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Prevalence of tuberculosis infection among patients undergoing regular hemodialysis: a multicenter study in Egypt

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Dear Editor,

About one-third of the human population is presently infected by *Mycobacterium tuberculosis*, and about 10% during their life develop active tuberculosis (TB) (5% during the first 2 years following infection) [1].

Diagnosis and treatment of TB Infection (TBI) have been considered core interventions to pursue TB Elimination [1]. The World Health Organization (WHO) recommends screening for, and treatment of TBI in the groups at higher risk of developing TB when infected [1]. Patients undergoing dialysis are among the risk groups WHO is recommending for TBI diagnosis and treatment [1,2]. Systematic diagnosis and treatment of TBI is still under implementation in several countries of the Middle East and North Africa like Egypt, where, in spite of the relatively low burden of TB (TB incidence is below 10 cases per 100,000 population in many countries), risk groups exist deserving clinical and public health attention [2].

The aim of this study is to determine the prevalence of TBI among patients undergoing hemodialysis in Egypt and identify the factors associated with TBI in the country using QuantiFERON TB Gold Plus (QFT-plus) assay, one of IGRA tests recommended by the WHO [1,2]. This multicenter cross-sectional study was conducted enrolling consecutive patients in 20 governorates throughout Egypt. Asuit, Sharkia, Alexandria, Gharbia, Menofia, Cairo, Kafr El Shikh, Sohag, Behaira, Ismailia, Qaliobia, Damietta, Daqahlia, Menia, Qena, Suis, Giza, Bani Swif, North Saini and Aswan. As this was a real-world study reflecting routine clinical practice, no strict inclusion criteria were applied beyond patient presentation for evaluation. Ethical clearance was obtained (document ref 6-2024/4) before initiating the study.

Blood samples were collected for laboratory examinations after patients signed an informed consent form and TBI was assessed using QFT-Plus according to the manufacturer's instructions as positive, negative or indeterminate result [2].

The following information was collected, ensuring anonymization as per legislation in force in Egypt: sociodemographic data; epi risk factors; other clinical conditions and/or co-morbidities which indicated the need for dialysis.

An individual was defined as smoker when the yearly consumption of tobacco products exceeded 100 packs-year.

A descriptive analysis was conducted, which included frequencies and proportions for categorical variables. The Chi-square test was utilized to assess associations between TBI positivity and categorical covariates, with a significance level set at $\alpha = 0.05$. The R Statistical Software (v4.1.2; R Core Team 2021) was used for analysis.

Overall, out of 22,313 individuals screened, 4,410, were QFT-plus positive (21.5%) as shown in Table 1.

Males yielded a higher QFT-plus positivity rate than females, with approximately 13.5% of positive results observed among males compared to 6.3% among females. Additionally, older age groups (between 40 and 60 years and above 60 years of age) showed higher positivity rates compared to younger individuals (age groups younger than 20 years or between 20 and 40 years).

The overall positivity rate for the QFT test was 21%, indicating a notable occurrence of positive results among the tested population. The proportion of indeterminate results was around 8% without any significant variation across the different age groups.

Stratifying by risk factor and medical conditions, as shown in Table 2, those smoking or with Hepatitis B or C Virus (HBV and HCV) had the highest QFT-plus positivity rate reported in the cohort at over 25%, followed by individuals with hypertension (21.9%), diabetes (21.6%), and HIV infection (18.8%).

Overall, HBV, HCV, smoking status and diabetes showed significant associations with QFT-plus results, while HIV and hypertension status did not (Figure 1).

There was no apparent association between specific medical conditions and the occurrence of indeterminate results, as the indeterminate rate remains relatively consistent across different conditions with the highest rate among diabetes and HBV, at a rate which is internationally considered acceptable (average 7 %; range 5.3-8.6%) and in line with previous reports demonstrating good performance and feasibility of use of QFT-plus in this high-risk group regardless of COVID-19 or SARS-CoV-2 vaccination [3].

Egypt is ranked as a medium-burden TB incidence country. A WHO descriptive analysis of TB burden in Egypt showed that the estimated incidence rate per 100 000 population decreased from 26 in 2000 to 10 in 2021), positioning the country among those at low TB incidence, thus able to implement the activities which are considered necessary to pursue TB Elimination [1]. In the WHO Global TB Report 2023 Egypt had an estimated TB incidence of 9.8 cases per 100,000 population (range: 8.4-11) with an estimated number of 11,000 TB cases per year (range 9,300-12,000) [1].

It is important to notice that the main social determinants considered relevant for TB in Egypt, in decreasing order of importance, are under-nutrition, smoking, diabetes, alcohol and HIV [1]. In our study the association between smoking/diabetes and TBI positivity has been confirmed, testifying the importance of continuing the screening in these risk groups. Similarly, the association with viral hepatitis (HBV and HCV) suggests the need to coordinate the screening efforts of pulmonary and infectious-diseases oriented services. Fortunately, the HIV positivity rate is estimated to be low in Egypt (0.008 per 100,000 population, rage 0.04-0.14) with 90 cases estimated to occur every year (range: 41-160) and low mortality (0.03 cases per

100,000 population, range 0.01-0.07) [1]. However, in view of the migration flows observed in the region it is important to continue quality surveillance in this risk groups as well.

In spite of the overall success achieved so far in reducing both incidence and burden of TB in Egypt, the proportion of TB-infected individuals is high among patients undergoing dialysis (about 1 out of 5 cases). Given the objective complexity of managing patients in dialysis and their vulnerability, the importance of strengthening their screening is underlined. These patients after being identified as infected, should undergo chest radiography to rule-out TB (disease) and then initiate without delay TBI treatment (TB preventive treatment-TPT as per WHO definition). It is of paramount importance to be able to describe the whole TPT cascade of care [2] as to ensure the highest possible completion of TPT regimens using the shorter options recommended by WHO [1]. This will accelerate the prevention of future cases and the trajectory of Egypt towards the pre-Elimination threshold (10 cases per million or 1 case per 100,000) [2]. From a programmatic point of view, in order to ensure effective implementation of TBI screening and TPT, these activities should ideally be included in a coherent and funded National Strategic Plan, as the Lebanon experience testifies [4].

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Table 1. Proportion of QuantiFERON-TB Gold Plus (QFT-Plus) positive (+), negative (-) and indeterminate results (ind) stratified by age and gender.

	Total	QFT-plus +	QFT-plus ind
Age			
Median (IQR)	55 (20)		
<=20	308 (1.4%)	28 (9.1%)	15 (4.9%)
20-40	4226 (19.3%)	530 (12.5%)	344 (8.1%)
40-60	10179 (45.9%)	1942 (19.1%)	819 (8.4%)
>60	7407(33.4%)	1862 (25.1%)	609 (8.2%)
Gender			
Male	13326 (60%)	2853 (21.4.5%)	1091 (8.2%)
Female	8884 (40%)	1326 (14.9%)	702 (7.9%)

Table 2. Proportion of QuantiFERON-TB Gold Plus (QFT-Plus) positive (+) and indeterminate (ind) stratified by risk factor/co-morbidity

Risk factor	Total	Patients with or without the condition %	QFT-plus + (%)	QFT-plus ind (%)
Diabetes	2441	12%	477 (21.6%)	232 (10%)
No Diabetes	18540	88%	3665 (21.6%)	1560 (8%)
Hypertension	12363	58%	2472 (21.9%)	1064 (9%)
No hypertension	8801	42%	1706 (21.2%)	730 (8%)
Smoking	1501	9%	365 (24.4%)	60 (4%)
No Smoking	15689	91%	3123 (46.2%)	558 (8%)
HIV	134	1%	24 (18.8%)	6 (4.5%)
No HIV	21841	99%	4326 (21.6%)	1789 (8.2%)
HCV	3547	16%	816 (25.1%)	285 (8.1%)
No HCV	18765	84%	3594 (20.9%)	1516 (8.1%)
HBV	446	2%	108 (26.9%)	43 (9.7%)
No HBV	21536	98%	4249 (21.5%)	1753 (8.2%)

HCV, hepatitis C virus; HBV, hepatitis B virus.

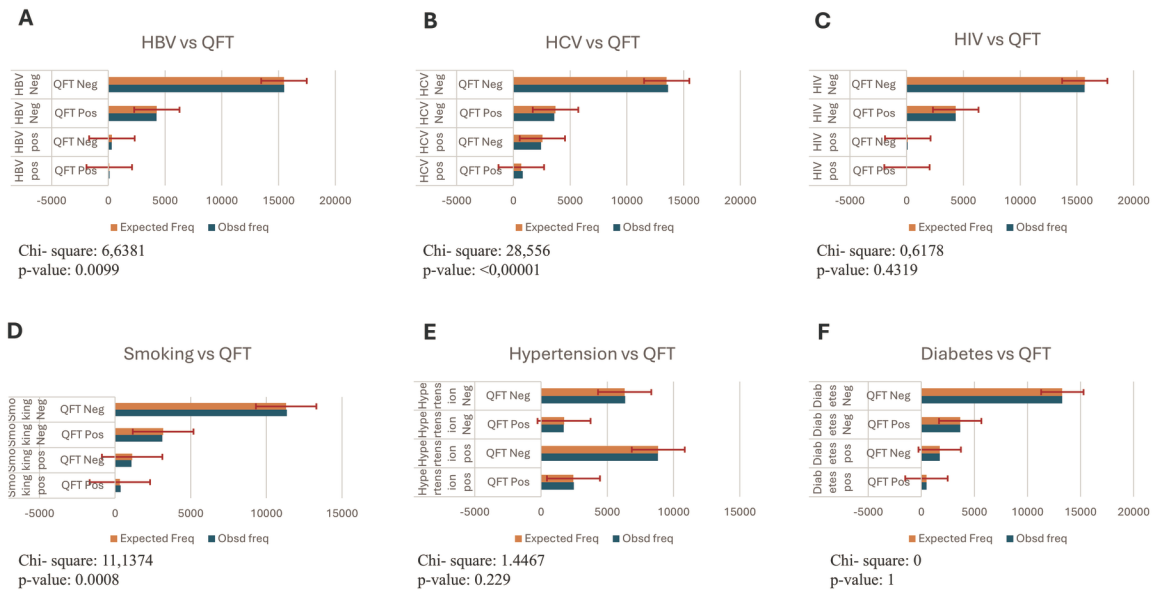

Figure 1. Association between risk factors/co-morbidities and QFT results.