

# AIDS-Defining Opportunistic Illnesses in Qatar, 2000-2016 : A Cohort Study

**Maisa Ali** (✉ [mali34@hamad.qa](mailto:mali34@hamad.qa))

Hamad Medical Corporation

**Mahmoud Gassim**

Hamad Medical Corporation

**Nada Elmaki**

Hamad Medical Corporation

**Wael Goravey**

Hamad Medical Corporation

**Abdulatif Alkhal**

Hamad Medical Corporation

**Muna Almaslamani**

Hamad Medical Corporation

**Hussam Alsoub**

Hamad Medical Corporation

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## Research Article

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# Abstract

## Background

Human immune deficiency virus (HIV) infection remains a major health problem since discovery of the virus in 1981. Globally, since introduction of antiretroviral therapy, AIDS related death fell by more than 25% between 2005 & 2011. Also, HIV related opportunistic infections (OIs) are less common, especially with use of prophylaxis to prevent such infections (3). We aim in this study to assess the incidence of HIV infection and related OIs in Qatar for 17-year period, and assess the spectrum of these infections, risk factors and treatment outcome.

## Methods

retrospective cohort study for all HIV infected patients registered in Qatar from 2000-2016. Incidence of HIV infection and related opportunistic illness was calculated per 100000 population. Demographic and Clinical characteristics were compared between two groups of patients with and without opportunistic illness.

## Results

of 167 cases with HIV infection 54 (32.3%) of them had opportunistic illness. The average incidence rate of HIV infection over 17 years is 0.69 per 100000 population, and the incidence rate for opportunistic illness is 0.27 per 100000 population, figure 1. The most common opportunistic illness is pneumocystis jirovecii pneumonia (PCP) 25% of cases, followed by CMV retinitis 7.2%, Tuberculosis 5.4%, Toxoplasmosis 4.2% and less than 2% for Kaposi sarcoma, lymphoma and cryptococcal infection.

## Introduction

Human immune deficiency virus (HIV) infection remains a major health problem since discovery of the virus in 1981. WHO reported that since beginning of HIV epidemic more than 70 million people were infected with the virus and about 35 million died of the disease (1). However, overall, the rate of new HIV infection continues to decline in many countries (2)

Globally, since introduction of antiretroviral therapy, AIDS related death fell by more than 25% between 2005 & 2011 (2). Also, HIV related opportunistic infections (OIs) are less common, especially with use of prophylaxis to prevent such infections (3). Many HIV infected patients now living longer with adherence to antiretroviral medication (4).

The incidence and spectrum of OIs has been reported from many developed countries (5), but few data have been reported from the middle east. In the Gulf region, study from Oman shows 58% of HIV infected patients had OIs, in which PCP and cryptococcal meningitis were commoner. (6)

In Qatar the first case of HIV was diagnosed in 1984 and antiretrovirals therapy was introduced in 1997, since then most of new line of medication are been used. In 2014, a study done by AlSoub et al, showed in 306 cases of HIV infected patients in Qatar, AIDS related OIs was in 54% with majority of cases were non-Qatari (7).

We aim in this study to assess the incidence of HIV infection and related OIs in Qatar for 17-year period, and assess the spectrum of these infections, risk factors and treatment outcome.

## **Material & Methodology**

This study was conducted as a retrospective cohort study to explore the incidence of HIV infection and related OIs per 100,000 populations in Qatar.

The study was done at HMC, the only governmental hospital in Qatar with 9 branches all over the country. All patient diagnosed with HIV will be registered at ministry of health & will be followed at compromised host clinic at communicable diseases center.

Data review of all medical records of patients diagnosed between January 2000 to December 2016. This include demographic data, clinical characteristic, viral load, CD4 count, percentage, and comparing these data between patients with and without OIS.

The spectrum of OIS, treatment outcome, use of antiretroviral therapy and prophylaxis was assessed.

### **Definitions**

We concentrate on pneumocystic jirovecii pneumonia (PCP), tuberculosis (TB), cytomegalovirus infections (CMV), cryptosporidium infection, toxoplasmosis, mycobacterium avium complex (MAC), Progressive multifocal leukoencephalopathy (PML), lymphoma & Kaposi sarcoma

## **Statistical analysis**

descriptive statistic in terms of counts and percentages for categorical variables and mean and standard deviation or median with range (where ever appropriate) for internal variables will be performed. chia square test to see significant differences of proportions of categorical variables with opportunistic infections and student t test or mann whitreny u test for internal variable will be performed. to see risk factors for opportunistic infections, multivariate logistic regression analysis will be performed separately for each infection. Adjusted odds ratio with 95%CI will be presented. P value 0.05 (two tailed) will be considered for statistically significant level. SPSS22.0 statistical package will be used for the analysis

## **Result**

Between 2000 and 2016, 339 patients were diagnosed with HIV in Qatar, unfortunately only 167 cases were included it in the study, as result of record were lost due to patient died or left the country.

Incidence of HIV infection and related opportunistic illness was calculated per 100,000 person-years.

The average incidence rate of HIV infection over 16 years is 0.69 per 100000 population, and the incidence rate for opportunistic illness is 0.27 per 100000 population. (Figure 1)

Demographic and Clinical characteristic were compared between two groups of patients with and without opportunistic illness. Most of our patients in both groups were young age, majority males, and almost half of them were Qatari. Patients age at the time of HIV diagnosis was lower in the group of patients without opportunistic infection (33.65 and 39.72, P value 0.002).

The CD4 count, CD4%, CD4/CD8 ratio and viral load were statistically significant risk factors in cases with opportunistic illness p value <0.05, however presence of comorbidities was lower in patients with opportunistic illness P value 0.032. (Table1)

The most common opportunistic illness is pneumocystic jirovecii pneumonia (PCP) 25% (42 of cases). Followed by CMV retinitis 7.2%, tuberculosis 5.4% ,toxoplasmosis 4.2% and less than 2% for Kaposi sarcoma, lymphoma and cryptococcal infection. (Figure 2)

The outcome of treatment of cases with opportunistic illness was: cure rate 59.3%, relapse within one year was 3.7%, mortality within 3 months of opportunistic illness was 3.7%, whereas 33.4% loss follow up (left the country).

## Discussion

Since the initial epidemic of HIV, the overall incidence of new HIV case were declining globally, however new cases were more in the Middle East. New HIV infections have been reduced by 47% since the peak in 1996. In 2017, there were 1.8 million new HIV infection and 9400000 died from AIDS related illness worldwide. ALSO 59% OF all people living with HIV were accessing the treatment. (8)

Qatar is a small country in the gulf area with increasing number of populations growing fast over the last 10 years, current population around 2.5 million, 25% were Qataris. We notice from our study the declining number of newly diagnosed HIV infected cases despite the raising in population, which can be explained with the overall declining of HIV incidence. (2).

Also, the incidence of HIV related OIs is decaling, explained by the use of antiretrovirals medication and prophylaxis (3).

In Qatar the use of HIV screening program for all premarital individual, antenatal screening and pre-employment screening for selected jobs, has contributed to early diagnosis of HIV infection and less rate of OIS. In addition, HIV screening test is done for all new comers who will stay more than one month in the country.

HIV treatment is available for all our patients, which also contributing in lower incidence of opportunistic infections among them.

In our study, Patients with OIS have significant decrease in CD4 count and CD4/CD8 ratio with high HIV viral load compared to patients without infection, same observation has been documented in other studies (10, 11, 12).

We also notice a smaller number of hepatitis B or C combined infection among HIV cases, this could be explained by blood donation screening program, along with low incidence of drug abusers among our HIV infected patients.

We notice the presence of comorbidities among our HIV cases, mainly due to diabetes, which may be related to overall high incidence of diabetes among Qatari population (9).

PCP remains the most common type of OIS, accounting for 25% (42 cases) of all diagnosed OIs in our study. Studies from other regional countries show similar prevalence; Oman 25% and Bahrain 15.1% (6, 10). A definitive diagnosis of PCP with a demonstration of organisms in induced sputum samples or BAL fluid was made in most of our studied cases. A total of 16 patients (9.6%) with HIV/AIDS had PCP as an AIDS-defining OI at their first presentation.

CMV disease/retinitis was the 2nd common OIs in our study representing 7.2% (12 cases of infected HIV/AIDS patients). Diagnosis of the disease mainly clinical based on positive CMV serology (IgM,IgG), high PCR titer and fundoscopic finding. In contrast to data from Oman where 17% of HIV patients had CMV retinitis. (6).

Although tuberculosis is common in the region due to high number of workers from high endemic area, combined HIV and TB cases were low, 5.4% (9 cases). This maybe explained that all new comers to the country will be screened and treated for latent TB infection. We also noticed none of the studied case had MDR TB as overall prevalence of MDR TB in Qatar is low and few associations between it and HIV (13).

Toxoplasmosis, caused by *Toxoplasma gondii*, is one of the major OIs afflicting HIV patients. Cerebral toxoplasmosis is the most common cause of focal neurological disorders in HIV patients. In our cohort, cerebral toxoplasmosis accounted for 4.2% (7 out of 167) of HIV infected patients. In a study from Oman, cerebral toxoplasmosis was reported in 12% of the HIV-infected patients. (6)

*Cryptococcus neoformans* is one of the causes of invasive fungal disease in patients with HIV worldwide. Meningitis is the commonest clinical manifestation of invasive cryptococcosis infection. In our study, *Cryptococcus* meningitis accounted for only 1.2% of all HIV patients. As a result, primary prophylaxis for invasive cryptococcal disease is not practice in Qatar.

Similar low incidence was seen in Indian reports show 6–8%, whereas it is about 5–11% in the USA, 33% in Africa, and 28.5% in Thailand. (14) Interestingly, in Oman reports incidence of cryptococcal meningitis

was high as 21% of all HIV infected patients. The exact explanation for such high incidence in Oman is unclear. (6).

*Cryptosporidium* infection was observed in only 2% in our study. Regional data showed similar low incidence, in Oman 3%. (6). This is in contrast to data from Ethiopia where 21% of HIV patients had *Cryptosporidium parvum* infection. (15). In patients with HIV, cryptosporidiosis usually causes chronic diarrhea however, it may cause potentially fatal complications, like bile duct perforation. (16). The rate of cryptosporidiosis has subsided in many countries because of the use of ART. (17)

Kaposi sarcoma and PML were rare opportunistic infections in our study group and worldwide. We have smaller of patients with cryptococcal meningitis in comparison to patients in Omani study (6). In our study none of the patient had MAC infection out of 167 HIV infected patients. This can be explained to routine use of primary prophylaxis in patients with CD4 count less than 50.

The proportion of treatment success among OIs patients in our study is 59.3%, however, one third of patients lost follow up as they left the country.

Conclusion: Qatar has a low prevalence rate for HIV infection and related opportunistic illness. Early diagnosis and use of antiretroviral therapy are important measures to decrease the rate of opportunistic illness.

## Declarations

Ethics approval: An approval from Hamad Medical Corporation, Medical Research Council (MRC) was obtained prior to submission of this manuscript.

Consent for publication: approved from Hamad Medical Corporation, Medical Research Council (MRC) , Qatar

All methods were performed in accordance with the relevant guidelines and regulations by MRC

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Inform consent: informed consent was not obtained from all subjects and/or their legal guardian(s) as per regulation of Medical Research Council, Hamad Medical Corporation, Qatar for retrospective observational study

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## Tables

Table 1

Demographic data, CD4%, absolute CD4 count, and CD4/CD8 ratio between HIV-infected patients with and without opportunistic illness

	HIV with opportunistic illness (n=67)		HIV without opportunistic illness (n=100)		
	Mean	Standard Deviation	Mean	Standard Deviation	P value
<b>Age at diagnosis</b>	39.72	11.246	33.65	12.920	0.002*
<b>CD4</b>	99.00	121.542	574.36	427.218	<0.001*
<b>CD4 percentage</b>	5.48	6.026	20.80	12.844	<0.001*
<b>CD ratio</b>	0.13	0.137	0.76	1.731	0.023*
	Frequency	%	Frequency	%	P value
<b>Nationality (n=167)</b>					
Qatari	32	47.8%	48	48.0%	0.976
Non-Qatari	35	52.2%	52	52.0%	
<b>Gender (n=167)</b>					
Male	51	76.1%	75	75.0%	0.869
Female	16	23.9%	25	25.0%	
<b>Marital status (n=167)</b>					
Single	22	32.8%	42	42.0%	0.349 <sup>a</sup>
Married	43	64.2%	57	57.0%	
Divorced	3	3.0%	3	3.0%	
<b>Mode of transmission (n=167)</b>					
Sexual transmission	57	85.07%	90	90.0%	0.336
Others	10	14.93%	10	10.0%	
<b>Hepatitis C infection (n=167)</b>	2	3.0%	3	3.0%	0.853
<b>Hepatitis B infection (n=167)</b>	3	4.5%	2	2.0%	0.610
<b>Co-morbidities (n=167)</b>	15	22.4%	24	24.0%	0.032*
<b>Viral load (n=167)</b>					
<100000	25	25.8%	72	74.2%	<0.001*

	HIV with opportunistic illness (n=67)		HIV without opportunistic illness (n=100)	
>100000	36	64.3%	20	35.7%
*Indicate statistically significant result				