

# Correlation between Silica Exposure and Risk of Tuberculosis in Lorestan Province of Iran

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**Background:** Tuberculosis is considered a prevalent and hazardous disease in developing countries. Recognition and control of TB risk factors are of special significance. This study sought to determine the frequency of occupational silica exposure in TB patients residing in Lorestan Province.

**Materials and Methods:** This cross-sectional study was conducted in 2012. List of registered TB patients was obtained from the Infectious Disease Control Center of Lorestan Province. Data were collected from 871 TB patients through interview and filling out a checklist. Also, 429 subjects presenting to Health Centers of Lorestan Province with respiratory complaints suspicious of TB (which was ruled out) were entered the study as the control group for comparison of frequency of silica occupational exposure. Understudy subjects based on the degree of silica exposure were categorized into 4 groups of no exposure, mild exposure, moderate exposure and severe exposure and compared in terms of frequency of TB incidence.

**Results:** Frequency of silica exposure was significantly higher in TB patients compared to controls ( $P < 0.001$ , OR: 3.39, 95%CI=2.63-4.36). Additionally, frequency of TB was greater in patients with probable silicosis and silica exposed subjects compared to those with no history of silica exposure ( $P < 0.05$ ). Logistic regression analysis revealed significant associations between moderate and severe silica exposure and TB frequency. Significant correlations were also detected between age, work experience, level of education, male gender and cigarette smoking with TB frequency ( $P < 0.05$ ).

**Conclusion:** The study results revealed that silica exposure was prevalent among TB patients and frequency of TB increased by increased intensity of silica exposure, older age, higher work experience, lower level of education, male gender and cigarette smoking. Provided that our study results are confirmed by prospective studies, TB screening is recommended for workers with occupational silica exposure particularly those with higher work experience.

**Key words:** Tuberculosis, Occupational exposure, Silica exposure, Worker

## INTRODUCTION

At present, TB is among the biggest public health hazards in developing countries (1, 2). TB prevalence in Iran was reported to be 6.8 in  $10^5$  populations in 2005. However, according to a report by the World Health Organization (WHO), the actual TB incidence rate is  $12/10^5$

populations in Iran. Underestimation of Tb prevalence is attributed to its misdiagnosis and under-reporting of TB cases (2).

Exposure to silica dust occurs in several industries and occupations worldwide. This is somehow expected considering the abundance of silica in earth's crust and its

extensive use in many products (3). The National Institute for Occupational Safety and Health (NIOSH) estimates that approximately 1.7 million workers in the US are at risk of exposure to respirable silica dust (4) and 119,000 individuals working in various industries are exposed to silica dust in concentrations over its safe threshold of occupational exposure (5). Workers are at risk of exposure to silica dust in various industries including mining, tunnel construction, casting, glass production, sandblasting, ceramic production, shingle production and cement and concrete manufacturing (6).

Strong epidemiologic evidence exists regarding the association of occupational silica exposure and development of various diseases such as silicosis, lung cancer, pulmonary tuberculosis, and chronic obstructive pulmonary disease (7).

The correlation of silicosis and tuberculosis came into the spotlight in early 20<sup>th</sup> century (8). Silicosis patients are at 2.8 to 39 times greater risk of pulmonary tuberculosis in comparison to healthy subjects (6, 8-11). Additionally, risk of extrapulmonary tuberculosis in silicosis patients has reported to be 3.7 times higher than in healthy subjects (10). Recent findings have demonstrated that exposure to silica without developing silicosis may be a predisposing factor for TB (10, 11, 8). However, this correlation has yet to be definitely confirmed and is in need of further scrutiny (12).

Calvert et al. reported that risk of TB becomes greater by increased duration (hours) of exposure to silica and risk of TB in workers with the longest exposure was 4 times higher than in workers with the least exposure. Additionally, they noticed that workers developed TB averagely 7 years after discontinuation of silica exposure which indicates that these workers are at risk of TB even after discontinuation of exposure (6).

In a cross-sectional study TeWaterNaude et al. evaluated the effect of silica exposure in absence of silicosis on prevalence of pulmonary tuberculosis in 520 gold miners in South Africa. Their study results revealed a significant association between the increased prevalence of TB and duration of silica exposure (11).

The majority of previous studies on this subject could not definitely confirm a correlation between silica exposure and TB due to their small sample size and not discriminating the silicosis patients from healthy workers with history of silica exposure. Considering the high prevalence of TB in Iran and high prevalence of silica exposure among Iranian workers, the present study was designed to assess the association of silica exposure and TB.

## MATERIALS AND METHODS

This cross-sectional study was conducted in Lorestan Province in Iran in 2012. List of TB patients (1,200 cases) registered during 2006-2011 aged over 15 years was retrieved from the archives of Infectious Disease Control Center of the Health Deputy of Khoramabad City, Lorestan Province. By showing up at their residence, patients were personally interviewed and a checklist specifically designed for this purpose was filled out for them. Data regarding personal information, medical history and occupational experience of patients were collected. Also, individuals over 15 years of age presenting to the Health Centers of Lorestan Province suspicious for TB (which was ruled out) were entered the study as the control group. Due to not finding their place of residence or their lack of cooperation, number of our test group subjects was reduced to 871 individuals. In the control group (non-TB patients), we only had access to 2,011 medical records out of which, 429 were available for the interview. Diagnosis of TB was made according to the national protocol of the Ministry of Health. According to this protocol, three sputum samples were obtained from patients complaining of cough for two weeks or longer. Sputum culture was also carried out whenever required and the diagnosis of TB was made according to the test results.

All understudy subjects were evaluated in terms of exposure to silica and categorized into two groups of positive and negative silica exposure according to the Ministry of Health protocol and the results of previous studies (6). Furthermore, understudy subjects were

grouped in terms of their degree of exposure to silica according to the classifications observed in previous studies (classification of occupations based on level of exposure) into no exposure, mild exposure, moderate exposure and severe exposure groups (6). In this study, participants were divided into 32 occupational silica exposure groups: casting, agriculture, underground mining, concrete manufacturing industry, construction industry, cement work, sand and gravel production, stone carving, ferrosilicon company and mine, glass production, sandblasting, tunneling and brick making in the severe exposure group, construction work, stonemasonry, plasterwork, road construction, stone milling, stone mining, asphalt company, limestone, granite stone and stone mine driver in the moderate exposure group and concrete production, installation, repair and maintenance of railways, tiling, tessellation, tile and ceramic manufacturing industries, stone cutting, mosaic manufacturing and pottery in the mild exposure group (6).

In order to diagnose silicosis in patients with suspicious chest x-ray, medical and occupational histories were obtained and physical examination, paraclinical assessments and consultation with pulmonologist were carried out. In other words, for subjects with silica exposure, a checklist specifically designed by the Ministry of Health for diagnosis of silicosis was filled out and the diagnostic workup was performed. Based on the test results and chest x-ray findings, 180 subjects with silica exposure were screened for possible silicosis. Following consultation with a pulmonologist and occupational medicine specialist and conduction of HRCT if required, 35 patients were specified with possible silicosis.

In descriptive analysis, mean, SD and range were employed for describing quantitative variables. Qualitative variables were reported as percentage and frequency. For comparison of quantitative variables between the two groups, independent t-test and for qualitative variables chi square test were applied.  $P < 0.05$  was considered statistically significant. Logistic regression analysis was

used in order to control for confounding factors and assess the correlation of silica exposure with TB. Also, Odds ratio (OR) with 95% confidence interval (95%CI) was applied to evaluate the effect of silica exposure and different factors on development of TB. Data were analyzed using SPSS version 11 software.

## RESULTS

In this study, of 871 TB patients, 484 (55.6%) were males and 387 (44.4%) were females. The mean age of patients was 41.89 years (range 15-65 yrs.). Of male patients, 177 (36.6%) had negative and 307 (63.4%) had positive silica exposure. Of females, 241 (62.3%) had negative and 146 (37.7%) had positive occupational exposure to silica. The difference in this respect was statistically significant ( $P < 0.001$ ).

Table 1 compares the demographic variables and frequency of silica exposure in the two groups of TB and non-TB patients. As observed, the two groups were not significantly different in terms of demographic factors (age, work experience, cigarette smoking, etc.) ( $P > 0.05$ ). However, comparison of the frequency of silica exposure between the two groups revealed that frequency of exposure to silica was significantly higher in TB patients compared to controls ( $P < 0.001$ , OR:3.39, 95%CI:2.63-4.36). This comparison between males in the two groups yielded a greater significant difference ( $P < 0.001$ , OR:4.4, 95%CI: 3.22-6.12).

Also, comparison of TB frequency in patients with possible silicosis, non-silicosis patients with positive silica exposure and subjects with no exposure to silica demonstrated that TB frequency was significantly higher in the first two groups compared to those with no silica exposure ( $P < 0.05$ ) (Table 2). The correlation between frequency of TB and history of silica exposure is demonstrated in Table 3. As observed, subjects with over 15 years of silica exposure had a significantly higher frequency of TB compared to non-exposure group ( $P < 0.05$ ). However, the difference in this regard between workers with less than 15 years of exposure and the non-exposure group was not statistically significant ( $P > 0.05$ ).

Table 4 compares the frequency of TB based on the intensity of exposure. As noted, frequency of TB was significantly greater in subjects with moderate or severe exposure to silica compared to non-exposure group ( $P<0.001$ ). However, the difference between the mild exposure and non-exposure groups was not statistically significant ( $P>0.05$ ).

The results of logistic regression analysis (Table 5) demonstrated that after adjusting for confounding factors, a significant association was found between moderate and severe silica exposure and TB frequency. Significant relationships were also detected between age, work experience, level of education, male gender and cigarette smoking with TB frequency ( $P<0.05$ ).

Table 1. Comparison of demographic variables and frequency of silica exposure between TB patients and non-TB subjects.

Variable	TB patients (n=871)	Non-TB subjects (n=429)	Level of significance
Age (yrs.)(mean)	41.80	39.74	>0.05
Level of education (yrs.)(mean)	11.12	11.03	>0.05
Work experience(yrs.)(mean)	14.16	14.19	>0.05
Male gender (number, percentage)	484 (55.56)	241(56.17)	>0.05
Cigarette smoking (number, percentage)	198(22.70)	95(22.10)	>0.05
History of silica exposure (number, percentage)	453(52.00)	107(24.94)	<0.001

Table 2. Frequency of TB based on silica exposure and probable silicosis.

Study groups	TB		Odds ratio	95% CI	Level of significance
	Yes	No			
No silica exposure	418	322	-----	-----	-----
Silica exposure only	422	103	2.85	1.13-3.42	0.027
Probable silicosis	31	4	4.08	2.44-5.85	0.001>

Table 3. Frequency of TB based on the history of silica exposure.

History of silica exposure (yrs.)	TB		Odds ratio	95% CI	Level of significance
	Yes	No			
No exposure	418	322	---	---	---
15 ≥	148	54	2.35	0.95-4.35	0.058
15<	305	53	4.46	2.31-7.01	0.001>

Table 4. Frequency of TB based on the intensity of silica exposure.

Intensity of silica exposure	TB		Odds ratio	95% CI	Level of significance
	Yes	No			
No exposure	418	322	---	---	---
Mild	235	64	2.18	0.85-3.26	0.061
Moderate	159	35	3.15	1.31-5.37	0.035
Severe	59	8	4.35	2.13-6.15	0.001<

**Table 5.** The correlation of silica exposure with frequency of TB using logistic regression analysis.

Variable	Status	Odds ratio	95% CI	Level of significance
Age (yrs.)	≤ 40	1	-----	----
	>40	2.73	1.12-4.15	0.038
Gender	Female	1	-----	-----
	Male	2.66	1.14-4.06	0.041
Cigarette smoking (Pack/year)	Non-smoker	1	-----	----
	≤ 5	2.97	1.36-4.72	0.027
	>5	3.25	1.42-5.09	0.011
Level of education	Over elementary	1	-----	----
	Elementary, illiterate	2.53	1.09-3.99	0.047
History of silica exposure (yrs.)	No exposure	1	-----	-----
	≤ 15	2.14	0.85-3.87	0.057
	>15	3.01	1.40-5.02	0.015
Intensity of silica exposure	No exposure	1	-----	-----
	Mild	1.84	0.56-3.20	0.066
	Moderate	2.63	1.11-5.01	0.045
	Severe	3.44	2.02-6.13	0.001>

## DISCUSSION

TB is among the most prevalent public health dilemmas of the 21<sup>st</sup> century (13). Despite the vast efforts made for control and eradication of this disease, TB control programs have not been very successful in communities with high exposure to silica, and TB-related morbidity and mortality are increasing in such areas (6). The present study evaluated silica exposure in TB patients. In our study, frequency of TB in the silica exposure group was 3 times higher than the rate in non-exposure group. Also, after adjusting for confounding factors, a significant association was found between the intensity of silica exposure and TB frequency. The results of similar studies also confirm the higher risk of TB in patients with silica exposure (2, 6, 14). Furthermore, some studies indicated an association between TB frequency and concentration of silica (8, 15).

In the current study, frequency of TB was significantly higher in subjects with more than 15 years of silica

exposure compared to the non-exposure group ( $P < 0.05$ ). But, no such correlation was noted in workers with less than 15 years of exposure ( $P > 0.05$ ). In a study by Chopra et al. 30% of TB patients had 16 to 20 years of silica exposure history; 65% of patients mentioned over 10 years of silica exposure (15).

In the present study, frequency of TB was 3 to 4 times greater in subjects with moderate or severe silica exposure in comparison to non-exposure group. This increase was statistically meaningful ( $P < 0.05$ ). In a study by Rosenman and Hall conducted in New Jersey, USA, occupational risk factors responsible for TB progression were discussed. Exposure to silica was among the most important risk factors in this regard (OR:3.96, 95%CI:0.34-44.02)(16). In a prospective study in Brazil it was revealed that risk of progression of pulmonary tuberculosis depended on the severity of silicosis. Workers with severe silica exposure developed TB 3.22 times more than those with the lowest exposure (17).

In our study, the frequency of TB was significantly higher in subjects over 40 years of age compared to those below the age of 40 ( $P < 0.05$ ). In another study in Hong Kong, it was reported that by advanced age in silica-exposed subjects, the frequency of pulmonary TB in them increased (18). Also, in a study by Chopra et al, in Rajasthan in India, 93% of TB patients were in the age range of 21 to 55 years; among which, the majority were 46-50 years of age (15).

In the current study, more than 90% of TB patients did not have university education and 34% were illiterate. Also, frequency of TB in subjects with maximum educational level of elementary school was significantly higher than in subjects with higher educational levels ( $P < 0.05$ ).

A study conducted in the United States demonstrated that TB patients with higher education had lower prevalence of silica-related TB than those with lower educational levels. Also, silica exposure was significantly more prevalent among those with lower educational levels and illiterate subjects had 68% silica exposure while this rate was 37% in those with high school education (16).

In our study, 75% of patients were non-smokers but silica exposure was significantly correlated with cigarette smoking and frequency of TB in smokers was significantly higher than in non-smokers ( $P < 0.05$ ). By increasing the rate of cigarette consumption to more than 5 packs/year, frequency of TB further increased.

In our study, frequency of TB was 4.08 and 2.85 times higher in patients with probable silicosis and silica-exposed subjects without silicosis, respectively (compared to the non-exposure group). This difference was statistically significant ( $P < 0.05$ ). Other studies also show very high frequency of TB in silica-exposed workers without silicosis (10, 19). Furthermore, Barboza et al. in their review study recommended isoniazid prophylaxis for silicosis patients and those with more than 10 years of silica exposure with tuberculin skin test of greater than 10 mm (20).

Reduced exposure to silica has a marked effect on TB control. Silica exposure can increase the risk of TB even in absence of silicosis (8, 11). Some researchers believe that reduced occupational exposure to silica particles is effective for reducing TB incidence (21, 22). Also, decontamination of work environment from silica particles can significantly reduce number of TB cases. This method can be employed as a TB control strategy especially in communities with high prevalence of TB and silica exposure (23).

The present study was among the most extensive researches on the occupations of TB patients in Iran and is the only one evaluating the correlation of TB and silica exposure in our country. However, it was a cross-sectional study; which has limitations for confirming a cause and effect relationship. Furthermore, we did not quantitatively measure silica exposure which further limited the estimation of occupational exposure.

## CONCLUSION

The present study results demonstrated that occupational silica exposure was common among TB patients and frequency of TB increased by increased intensity of silica exposure, advanced age, higher work experience, lower educational level, male gender and cigarette smoking. Provided that our study results are confirmed by prospective studies, TB screening is recommended among silica-exposed workers especially those with higher work experience.

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