## Environmental and Host-Related Factors Predisposing to Tuberculosis in Karachi: A Cross-Sectional Study

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# -ABSTRACT-

**BACKGROUND:** To study the environmental and host-related factors predisposing to tuberculosis (TB) in Karachi.

METHODS: This was a descriptive crosssectional study, which was conducted at two tertiary care government hospitals. The duration of the study was from September 2009 to February 2010. A total of 250 sputum smearpositive TB patients were included in the study. A questionnaire containing information on age, sex, education and occupation was completed by two separate investigators from each setting. Recall information was elicited about the presence of co-morbidities, any form of immunosuppression, addiction or BCG vaccination and close contact with a tuberculosis patient.

**RESULTS:** Questionnaires were completed for 250 sputum smear-positive pulmonary TB patients. The mean duration of positive sputum TB was  $5.39 (SD \pm 4.76)$ 

months. 54% patients were male. Diabetes had the maximum prevalence, with approximately 25% patients reporting to have diabetes. Most common addiction was smoking (48%), and 10% of the smokers belonged to the high-risk group (20 or more cigarettes per day). 69.6% patients (N=174) lived in over-crowded houses ( $\geq$ 3 persons/room).

**CONCLUSIONS**: Multiple environmental and host-related factors are present in the sputum smear-positive cases of Karachi. Thus, an understanding of these risk factors will contribute in the appropriate management of this disease. Conflicting Interest: None declared

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### INTRODUCTION

Among the infectious diseases, TB holds one of the highest mortality rates worldwide. Eighteen people are affected with TB every minute globally and three of them die per minute. WHO ranks Pakistan 8<sup>th</sup> among the 22 high-burden TB countries.[1]

Tuberculosis is a multi-factorial disease in which complex environmental interactions with host related factors contribute to the overall disease phenotype. Understanding the individual balance between degree of exposure and inherited genetic susceptibility to infection will have strong implications on tuberculosis control and prevention.[2]

Several approaches can be considered to target tuberculosis control and there is an urgent need to design new interventions against tuberculosis, integrating the epidemiologic and sociologic approaches.[3] Comparison of the prevalence of individual risk factors for TB in various populations using standardized indicators would elicit useful information. In Pakistan, few studies have been carried out to understand the effect of individual factors on the development and progression of the disease. Unfortunately, no study integrating the total sum of these factors has been carried out.

This study intends to help health system policy makers, health officials, faculty in medical institutions, nongovernmental organizations and health care providers in Pakistan, particularly in Karachi, to understand the predisposing factors that are most alarming in our society and will also help them in concentrating their resources in those towns of Karachi which are most affected by TB.

#### MATERIALS AND METHODS

This descriptive cross-sectional study was conducted at two tertiary care government hospitals in Karachi, Civil Hospital and Ojha Institute of Chest Diseases, from September 2009 to February 2010. Initially a pilot study was done by interviewing 30 sputum smear-positive cases of tuberculosis. In the actual study, two separate investigators collected data from each setting to minimize bias. Sputum smear-positive cases of pulmonary TB, including newly diagnosed, relapsed and follow-up patients, residing in Karachi for at least twelve months were included. Informed consent was taken from each patient. Height and weight of the patients was measured. Information about age, sex, marital status, education, occupation and monthly income was taken by the investigator. The town of Karachi where the patients have been residents for the last 12 months was also noted.

Recall information about BCG vaccination and close contact with a tuberculosis patient was noted as well as the patient examined for a BCG scar. The presence of co-morbids (i.e. asthma, diabetes, chronic renal disease, hepatitis, measles) and any form of addiction (i.e. illegal drugs, alcohol and smoking) was noted. Any feature causing immunosuppression (i.e. use of oral/injectable steroids, cancer, HIV, chemotherapy and radiotherapy) was also inquired. Approval to conduct this study was obtained from the institutional review board of Dow University of Health Sciences, Karachi.

To simplify the complex association between the factors and tuberculosis, the risk factors were grouped into two major categories, (1) Host-related factors: age and sex, immunosuppression, HIV infection, diabetes, comorbids (asthma, hepatitis, measles, chronic renal disease), alcoholism, smoking, BCG vaccination, malnutrition (2) Environmental factors: socioeconomic status, overcrowding, close contact with diseased individual, unemployment, homelessness and illicit drug use. Frequencies were determined for each risk factor and standard deviation and mean determined where appropriate.

#### RESULTS

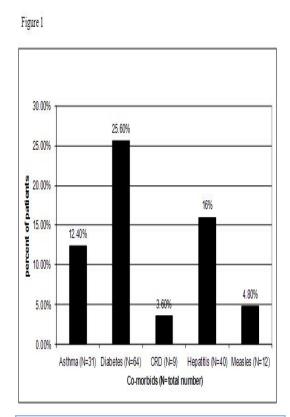
Questionnaires were completed for 250 sputum smear-positive pulmonary TB patients from the two centers. Of them, 187 (74.8%) were interviewed at Ojha Institute of Chest Diseases and 63 (25.2%) at Civil Hospital, Karachi. The mean duration of positive sputum smear for TB was 5.39 (SD $\pm$ 4.76) months. Of these, 54 (21.6%) also had previous infection of pulmonary TB.

Regarding age, patients were categorized into three groups: young (0-15 years), middle age (16-64 years) and old (65 years and above). 231 (92.4%) patients belonged to the middle aged group. For all age groups, the number of males and females was comparable. Of all the patients, 135 (54%) were males and 115 (46%) were females. 60% of patients either had been vaccinated or had a BCG scar while 40% (N=100) had no vaccination or scar present. The approximate weight loss during the disease was 4.61 (SD=4.4) kg while mean BMI before infection was 20 (SD=4.3) kg/m<sup>2</sup>.

	Town	Frequency	Percent (%)
1	Lyari Town	29	11.6
2	Saddar Town	26	10.4
3	Kemari Town	23	9.2
4	Baldia Town	20	8
5	Landhi Town	20	8
6	New Karachi Town	18	7.2
7	Korangi Town	18	7.2
8	Orangi Town	17	6.8
9	Malir Town	17	6.8
10	Liaquatabad Town	12	4.8
11	Gulshan Town	11	4.4
12	SITE Town	8	3.2
13	Shah Faisal Town	6	2.4
14	Gadap Town	6	2.4
15	North Nazimabad Town	5	2
16	Bin Qasim Town	5	2
17	Jamshed Town	5	2
18	Gulberg Town	4	1.6
	Total	250	100

<u>**Table 2:**</u> Distribution of the sample sputum smear TB patients in various towns of Karachi (N=250)

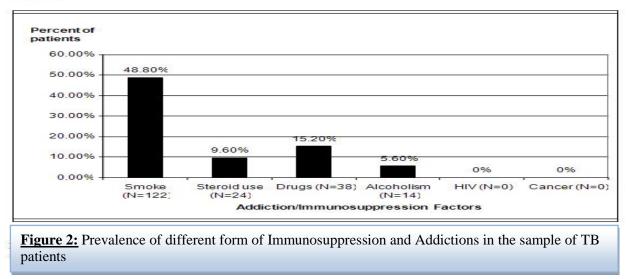
		Total number (N)	Frequency (%)
Employment	Unemployed	51	20.4
	Employed	199	80%
	Govt. service	20	8
	Private service	20	8
	Personal business	49	19.6
	Unskilled labor	44	17.6
	Skilled labor	32	12.8
	Others	34	13.6
Monthly Income	<5000	156	62.40%
	>5000	94	37.60%
Education	Illiterate	74	29.60%
	Read and write	26	10.40%
	Primary	58	23.20%
	Secondary	41	16.40%
	Above Secondary	51	20.40%
TB Contact History	Yes	95	38%
	No	155	62%
Crowding	Non Crowded (<3person/room)	76	30.40%
	Overcrowded (≥3persons/room)	174	69.60%



<u>**Table 1:**</u> Prevalence of environmental factors in sputum smearpositive patients (N=250)

Figure 1: Prevalence of different comorbids in the sample Tb patients

Figure 2:



#### DISCUSSION

The main objective of our study was to determine the prevalence of a number of risk factors in TB patients residing in Karachi. In our study, most TB patients belonged to the middle aged group with a male dominance as compared to female (54% males versus 46% females). Age and sex variations in the prevalence of tuberculosis infection and disease have been reported worldwide, in both developed and developing countries.[5,8] Early tuberculin skin test surveys have shown that infection with *M. tuberculosis* increases with age and then declines in older adults. The prevalence of tuberculin sensitivity is usually similar in both genders until adolescence, after which prevalence is higher among males.[8] This difference after adolescence may reflect greater exposure among adult males because of differentiated social roles and economic activities[9], but it also may reflect a genuine sex difference in susceptibility to tuberculosis infection related to a different predisposition to responsiveness to delayedtype hypersensitivity.[10] It is probable that, in addition to genuine age and sex differences in susceptibility related to biologic mechanisms, socioeconomic and cultural factors may play a role in determining age and sex differences in the rates of infection, progression to disease, and treatment outcome.[9]

In contrast to our study, HIV infection has come forward as the most important risk factor for development of tuberculosis in persons infected with M. tuberculosis in the world.[11,12] Because of the immunosuppression caused by HIV infection, persons with latent tuberculosis as well as newly infected persons may progress rapidly to clinical disease.[13] The estimated risk of clinical disease in HIV-infected persons is between 6 and 26 times the risk in non-HIVinfected persons. In our study, 25% of the patients also had diabetes. In a previous study, a review was made of the records of all patients with pulmonary tuberculosis and diabetes mellitus admitted over a period of 5 years to a teaching hospital in Karachi, Pakistan. Among 42358 patients, the total number with both tuberculosis and diabetes was 173. The prevalence of tuberculosis in diabetic patients was 10 times higher than in nondiabetic patients and prevalence increased with duration of diabetes.[14] In our study, we took a look at the prevalence of five co-morbids in TB patients. Sos et al. in a retrospective study of patients hospitalized for Mycobacterium tuberculosis infection compared two populations. immunodepressed versus nonimmunodepressed. 75 patients aged 20 to 91 were included, 41 patients were considered immunodepressed and 34 non-immunodepressed.

The causes of immunodepression were: HIV infection (n = 2), diabetes (n = 4), chronic alcoholism (n = 12), chronic respiratory diseases treated with corticosteroids (n = 6), neoplasia (n = 9), and inflammatory diseases (n = 7). [15]

The most common addiction in our patients was smoking (48.8%). Evidence exist showing a link between tuberculosis and smoking. There is epidemiological evidence from the UK, China, India and the USA, that there seems an association that an increase in tuberculosis case rates of between twoand four-fold for those smoking in excess of 20 cigarettes a day. A possible explanation is that nicotine stops the production of TNF-alpha by the macrophages in the lungs, making the patient more susceptible to the development of progressive disease from latent Mycobacterium tuberculosis infection.[6] Shevchenko studied pulmonary TB in alcoholics. Pulmonary TB was found to occur in chronic alcoholics more frequently than in those without chronic alcoholism, to run relatively badly, therapeutical efficiency was reduced and long-term prognosis was under question.[16]

Malnutrition is a strong risk factor for becoming unwell with TB,[17] and TB itself is a known risk factor for malnutrition. It is also well known that malnourished patients with TB (BMI less than 18.5) are at an increased risk of death even with appropriate antibiotic therapy. Baldwin et al. underscored the importance of access to nutritional enhancements, which they showed in turn interface well with a prevalent ethno-medical worldview that may minimize diagnostic delays, and fortify adherence to requisite TB treatment regimes.[18]

Historically, tuberculosis has been linked with poverty. Poverty conditions during the industrial revolution in the 19th century in Europe were accompanied by disease and death due to tuberculosis.[19] Disease rates in Europe declined constantly between the early 19th century (when approximately one death in four was caused by tuberculosis) and the mid-1980s. Because this decline started long before effective chemotherapy or vaccines were available, it has been attributed to the combined effects of isolation of infectious tuberculosis patients in sanitariums as well as socioeconomic development.[19] In a recent study in rural Malawi, Glynn et al. found that schooling and quality of housing were positively and independently associated with an increased risk of tuberculosis disease, after adjustment for baseline HIV status, age, and sex.[20]

In our study, overcrowding (≥3persons/room) was a significant finding (69.60%). In crowded houses, a greater degree of shared airspace increases exposure to *M. tuberculosis*, which can even be increased by limited air movement in closed spaces-hence a greater risk of infection. Crowding also has been reported to increase the risk of tuberculosis disease. In a study investigating the influence of the "social complex" on tuberculosis notification and mortality in Glasgow, Scotland, Stein found a highly significant association of tuberculosis disease with various social variables, the strongest being crowding (average number of persons per house).[21] Later, Lienhardt found that tuberculosis mortality between 1950 and 1952 in Glasgow was highly correlated with crowding, and that the number of new tuberculosis cases was highly correlated with overcrowding (defined as the proportion of houses with more than two persons per room).[7] Jail inmates are at an increased risk of contracting tuberculosis because the likelihood of contract between susceptible persons and infectious tuberculosis as well as intimacy of exposure is high. In a study conducted at Karachi juvenile jail, the prevalence of TB among inmates was found to be 3.9%; significantly higher than the estimated 1.1% prevalence in general population.[21] There is a significant transmission of tuberculosis from a patient of pulmonary tuberculosis to contacts.

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According to a study at Civil Hospital, Lyari General Hospital and Ojha Institute of Chest Diseases, Karachi, in which 287 close contacts of 50 diagnosed cases of tuberculosis were included, 26 contacts (15.3%) were found to be suffering from TB. These included 13.3% of smear-positive patients and 2 (2%) contacts of smear-negative patients (P value = 0.000396).[22] Another study at Umerkot, Sindh, confirms the prevalence of tuberculin skin test (TST) positivity among household contacts of acid-fast bacilli (AFB) sputum smear-positive TB patients; the prevalence of TST positivity in them was found to be was 49.4%. [23]

In a study conducted by Coker R et al. in St Petersburg, Russia, the odds ratio of risk for developing tuberculosis among the unemployed individuals was 6.10, and the odds ratio of risk for developing tuberculosis among the illicit drug users was 8.74.[24]

There are several limitations of this study. The validity of information obtained by patient recall can not be established with certainty. Another limitation is that the study does not prove whether these patients had these risk factors by chance or if TB could predispose to these factors. Thus, further studies linking the relationship of these factors to the occurrence of the disease need to be carried out. This will contribute to developing a holistic approach in the management of TB.

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