

The clinical outcome of HIV infection at a tertiary care center in Riyadh, Saudi Arabia

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ABSTRACT

الأهداف: دراسة الخصائص السريرية ونتائج الأشخاص المتعايشين مع فيروس نقص المناعة البشرية (PLWHIV) في مركز الرعاية الثالثية في الرياض، المملكة العربية السعودية.

المنهجية: أجريت الدراسة الحالية بأثر رجعي بين 2000-2019 م في مدينة الأمير سلطان الطبية العسكرية، الرياض، المملكة العربية السعودية. تم جمع الخصائص الديموغرافية والسريرية لـ 137 مريضاً مصاباً بفيروس نقص المناعة البشرية من خلال مراجعة سجل البيانات الطبية.

النتائج: من بين إجمالي عدد المصابين بفيروس نقص المناعة البشرية 137، 78.8% ذكور و 21.2% إناث. عند دخول الرعاية، فإن كانت معظم الإصابات الانتهازية التي تم العثور عليها هي عدوى الفيروس المضخم للخلايا. عدوى الفيروس المضخم للخلايا (CMV) في 13.8% من المرضى، السل (8%)، الأورام الخبيثة المرتبطة بالإيدز (10.9%)، التهاب الكبد ب (5.8%)، و NTM (3.6%)، التهاب الكبد سي (2.2%). في هذه الدراسة، تلقى أكثر من نصف المرضى العلاج المركب القائم على التكامل. تم تشخيص أعلى عدد (n=20) من المرضى في عام 2018م.

الخلاصة: تصف النتائج التي توصلنا إليها إلى الخصائص والنتائج السريرية للمصابين بفيروس نقص المناعة البشرية في مستشفى إحالة ثالث رئيسي في المملكة العربية السعودية. المرض غير المتعلق بالإيدز هو السبب الرئيسي لوفاة بين المصابين بفيروس نقص المناعة البشرية. أدى التشخيص المبكر وبدء العلاج المضاد للفيروسات القهقرية إلى انخفاض كبير في المراضة والوفيات.

Objectives: To investigate clinical characteristics and the outcome of people living with HIV (PLWHIV) at tertiary care center in Riyadh, Saudi Arabia.

Methods: The present retrospective, observational study was carried between 2000-2019 at Prince Sultan Military Medical City (PSMMC), Riyadh, Saudi Arabia. The demographic and clinical characteristics of 137 PLWHIV patients were collected by reviewing the medical data record.

Results: Of the total 137 PLWHIV, 78.8% were male and 21.2% were female. At care entry, the most opportunistic infections found were the cytomegalovirus infections. cytomegalovirus (CMV) infections in 13.8% of patients, tuberculosis (8%), AIDS associated malignancy (10.9%), hepatitis B (5.8%), NTM (3.6%), hepatitis C (2.2%). In the

present study, more than half of the patients received integrase based combination therapy. The highest number (n=20) of patients were diagnosed in 2018.

Conclusions: Our findings describe the clinical characteristics and outcomes of PLWHIV at a major tertiary referral hospital in Saudi Arabia. The non AIDS related disease is the major cause of death in HIV infected patients. Early diagnosis and initiation of antiretroviral therapy resulted in a significant decrease in morbidity and mortality.

Keywords: AIDS, HIV, TB, PCP, toxoplasma, malignancy, CMV, antiretroviral therapy

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The human immune deficiency virus (HIV) epidemic causes approximately 77.3 million infection since the beginning and 35.4 million have died from AIDS related diseases, globally.¹ The sub Saharan Africa is the worst affected in the world, accounting for 74% of the total death from HIV.² In Kingdom of Saudi Arabia (KSA), HIV is increasingly recognized as a major health problem.^{3,4} In 1984 the first HIV case was identified in Saudi Arabia. After 10 years, the National AIDS Prevention System was created, which implemented multisectoral and systematic disease-fighting strategies.

Since then, the knowledge about HIV cases from different regions of KSA has begun to enter the Ministry of Health. However, HIV/AIDS surveillance still faces many hurdles.⁵

AIDS is multifactorial disease with the complex etiology. Several factors have been suggested as the risk factors for the development of disease including age, race, and gender of the host.⁶⁻⁸ The widespread use of antiretroviral (ART) in mid 1990s has led to a remarkable decline in AIDS related mortality among people worldwide living with HIV infection.^{6,7,9} The HIV epidemic has been transformed into a chronic disease with a near-normal life expectancy, especially in high-income countries.¹⁰⁻¹³ The decline in mortality is especially evident in high-income developed countries where access to health care and antiretroviral therapies is more readily available.¹⁴

In adults, 25 antiretroviral drugs belonging to 6 different therapeutic groups are currently recommended for treatment or prevention of HIV infection.¹⁵ Therefore, in most patients taking medication, the classic AIDS related conditions are becoming less common, achieving lifelong viral suppressions. It has also prolonged disease-free survival, immunologic (CD4 cell) repletion, and reductions in hospitalization rates.^{15,16} Previous studies have reported that the extensive use of ART since, 1996 in the United States and Europe leading to significant reduction in AIDS related deaths and opportunistic diseases.^{8,10-13} Although ART results in a decrease in the hospitalization rate for AIDS-related disease, it increased the risk of many complications related to “non-AIDS” as a cause of death and hospitalization.¹⁷⁻²¹

Until now, a comprehensive literature survey has revealed the scarce of information in Saudi Arabia concerning diseases among PLWHIV whose HIV infection is under control and the conditions that lead to deaths. The present research study was therefore designed to examine the prevalence of PLWHIV related AIDS diseases, data profiling levels AIDS-related illness and death among patients treated at PSMC in Riyadh, Saudi Arabia.

Methods. The present retrospective, single center, observational cohort study was conducted between

January 2000 and December 2019 at HIV outpatient clinic, Riyadh, KSA. The patient’s medical information of PLWHIV was collected by reviewing the chart of the medical data record to collect demographic and clinical characteristics of PHWLIV such as age at the time of visit, mode of transmission, symptoms, laboratory analyses, ART, opportunistic infections, and outcomes.

The ethical approval was obtained from the Institutional Review Board, PSMC, Riyadh prior to conducting this study. We included only those patients whose age was 18 year or older, diagnosed between January 2000 and December 2019, received follow-up care at least once a year since treatment was started. We excluded all those patients whose age was below 18 years and also who did not fulfill the above-mentioned inclusion criteria.

Statistical analysis. The statistical analysis was carried out by using the Statistical Package for Social Sciences, windows version 20.0 (Chicago, IL, USA). Descriptive analysis including quantitative variables such as age was summarized by median (min-max). Qualitative variables such as gender, resistance and co-morbidities were summarized by frequencies and percentages. Association of the CD4 and co-morbidities and other infections (OIs) variables were determined using the Chi-square test. The values were presented as crude odds ratio (OR) and 95% confidence intervals. $p < 0.05$ was considered as significant.

Results. A total of 137 PLWHIV patients were included in the present retrospective cohort study. In our study, 108/137 (78.8%) were male and 29/137 (21.2%) female, the median age of patients was 42 years ranging between 18-89 years. Most patients were married (54.7%), 19.7% were single, 2.2% divorced, and 23.4% unknown. The mode of transmission data revealed 40.1% were secondary to heterosexual transmission, 2.2% were homosexual, and 1.5% transmission was via blood transfusion. One of the patients was known to have hemophilia and acquired the virus through the blood transfusion. The status of partner for HIV infection showed 20.5% were positive, 18.3% were negative while 61.4% were unknown status. The viral load data stratification have shown 42.3% of patients were above the viral load cut off ($>150,000$), approximately 40.9% had a baseline viral load of ≥ 50000 with a median of 107,721 copies. The median nadir HTC was 128 cells in more than half of the cohort. The resistance against ART was reported in 8.8% (**Table 1**). The annual incidence of HIV infection progressively increased during the last few years. We presented the incidence of HIV

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infection per year at a tertiary care center in Riyadh, Saudi Arabia in **Figure 1**. The highest incidence rate was observed in 2018. Data analysis for opportunistic infections and AIDS associated malignancies revealed that cytomegalovirus (CMV) infection was the most frequent (13.8%) opportunistic infections followed by *Pneumocystis carinii* (7.2%), *Mycobacterium tuberculosis* (8%) pulmonary TB (6.6%) and extra pulmonary TB (1.5%). Non-TB mycobacterium was found in 3.3% of patients. Notably, all were *Mycobacterium avium* complex (MAC) except one was *Mycobacterium riyadhense*. Toxoplasma was reported in 2.9% of patients and only one case (0.7%) of *Cryptococcus* was recorded in our study. Cytomegalovirus invasive disease was reported in only 0.7% in the form of colitis, encephalitis, esophagitis, pneumonitis and retinitis. It is of note that co-infection with hepatitis B was found in 8 (5.8%) patients and hepatitis C was found in 3 (2.2%) patients. AIDS associated malignancies was accounting for 7.3% of lymphoma and 3.7% of Kaposi sarcoma (**Table 3**). The international and national guidelines were followed for the treatment of HIV infected patients. The ART was individualized according to the patients tolerance, interaction and genotypic mutations.

Discussion. Our findings demonstrate that number of male patient infected with HIV was higher than female, more than half of the patients were married, and the primary mode of HIV transmission (40.1%) was heterosexual contact, while 55.5 % were unknown for the mode of transmission. The mean age of diagnosis was 42 years (**Table 1**). Our findings are in agreement with the previous report conducted at King Faisal Specialist Hospital and Research Center (KFSHRC), a referral center for HIV infection from all regions of Saudi Arabia.⁴ A total of 15,213 of PLWHIV patients were collected between 1984 and 2009 including patients under 15 years of age. Similar to our data, they have also reported 61.4% unknown for their HIV infection status. Human immunodeficiency virus baseline testing data confers high number of patients were above the viral load (>150,000) and helper T cells cut off (>200) as shown in **Table 1**. The baseline test results can be used to guide choices about HIV treatment and track the efficacy of ART. Of the total, only 3 patients were found before 2004 at our tertiary care center, then the cases increase and highest number 20 was reported in 2018 (**Figure 1**). The recent increment in new cases reflects the necessities of the wide spread use of HIV screening program in Saudi population. The first report of the HIV epidemic in the KSA, since it emerged in 1983-2003, has shown that

sexual transmission accounts for 46% of transmission, and there has been a decline in blood transfusion related cases since 2001.²² Conversely, 54% and 26% of a 410 Saudi cohort acquired HIV via blood product transfusion, which is expected during that period owing to lack of the proper tools for blood screening.^{23,24} Thus, screening of pre-marital couple, antenatal and some professionals like medical and military careers prior to the blood and organ donation is crucial.

In the present study, opportunistic infections data analysis have shown CMV is major source of opportunistic infection followed by tuberculosis, malignancies, hepatitis B, NTM, hepatitis C (**Table 2**). Our cohort study revealed the existence of CMV syndrome viremia with or without invasive disease. It worth's mentioning, CMV co-infection is predominantly reported in developing countries, which contributes to mortality and morbidity. The presence of CMV viremia has shown to be an independent predictor

Table 1 - Demographical and clinical characteristics of HIV infected patients at a tertiary care center in Riyadh, Saudi Arabia.

Variables	n (%)
Age (range) in years	42 (18-89)
Gender	
Male	108 (78.8)
Female	29 (21.2)
Marital status	
Married	74 (54.7)
Single	31 (21.9)
Divorced	32 (23.4)
Mode of transmission	
Heterosexual	55 (40.1)
Homosexual	3 (2.2)
Bisexual	1 (0.7)
Blood transfusion	2 (1.5)
Unknown	76 (55.5)
Partner status	
HIV positive	28 (20.5)
HIV negative	25 (18.2)
Unknown	84 (61.4)
VL baseline	
>150000	58 (42.3)
<150000	56 (40.9)
Unknown	23 (16.8)
HTC baseline	
>200	75 (54.7)
<200	46 (33.6)
Unknown	16 (11.7)
Resistance	
Yes	12 (8.8)
No	7 (5.1)
Unknown	118 (86.1)

VL: viral load, HTC: helper T cells

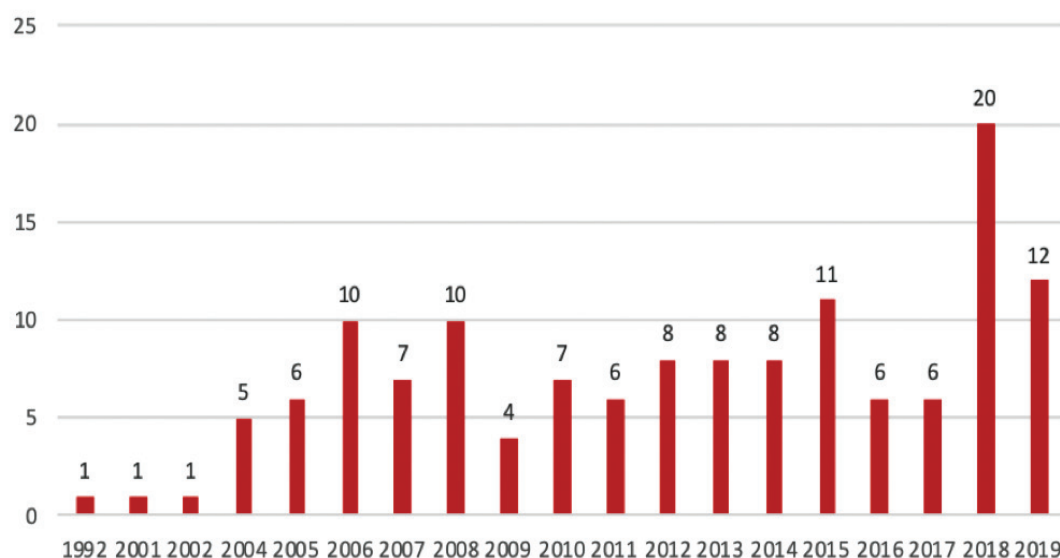


Figure 1 - Incidence of HIV infection per year at a tertiary care center in Riyadh, Saudi Arabia.

Table 2 - Initial opportunistic infections (OIs) of HIV infection at a tertiary care center in Riyadh, Saudi Arabia.

Variables	n	(%)
Tuberculosis (TB)	11	(8.0)
Pulmonary TB	9	(6.6)
Extra-pulmonary TB	2	(1.5)
NTM	5	(3.6)
MAC	3	(2.2)
M. Rhyadansae	1	(0.7)
Cytomegalovirus	19	(13.8)
PCP	11	(8.0)
Toxoplasma	4	(2.9)
Cryptococcus	1	(0.7)
Hepatitis B		
Positive	8	(5.8)
Negative	10	(7.4)
Unknown	23	(16.8)
Hepatitis C		
Positive	3	(2.2)
Negative	107	(78.1)
Unknown	27	(19.7)
Malignancies	15	(10.9)
Lymphoma	10	(7.3)
Kaposi sarcoma	5	(3.7)

of mortality in Africa.^{25,26} On the other hand, there was a tremendous decrease in CMV related mortality in developed countries as a result of early ART initiation.²⁷ Tuberculosis is highly prevalent in our region, previous report from the HIV clinic in the eastern province of Saudi Arabia has shown a close relationship between HIV and TB, especially among IVDU and prisoners.²⁸ A systematic review of data from low and middle-income countries illustrates the efficacy of ART in the reduction of OIs after one year, with the magnitude of the effect on oral candidiasis, cerebral toxoplasmosis and PCP contrary to TB.²⁹ Interestingly, *Mycobacterium riyadhense* is a new species of non-tuberculous mycobacterium which has emerged from Saudi Arabia and is described in a recent report from 2 HIV patients. *Mycobacterium riyadhense* necessitated treatment for one year with anti TB according to the susceptibility, which in the most cases is susceptible to Ethambutol, Clarythromycin and amikacine. However, a good response to the standard first line anti-TB has been shown, despite in vitro resistance.^{30,31} Corresponding to the progress in the ART and the use of prophylaxis against PCP, the incidence of PCP in PLWHIV was reduced in most of the developed countries. However,

it remains the most common in many countries.^{32,33} Our data is in line with other studies, which have shown a favorable prognosis and incommensurate presentation in HIV patients, compared to non-HIV patients who have a higher mortality 1-15% versus 30-40%, consecutively.³⁴⁻³⁶ The prevalence of PCP was estimated to be 27% from a tertiary care center in Saudi Arabia, and had a mortality rate of 8%. The prevalence of Toxoplasmosis is considered the lowest amongst the OIs (up to 2.9%), only 4 patients presented with toxoplasmosis based on brain ring enhancing lesions with a positive toxoplasma IgG who had a favorable response to anti toxoplasma treatment. Cryptococcus meningitis was recorded only in one patient compared to four from the Saudi literature.²³

Data from coinfections with other viral hepatitis in Saudi Arabia are scarce, single center studies have shown that coinfection with HCV in 12% hepatitis B in 3% patients.³⁷ Multiple factors contributing to the increase of lymphoma among HIV patients including the disease-related immunosuppression, cytokine deregulation, and, coinfections with other lymphotropic herpes viruses such as Epstein-Barr virus and human herpes virus.³⁸ As a result, lymphoma and Kaposi sarcoma were recorded in 6.6% and 3.3% subsequently in our cohort.³⁹ The failure of the CD4 increment, despite the ART, is a predictor of lymphoma; thus, using combined chemotherapy treatments and ART have led to an improved prognosis.⁴⁰ The majority of the patients (55.5%) are on an integrase-based combination therapy, which is consistent with international recommendations.⁴¹ We have reported 8.8% of the total infected patients who have shown resistance to ART. Interestingly, up to 23.3% of the experienced patients had a mutation in M184V, which is significantly lower than other parts of the world and Saudi Arabia.⁴²⁻⁴⁴ Of note, having this mutation alone does not contribute to treatment failure. Our report cannot be generalized to the whole PLWHIV because it is selective for certain category of the population.

Study limitations. Its retrospective design and certain category of the PLWHIV who are eligible to be treated in our center were included.

In conclusion, this report from a single-center in Saudi Arabia describes the prevalence of OIs in a particular population during the period 2009-2019. Results are compatible with previous results of delayed presentation and diagnosis of HIV-infection, which resulted in high rates of opportunistic infections and mortality. Following an expanded screening program and prompt initiation of ART subsequently, patient's outcome improved significantly.

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