Review article

Tuberculosis Screening Among Expatriate in Bahrain

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Abstract

The Majority of expatriate TB cases were identified in Bahrain mainly through passive case finding. Expatriate with LTBI have a 10% risk of developing active TB during their lifetime, with the greatest risk being within 2, 3 years of country entry. Expatriate TB was highest in labors between 20-49 years age group. The key to control TB in Bahrain is either to add PPD testing or doing IGRA, for all pre-employment during expatriate entry to the Kingdom. PPD testing is remaining the preferred method with IGRAs as a supplemental assay in subjects more than 2 years of age. If either TST or IGRA are positive, then active disease must be excluded by chest X-ray and sputum for microscopy and culture. Diagnosis and treatment of latent tuberculosis infection are considered an essential component of TB control strategy and should be a major component of the overall public health plan for controlling TB in Bahrain.

Keywords: *Mycobacrium Tuberculosis, tuberculin skin testing, Purified Protein Derivatives*

Introduction

The majority of TB patients in the Bahrain were expatriates (71. 8 [1] - 75.7% [2]), which is possibly related to the limitation of a screening program to only chest radiography for laborers without implementation of PPD to all expatriate workers upon entry to the Kingdom of Bahrain. The total incidence rate of TB in Bahrain was 32.3/100,000 population (low-intermediate TB burden) [1 – 2] (figure 1) [2], while the incidence was higher among non-Bahrainis ranging from 47.4 to 75 per 100,000, however decreased to 26 cases/ 100, 000 in years 2013-2014 among the domestic working class. [1] Nonetheless the incidence in Bahraini population decrease from 10 to 5 cases/ 100.000 developed countries was 5-6 /100 000 population in the years 2013-2014. [3] The total TB positive smears were 225 cases in 2014.

The definition of low- TB incidence burden is the countries which set the cutoff at 20 TB cases /100,000 populations (Western Europe and North America, as well as Australia and New Zealand). [4, 5]

Patients born, raised or recently arrived from high TB-burden countries, like expatriate labors are at higher risk of contracting TB (active TB) or having latent tuberculosis infection (LTBI); which TB bacillus infection is controlled by the immune system. [2, 5] People with LTBI have a 10% risk of developing active TB during their lifetime, with the greatest risk being within 2 years of country entry. [6]

Overall, TB disease are divided either to extra pulmonary TB disease (EPTB) or pulmonary TB disease (PTB), in Bahrain EPTB was 39% while 61% with the PTB. The most common site of EPTB (50%) was the lymph nodes (figure 2). [2]

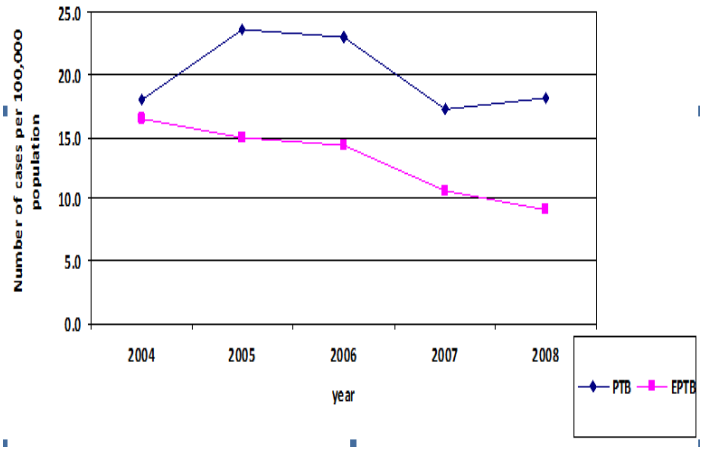


Figure 2: Incidence of PTB and EPTB per 100,000 (2004-2008). [2]

The contribution of Non-Bahraini to the total TB patients was variable among different age groups; it

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is highest in labors between 20-49 years age group (figure 3).

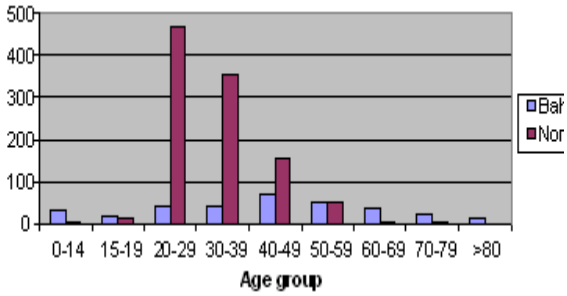


Figure 3: Number of TB Cases among different age groups. [2]

Objective

To provide evidence tests that general practitioner should order regularly for screening TB in expatriate labors.

Discussion

World Health Organization (WHO) puts goals for Tuberculosis (TB) control, wherein dramatically reduce the global burden of TB by 2015 (The Stop TB Strategy). [7, 34]

The Majority of TB cases were identified in Bahrain mainly through self-referral of symptomatic individuals to health facilities (passive case finding). While less TB cases were identified through active TB case finding (ACF). ACF are the strategies to screen and treat suspected people in early TB disease. [8, 33]

Table 1: Populations at increased risk of exposure to TB. (4)

- **Elderly patients – the incidence was far higher in EPTB.**
- **Migrants or expatriate workers from high TB-burden countries- the incidence was far higher in PTB.**
- **Healthcare workers or whom have been working from high burden countries.**
- **Negative Lifestyle (e.g., crowded accommodation, illicit drug use or alcoholism).**
- **Imprisonment.**
- **Related to underlying co-morbidities illnesses.**
- **Contacts of active TB cases.**
- **Patients and staff in psychiatric facilities.**
- **Patients in residential care.**

Most TB cases, presentations were atypical, so physicians should always have a high index of suspicion among populations with an increased risk of exposure to TB (*Table 1*), also to identify the risk factors for TB reactivation of TB cases reactivation (*Table 2*). Populations at increased risk of exposure to are many such as; elderly, immigrant, health care workers, imprisonment) and people with negative lifestyle alteration (e.g., crowded accommodation, illicit drug use or alcoholism). [9, 10, 33]

TB incidence rates in risky groups often dramatically exceed background incidence. [1, 2]

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Table 2: Risk factors for TB reactivation. [4]

- Recently acquired infection (within the first 2 years).
- Immune-compromised states including HIV infection.
- Medicines related (eg. immune modulators, chemotherapy and post-transplantation)

Conversely, commitment of high risk groups with ACF is often more difficult, resulting in hindered diagnosis, onward transmission, poor treatment adherence and a consequent disproportionate contribution of these population groups to the TB burden. [11]

Diagnostic tools for ACF to consider TB by following the TB flow chart (figure 4).

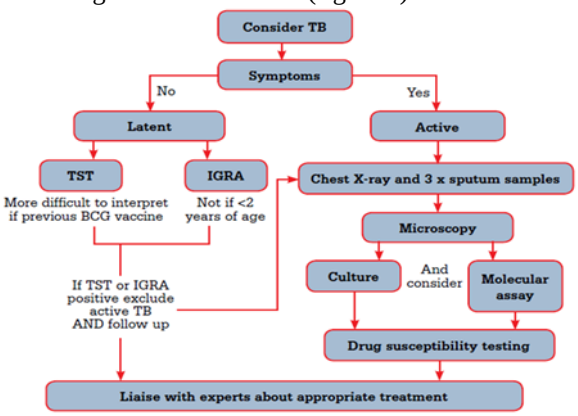


Figure 4: Investigations when considering a diagnosis of TB. [4]

Settings national standardized symptom enquiry questionnaire for early active pulmonary TB identification (PTB) (e.g., cough lasting more than 2–3 weeks, no wheezing, hemoptysis, fever, night sweats, Pleuritic chest pain, difficult breathing, new sputum production, current smoker and weight loss) requires urgent chest X-ray and microbiological testing. [12, 13]

The combined symptom enquiry questionnaire shows moderate to high sensitivity (65–90%), while with low to moderate specificity (30–68%) to detect microbiologically confirmed TB. [14]

Typical changes include 3Cs changes (air space Consolidation, Cavitation and fibrous Contraction)

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in one/both upper lobes or superior parts of the lower lobes ± Pleural Effusion ± Hilary Lymphadenopathy [12] (figure 5).



Figure 5: Chest X-ray of a man, 47 years of age, with typical pulmonary tuberculosis.

The sensitivity and specificity of CXR screening for active PTB can be as high as 82% and 99%, respectively. [15]

Microbiologically sputum test should be obtained during ACF; usually following a positive result from either a symptom questionnaire or CXR finding. The predictive value of sputum smears depends on TB prevalence, the quality of the sample collection, the number of smears taken and overall quality control. [16, 33]

Microbiologically sputum tests should be taken on three early morning specimens (for Acid-fast microscopy and culture) to maximize yield. Molecular assays identify DNA specific for Mycobacrium tuberculosis (MTB complex) and new rapid polymerase chain reaction (PCR) test (Xpert® MTB/RIF assay, Cepheid, Sunnyvale CA.) are both with have high sensitivity (86–97%) and specificity (85–99%). [17, 18, 33]

Diagnosis of LTBI is dependent on the levels of immune recognition of MTB antigens with either tuberculin skin testing (TST) (PPD) or the interferon gamma release assays (IGRA) for pre-employment purposes, healthcare workers TB screening, and as part of the post exposure evaluation. [19, 35]

Contact screening usually aims to detect individuals with latent TB infection (LTBI), or to diagnose early TB disease. Diagnose and treatment of LTBI is very important to halt active TB development by 60–90% and to eradicate the potential for transmission. The risk of disease progression is greatest within the first 2–3 years [20, 35] (table 3, figure 6). [30-32]

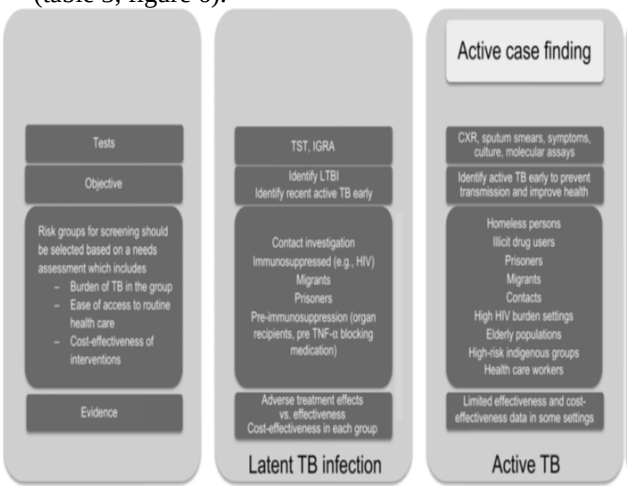


Table 3: Active, latent TB case finding.

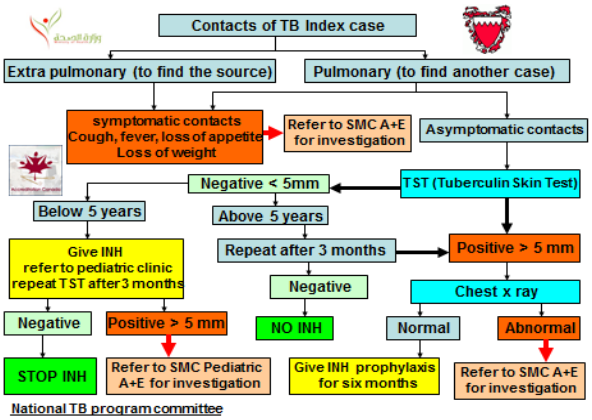


Figure 6: Contact screening for TB index case.

The key to control TB in Bahrain is either to add PPD testing or doing IGRA, for all pre-employment during expatriate entry to the Kingdom, besides to all expatriate preschool entry. [21, 22, 35] (figure 7, 8) [32, 33]

The PPD test problems are; to be read 48–72 hours after administration, high false positives can result from previous bacilli Calmette-Guérin (BCG) vaccination in addition, patient exposure to other Mycobacterium species [35] (table 4). [32, 33, 35]

IGRA assays are unaffected by previous BCG vaccination and not need for a second visit for reading. TST are remaining the preferred method with IGRAs as a supplemental assay in subjects more than 2 years of age [23, 24, 33-35] (table 5) [6].

If either TST or IGRA are positive, then active disease must be excluded by chest X-ray and sputum for microscopy and culture. [23, 33-35]

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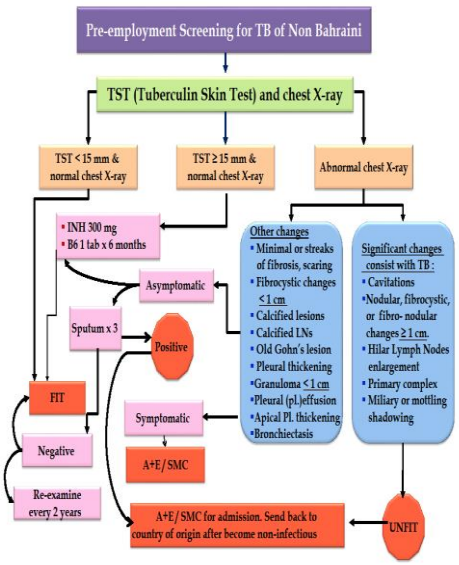


Figure 7: Pre-employment screening for TB for expatriate

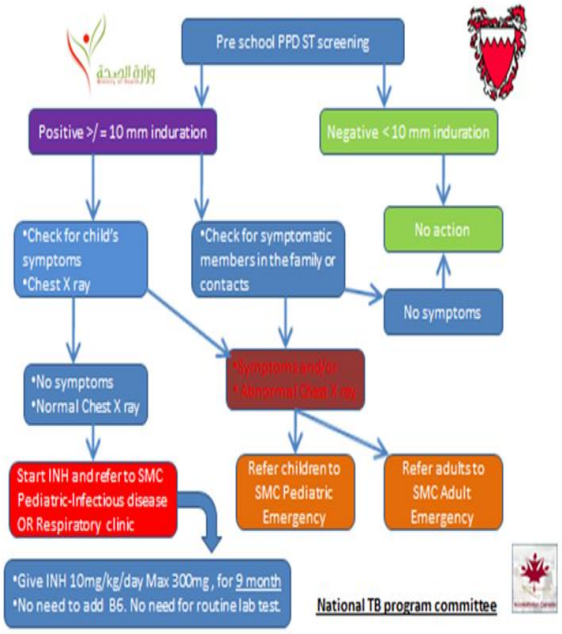


Figure 8: Pre-school PPD screening test.

Table 4: Positive screening tuberculin skin test (mantoux).

Mantoux - Tuberculin Skin Testing in Screening		
Diameter of induration	**Positivity** (degree of hypersensitivity to tuberculin protein).	**Interpretation**
Less than 5 mm	Negative - (no significant hypersensitivity to tuberculin protein).	• Previously unvaccinated individuals may be given BCG provided there are no contra-indications. • Suggests no TB infection but beware false negatives.
5 mm or greater	Positive - (hypersensitive to tuberculin protein).	Considered positive in: • HIV-infected persons. • A recent contact of a person with TB disease. • Persons with fibrotic changes on chest radiograph consistent with prior TB. • Patients with organ transplants. • Persons who are immunosuppressed for other reasons (eg, taking the equivalent of >15 mg/day of prednisone for one month or longer, taking TNF-antagonists).
10 mm or greater	Strongly positive - (strongly hypersensitive to tuberculin protein).	Considered positive in: • Recent immigrants (<5 years) from high-prevalence countries. • Injection drug users. • Residents and employees of high-risk congregate settings. • Mycobacteriology laboratory personnel. • Persons with clinical conditions that place them at high risk. • Children <4 years of age. • Infants, children, and adolescents exposed to adults in high-risk categories.
15 mm or greater	Strongly positive - (strongly hypersensitive to tuberculin protein).	An induration of 15 or more millimetres considered positive in any person, including persons with no known risk factors for TB. However, targeted skin testing programmes should only be conducted among high-risk groups.

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Table 5: Comparison of important features of the two main types of tests for detecting LTBI

	TSTs	IGRAs
cost	Low cost	High cost
Specificity – influenced by previous BCG vaccination	Yes	No
Specificity – influenced by previous infection by environmental mycobacteria	Yes	Less than with TST (but test antigens also found in *M. marinum*, *M kansasii* and *M. szulgai*)
Special precautions	Store tuberculin re-agent at –8°C and protect from light	Blood must be processed within 16 hours
Suitable in children <2 years of age	Yes	No
Hypersensitivity reactions	Possible – anaphylaxis rare	No
Number of visits to complete test	Two	One

All patients with TB should be screened for HIV infection and chemical /infective hepatitis, additionally, TB patients should be screened for drug induced neutropenia or thrombocytopenia and vitamin D deficiency by doing liver enzymes and hepatitis B and C profiles, regular full blood examination and vitamin D level are all indicated. [25, 36]

Expatriate screening could be done before entry (pre-departure = country of origin screening), at entry (on arrival = port-of-entry screening) or after arrival (post-entry screening). On the other hand, the post entry transmission of infection between migrants could be attributed either to higher TB incidence in the country of origin or contributions from a range of poor socioeconomic factors (living in deprived, overcrowded sharing accommodation settings). [26, 27]

The TB screening requirement should comply with migrants' rights and responsibilities, such as when there is an obligation for pre-entry TB health clearance screening as a condition for obtaining a residence/ work visa from a designated center in their country of origin. Pre-entry screening with CXR, combined with smears and culture, was associated with a reduction in TB occurring among migrants within 6 months of arrival. [28]

National post-entry screening programmes should be used in Bahrain to target migrants from countries with an incidence of TB exceeding 150 per 100 000 population was found to be cost-effective (Most African countries, Philippines, Pakistan, India, Indonesia, Korea, Vietnam, Afghanistan, etc.) [29, 30, 33, 34]

Alkhawaja et al. claimed that effective TB screening program for all groups of expatriate workers is mandatory for the success of the TB control program. [2] Diagnosis and treatment of latent tuberculosis infection is considered an essential component of TB control strategy and should be a major component of the overall public health plan for controlling TB in Bahrain. [31, 32]

Recommendation

1) Settings national standardized symptom enquiry questionnaire for early active pulmonary TB identification.
2) Training primary care physicians for early TB chest x ray finding.
3) The key to control TB in Bahrain is either to add PPD testing or doing IGRA, for all pre-employment during expatriate entry to the Kingdom.
4) Obligation for pre-entry TB health clearance screening for obtaining a residence/ work visa.
5) BCG should be given to all non-Bahraini newborns or one/both originally non Bahrain parents.

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