.3)
Dementia	3 (2.3)
Kaposi sarcoma	2 (1.5)
Osteoporosis	2 (1.5)
Inflammatory bowel disease	2 (1.5)
Heart Failure	1 (0.8)
Hepatitis C	1 (0.8)
Left atrial enlargement	1 (0.8)
Peripheral neuropathy	1 (0.8)

[a] Lymphoma cases included seven Burkitt's lymphoma, five diffuse large B-cell lymphoma, and one Hodgkin's lymphoma.

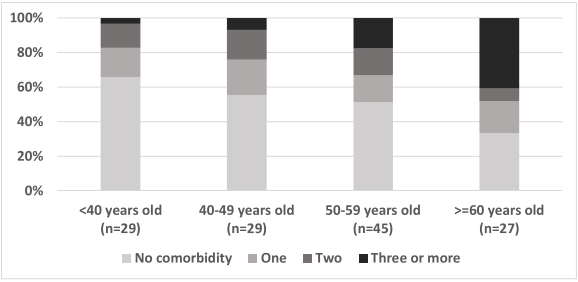

Fig. 1. Proportions of multimorbidities among the studied patients.
Fisher's Exact test, p value = 0.047.

been reported in 40.7% of patients aged 60 and above, compared to (17.8%) of patients aged 50–59 (n = 8 cases), (6.9%) among those 40–49 years old (n = two cases), and (3.4%) of patients less than 40 years old (n = one case).

A Significantly higher proportion of chronic conditions among elderly patients was observed among those with documented chronic kidney disease ($p = 0.01$), hypertension ($p = 0.001$), cardiac disorders ($p = 0.001$), and diabetes mellitus ($p = 0.02$). However, no statistical differences according to age categories were identified in the dyslipidemia, psychiatric, lymphoma, hepatitis B infection, and respiratory disorders. Moreover, the majority of patients diagnosed with psychiatric disorders, lymphoma or hepatitis B infection, and all patients diagnosed with respiratory problems were less than 60 years old (Fig. 2).

The proportions of having at least one comorbidity were the highest among patients who used protease inhibitors (75.9%); however, 60% of patients on other ART medication classes had at least one comorbidity (range 59.3 %–61.9 %) (Fig. 3).

Logistic regression analysis was shown in Table 4. Only patients aged 50 or above were more likely to have at least one comorbidity (OR = 7.59, 95%CI = 2.25, 25.61).

Discussion

This study revealed that increased multimorbidity prevalence corresponded with increased age among HIV infected individuals who were diagnosed and on-follow up in Jeddah, western Saudi Arabia. This finding was consistent with several previous studies from Japan [24], Canada [25], Portugal [26], and South Africa [7]. Almost half of the patients in the current study had at least one chronic comorbidity, which was higher compared to previous reports. For example, in Kendall et al. [25] and Lorenc et al.

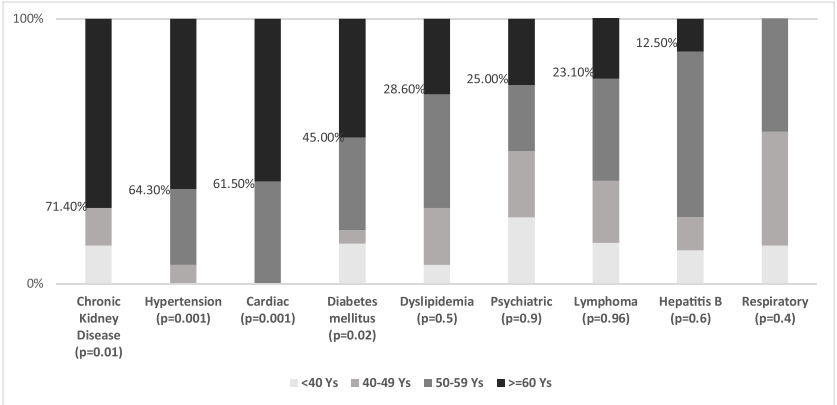

Fig. 2. Distribution of comorbidities according to age categories.
Percentages on the columns represent patients aged 60 years or above.
Lymphoma cases included seven Burkitt's lymphoma, five diffuse large B-cell lymphoma, and one Hodgkin's lymphoma.

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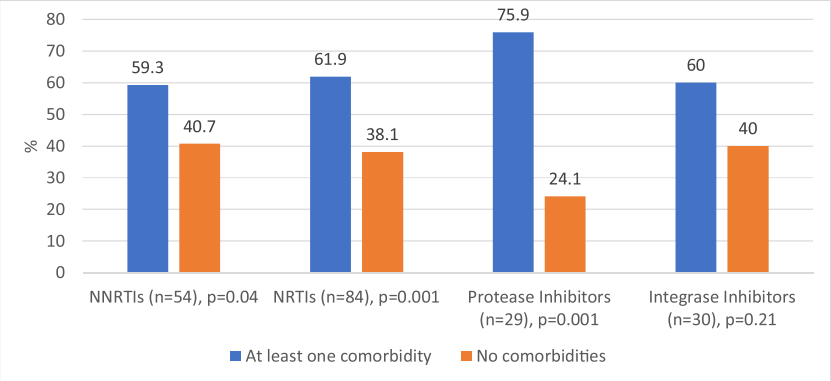

Fig. 3. Proportions of comorbidities according to ART medications.
NRTIs = nucleoside/nucleotide reverse transcriptase inhibitors.
NNRTIs = non-nucleoside reverse transcriptase inhibitors.

Table 4
Logistic regression analysis of factors associated with occurrence of comorbidities.

Variables	Comorbidities		Odds Ratio (95% Confidence Interval)	*P* value
	NO	YES[a]		
Age in years,				
<40 years	19 (65.5)	10 (34.5)	1	1
40–49 years	16 (55.2)	13 (44.8)	2.29 (0.65, 7.96)	0.19
> = 50 years	32 (44.4)	40 (55.6)	7.59 (2.25, 25.61)	0.001
Gender,				
Female	22 (59.5)	15 (40.5)	1	1
Male	45 (48.4)	48 (51.6)	2.9 (0.90, 9.23)	0.07
BMI,				
Below 18.5 (underweight)	5 (41.7)	7 (58.3)	1	1
18.5–24.9 (Normal)	14 (42.4)	19 (57.6)	0.87 (0.19, 3.93)	0.85
25.0–29.9 (Overweight)	8 (38.1)	13 (61.9)	0.93 (0.18, 4.82)	0.94
30.0 and above (Obese)	11 (45.8)	13 (54.2)	0.83 (0.13, 5.27)	0.85
Type of prescribed antiretrovirals,				
Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs)	22 (40.7)	32 (59.3)	3.01 (0.91, 9.92)	0.07
Non-Nucleotide Reverse Transcriptase Inhibitors (NNRTIs)	32 (38.1)	52 (61.9)	0.82 (0.25, 2.72)	0.74
Protease inhibitors (PI)	7 (24.1)	22 (75.9)	1.77 (0.46, 6.82)	0.41
Integrase inhibitors	12 (40.0)	18 (60.0)	1.05 (0.30, 3.69)	0.94
Years since diagnosis till date or death,				
<6 years	27 (46.6)	31 (53.4)	1	1
> = 6 years	38 (55.9)	30 (44.1)	1.08 (0.36, 3.26)	0.907

[a] At least one comorbidity.

[11], (34.4%) and (29%) of the studied populations had at least one chronic comorbidity, respectively.

In concordance with other data, the most common prevalent comorbidities were diabetes, dyslipidemia [12,25] and hypertension [12,25,27]. Among elderly patients, cardiac disorders, chronic kidney disease, diabetes mellitus and hypertension were significantly high, a finding that was also supported by previous studies [24,27–30]. Our finding of increased psychiatric (depression, dementia), malignancy (lymphoma), hepatitis B infection, and dyslipidemia conditions in young age patients require further investigation in a larger study. Ruzicka et al. had a similar observation for the psychiatric problems and hepatitis B infections [24]. However, the increased occurrence of lymphoma in younger age patients in the current study reflects late diagnosis of HIV infection and a lack of screening programs. In Ruzicka et al.'s study, a low incidence of lymphoma and Kaposi sarcoma was attributed to the start of antiretroviral medications at an earlier stage [24]. Several factors could contribute to the occurrence of dyslipidemia in young age patients including the effect of ART medications.

The association between antiretroviral medications (ART) and chronic comorbidities has been discussed in previous studies [10,12,27]. Schouten et al. found that the duration of immunodeficiency was a significant factor contributing to the occurrence of chronic comorbidities among HIV patients, which was confounded by other factors of HIV infection duration and ART use [27]. The current study did not find an association between the duration of HIV infection since diagnosis and the occurence of chronic comorbidities; an increased age of 50 years or more was the only significant predictive factor. Lorenc et al. [11] had a similar finding, where time since HIV diagnosis was not associated with comorbidities, suggesting additional risk factors or an aggregate effect of independent risk factors that contributed to the incidence of some conditions. In their cohort of HIV-infected patients, Blanco et al. found that an age of 50 years or older as a cut-off was associated with a lesser immunological response and reduced survival after starting ART, with no effect on the virological response [31]. Some ARTs are associated with mechanisms that may result in premature cellular changes (e.g., endothelial dysfunction) [32]. However, specific inflammatory and immune system mechanisms that contribute to the incidence of comorbidities among HIV patients are still an area for future longitudinal research and investigation.

The relatively small sample size in the current study limits the generalizability of the findings. This study also did not include people living with HIV who are unaware of their condition. Due to the cross-sectional design of the study, it was not possible to draw inferences on the causal association between HIV infection or the use of antiretrovirals and comorbidity incidence. Further, the current study did not include information on adherence to HIV

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medications or on co-medications which should be investigated in future studies due to potential drug-drug interactions (DDIs) [24] Additionally, this study reviewed medical records over an eighteen-year period, and data on several ART medications (dose and duration) were missing.

In conclusion, this study highlights the substantially increased burden of chronic comorbidities among HIV patients. The prevalence of some chronic conditions is similar to the general population; however, the burden is higher among older age individuals, with an increasing number of comorbidities per patient. Moreover, those people are on complex medications that require particular care and capable resources at primary-and tertiary-care levels. Proper counseling for HIV patients is highly recommended-not only for prevention of other infectious diseases (e.g., vaccination), but also for lifestyle modification and self-management for those with chronic conditions. Future research should focus on further understanding of the underlying mechanisms of HIV non-AIDS comorbidities and estimating the burden of these comorbidities in terms of cost, hospitalization, and the impact of new medication regimens.

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Competing interest

None declared.

Ethical approval

Not required

Author contributions

Farahat F: Study conception, design, and analysis, interpretation of data, drafting the article and approval of the final revision of the manuscript.

Alghamdi Y, Farahat A, Alqurashi A, Alburayk A, Alabbasi A: Study design and acquisition of data.

Alsaedi A, Alshamrani M: Critical revision of the manuscript and approval of the final version to be submitted.

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