Silicosis-Associated Tuberculosis: Management and Control

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Abstract Silica-associated diseases, including tuberculosis and other related diseases, such as COPD, lung cancer, autoimmune diseases, renal diseases, etc. remain an important public health concern in the 21th century. Silica exposures and silicosis increase the risk of active tuberculosis development by approximately 30-40 times, compared to populations without silica exposure. Workers with periods of silica exposure longer than 10 years should be provided tuberculosis chemoprophylaxis. Although evidences of silicosis are not detected, the risk of active tuberculosis can increase. However, further studies are urgently needed to identify the best chemoprophylaxis regimen for tuberculosis.

Keywords: *silicosis, silicosis-associated tuberculosis, silica, tuberculosis*

Cite This Article: Attapon Cheepsattayakorn, and Ruangrong Cheepsattayakorn, "Silicosis-Associated Tuberculosis : Management and Control." *American Journal of Public Health Research*, vol. 6, no. 2 (2018): 125-129. doi: 10.12691/ajphr-6-2-17.

1. Introduction

Silicosis, a preventable occupational lung disease is associated with several other diseases, including tuberculosis (TB) [1]. Silicosis can occur as a consequence of occupational exposure to respirable crystalline silica-containing dust [2]. Although in the absence of clinically apparent silicosis, individuals who have been exposed to high level of silica dust may be at increased risk of developing TB [3]. Positive tuberculin-skin-testing individuals with silicosis have a 30 times' higher risk of developing active TB as compared to a control population regardless to tuberculin-skin-test status [4]. Silica-associated diseases remain an important public health concern in the 21th century due to a handful of toxins of crystalline silica that causes multiple serious diseases and increased mortality [5]. Silica exposure leads to serious epidemics of TB in southern Africa and other low-income regions of the world. Silica exposure is still common in both low- and high-income countries. At least 1.7 million workers in the United States are potentially exposed [3]. An estimated 119,000 workers are overexposed in some industries [6]. Silica-associated diseases include silicosis, a fibrotic-nodular-lung disease, pulmonary TB, chronic obstructive pulmonary disease (COPD), lung cancer, renal diseases, and autoimmune diseases [7]. Table 1 demonstrates diseases associated with respirable crystalline silica [8].

Table 1. Diseases associated with respirable crystalline silica

Pneumoconioses
-Accelerated silicosis
-Chronic silicosis
-Progressive massive fibrosis (PMF)
Mineral dust airway disease (MDAD)
Emphysema
Chronic bronchitis
Mycobacterial diseases
-Pulmonary and extra-pulmonary tuberculosis
-Non-tuberculous mycobacterial (NTM) diseases
Lung cancer
Renal diseases
Autoimmune diseases
-Rheumatoid arthritis
-Systemic lupus erythromatosis
-Scleroderma

Source Modified from Murray and Nadel's Textbook of Respiratory Medicine (Table 61.2), with kind permission from Elsevier Saunders [8]

In Thailand, there was first-case report of silicosis, reported by Dr. Ninnard Chinachote in 1954 in Kanchanaburi province (unpublished article). In 1995, Aungkasuvapala *et al* reported a study conducted in Saraburi province, Thailand that 31(93.9 %) of 33 factories in 3 subdistricts of Saraburi province had amounts of either total dust or respirable dust exceeding the threshold limit values

with average levels of total dust and respirable dust of 24.3 +/-34.6 and 2.4+/-1.6 mg/m^3, respectively [9]. Roentgenographic findings revealed that 61 workers (9.0 %) were diagnosed of suspected silicosis and 13 workers (1.9 %) were diagnosed of suspected pulmonary TB [9]. The prevalence of silicosis and pulmonary TB was significantly associated with years of work [9]. From annual report between 1995 and 2001, reported by the Ministry of Public Health, Thailand demonstrated that there was incidence rates of silicosis in Thailand between 7.1 to 20.7 cases per 1,000 silicosis-risk persons and reported that there was 3.7 cases of TB per 1,000 silicosis-risk persons (unpublished article). These reports also demonstrated that there was incidence of 0.44 cases of silicosis-associated TB per 1,000 silicosis-risk persons (unpublished article). In 1987 and 1989, there were reports of 15 % and 30 % of patients with silicosis in Saraburi province and Phayao province, Thailand, respectively (unpublished article). In Thailand, disease surveillance of silicosis, silica-associated diseases, and silicosis-associated or silica-associated TB should be regularly performed to achieve controlling of these silica-related diseases in the near future.

2. Objective of the Study

This study focuses on sources of silica exposure, silicosis, and silica-associated tuberculosis, which is of particular concern in low- and middle-income countries, and aspects of management, prevention, and control.

3. Sources of Respirable Silica Exposure

Surprisingly, a large number of industries generate respirable silica dust. A comprehensive description of silica exposures is available from various sources [3,10]. The most common exposures occur in mining and mining-related occupations, such as tunneling, excavation, quarrying, and milling ores. Industries with well-known silica risks include foundries, construction, and ceramics. Occupations having a long history of producing silica-associated diseases include cutting and polishing gem stones, stone-working or cutting, furnace masonry, and those in which fine silica material are used. Abrasive blasting with sand is particularly dangerous, and recommendations have been made to ban sand blasting in some countries [11].

4. Silicosis

Accelerated silicosis occurs after 3-10 years of exposure. Even the changes are similar to those identified in chronic silicosis, the pulmonary nodules develop sooner and are more cellular than fibrotic in nature. Alveolar lipoproteinosis, an uncommon feature develops after intense short exposures, sometimes only months, to fine dust with a high silica content [12,13]. The alveolar spaces become filled with granular lipoproteinaceous material, comprising alveolar surfactant. While duration and intensity of exposure are not the only determinants of the pathogenicity of silica dust, host factors influence personal susceptibility, and smaller particles increase the fibrogenicity of the dust [14].

5. Clinical Manifestations

The silicosis itself not producing symptoms, whereas chronic silicosis is often a radiological diagnosis. If silicosis progresses to PMF, or if TB, COPD or lung cancer develops exertional dyspnea may occur. Patients with acute silicosis may become disabled within months of exposure, with clinical manifestations similar to alveolar proteinosis of other etiologies. The clinical manifestations of accelerated are similar to those of chronic silicosis, but develop sooner. A productive cough may be present and is usually due to chronic bronchitis, nevertheless, it may due to TB or lung cancer. Systemic symptoms, such as fever and body weight loss of clubbing of fingers, should be due to TB or lung cancer until proven otherwise.

6. Thoracic Imaging in Silicosis and Silicosis-Associated Tuberculosis

In most cases, routine chest roentgenograms is sufficient for the diagnosis of silicosis [15,16]. The characteristic chest roentgenographic finding is the presence of multiple, diffusely distributed nodules smaller than 10 mm. in diameter, predominantly in the superior and posterior regions of the lungs. These nodules can coalesce and form opacities greater than 10 mm. in diameter, which indicates progressive massive fibrosis. The size (equal or less than 1.5 mm.; 1.5-3 mm.; or more than 3 mm.), type (regular or irregular), and profusion of these nodules form the basis for the International Labour Organization Classification [17]. "Eggshell" calcification of hilar and mediastinal lymphadenomegaly is highly suggestive of the diagnosis of silicosis [16]. These alterations are present in the accelerated and chronic forms. The acute form, is characteristically present with perihilar and ground-glass alveolar opacities, which resemble alveolar proteinosis, providing rise to the term "silicoproteinosis" [16]. Chronic silicosis is characterized by symmetrically distributed, small (usually 1-3 mm. in diameter) rounded opacities, initially in the upper regions of the chest roentgenograms [18]. Surprisingly, high resolution computed tomography (HRCT) of the chest has not been demonstrated to be consistently more sensitive than chest roentgenograms in detecting early silicosis [19].

It is extremely important to exclude the coexistence of active pulmonary TB in patients with silicosis [20]. Nevertheless, the diagnosis of pulmonary active TB superimposed on silicosis by the roentgenographic alterations can be very difficultly indistinguishable from those resulting from the preexisting silicosis [21]. Initially, it is recommended that sputum smear microscopy and sputum culture, as well as chest roentgenograms (Figure 1) should be performed [20,22]. In cases with doubts about the presence of active pulmonary TB, bronchoscopy with bronchoalveolar lavage (BAL) can be used, in conjunction with transbronchial biopsy when possible [23]. Imaging patterns suggestive of silicotuberculosis have also been

identified on chest computed tomography by the presence with thick-wall cavities (Figure 2), a tree-in-bud pattern, asymmetrical nodularity, consolidations, and rapid disease progression [22,24,25].
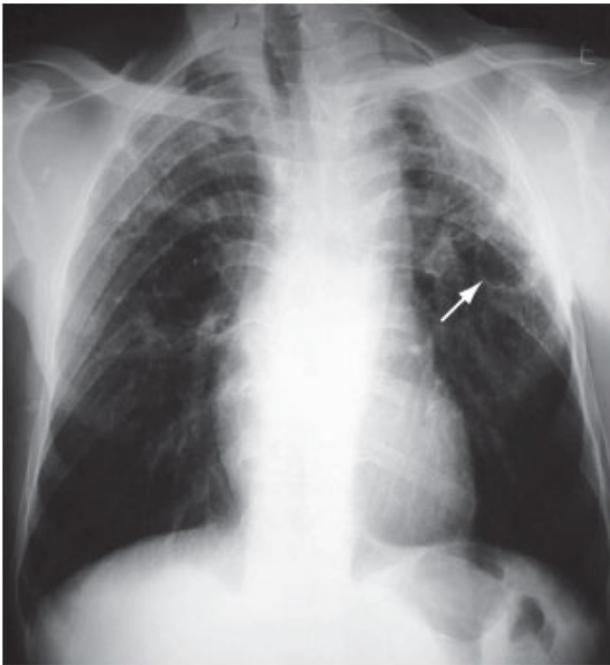

Figure 1. Chest X-ray of a patient with silicosis and pulmonary tuberculosis. The patient was a well driller. Note the thick-walled cavity in the left middle lung field (arrow) (Source Barboza et al. J Bras Pneumol, 34, Nov. 2008 [26])
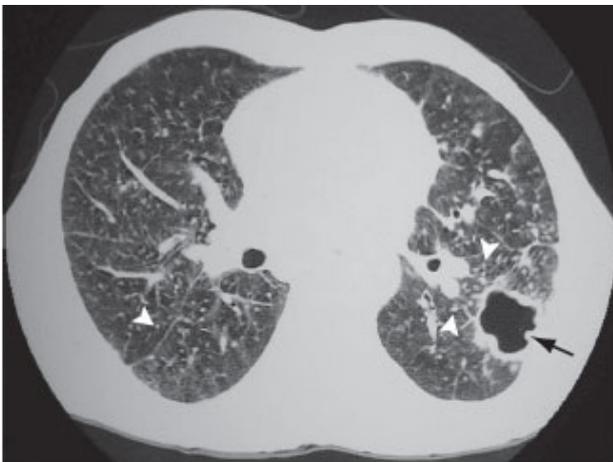

Figure 2. Tomography scan of the chest of the same patient. Note the thick-walled cavity with an irregular surface in the left lower lobe (black arrow), as well as multiple, diffusely distributed nodules, predominantly in the left lung (white arrowheads) (Source Barboza et al. J Bras Pneumol, 34, Nov. 2008 [26])

TB rates in individuals with advanced simple silicosis in high background TB settings can be very high, up to three-fold higher than those in the same workforce without silicosis [27].

7. Chemoprophylaxis

A randomized, double-blind, placebo-controlled trial evaluated the effect of three chemoprophylaxis regimens in 652 patients with silicosis who did not have active TB and had never been treated for TB [28]. The subjects were randomized to receive, in an unsupervised manner, one of the following regimens: 300 mg/day of isoniazid for 24 weeks; 300 mg/day of isoniazid and 600 mg/day of rifampicin for 12 weeks; 600 mg/day rifampicin for 12 weeks; or placebo for 24 weeks. After 5 years, the use of chemoprophylaxis reduced the risk of developing TB by around 50 %. The proportion of individuals with active TB in the groups using chemoprophylaxis was 13 % (combined result of the three different regimens; $p < 0.01$), compared with 27 % in the placebo group. The annual TB incidence was 4 % in the groups using chemoprophylaxis and 7 % in the placebo group. There was no significant difference in term of efficacy among three chemoprophylaxis regimens [28]. A previous study of HIV-infected gold miners with a high prevalence of silicosis revealed a reduction in TB incidence of 38 % overall, after routine isoniazid preventive therapy [29]. Nevertheless, screening for latent TB can be problematic. In countries with low background rates of TB, tuberculin skin tests are used to diagnose latent TB, after which a 9-month course of isoniazid is recommended [30].

8. Management

Due to incurability of silicosis, the management goals are to detect early cases of silicosis and TB via monitoring of both currently and formerly exposed workers; to slow progression; to prevent TB; to reduce disability; and to establish surveillance programs. The interaction between silica exposure and smoking in the development of TB, COPD, and lung cancer [31].

9. Primary Prevention and Control of Silica Dust

TB is the only cured silica-associated disease among other non-cured silica-associated diseases. Thailand and South Africa are examples of a number of countries that have established national silicosis elimination programs under the guidance of the ILO/WHO global elimination campaign. Components of these programs include compensation, education, awareness, improved case finding, strengthening enforcement of standards, and targeting priority industries for silica dust control. The optimum form of primary prevention of silicosis is the control of silica dust to concentrations at which disease will not occur that is more comprehensively covered in industrial hygiene publications. There are at least two important reasons to reduce silica concentrations to the achieved lowest level even if silica concentrations cannot be lowered to the levels that will prevent all silica-associated diseases. First, for prevention of serious silica-associated diseases [6,32]. Second, although over control limits of silica exposure dramatically have been identified to increase the risk of silicosis [33].

The risk of silicosis following a lifetime of silica exposure at 0.05 mg/m^3 is probably to be 20 % to 40 % [34], whereas the American Conference of Governmental

Industrial Hygienists (ACGIH) has recommended a threshold limit value (TLV) of 0.025 mg/m^3 [6,35]. These low levels of silica exposure is challenging and may not be protective against some silica-associated diseases, such as TB, particularly in small enterprises and low-income countries [5].

10. Discussion

In communities with high silica exposure, TB control programs have not been very successful [36]. A previous study demonstrated that 30 % of TB cases had significantly silica exposure with 16-20 years of silica exposure [37]. A previous study conducted in New Jersey, USA revealed that silica exposure was among the most importantly occupational risk factors responsible for TB progression (OR: 3.96, 95 % CI: 0.34-44.02) [38]. This study also revealed that TB patients with higher education had lower prevalence of silica-associated TB than those with lower educational levels [38]. Silica exposure was significantly more prevalent among those with illiteracy and lower educational levels with 68 % of silica exposure whereas 37 % of exposure was found in those with high school education [38]. A previous prospective study conducted in Brazil demonstrated that workers with severe silica exposure developed TB 3.22 times more than those with the lowest silica exposure [39]. TB control is markedly affected by reducing silica exposure, hypothesized by some investigators [40,41]. This TB control strategy is much effective in communities with high silica exposure and high prevalence of TB [42]. Increasing the risk of TB can be due to silica exposure without evidence of silicosis [43,44].

Previous studies on compensation conducted in southern Africa demonstrated that many retired gold miners who returned to rural labour-sending areas were identified undiagnosed and uncompensated persons [45,46]. Although in the absence of respiratory symptoms or impairment, workers with silicosis may be excluded from many jobs because of an abnormal chest roentgenograms, thus, compensation benefits are generally provided. Workers' compensation benefits in poor countries may be critical in providing financial support for covering medical costs and for families.

11. Conclusion

Sweden and other high-income countries demonstrate that silica-related diseases including TB can be prevented. In low-income countries, new cases of silicosis and silica-related TB, related COPD, and related lung cancer are probable for decades to prevent these silica-related diseases, particularly TB due to taking time to achieve. Protective standards have not been established for some silica-related diseases, such as TB. Management of silicosis, a prevalent and untreatable disease should focus on removing workers from the source of silica exposure. Regarding silica-exposed workers who do not have the disease, considering this population also at risk for TB, it would be suggestive to provide chemoprophylaxis in those with periods of silica exposure longer than 10 years and

with strongly positive tuberculin skin test results. Nevertheless, further investigations are urgently needed for identifying the best regimen whereas study protocols designed to validate this treatment have to be developed.

Acknowledgements

Statement of Competing Interests

The authors declare no competing interests.

Abbreviations

ACGIH: American Conference of Governmental Industrial Hygienists, BAL: Bronchoalveolar Lavage, CI: Confidential Interval, COPD: Chronic Obstructive Pulmonary Disease, HRCT: High Resolution Computed Tomography, ILO: International Labour Organization, MDAD: Mineral Dust Airway Disease, NTM: Non-tuberculous Mycobacterial, OR: Odd Ratio, PMF: Progressive Massive Fibrosis, TB: Tuberculosis, TLV: Threshold Limit Value, USA: United States of America, WHO: World Health Organization.

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