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REVIEW

Silicosis and tuberculosis: A systematic review and meta-analysis

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KEYWORDS Abstract Introduction: Silicosis mostly happens in workers with high silica exposure and may accompany Silicosis: Tuberculosis: the development of various diseases like tuberculosis, cancer, or autoimmune diseases. The term silico-tuberculosis describes a condition in which an individual is affected by both silicosis Systematic review and tuberculosis at the same time. This systematic review and meta-analysis study was conducted to evaluate the risk of tuberculosis in silicosis patients and individuals exposed to silica dust Methods: We performed a systematic search for relevant studies up to 6 September 2022 using PubMed/ Medline, and Embase with the following keywords in titles or abstracts: "silicosis" OR "silicoses" OR "pneumoconiosis" OR "pneumoconioses" AND "tuberculosis". Cohort and casecontrol studies containing relevant and original information about tuberculosis infection in silicosis patients were included for further analysis. Pooled estimates and 95% confidence intervals (CI) for the relative risk of tuberculosis in individuals with silicosis compared to those without;

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these were evaluated using the random effects model due to the estimated heterogeneity of the true effect sizes.

Results: Out of 5352 potentially relevant articles, 7 studies were eligible for systematic review, of which 4 cohort studies were included for meta-analysis. The total population of all studies was 5884, and 90.63% were male. The mean age of participants was 47.7 years. Our meta-analysis revealed a pooled risk ratio of 1.35 (95%CI 1.18-1.53, I ²: 94.30%) which means an increased risk of silicosis patients and silica-exposed individuals to tuberculosis infection.

Conclusion: Silicosis and silica dust exposure increase the risk of tuberculosis. Therefore, we suggest that individuals with long-time silica exposure, like mine workers, be routinely considered for both silicosis and tuberculosis screening programs.

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Introduction

Silicosis is an occupational lung disease caused by chronic exposure to silica dust, mainly composed of quartz dust, a human carcinogen.¹ Silicosis is caused by the deposition of silica particles in the lower respiratory tract leading to chronic inflammation, collagen deposition, and fibrotic lesions, which may vary from subclinical pathological changes to severe lung tissue damage and reduce life expectancy.^{2,3} Although silicosis may be fatal and irreversible, it can be prevented. ⁴ It mainly affects industrial workers with prolonged and intensive exposure, such as coal miners,² and it is prevalent in low-income countries with annual global mortality higher than 10,000 people.⁵ Although its notification rate is high, several cases are not diagnosed.⁶

There is not a specific diagnostic test for silicosis, however, occupational history and chest radiological abnormalities (i.e., nodular opacity) can confirm the diagnosis.⁷

Silicotuberculosis is a condition characterized by the coexistence of silicosis and tuberculosis (TB). The incidence of tuberculosis in patients with silicosis is 21.8 times higher than that recorded in the general population.⁸ The most important risk factors for developing silicotuberculosis are: exposure to crystalline silica and sandblasting and its duration, age (>30 years), being male, HIV positive, smoking, chronic obstructive pulmonary disease, being migrant from endemic countries, and silicosis severity. ⁹

High silica impairs the activity of alveolar macrophages, leading to apoptosis and susceptibility to mycobacterial infection.9-13 After inhalation of silica particles, they enter the alveolar space and interact with macrophages, and then, they sink into the phagosome. A macrophage receptor with a collagenous structure (MARCO), is a Class A protein scavenger receptor on the surface of macrophages that intercedes binding and ingestion of unopsonized environmental particles such as TiO2, Fe₂O₃, silica, and other nanosized substrates. MARCO has been described as the main molecule responsible for the recognition and uptake of silica and there will be no particle uptake or cell death in the absence of this recepeptor. $^{\rm 14,15}$ Some pattern recognition receptors, such as Toll-like receptors (TLRs), play an essential role in responding to bacterial infections. Significant downregulation of TLR2 following silica exposure may contribute to higher TB susceptibility.¹⁶ Genetic polymorphisms of tumor necrosis factor-alpha (TNF- α), natural resistanceassociated macrophage protein 1, and inducible nitric oxide synthase (iNOS) of macrophages were shown to affect the response to exposure to silica. $^{17,18}\,$

This systematic review and meta-analysis study was conducted to evaluate the risk of tuberculosis in silicotic patients and individuals exposed to silica dust.

Methods

This review conforms to the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) statement (PROSPERO pending ID: 388636).¹⁹ Also, the PRISMA 2020 item checklist is available in supplementary 1.

Search strategy

We searched Pubmed/Medline, and Embase, for studies reporting the association between silicosis and pulmonary TB published up to 6 September 2022. There was no specific limitation for the starting date of search. The following search strategy was used: ("silicosis"[MeSH Terms] OR ("silicosis"[Title/Abstract] OR "silicoses"[Title/Abstract] OR "pneumoconiosis"[Title/Abstract] OR "pneumoconioses"[Title/Abstract]) OR "pneumoconiosis"[MeSH Terms]) AND ("tuberculosis"[MeSH Terms] OR "tuberculosis"[Title/ Abstract]).

Study selection

The records found through database searching were merged, and the duplicates were removed using EndNote X8 (Thomson Reuters, New York, NY, USA). Two reviewers (MA and BM) independently conducted title and abstract screening to exclude irrelevant studies. Two other reviewers (MA and BM) retrieved and assessed the full text of potentially eligible records. Inclusion criteria were: populations exposed to silica and silicosis patients; studies reporting comparative effect estimates, specifically case-control or cohort studies reporting relative risks or odds ratios across groups with and without silicosis (including different grades). Only Englishmedium papers were considered.

Studies without comparison between those with and without the disease, studies focused on latent TB infection, cross-sectional and mortality studies, and autopsy-based studies were excluded. Review articles, duplicate publications, conference abstracts, editorials, postmortem studies,

and those in which the full text of papers was not found were also excluded.

Data extraction

The data extraction form was designed by PJ and the following data were extracted by BD, BM, MA, and FK: first author's name, type of study, year of publication, study period, the country/ies where the study was performed, study population, age, gender, occupation, mentioned confounding factors, diagnostic approach for silicosis and tuberculosis, duration and grade of silicosis, follow-up duration and technique, the estimated effect measures of silicosis and TB, and the total number of following items: TB population, silicosis population, TB population with and without silicosis, silicosis without TB, and the total number of non-silicosis individuals.

Quality assessment

The Newcastle-Ottawa Scale (NOS) for observational studies was used to perform a study quality assessment.²⁰ The NOS scale assesses the risk of bias in observational studies with three domains: 1) selection of participants, 2) comparability, and 3) outcomes. A study could be given a maximum of one point for each numbered item within the selection and outcome areas, and a maximum of two points allocated for

comparability. The low, moderate, and high-quality studies were given scores of 0-3, 4-6, and 7-9, respectively.

Data synthesis and analysis

Statistical analyses were conducted using Comprehensive Meta-Analysis software, version 2.0 (Biostat Inc., Englewood, NJ, USA). Pooled estimates and 95% confidence intervals (CI) for the relative risk of TB in silicosis individuals compared to those without silicosis ones were evaluated using the random effects model due to the estimated heterogeneity of the true effect sizes. The between-study heterogeneity was assessed by Cochran's Q and the I2 statistic. Publication bias was evaluated using Begg's tests (P < 0.05 was indicative of a publication bias) and forest plot.

Results

The primary search identified a total of 5,352 potentially relevant publications. Removing 1,604 duplicates, 3,748 records were screened, and 172 full-text articles were further assessed for eligibility. Finally, 7 studies met the inclusion criteria and were selected for qualitative analysis, $^{21-27}$ of which 4 cohort studies $^{21-24}$ were included for further meta-analysis (Fig. 1).

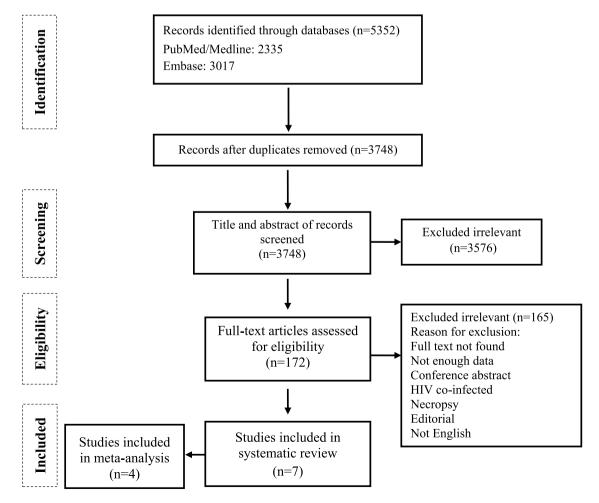


Fig. 1 PRISMA Flow chart of study selection for inclusion in the systematic review and meta-analysis.

Table 1	Quality as.	sessment of the coho	ort studies inclu	uded in the meta-an	Table 1 Quality assessment of the cohort studies included in the meta-analysis (The NOS tool) ²⁰	20					
Author			Sel	Selection		Comparability	bility	Outcome			Total
	_ 2	Representativeness of Exposed Cohort	Selection of non- exposed Cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at the start of the study	Adjust for the most important risk factors	Adjust for other risk factors	Assessment of outcome	Follow-up length	Loss to follow-up rate	quality score
Westerholm et al. ²⁴	E	0	0	-	-	-	0	£	t	+	6
Cowie et al. ²¹	21	-	+	-	-	-	0	1	1	-	8
Ross et al. ²³	e 9	-	-	-	-	-	-	-	-	-	6
Meel et al. ²²	22	-	-	-	0	-	0	-	-	-	7
NOS: The N	Newcastle-C	NOS: The Newcastle-Ottawa Scale									

Quality of included studies

Based on the Newcastle-Ottawa Scale (NOS), which was used to assess the quality of the cohort studies, the mean (standard deviation [SD]) NOS score was 7.5 (1.29), which is suggestive of a high methodological quality and a low risk of bias of the included studies (Table 1).

Characteristics of the included studies and populations

Five articles described cohort studies^{21,23-25,28} and two casecontrol studies.^{26,27} Publication dates ranged from 1984 to 2013. Most of the studies were conducted in South Africa (n= 4, 57.14%),^{21-23,26} one (14.28%) in Sweden,²⁴ one (14.28%) in Hong Kong, ²⁵ and one (14.28%) in Iran.²⁷ The total population was 5,884 persons. The male gender was dominant (n=5,333, 90.63%), and the mean age was 47.70 years (Table 2 and Table 3).

The diagnosis of silicosis was mainly based on chest X-ray findings; however, occupational history and physical examination were helpful. The most prevalent methods for tuber-culosis diagnosis were sputum smear microscopy and culture (Table 2).

The follow-up duration reported in articles ranged from 3 to 20 years. The most common follow-up techniques were clinical evaluation, radiologic imaging, sputum examination, pulmonary function tests, and questionnaires (Table 2).

All studied populations were silicosis-confirmed patients, except one study,²⁷ which stratified the population into silicosis and silica-exposed individuals without silicosis.

Disease severity classification was based on the level of exposure to silica²⁷ and X-ray images were classified according to International Labor Organization (ILO) standards^{21,22,26} (Table 3).

All studies established the substantial effect of silicosis on tuberculosis development, with the estimated effect measures ranging from 1.86 to $8.6^{23,25}$ (Table 3).

Several confounding factors were mentioned in our reviewed studies, including occupation, age, gender, height, HIV, smoking, duration of employment as an indicator for the time of silicosis or silica exposure, the severity of silicosis, co-existence of other pulmonary diseases, progressive massive fibrosis, baseline lung function, using anti-TB medications before silicosis diagnosis, and level of education (Table 3).

Since no data for confounding factors were available, we could not perform any stratification analysis.

One study evaluated tuberculosis risk factors in a silicosis cohort in Hong Kong and identified four TB risk factors as follows: no anti-tuberculosis treatment before the date of silicosis diagnosis (RR 4.51, 95%CI 2.46–8.24), progressive massive fibrosis (RR 3.78, 95%CI 2.25–6.36), small opacities exceeding 1.5 mm (RR 2.17, 95%CI 1.38–3.42), and caisson work (RR 1.56, 95%CI 1.01–2.41).²⁵ Almost all samples had a history of mine work or dusty jobs. One study reported that 48.4% of their silicosis population had worked in the mines for 11 to 20 years.²²

According to two studies^{22,27} older silicosis patients were mentioned as having a higher risk for TB. One study demonstrated that TB was most common in the age group of 36 to

Authors	Type of Study	Year of publication	Study time	Country	Silicosis diagnosis method	TB diagnosis method	Follow-up duration	Follow-up technique
Westerholm et al. ²⁴	Retrospective Cohort	1984	1959-1980	Sweden	CXR	CXR + Sputum smear /culture	20 years	CXR
Cowie et al. ²¹	Cohort	1994	1984-1991	South Africa	CXR	Sputum smear and culture (3 times), CXR, Mantoux test with 5TU, Tuberculin skin test, and when indicated, histologic examination	7 years	Clinical evalua- tion, 100-mm CXR
Corbett et al. ²⁶	Case-control	1999	1975-1990	South Africa	CXR	Sputum smear and culture and fluorescent microscopy	NA	NA
Chang et al. ²⁵	Cohort	2000	1988-1999	Hong Kong	Pneumoconiosis Medical Board (PMB) consists of a consultant chest physician, a senior medi- cal officer, and an occupational health officer.	One of these criteria: 1) two or more positive cultures for Mycobacterium tuberculosis; 2) one positive culture for M. tuberculosis plus compatible clinical history and radiolog- ical picture; 3) one or more positive smears for acid-fast bacilli plus compatible clini- cal history and radiological picture; 4) a compatible clinical history and a radio- logical picture or histologi- cal evidence plus improvement after anti- tuberculosis treatment.	95.00 ± 2.44 months	Clinical evalua- tion, radiologic imaging, and sputum examination
Ross et al. ²³	Retrospective Cohort	2010	1995-2000	South Africa	Mass Miniature Radiography (ILO Classifica- tion System)	Sputum smear and culture (3 times)	3 years	Radiological screening for TB + PFT + a questionnaire eliciting respi- ratory, smok- ing, and occupational information
Meel et al. ²²	Retrospective Cohort	2013	1997-1999	South Africa	CXR & physical examination	CXR & physical examination	NA	NA

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Authors	Type of Study	Year of publication	Study time	Country	Silicosis diagnosis method	TB diagnosis method	Follow-up duration	Follow-up technique
Yarahmadi et al. ²⁷	Case-control	2013	2006-2011	Iran	CXR, medical & occupational history, and physical exami- nation, consul- tation with a pulmonologist	Three sputum smears with or without sputum culture	NA	Clinical evalua- tion, radiologic imaging, and sputum examination

NA: Not Available; PFT: Pulmonary Function Test; CXR: Chest X-Ray.

Authors	Study population	Mean age	Gender	Occupation	Mentioned confounding factors	Grade of silicosis	Duration of silicosis History	Correlation between silicosis & TB	Estimate (95% CI) (silicosis vs. non-silicosis)
Westerholm et al. ²⁴	1522 (Exposed:712, non-exposed: 810)	NA	1522 M	Mining, Quarry- ing, tunneling, and steel and iron foundries	Occupation, age at first exposure to silica, calendar year of first exposure to silica	NA	NA	Yes	NM
Cowie et al. ²¹	1153 (Exposed: 818, non-exposed: 335)	49.2	1153 M	Gold miner	Occupation, age, date of diagnosis	Based on nodule profusion using the ILO standard guidelines, on entry to the study: Category 0 (n=335) Cate- gory 1 (n=418) Category 2 (n=355) Cate- gory 3 (n=45)	NA	Yes	RR: 2.8 (1.9 to 4.1)

Authors	Study population	Mean age	Gender	Occupation	Mentioned confounding factors	Grade of silicosis	Duration of silicosis History	Correlation between silicosis & TB	Estimate (95% CI) (silicosis vs. non-silicosis)
Corbett et al. ²⁶	561 (Case: 381, Con- trol: 180)	> 35yr: 134, 35–44yr: 234, > 45yr: 293	561 M	Driller, miner, scraper winch, rock transport, dusty job	Occupation, age, duration of employment, HIV, grade of silicosis	Based on a six- point scale mod- ified from the ILO classification system designed for use with standard-size chest radio- graphs: None: 340 (TB:198, control:142) Pos- sible: 69 (TB:50, control:19) Prob- able: 48 (TB:40, control:8) Early: 43 (TB:37, con- trol:6) High grade: 47 (TB:43, con- trol:7)	NA	Yes	Multivariate OR categorized by the grade of sili- cosis none:1 (<0.001), possi- ble: 1.6 (0.86–2.90), probable: 2.8 (1.24–6.46), early/high- grade: 4.9 (2.32–10.58)
Chang et al. ²⁵	707	53	702 M, 5 F	Caisson work	Occupation, age, gender, anti-tuberculosis treatment before the date of silicosis diag- nosis, progres- sive massive fibrosis, size of opacities in CXR	NA	Simulta- neous diagnosis of TB and silicosis: 71, <2 months after diagnosis of silico- sis: 37, >2 months after diagnosis of silico- sis: 143	Yes	RR: 8.6 (NM)
Ross et al. ²³	370 (Exposed: 185, non-exposed: 185)	43.95	370 M	Gold miner	Age, height, baseline lung function, years of employment, smoking, other respiratory diagnoses	NA	NA	Yes	OR: 1.86 (1.03- 3.37)

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Authors	Study population	Mean age	Gender	Occupation	Mentioned confounding factors	Grade of silicosis	Duration of silicosis History	Correlation between silicosis & TB	Estimate (95% CI) (silicosis vs. non-silicosis)
Weel et al. ²²	271	51.6	300 M	Former mine worker (mostly worked in the mining industry for 11-15 years)	Age, duration of employment	X-ray images were classified according to International Labor Organiza- tion (ILO) stand- ards and were entered in the Epi-info 6 pro- gram and then analyzed Probable: 26 Slight: 16 Marked: 19 Severe: 4	<10 years: 23 11-20 years: 31 >21 years: 10	Yes	OR: 5.08 (2.58- 9.88)
Yarahmadi et al. ²⁷	1300 (Case: 871, Control: 429)	40.77	725 M, 575 F	Casting, agricul- ture, under- ground mining, concrete manufacturing industry, con- struction industry, cement work, sand and gravel produc- tion, stone carving, ferrosil- icon company, mine, glass pro- duction, sandblasting, tunneling, brick making, con- struction work, stonemasonry, plaster work, road construc- tion, stone mill- ing, stone mining, asphalt company, lime- stone, granite stone, stone mine driver con- crete	Age, gender, the intensity of silica exposure, dura- tion of employ- ment, level of education, ciga- rette smoking	Degree of expo- sure to silica according to the classification of occupations based on level of exposure: No exposure: 740 (TB: 418, con- trol: 322) Mild: 299 (TB: 235, control: 64) Moderate: 194 (TB: 159, con- trol: 35) Severe: 67 (TB: 59, con- trol: 8)	15 years≥ silica exposure: 148 TB, 54 Non- TB; 15y< silica exposure: 305 TB, 53 Non-TB	Yes	OR: 4.08 (2.44 5.85)

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45 years, and the age groups that were least susceptible to TB were those aged <35 years (2.6%) and 66+ years (7.4%).²²

The frequency of TB increased along with the duration and intensity of silicosis/silica exposure. One case-control study showed that individuals with >15 years of moderate to severe silica exposure had the highest TB rate.²⁷ Another study reported that the largest group of subjects with TB had a mining history of 11-15 years.²² Moreover, one study found that probable, early, and high-grade silicosis, as well as the period of employment, were significant risk factors for TB.²⁶

No significant publication bias was found in the selected studies (Begg's test P>0.05 and forest plot qualitative analysis) (Fig. 2). Pulmonary silicosis increased the risk of pulmonary tuberculosis, with a pooled risk ratio of 1.35 (95%CI 1.18-1.53) with an 1² of 94.30% (Fig. 3). Considering the large outlier effect size of Westerholm et al.,²⁴ we repeated the analysis without this study; however, the result did not significantly differ (RR 1.85, 95%CI 0.45-7.60, 1²: 94.41%) compared with the previous estimate.

Discussion

In the present meta-analysis study, we found an increased risk of tuberculosis in silicosis patients and individuals exposed to silica dust.

The presence of silica particles in the lung and silicosis may facilitate the occurrence of tuberculosis infection and progress to disease, increasing the disease severity and favoring poor outcomes.²⁹ According to some studies, exposure to silica affects the fibrotic tissue of the lung, and the chronicity and immunomodulation of silicosis cause susceptibility to *Mycobacterium tuberculosis*, leading to a significant incidence of tuberculosis in silica-exposed populations.^{3,29,30} Free silica can kill or damage alveolar macrophages, which play a major role in controlling tuberculosis bacilli.^{31,25} Silica exposure decreases cellular function and dendritic cell activation, leading to a nonspecific and impaired inflammatory response.³ Thus, susceptibility to bacterial infections, mainly *Mycobacterium tuberculosis* and other mycobacterial species, increase.³

Evidence supports a greater risk of HIV-infected silicosis individuals for TB, based on the existing defect in cellular immunity of HIV patients.^{31,25} The HIV epidemic impact on TB incidence in miners partly depends on the interaction between HIV and silicosis as risk factors for TB. The results from a study in South African miners demonstrate a high incidence of both silicosis and TB in HIV-positive miners, which are compatible with a multiplicative effect of silicosis and HIV infection.³ HIV's effect on the incidence of silico-tuberculosis was also discussed by studies included in our systematic review. Corbett et al. showed that HIV infection was a significant risk factor for both TB and nontuberculous pulmonary mycobacterial diseases in South African gold miners.²⁶. They also suggested that as the South African HIV epidemic progresses, HIV infection may well make a significantly increasing addition to the already elevated rates of occupational mycobacterial diseases.²⁶ This was supported by Cowie et al. in their epidemiologic study on South African gold miners.²¹ Another study found that HIV status at the time of TB diagnosis was not

Table 3	Table 3 (Continued)								
Authors	Study population	Mean age	Gender	Occupation	Mentioned confounding factors	Grade of silicosis	Duration of silicosis History	Correlation between silicosis & TB	Estimate (95% CI) (silicosis vs. non-silicosis)
				production, installation, repair, and main- tenance of rail- ways, tiling, tessellation, tile and ceramic manufacturing industries, stone cutting, mosaic manufacturing, and pottery					
ILO: Interr	ILO: International Labor Office.								

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Funnel Plot of Standard Error by Log odds ratio

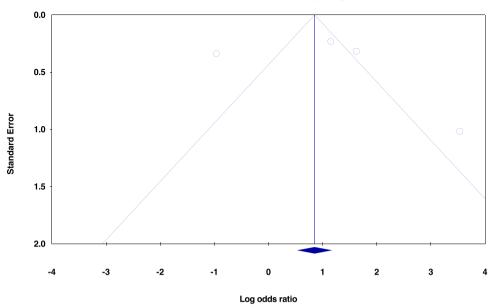


Fig. 2 Forest plot indicating no publication bias of the selected studies.

Study name				Ri	sk rat	io and	1 95%	CI
	Risk ratio	Lower limit	Upper limit					
Westerholm et al.	32.992	4.506	241.574	T	1	1	+	
Cowie et al.	2.760	1.815	4.197				•	
Ross et al.	0.771	0.622	0.957					
Meel et al.	1.665	1.402	1.976					
	1.350	1.188	1.533			•		
				0.01	0.1	1	10	100

Fig. 3 Forest plot of the cohort studies indicating the impact of silicosis on the risk of tuberculosis.

associated with loss of lung function. However, HIV status could not be analyzed as a confounder because it was tested only in the TB group.²³

Occupation type is another major risk factor for developing silicosis and silico-tuberculosis.¹³ In the study by Farazi et al., the incidence of tuberculosis in silicosis patients was 28 to 39 times higher than that of the average population.⁸ Also, previous studies suggested that even silica exposure without the clinical diagnosis of silicosis may be a risk factor for tuberculosis.^{13,32,33} Workers may be at high risk for silica dust exposure in many occupations across a variety of industries. Calvert et al. estimated occupational silica exposure in several industries, using death certificates from the United States. They demonstrated that metal and coal mining, crude petroleum and natural gas extraction, non-metallic mining and quarrying, construction, cement, concrete, gypsum, and plaster products, pottery and related products, miscellaneous non-metallic mineral and stone products, iron and steel foundries, construction and material handling machines, and non-specific manufacturing industries were among the high-risk occupations regarding the silica exposure.³⁴ Almost all of our studied population were employed in some of the mentioned industries (e.g., metal and coal

mining, quarrying, tunneling, steel iron foundries, construction, etc.).

The majority of our reviewed studies made no mention of any specific duration for silicosis or silica exposure among patients; in some cases, the duration of service was presumed to be the estimate for time of the silica exposure; most of the former mine workers had work experience in diverse mining settings. Due to the dramatically varying dust-controlling efforts and systems from one mine to another, one cannot simply correlate years of service and the type and severity of lung disease. Thus, the measured dust levels in the mines and other related workplaces cannot offer reliable risk-assessment data for former workers whose lung diseases are due to lung tissue irritations occurring several years ago.

A cohort study on patients with silicosis in Hong Kong revealed that a multiplicative positive interaction might exist between silicosis and smoking effecting mortality rates of pulmonary tuberculosis.³⁵ In another prospective cohort study on Chinese patients with silicosis, further support for a causal link between smoking and TB was found.³⁶

However, we could not perform a subgroup analysis due to inadequate data on smoking status in the studies we included.

Various other risk factors have been demonstrated including older age, male sex, chronic obstructive pulmonary disease, to be migrated from endemic areas, the severity of the silicosis, exposure to toxic materials, intensity of the exposure, poor nutritional status, and low BMI.^{9,37,38} Further investigations with greater populations are required to elucidate the extent of each of the mentioned risk factors in TB development and progress.

Strengths and limitations

The final result of our study is along with the Ehrlich et al. meta-analysis published in 2021 which demonstrated an

increased risk of tuberculosis in silicosis patients.³² However, our study has some strengths and is different in some ways. We included studies focused purely on the relationship between silicosis and silica dust exposure and tuberculosis. Postmortem studies or studies in which the sample population had specific comorbidities (e.g., end-stage renal disease) were excluded to lessen the potential effect of the confounding factors. Also, we excluded the articles in which the full text was not found. Against this, we included two other studies that not previously included.^{22,23} Our calculated pooled risk ratio (1.35, 95%CI 1.18-1.53) was a little lower than Ehrlich et al. (RR 1.92, CI 95% 1.3-,2.73) but in

line with its direction and statistical significance. The major limitation of our study is its originality, as the data on the association between silicosis and tuberculosis has been known and ascertained for some time and also reported by international agencies NIOSH (2003), OSHA (2004) regarding the need for health surveillance for tuberculosis in silicosis patients and people at risk of silicosis. However, that association has resulted in very high rates of tuberculosis in countries with poor tuberculosis and silica exposure control and an update of data relating to scientific evidence can still have value.

Some other limitations of our study are associated with the studies we included and are as follows: First, there have not been any recent cohort and case-control studies on the topic and the most recent one was published in 2013. Further new investigations with a large number of populations are required to elucidate the issue. Second, the male gender was dominant in almost all of our included studies and only one study.²⁷ had an equal male-to-female proportion. This could be because mine workers are mainly males but females can also be affected by working and living near workplaces.³⁹ We suggest future studies to consider this issue. Third, several confounding factors were mentioned in our study which despite our inability to subgroup analysis, due to insufficient and inconsistent data, can inspire future research in this field.

Conclusions

Silicosis and silica dust exposure increase the risk of tuberculosis. Therefore, individuals with long-time silica exposure, like mine workers, should be routinely considered for both silicosis and tuberculosis screening programs. Dust control measures should be enforced and followed by focused tuberculosis control programs for individuals in high-risk jobs. Also, surveillance and reporting methods among these highrisk workers should be improved to monitor the effectiveness of preventive programs.

Authors contribution

All authors participated in the drafting and revision of the manuscript and the approval of the final version.

Conflicts of interest

None.

Acknowledgment

None.

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