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Prevalence of concomitant pulmonary tuberculosis in patients with newly diagnosed silicosis in a tertiary care center in South India

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ABSTRACT

Background: Long-term exposure to silica dust makes people prone for silicosis which raises the risk of the individual in developing pulmonary tuberculosis (PTB). Silicosis is a progressive lung disease characterize with shortness of breath, cough, fever, and bluish skin, caused due to inhalation of crystalline silica dust found in abundance in sand, rock, and quartz. **Aims and Objectives:** The disease is known to effect the functioning of macrophages making it unable to defend mycobacterium species, thus allowing the bacterium to invade and develop tuberculosis. **Materials and Methods:** A retrospective cross-sectional study is carried out to estimate the prevalence of PTB in newly diagnosed silicosis patients at Madurai Medical College, Madurai, Tamil Nadu. All the patients who got registered in Occupational Lung Diseases Registry from January 2016 to December 2021 are included in the study. Silicosis patients tested positive on sputum CBNAAT are considered as silicotubercular patients, whose prevalence is calculated. **Results:** Our study included a total of 54 subjects (90.8% males and 8.2% female) with mean SD age of 38 ± 6.7 years ranging from 26 to 53 years. Of which 22 patients, 40.7% tested positive for *Mycobacterium tuberculosis* (MTB) on sputum CBNAAT. The prevalence of MTB in among silicosis patients was found to be 40.7%. **Conclusions:** Association of TB and silicosis is very strong with the prevalence of TB among silicosis patients as 40.7%. Our study also observed the male sex and elder age as elevated risk of developing silicotuberculosis. All the people getting exposed to silica dust need to be educated in the usage and usefulness of protective equipment.

Key words: Silicosis; Silicotuberculosis; *Mycobacterium tuberculosis*; Lung diseases; Prevalence

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INTRODUCTION

Silicosis is an occupational lung disease caused due to repetitive, long-term exposure to crystalline silica dust which is found in abundance in sand, rock, and quartz. It is a progressive lung disease characterized with dyspnea, cough, fever, and bluish skin.[1] The disease is commonly seen in people working in coal mining, glass manufacturing, building construction, brick manufacturing, road repairs, concrete manufacturing, etc., and is presented after weeks to months to years after exposure.[2] Silica (SiO_2/silicon dioxide) exists in 2 forms, namely, amorphous and crystalline forms. The amorphous form of the silica inhalation do not cause any health illness, but is caused on inhalation of crystalline form.[2] Silicosis is a progressive lung disease characterized with fibroblast infiltrations in a nodular pattern due to release of inflammatory cytokines and apoptosis of parenchymal cells and macrophages.

On inhalation of crystalline silica, it deposits in the alveoli and terminal bronchiole which activates alveolar macrophages and results in cellular damage and release of inflammatory cytokines, along with generation of free radicles. The release of inflammatory cytokines results in promotion of fibrosis.

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This leads to radiological nodular opacities in lung filed.[3,4] It is known that the silica can influence the capability of macrophages in defended mycobacterium species, leading to its invasion and developing tuberculosis (TB).[5]

Patients with silicosis have an increased risk of developing TB with a relative risk of 2.8 in men with silicosis than in men without silicosis.[6] There is a life-long risk even if the exposure to silica is ceased. Due to this elevated risk of TB in patients with silicosis, WHO has made few guidelines in screening the patients with silicosis. According to the WHO guidelines, silicosis patients are to screen with interferon gamma release assay or tuberculin skin test in case of latent pulmonary TB (PTB). The association of TB and silicosis is very high in countries with poor safety/control measures.[7]

As per the reports of ICMR (Indian Council of Medical Research) in 1999, approximately 3.0 million workers are at high risk of silica exposure which is more prevalent among states such as Gujarat, Rajasthan, Pondicherry, Haryana, UP, Bihar, Chhattisgarh, Jharkhand, Orrisa, and West Bengal. Silicosis prevalence in India was found to be as less as 3.5% in ordnance factory to as high as 54.6% in slate pencil industry.[1] The present study aims at estimating the prevalence of TB among newly diagnosed silicosis patient in a tertiary care center in South India through a retrospective cross-sectional study.

Aims and objectives

The primary objectives of this study were to estimate the prevalence of TB in newly diagnosed silicosis patients in a tertiary care hospital in South India. The secondary objectives of this study were to analyze the association of comorbidities (Diabetes and hypertension) and TB in newly diagnosed silicosis.

MATERIALS AND METHODS

A retrospective cross-sectional study is conducted at Madurai Medical College, Madurai, Tamil Nadu, to estimate the prevalence of TB in newly diagnosed silicosis patients.

Ethical consideration

The study was approved by the Institutional Human Ethics Committee and Institutional Review Board. Data confidentiality was maintained.

Selection of subjects

All the patients who got registered in Occupational Lung Diseases Registry from January 2016 to December 2021 are the study population.

Inclusive criteria

The following criteria were included in the study:

1. Newly diagnosed silicosis patients registered in occupational lung diseases register during the study period
2. Patients of any sex and age group.

Exclusion criteria

The following criteria were excluded from the study:

1. Patients with previous history of PTB
2. Patients diagnosed with silicosis earlier and under follow-up.

Sampling technique

All the silicosis patients registered in the occupational lung diseases register from January 2016 to December 2021 at Madurai Medical College, Madurai, Tamil Nadu, were directly recruited in the study.

Methodology

Occupational lung diseases register of the Department of Respiratory Medicine, Madurai Medical College was reviewed from January 2016 to December 2021 and study population is pooled.

The diagnosis of silicosis was based on the occupational exposure history, clinical presentation, and radiological diagnosis. All silicosis patients were screened for TB at their first visit with sputum CBNAAT as per institution protocol. The results of same were used to group the population into *Mycobacterium TB* (MTB) detected and not detected.

Statistical analysis

Computed tomography (CT) chest findings and Sputum CBNAT report were considered as primary outcome, where the occupational exposure/year, years of exposure, comorbidities etc., were considered as explanatory variables. Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency, and proportion for categorical variables. Categorical outcomes were compared between study groups using Chi-square test. $P<0.05$ was considered statistically significant. Data were analyzed using SPSS software, V.22.[8]

RESULTS

The study included a total of 54 subjects, of which 90.8% (49) were male and 9.2% (5) were female with mean±SD age of 38±6.7 years ranging from 26 to 53 years. Majority of the population 63% (34) was with age >35 years and only 37% (20) patients are with age <35 years.

Of 54 patients, 38.9% (21) patients had an occupation of quarry working followed by 18.5% (10) patients that had occupation of bore well digging and tile working. About 11.1% (6) population had occupation of tooth powder factory working, 7.4% (4) patients had road laying,

3.7% (2) had glass factory working, and the least 1.85% (1) had occupation of ceramic factory. Table 1 provides information on the number and percentage population with different occupations.

CT chest findings of the silicosis patients showed various radiological features such as mediastinal calcification, cavities, diffuse nodules, focal nodules, progressive massive fibrosis (PMF) pleural thickening, and pneumothorax. Mostly observed radiological feature was mediastinal calcification in 83.3% patients, followed by cavities and diffuse nodules in 48.1% and 37.0%, respectively. Equal percentage of patients (33.3%) showed focal nodules and PMF. Pneumothorax is the radiological feature seen in a lowest patient of only 1%. Table 2 provides the details of various radiological features seen in silicosis patients of our study.

Among 54 silicosis patients in the study, 40.7% (22) patients tested positive for MTB on sputum CBNAAT and 59.3% (32) patients tested negative. The prevalence of MTB in silicosis patients is calculated as,

Prevalence of MTB cases

$$\frac{Number\ of\ cases\ positive\ for\ MTB}{Overall\ cases\ of\ silicosis} = \frac{22}{54}$$

Prevalence of MTB = 40.7%

Various radiological features observed in the silicosis patients were compared between the patients detected with MTB on sputum CBNAAT and with those not detected with MTB. Significant different is tested statistically using Chi-square test and corresponding p-values are calculated and presented in Table 3. None of the radiological feature showed significant difference ($P>0.05$) between the patients tested positive and negative except for the cavities ($P<0.05$). All the radiological features seen in silicosis patients have an equal chance of observing in both the patients with concomitant MTB and without MTB. None of the radiological feature can be identified as specific for silicosis with MTB.

Table 1: Number and percentage population of silicosis with different occupations

Occupational exposure/Years		
Quarry worker	21	38.89%
Bore well digging	10	18.52%
Tile work	10	18.52%
Tooth powder factory	6	11.11%
Road laying	4	7.41%
Glass factory	2	3.70%
Ceramic factory	1	1.85%

Table 2: Various radiological features seen in CT chest of silicosis patients

CT chest findings	Frequency	Percentage
Mediastinal calcification	45	83.33
Cavities	26	48.10
Diffuse nodules	20	37.00
Focal nodules	18	33.33
PMF	18	33.33
Pleural thickening	9	16.70
Pneumothorax	1	1.90

PMF: Progressive massive fibrosis, CT: Computed tomography

The mean±SD of duration of exposure to the silica was found to be 5.31±1.98 years with range of 1 year–8 years. The duration of exposure and the probability of developing MTB in silicosis patients are tested statistically by grouping the years of exposure as 1–3 years, 4–6 years, and 7–10 years and calculating P-values Chi-square test. P-value reported no significant difference in the number of patients developing MTB and not developing MTB across the various duration of exposures. Within the patients developed MTB, majority of patients (53.85%) were exposed to silica for about 1–3 years. Table 4 provides number and percentage of patients detected with MTB on sputum CBNAAT in various duration of exposures.

Among 54 patients, nine patients were diabetic mellitus (DM), six were hypertensive (HTN), and five were both diabetic and HTN. Among the nine DM patients, six patients (66.67%) had developed PTB along with one in each of HTN and DM/HTN patients. There was no statistically significant difference seen across comorbidities and CBNAAT positive with p-value 0.18 as tested Chi-square test.

Table 5 provides a glance on the number and percentage of patients with comorbidities and CBNAAT-tested positive and negative.

DISCUSSION

Our study objective was to estimate the prevalence of concomitant TB with silicosis which is found to be 40.7%. The results of our study are in great understanding with the exiting literature. The only limitation of the study is being retrospective, the patients tested negative for MTB on sputum CBNAAT are not followed up to check for any progression in the radiological features to suspect TB.

A systemic review and meta-analysis on association of silicosis and TB carried out by Ehrlich et al.,[9] concluded that an elevated risk of TB was found with radiological silicosis with low disease severity. The same study also

Table 3: Different radiological features seen in patients detected with and without MTB in silicosis patients with corresponding Chi-square and P-values

CT findings	Sputum CBNAAT		Chi-square	P-value
	MTB detected/R-S (n=22) (%)	MTB not detected (n=32) (%)		
Diffuse nodules	9 (40.91)	11 (34.38)	0.239	0.625
Focal nodules	6 (27.27)	12 (37.5)	0.614	0.433
PMF	7 (31.82)	11 (34.38)	0.038	0.845
Mediastinal calcification	19 (86.36)	26 (81.25)	0.245	0.723
Cavities	15 (68.18)	11 (34.38)	5.968	0.015
Pneumothorax	0 (0)	1 (3.13)		*
Pleural thickening	3 (13.64)	6 (18.75)	0.245	0.723

*No statistical test was applied- due to o subjects in the cells, PMF: Progressive massive fibrosis, MTB: *Mycobacterium tuberculosis*

Table 4: Number and percentage of patients detected with MTB on sputum CBNAAT in various duration of exposures

Sputum CBNAAT	Years of exposure			P-value
	1–3 years (n=13) (%)	4–6 years (n=24) (%)	7–10 years (n=17) (%)	
MTB detected/R-S	7 (53.85)	11 (45.83)	4 (23.53)	0.195
Negative	6 (46.15)	13 (54.17)	13 (76.47)	

MTB: *Mycobacterium tuberculosis*

Table 5: Comorbidities seen in patients detected with and without MTB

Comorbidities with sputum CBNAAT	Sputum CBNAAT		Chi-square	P-value
	MTB Detected/ R-S (%)	MTB not detected (%)		
DM (n=9)	6 (66.67)	3 (33.33)	4.840	0.184
HTN (n=6)	1 (16.67)	5 (83.33)		
HTN/DM (n=5)	1 (20)	4 (80)		
None (n=34)	14 (41.18)	20 (58.82)		

HTN: Hypertensive, MTB: *Mycobacterium tuberculosis*

concluded that an uncertain effect estimate was found between silicosis without radiological features and TB.

Diagnosis of concomitant TB with silicosis is quite difficult, specifically in initial phase of the disease, where the clinical and radiological findings can misguide to pre-existing silicosis. However, radiological findings of new opacities and pleural effusion in silicosis patients can be suspected for TB.[10] To be specific, progression in nodular profusions or size and changes in distinct patterns may be an indication of concomitant TB.[11] Even in the absence of TB bacilli in the sputum, radiological presentation can be considered for diagnosing TB.[12] In our study, identification of MTB bacilli in sputum is considered as confirmation since the radiological presentation of silicosis patients are not followed to check the progression of the radiological features to confirm the same. Even more, since our study is of retrospective and the data were obtained from the registry the data pertaining to the follow-up of patients was not available, the limitation of the study. The same could be considered as the limitation in identification of concomitant TB in silicosis patients in lower-middle and lower-income countries.

A cohort study conducted in south African gold miners by Hnizdo and Murray[13] reported that an average of 7.6 years is observed for developing PTB after exposure to silica dust is ceased and about 90.2% of PTB+silicosis patients had silicosis preceding to PTB making silicosis as a risk factor for PTB. A cross-sectional study conducted on the similar community by teWaternaude et al., reported older in-service miners with a high prevalence PTB and an strong association of exposure to dust or silica increased the risk of TB even in the absence of silicosis.[13,14]

There are several case reports published that reported silicosis with active/relapsed TB. Among all, Milovanovic et al., reported two males patients of age 52 years and 50 years who had a history of exposure to silica dust for 20 years and 10 years, respectively, and 1 patient died due to respiratory failure and chronic respiratory heart and the other patient was alive at the time of reporting/publishing. Both the patients presented diffuse lung fibrosis, small nodular opacities, and homogenous calcifications noted predominantly in the upper and middle lobes.[15] The other case study published by Mulliez et al.,[16] reported 65-year-old male patient with silicotuberculosis developed broncholithiasis. A case of silicotuberculosis in a 76-year-old woman who has exposure of 3 years to silica dust was complicated by broncholithiasis and oesophagobronchial fistula and relapsed TB even on 9 months of anti-TB treatment.[17] It is noted that most of the cases are reported from lower- and lower-middle income countries, reason, no

required safety measures are deployed for the workers and lack of knowledge and no regular screening of the people exposed to the silica dust.

Most of the existing literature suggests that male sex and the age of 25–54 years are the greater risks of developing silicosis/silicotuberculosis.[10,13,14] The same is also observed in our study.

An epidemiological study conducted by Chen et al., to estimate the risk of silicosis by various occupation related exposure to silica dust reported workers working in the tin mine workers have higher risk followed by tungsten mine workers and pottery workers. However, the study has limitations in that it included only three workplaces, namely, tin, tungsten, and pottery workers and the characteristics of silica dust are not the same in the considered workplaces, affecting the results.[18] Normalizing this limitation, study conducted by Harrison et al., concluded that per unit cumulative respirable exposure of silica dust pottery workers is found to be at higher risk, followed by tin and tungsten mine workers. However, even this study has the limitation of considering only three workplaces.[19] Another study conducted to estimate the risk of gold mine workers developing silicosis by Tse et al., reported that 29.1% population presented with accelerated silicosis, in which the population has far exceeding limits of acceptable exposure to the silica dust. One of the limitations of this study alongside with only the male population being included and only gold mine workers being included in the study.[20] In contrast, our study has included diverse population, in which population from seven different workplaces were presented with silicosis. Amongst all, as described in the Table 1, Quary dwelling workers are presented the most followed by bore well workers.

Radiological features as seen in case series published by Dee P et al., it can be inferred that the radiological presentations in acute silicosis may differ from classical and chronic silicosis.[21] In acute silicosis multiple patchy ground glass opacities, multiple bilateral centrilobular opacities and consolidations are seen. In contrast, multiple small nodules with calcifications that are diffusely distributed through upper lobe involving posterior region along with perilymphatic distribution of nodules are seen in classical form and focal soft tissue masses with irregular margins, calcifications are seen in upper lobes but in both apical and posterior regions in complicated/chronic silicosis.[22] The similar radiological findings were also reported in a study conducted by Antao et al., in which only stone carvers were evaluated, limitation of the study and also in study conducted by Bégin et al.[23,24] However, as described in Table 2, majority of our study population presented with mediastinal calcifications followed by cavities and diffuse nodules instead of centrilobular opacities and calcifications distributed predominantly in posterior or apical regions of upper lobe as seen in existing literature.

Limitations of the study

Our study has certain limitations like it is retrospective, cross-sectional in design, single center study, the study population being represented by only a few surrounding districts and hence could not give the picture of a large geographical area.

CONCLUSIONS

Our study concludes that association of TB and silicosis is very strong with prevalence of TB among silicosis patients as 40.7%. With our results, we strongly recommend that population getting exposed to silica dust need to be educated in the usage and usefulness of protective equipment.

Our study observed that DM is more seen in patients with silicotuberculosis. However, no statistical significance is seen among all the comorbidities as seen between both the groups, namely, MTB detected and not detected. Our study also observed the male sex and elder age as elevated risk of developing silicotuberculosis. However, no statistically significant difference is seen between the population developing silicotuberculosis and duration of exposure to the silica dust.

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Authors Contribution:
SR- Has conceptualized the study and played primary role in compiling, analysis and interpretation of the data. All the drafts were prepared, reviewed and final draft was approved by **NM, SR, KMA**; **NM, SR, KM**- Have contributed in fine tuning of the proposal, contributed in data collection and entry. Reviewed the results and contributed to preparation and review of drafts. All the authors have read and approved final version of the manuscript. All the authors take complete responsibility for the content of the manuscript.

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