

# What is the Rate of Latent Tuberculosis Infection in Human Immunodeficiency Virus (HIV) Infected Patients in Saudi Arabia?

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**Abstract Background/Objectives:** Despite significant investments in Tuberculosis (TB) control over 15 years, TB remains an important public health problem in Saudi Arabia (SA) affecting all age groups, and on the other side there is a notable increased in the number of people living with Human Immunodeficiency virus (HIV) in SA. This study was designed to estimate the prevalence of Latent Tuberculosis Infection (LTBI) among HIV-infected patients in a tertiary care hospital in Saudi Arabia (SA). Our study is the first study in the Middle East up to our knowledge and literature review in HIV-infected subjects. **Material/methods:** Retrospective study was conducted with a total of 61 HIV seropositive patients attended and followed up at data was collected and recorded from patients' charts, electronic health record system and HIV data base for age, gender, nationality, chest- XR and CD4 count and also for Quantiferon test (QFT) which was used as screening test for detection of LTBI. **Results:** Among our patients, 46 were male (75.4 %) and 15 were female (24.6 %), the mean age was 44.4 years (age range 19-77 years), 57 were Saudi (93.4%) and 4 were non- Saudi (6.6 %). The mean baseline CD4 count for all patients was 285 cells/mm<sup>3</sup>. QFT was done for 40 patients (66.7%), 2/40 patients were positive (5.0 %), 35/40 patients were negative (87.5%) and 3/40 patients were intermediate (7.5%). **Conclusions:** We found an overall prevalence of LTBI is 5 % among HIV-infected individuals in SA, which is relatively low especially in TB endemic country, more epidemiological studies are needed in this high-risk group of patients for latent Tuberculosis in SA.

**Keywords:** Latent TB, HIV, Saudi

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## 1. Introduction

Tuberculosis (TB) and HIV have been closely linked since the emergence of Acquired Immunodeficiency Syndrome (AIDS). Worldwide, TB is the most common opportunistic infection affecting HIV-seropositive individuals, and it remains the most common cause of death in patients with AIDS [1]. Globally, people living with HIV are 26 times more likely to develop TB disease than those who are HIV-negative. In 2014, an estimated 1.2 million (12%) of the 9.6 million people who developed TB worldwide were HIV-positive and HIV-associated TB deaths accounted for 25% of all TB deaths (among HIV-negative and HIV-positive people) and one third of the estimated 1.2 million deaths from HIV/AIDS [2].

Pulmonary tuberculosis is a common disease in Saudi Arabia. As most cases of tuberculosis are due to reactivation of latent infection [3], The total number of reported tuberculosis cases in the year 2008 was 3918

cases in a population of approximately 24,807,273, However WHO 2007 estimation of the incidence of TB new cases was 46/100 000 population/year [4]. Available recent prevalence in 2011 of tuberculosis (pulmonary and extra-pulmonary) was estimated to be 13.7 per 100,000 populations in Saudi Arabia [9]. According to Saudi Ministry of Health also the estimated number of people living with HIV in KSA since the beginning of 1984 and up to the end of 2013 amounted to 20,539 cases, of which 5,890 cases were Saudis and 14,649 were non-Saudis, In 2013, 1,777 new AIDS cases were detected, 542 of which are Saudis and 1,235 non-Saudis, There is a notable increase in the detected cases of AIDS among Saudis by 26% in 2013, compared to the detected cases in 2012, and by 18% for the preceding year, 2011.

Among pulmonary TB with HIV infection in SA, TB incidence is 30 times higher than in the general population, with significant mortality despite early diagnosis, treatment and tertiary care support [19]. Latent TB infection is an infection without clinical, bacteriological and radiological signs [6], Testing and treatment of persons at increased risk for latent tuberculosis infection

(LTBI) is a core element of the tuberculosis (TB) elimination strategy [7]. Preventing TB deaths among HIV-positive people requires intensified scale-up of TB prevention, diagnosis and treatment interventions [2].

## 2. Method

### 2.1. Ethics Statement

This study was approved by King Abdullah International Medical Research Centre at King Saud bin Abdulaziz University for Health Sciences, Riyadh - KSA, before starting data collection as the study does not disclose patient identity, and poses no risks to patients (Reference N. RC13/217).

### 2.2. Study Design and Analysis

We conducted a retrospective study to determine the prevalence of Latent Tuberculosis Infection (LTBI) among all human immunodeficiency virus (HIV) seropositive patients who treated and attended at King Abdulaziz Medical City (KAMC), Riyadh- SA, for the period from January 2005 to November 2015. Data was data was collected and recorded from patients' charts, electronic health record system and HIV data base for a total of 61 HIV positive enrolled in this study, all were adult 19 years and older, not affected with active Tuberculosis (TB) or previously treated from TB at the time of screening by Quantiferon test ( Interferon-gamma release assays (IGRAs)) (QFT). Age, sex, nationality, QFT, CD4 count and chest- XR data were collected, QFT is not routinely done for HIV patients in our hospital. Flow cytometry was used for absolute CD4 count measurement. All obtained data was analyzed by using SPSS analytic system.

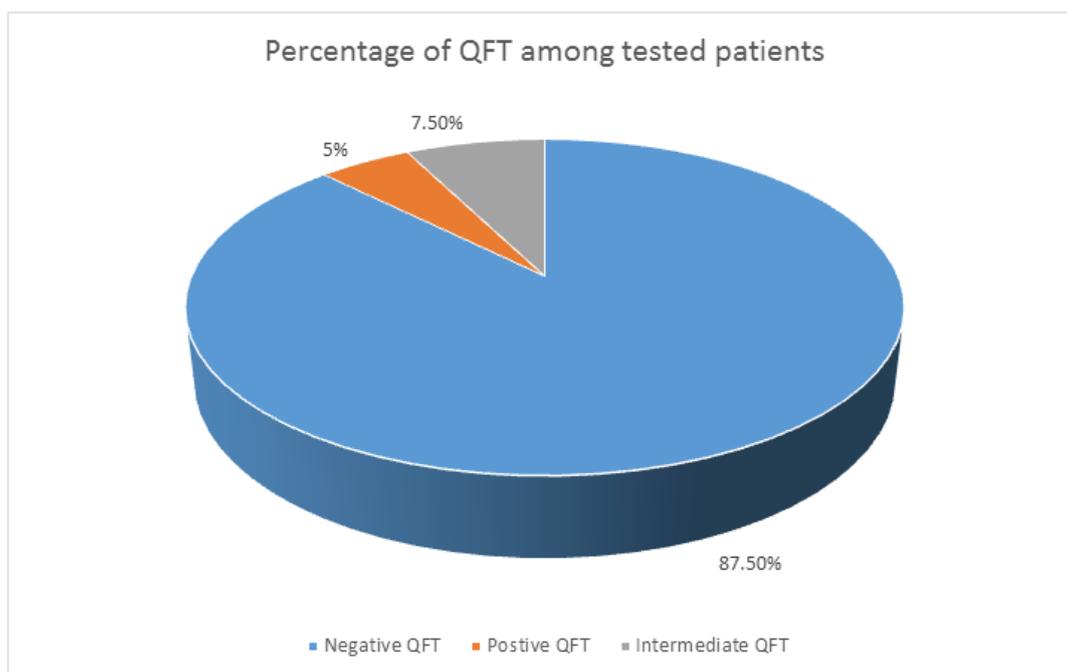
KAMC is a distinguished healthcare provider in Saudi Arabia with a capacity of more than 800 beds and located in Riyadh city.

## 3. Results

A total of 61 HIV seropositive patients were involved in this study, 46/61 were male (75.4 %) and 15/61 were female (24.6 %). The mean age was 44.39 +- 13.4 years (19-77), 57/61 patients (93.4%) were Saudi and 4/61patients (6.6 %) were non- Saudi. QFT was done for 40/61 patients (65.6%), 2/40 patients were positive (5.0 %), 35/40 patients were negative (87.5%) and 3/40 patients showed intermediate result (7.5%) (Figure 1) (Table 1).

**Table 1. General characteristics of the population at baseline and Quantiferon Test relation with different variables**

Parameters	Value/Number	Percentage
Total	61	100%
1. Median age in years (range)	44.393	-
2. Sex		
Male	46	75.4
Female	15	24.6
3. Nationalities		
Saudi	57	93.4%
Non-Saudi	4	6.6%
4. Quantiferon Test		
Positive	2/40	5.0
Negative	35/40	87.5
Intermediate	3/40	7.5
5. Chest -XR		
Normal	43/56	76.8
Abnormal	13/56	23.2
6. Gender distribution of positive Quantiferon Test		
Male	2/40	100%
Female	0/40	0%
7. Gender distribution of intermediate Quantiferon Test		
Male	3/40	100%
Female	0/40	0%
8. Quantiferon positive Test and CD4 count.		
CD4 <= 200 cells/mm <sup>3</sup> )	2/40	100%
CD4 >=200 cells/mm <sup>3</sup> )	0/40	0%
9. Quantiferon Intermediate Test and CD4 count.		
CD4 <= 200 cells/mm <sup>3</sup> )	3/40	100%
CD4 >=200 cells/mm <sup>3</sup> )	0/40	0%



**Figure 1.** Showed the percentage of positive QFT among HIV patients tested for Latent TB infection (QFT: Quantiferon Test, TB: Tuberculosis)

Chest-XR was done for 56/61 patients (91.8%), 43/56 patients had a normal Chest-XR (76.8%) and 13/56 patients had an abnormal Chest-XR (23.2%). Patients with positive result of QFT with a normal Chest-XR was 2/2 (100%), and with CD4 count less than 200 cells/mm<sup>3</sup> was 2/2 (100%). Patients with Intermediate QFT all were male (100%) and CD4 count less than 200 cells/mm<sup>3</sup> was 3/3 (100%) (Table 1).

## 4. Discussion

Despite a significant investments in TB control over 15 years, TB remains an important public health problem in SA affecting all age groups Saudis and non-Saudis people [13], the published data showed that TB in Saudi Arabia is still not fully controlled despite the government's efforts to eradicate the disease. Even though the directly observed therapy short course (DOTS) program in the country was implemented in 1999 as part of the national tuberculosis control program (NTP), the treatment success rate (62%) still remains below the international target set by the WHO (85%) [14,15].

Our study was done to reveal the prevalence of LTBI in HIV positive patients in SA, which is first study in this group of population in the Middle East up to our knowledge and as literature review, but many studies was done to know the prevalence of LTBI in HIV patients outside the KSA [10,11,12].

We found that the overall prevalence of LTBI (defined by a positive QFT test) is 5% among HIV positive in our study, which is relatively low compared to other studies done outside SA with reported incidence of 40 %, 7.5% and 6.7% respectively [10,11,12] and slightly higher than in other studies 4.6%,18.5%, 12 % and 2.2% [9,10,11,16].

The prevalence of LTBI in HIV patients in this study is low compared with prevalence of LTBI in general population in SA, *Al Kassimi et al* in 1993 conducted the first comprehensive and nationwide tuberculin survey in the Saudi Arabian general population with urban/rural stratification, using a definition of a positive tuberculin test of 10 mm or more, 33% of the subjects had a positive TST [3]. But the prevalence is still low in compared with rate of LTBI among Health Care Workers (HCW) in SA, which was 22.5% (47 out of 208) [17] and also 291(11%) out of 2650 HCWs in other study [18]. In general, the global rate of LTBI in low endemic countries is very low prevalence (0–3%) [9]. In an intermediate endemic burden country, the prevalence of LTBI in the general population was low 4%, increasing to 21% in contacts of sputum positive TB patients, in TB high endemic regions, the prevalence of LTBI in population was 30% [9].

Gender distribution in this study showed the prevalence of LTBI as, all were male patients with no female infection, also all patients with Intermediate QFT result were male with no female involvement, the prevalence in HCW was 22% in men and 23% in women [17].

Chest –XR was normal in 76.8 % and abnormal in 23.2% in our patients, it was 100% normal in patients with positive QFT, but it was 10% positive in HCW with signs suggestive of inactive TB in their CXR examination (none had CXR evidence of active TB) in study [17]. A total of 330 HCWs with positive TST or QFT underwent standard chest radiography, of these 330, 113 radiographs (34.2%)

were finally classified as normal, 206 (62.4%) had lesions suggestive of inactive TB, and 11 (3.4%) had features suggestive of active TB [20].

The CD4 count in our patients with positive and intermediate QFT result showed very immunocompromised state, all patients with QFT positive had CD4 count less than 200 cells/mm<sup>3</sup> and all patients with intermediate QFT result had CD4 count less than 200 cells/mm<sup>3</sup> (actually CD4 count was less than 100 cells/mm<sup>3</sup> for all patients with positive and intermediate QFT result). In other study patients with positive QFT and CD4 less than 200 cells/mm<sup>3</sup> was 10% and Intermediate with CD4 count less than 200 cells/mm<sup>3</sup> was 54.4% [12], also in other study there was no patients with positive QFT and CD4 count less than 200 cells/mm<sup>3</sup> but there was 9.1% of patients with CD4 count more than 200 cells/mm<sup>3</sup> [10].

## 5. Limitations

This study has a limitation of small sample size and being only descriptive of an original data with some difficulties of reaching all the desired information.

## 6. Conclusion

We found an overall prevalence of LTBI is 5 % among HIV-infected individuals in our study, which is relatively low especially in TB endemic country in SA, more epidemiological studies are needed in this high-risk group of patients for latent Tuberculosis in SA.

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