Silicotuberculosis in African underground Miners

La Silicotuberculose chez les Travailleurs des Mines Souterraines en Afrique

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Résumé

Objectif. La silicose, une pathologie pulmonaire causée par l'inhalation de silice, est l'une des maladies professionnelles les plus fréquentes et représente un problème de santé publique dans le monde. Elle peut être associée à la tuberculose pulmonaire (TB)
Méthodes. Les auteurs font une revue de la littérature sur l'association exposition aux poussières de silice et la TB, plus particulièrement chez les employés des mines souterraines d'Afrique. Un total de 873 articles a été récensé à partir des moteurs de recherche ont été extraits des moteurs de recherche Pubmed, Embase, et CINHAL ; 44 correspondaient aux mots-clés de notre revue, et une observation clinique locale fait suite à cette revue.
Résultats. Du lot de 44 articles reprenant nos mots-clés, 11 avaient trait aux mineurs Africains.Six articles traitaient de l'exposition aux poussières de silice avec la tuberculose, 5 étaient sur la silicotuberculose dans les mines d'or sud-africaines dont 2 cas-cliniques, 1 étude cas-témois, et 2 études de cohorte. Les deux études de cohorte décrivaient des taux de prévalence respectivement de 2,7% et 6,8%. Le cas du mineur congolais concerne un employé depuis plus de 20 ans, dans des mines de cuivre et de cobalt, dans la province du Katanga en RDC. Le tableau clinique et paraclinique sont repris dans le commentaire ci-dessous.
Conclusion. La silicotuberculose est un risque présent dans les mines de la province du Katanga. Des mesures de prévention et de sécurité au travail doivent être encouragées et implémentée.

Mots-clés: Silicotuberculose, mineurs, Afrique
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Summary

Objective. Silicosis, a lung disease caused by the inhalation of crystalline silica dust, is one of the most prevalent occupational diseases and represents a public health issue in the world.This paper is a review of the literature on the association between silica dust-exposure and TB.
Methods. A review of literature was conducted which included articles related to silica dust-exposure and TB,peculiar in minors in Africa.A total of 873 articles was extacted from 3 search engines : Pubmed, Embase and CINHAL. Among them, 44 corresponded to the review topic. In addition, a case report is described. R***esults***. Of the 44 articles that matched the keywords, 11 were related to African miners: 6 articles were related to the association between silica dust-exposure and TB, 5 consisted of reports on silicotuberculosis in South African gold miners, including 2 case reports, 1 controlled clinical trial and 2 cohort studies. The latest studies showed a prevalence rate of 2.7% and 6.8%, respectively.The casereport is about a Congolese copper and cobalt miner, with a history of chronic dust-exposure (more than 20 years) in Katanga province.Clinical and paraclinical features are presented in the following text.
Conclusion. Silicotuberculosis represents a real threat in the mines of Katanga province.Health preventive measures need to be encouraged and implemented in this sector.
Key words: Africa, Occupational dust exposure, Silicotuberculosis, Minors, Africa.
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Introduction

Definitions and epidemiology

Silicosis is a parenchymal lung disease caused by the inhalation of crystalline silica dust (1, 2). It is a preventable occupational lung condition without any effective treatment. Silicosis is one of the most prevalent occupational diseases and represents a public health issue in the world (3, 4). Occupational exposure to air-borne crystalline silica is considered a major health hazard that is encountered in occupational settings such as mining, pottery, foundry, glass, cement and concrete production; however, the mining sector is thought to account for the majority of individuals who suffer from silicosis in some countries (2, 4-6).

Several million workers are believed to be exposed to crystalline silica worldwide, including around two mil-

lion in the US. Inhalation of crystalline silica leads to the infiltration of inflammatory cells such as neutrophils, macro-phages and lymphocytes into the lung, causing an inflammation and the development of lung fibrosis afterwards, an irreversible and incurable condition known as silicosis. Tuberculosis (TB), a bacterial infection caused by *Mycobacterium tuberculosis*, remains one of major public health issues worldwide, infecting several millions and killing about 2 million people annually; and the TB burden is greater in developing countries (7). Exposure to silica dust may increase the risk of tuberculosis (8); and the term silicotuberculosis refers to the association of silicosis and TB.

Importance of the mining sector in Africa

The economics of many sub-saharan african countries rely on the export of underground resources. For example, South African Republic, a country located in the southern African region, is a world leader in mining with abundant mineral resources and reserves, for gold in particular. The country hasthe world fifth largest mining sector in terms of GDP value (9). In the central region, the Democratic Republic of Congo (DRC) is considered to have a vast mineral resource, too. Mining industry currently represents an estimated 60-80% of DRC's foreign direct investment (FDI) stock (10). However, in most countries of the Sub-Saharan Africa, precautionary measures in dusty mining sites are generally poor due to theabsence or insufficient implementation of occupational safety measures. In such working conditions, miners are at risk of developing silicosis and lung cancer.

This paper provides a review of the existing scientific literature on the association between silicosis and TB in African underground miners and, additionally, a clinical case is reported on a Congolese copper and cobalt miner with a history of chronic dust-exposure who developed Silicosisin Lubu-mbashi, Katanga province, Democratic Republic of Congo (DRC).

Review of the literature

A literature and database search was conducted for data on the association silicosis and TB in African underground miners. The following scientific databases were used for the review: Medline (Pubmed), CINHAL and EMBASE. 'Silicosis','tuberculosis','silicotuberculosis', 'miner'and 'Africa' were the main keywords that were used. To enter the keywords in the database search engines, a combination of two to three of them was used to retrieve related articles and abstracts.

Relationship between silica dust-exposure and tuberculosis, and silico-tuberculosis in African underground miners

In total, 873 articles and abstracts were obtained after checking reports that included twice in the list. Of the remaining articles, only 44 corresponded to the association silica exposure and tuberculosis, and also silicotuberculosis in miners; of them, 11 articles were related to African miners (5 for silicotuberculosis, 6 for silica exposure and TB development). Of the 5 articles related to silicotuberculosis in African mining workers, there were 1 controlled clinical trial, 2 cohort studies and 2 case reports. All patients consisted of South African gold miners.

The first scientific report on silicotuberculosis in Africans was published in 1984 by the South African Medical Journal (11); it was about a clinical trial in which 94 South African gold miners who were diagnosed with silico-tuberculosis underwent anti-TB medication. A corresponding number of pulmonary TB patients was used as controls. In cohort studies, silica dust-exposed gold miners were followed up for 7 years or more, and they underwent periodic radiological examination to determine the rates of workers who developed silicosis and TB. Reports published in 1994 and 1996 showed a silicotuberculosis prevalence rate of 2.7% and 6.8%, respectively. The remaining two other reports consisted of one case each (12-15) (Table 1).

Table 1: Review matrixtable of silicotuberculosis reports in African miners

Reference / category of worker	Country	Type of study or report	Sample size	Prevalence-rate
Cowie RL, 1994 (gold miners)	South Africa	Cohort	818	2.7
Cowie RL, 1996 (gold miners)	South Africa	Cohort	382	6.8
Martins *et al*., 2010 (gold miner)	South Africa	Case report	1	-
Oni *et al*., 2015 (gold miner)	South Africa	Case report	1	-
Our paper, 2016 (copper & cobalt miner)	Congo DR	Case report	1	-

Silicosis continues to be a major health issue worldwide, both in rich and developing countries ad it affects workers from different occupational settings, including miners, constructions workers, foundry workers etc. High silicosis morbidity has been reported and, given the absence effective treatment, the mortality of this condition is extremely high (16-17). The relationship between dust-exposure in mining settings and occupational lung diseases has been document since the 1500s. Recently, a number of scientific reports have supported the association between silicosis and lung cancer, and the International Agency for Research on Cancer (IARC) has classified crystalline silica as carcinogenic to humans (18-20). It was only in the twenty-first century that the relationship between silicosis and TB took another dimension due to the growing HIV epidemic in developing countries (21). Cowie has reported high rates of active TB in silicotic patients than in those without silicosis; he suggested that the severity of silicosis, the prevalence of silicosis in the general population from which the workforce is drawn, age, the general health status and HIV status are factors influencing the development of TB in patients with silicosis (12).

Though TB is a prevalent disease in miners, there are few scientific reports regarding studies on the association silicosis and TB in African miners. Table 1 shows that two cohort studies conducted in South African goldminers have been published in 1994 and 1996, with a silicotubercosis prevalence rate of 2.7% and 6.8% (12-13), respectively. Two other reports consisted of case reports on silicotuberculosis also in South African goldminers. This suggested that despite the fact that TB, which is an endemic infectious disease in most Sub-Saharan African countries, is associated to both silica dust-exposure and silicotuberculosis, this health issue has not yet been a focus by researchers in the field of occupational safety and health.

Case report

Table 2: Clinical, lung function parameters and radiologic features of the patient

History, physical examination& medication	Lung function (Spirometry)	Radiologic features (CXR and CT)
Chronic dust exposure	FEV1 : 51% predicted	Calcified small rounded opacities:
Pulmonary TB	FVC : 63% predicted	• q/q 1/1 type, according to ILO classification of chest radiographs of pneumoconiosis)
Dyspnea, cough, chest and back pain, wheeze sometimes	FEV1/FVC : 80%	• localized on upper and middle lung zones
Bronchial rales bilaterally		Enlarged, calcified lymph nodes
Spinal cord deformation		Destruction of T7, T8 on the spinal cord
Hypoesthesia of the chest		Mastoiditis, sinusitis, cerebral atrophy
Positive Mingazzini and Barré signs		
Anti-TB medication (positive tuberculin skin test)		

* Footnotes: TB, tuberculosis; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; CXR, chest X-ray; CT, computerized tomography; T7, 7th thoracic vertebra; T8, 8th thoracic vertebra

Description and discussion

Authors report on a male miner, aged 59 years, whohas been smoking for 30 years; he quit smoking three years prior to his admissionto the hospital in 2014. The patient has worked in underground copper and cobalt mines for more than 20 years (1975-1996) and as an elevator maintenance technicien in a building for 10 years for the same company. He hada history of pulmonary tuberculosis (with positive sputum test) for which he underwent anti-TB medication without improvement of his health status.

Physical examination

The patient's main complaints were dyspnea, breathlessness, cough, chest and back pain, fatigue and sometimes wheeze. In addition, he had difficulty walking. The palpation and auscultation of the chest revealed chest pain and bronchial rales, respectively, in both lung fields. In addition, the patient had a deformation of spinal cord. The neurological examination revealed hypotonic lower limbs with positive Mingazzini and Barré signs, as well as hypoesthesia on the chest, suggesting the presence of neurological damage.

Pulmonary function test (spirometry)

Spirometry was performed at a regional referral hospital belonging to a mining company in Lubumbashi; forced expiratory volume in one second (FEV1) was 51% (1.55 L) of predicted value, forced vital capacity (FVC) was 63% (2.51 L) of predicted value and the ratio FEV1/FVC was 80%, indicating a mixed ventilatory defect. The patient died due to respiratory failure.

Chest radiography and CT images

Chest x-ray (CXR) revealed the presence of calcified small rounded opacities of low profusion (nearly similar to those on ILO standard film q/q, 1/1) on upper and middle lung zones, calcified lymph nodes in both lung zones (Fig. 1A,B). Most of those lung features were also visualized on the chest computed tomography (CT) film (Fig.2A). On the other hand, cerebral atrophy (Fig.2B), a mastoiditis and sinusitis were also noted by the radiologist. In addition, the destruction of T7 and T8 on the spinal cord was observed on the dorsal area, suggestive of a fracture (Fig.1B).

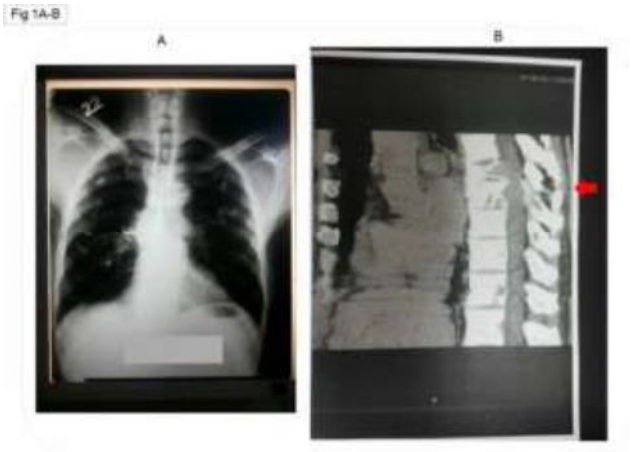

Figure 1A, B. Chest X-ray (A) and CT-SCAN (B) images of the patient

Figure1A shows a poorly processed chest radiograph (quality 3 film due to overexposure) with overlapping scapula bilaterally, with low profusion calcified small rounded opacities (q/q 1/1 type) in upper and middle zones of both lungs, and enlarged and calcified right hilar lymph nodes. On the other hand, figure 1B shows the dorsal and lumbar regions with osteolytic-blasting destructions involving spinous process and lamina with skip lesion (red arrow)

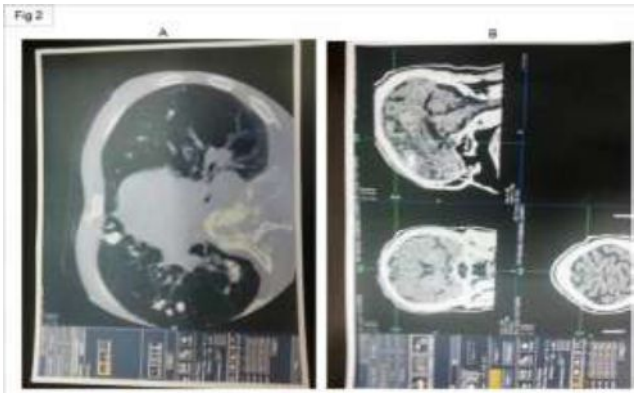

Figure 2 A, B. Thorax and headCT-SCAN images of the patient

The figure 2 Ashows multiple calcified nodules in both lungs and calcified right lobar lymph nodes. On the other hand, figure 2B shows the CT film of the patient's brain with a diffuse cerebral atrophy.

Discussion

This case report consists of a silicotic patient who have been treated for TB. He was a Congolese miner with a more than 20-year history of exposure to dust in underground cobalt and copper mines. He presented with lung parenchymal abnormalities suggestive of work-related silicosis, bone (spinal cord) abnormalities and cerebral atrophy probably caused by *Mycobacterium tuberculosis* infection. He was admitted in October 2014 and died of respiratory failure some weeks later. Both TB and silicosis can cause most of lung features described in this report, and smoking might have played an important role in precipitating the development of either TB, silicosis or both.

In fact, TB is reported to be a complication associated with silicosis and their association has been studied since the beginning of the twentieth century; and the risk for a patient with silicosis to develop TB has beenreported to be 2.8 to 39 fold higher than in healthy patients (22-23). In addition, it is estimated that pulmonary TB occurs in 25% of patients with acute or classic silicosis. Both lung diseases share similar radiologic features, including small opacities (pulmonary nodules which may appear calcified), enlarged lymph nodes and calcifications. The presence ofa rapid disease progression and cavitation in silica dust-exposed individuals are considered indicators of silicotuberculosis (24-27). In silicosis, not in pulmonary TB, calcified pulmonary nodules as well perihilar conglomerate masses are bilateral and symmetric. Thus, lung abnormalities found in these patients could probably be attributable to silicosis.

The radiological features of the spinal cord reported in this paper are subject to discussion, as both silicosis and TB can induce such abnormalities. Firstly, *Mycobacterium tuberculosis* is also known to cause extra-pulmonary abnormalities, and the spinal cord is one of its targets, leading to fracture. Secondly, crystalline silica is a recognized carcinogen, and lung cancer has been one of the complications of silicosis (28), and the spinal cord can be one of the locations of metastatic tumor from a primary cancer of the lung. However, in this patient, it is difficult to confirm a metastatic bone cancer from the lung, given there was no visible radiological findingin CXR and CT film that could suggest the presence of pulmonary malignancy. Thus, a bone disease resulting from *Mycobacterium tuberculosis* might be a plausible hypothesis that can justify spinal cord fracture. Moreover, the CT scan image of the head showed an atrophic brain but could not present a tumor-like image, suggesting that abnormality of the brain might be caused by a disease other than a tumor.

Ithas been reported that *Mycobacterium tuberculosis* can affect the central nervous system (CNS) and cause tuberculous encephalitis, which is also known as one of the causes of cerebral atrophy (29). This complication is reported to accounts for approximately 5 to 10% of all TB cases in the US (30-31), whereas a Canadian cohort study showed that the risk of developing CNS-TB was 1%, and it increased in immigrant and aborigine populations (32). In the Congolese case presented in this report, the history of dust exposure in mines, the bilateral distribution of lung parenchymal abnormalities in both right and left lung fields, the rapid progression of the disease, the history of active TBand the spinal cord fracture, cerebral atrophy and the absence of plausible evidence of a primary lung parenchymal tumor or a metastatic bone or brain mass make silicotuberculosis the more likely diagnosis of this case.

Nonetheless, this case report has limitations; the issues related to the difficulty of the diagnosis and the management of the case. In the absence of periodic radiological evaluation of the patient's condition, changes in lung abnormalities and the disease progression could not be comprehended. In addition, the histopathological examination of the lung and spinal fluid, which could provide more

information on the nature of the disease, were not performed inhealth settings were the patient was taken care. Knowledge on the pathology of silicosis and silicotuberculosis is important as it facilitates the differential diagnosis. In a classic silicosis, nodules are composed of mature collagen in the central portion with peripheral macrohages that appear different from the surrounding lung parenchyma. The collagen appears as a whorled "onion peel" in which varying amounts of dust are embedded. In particular, with the use of polarized light microscopy, the presence of birefringent silicate crystals can be identified at the cellular level. In addition, in the case of association between silicosis andTB, other TB specific histological features such as giant cells andgranuloma can be found in lung specimens,as well as caseation andepithelioid cells in enlarged lymph nodes (33-35). However, the poor quality of available patient's films could not allow to detect those features.

In the literature, some previous works have provided knowledge on the mechanisms that explain the reason why the risk of developing pulmonary and extra pulmonary TB is increased in patients with silicosis (36). A number of experimental studies suggested that silica modifies the immune response of the lungs, impairs the function of pulmonary macrophages, and, with frequent exposure, causes macrophage apoptosis (37-38). An additional element involved is surfactant protein A (SP-A), which appears at high levels in the bronchoalveolar lavage fluid (BALF) of patients with silicosis. An excess of this protein seems to be associated with higher susceptibility to tuberculosis, possibly because it allows Mycobacterium to enter the alveolar macrophages without triggering cytotoxicity and inhibits the formation of reactive nitrogen species by the activated microphages (39-40). Unfortunately, our medical setting did not have necessary equipment to quantify these specific markers. It is also thought that the bacilli can remain encapsulated within the silicotic nodules, which would be responsible for the reactivation of tuberculosis in such patients and the extension of the infection to other organs (36).

Our patient presented also with a diffuse cerebral atrophy, which possibly suggests an infectious origin given the absence of a mass. This might be another complication of TB or other infectious disease. Normally, cerebrospinal fluid (CSF) should have been collected and analyzed to identify the cause. This is another limitation of this case report as laboratory investigation of CSF was not performed.

Conclusion and recommendation

Working conditions inside underground mines create a high-risk environment for the development of silicosis and TB transmission as well (41-42) particularly in the Sub-Saharan African countries where mining industry is the main economic resource and occupational safety neglected. Hence, there is a crucial needto organize and implement occupational safety measures in mining settings. Given that TB is endemic in the area, there is a possibility that some silicosis cases are treated as TB, and silicotuberculosis misdiagnosed, leading to unsuccessful treatment. As a conclusion, the present report highlights the importance of training health care providers in the diagnosis and management of occupational lung diseases, and promoting occupational safety for workers exposed to dust, as well as the sensitization of local population in mining areas with risk of environmental exposure to such hazards.

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References

1. Yang HS, Kim JI, Ye BJ, Yoo TJ, Lee SW, Jung KY. A case of complicated silicosis with a complex clinical course in a glass manufacturing worker. *Ann Occup Envir Med* 2014; **26** : 10.
2. Greenberg MI, Waksman J, Curtis J. Silicosis: a review. *Dis Mon* 2007; **53**: 394–416
3. World health Organization (WHO). The Global Occupational Health Network newsletter: elimination of silicosis. 2007. Accessed on 19 January 2016. http://www.who.int/occupational_health/publications/newsletter/gohnet12e.pdf
4. Centers for Disease Control and Prevention (CDC). Silicosis mortality, prevention, and control—United States, 1968-2002. Accessed 19 January 2016.
5. Satpathy SR, Jala VR, Bodduluri SR, Krishnan E, Hedge B, Hoyle GW, Fraig M, Luster AD, Haribabu B. Crystalline silica-induced leukotriene B4-dependent inflammation promotes lung tumor growth. *Nat Commun* 2015; **6**:7064. doi: 10.1038/ncomms8064.
6. Takako H, Yasui M, Ichikawa Y, Waseda Y, Inuzuka K, Nishizawa Y, Tagami A, Fujimura M, Nakao S.The specific chymase inhibitor TY-51469 suppresses the accumulation of neutrophils in the lung and reduces silica-induced pulmonary fibrosis in mice. *Exp Lung Res* 2011; **37**(2): 101–108.
7. Field SK, Fisher D, Jarand JM, Cowie RL. New treatment options for multidrug-resistant tuberculosis. T*her Adv Respir Dis* 2012; **6**(5): 255-268.
8.Corbett EL, Churchyard GL, Clayton T, Herselman P, Williams B *et al*. Risk factors for pulmonary mycobacterium disease in South African gold miners. A case control study. *Am J Respir Crit Care Med* 1999; **159** (1): 94-99.
9. Kearney L. Mining and minerals in South Africa. South Africa Info, report, August 2012. Available from:www.southafrica.info/business/economy/sectors/mining.htm#.V9YJQI9OKUk
10. Oxford Policy Management. The impact of mining in the Democratic Republic of Congo Performance to date and future challenges (Report, October 2013). Available from: http://www.opml.co.uk/sites/default/files/DRC%20mining%20report%20-%20OPM%20-%20Final%20Eng.pdf
11. Escreet BC, Langton ME, Cowie RL. Short-course chemotherapry for silico-tuberculosis. S Afr Med J 1984; **66** (9): 327-330.
12.Cowie RL. The epidemiology of tuberculosis in gold miners with silicosis. *Am J Respir Crit care Med* 1994; **150**: 1460-1462.
13. Cowie RL. Short course chemoprophylaxis with rifampicin, isoniazid and pyrazinamide for tuberculosis evaluated in gold miners with silicosis: a double-blind placebo controlled trial. *Tuber Lung Dis* 1996; **77**(3): 239-243.
14. Martins P, Marchiori E, Zanetti G, Muccillo A, Ventura N *et al*. Cavitaed conglomerate mass in silicosis indicating associated tuberculosis. Case report in Medicine 2010; 2010. doi: 10.1155/2010/293730.
15. Oni T, Ehrlich R. Complicated silicotuberculosis in a South African gold miner: A case report. *Am J Ind Med* 2015; **58**: 697-701.
16. National Institute of Occupational Safety and health (NIOSH). The work-related lung disease surveillance report, 2002. Cincinnatti, OH: NIOSH, 2003.
17. International Labour Office. Encyclopedia of occupational health and safety, 4th edition. Geneva: International Labour Office, 1997.
18. Wong O. The epidemiology of silica, silicosis and lung cancer: some recent findings and future challenges. *Ann Epidemiol* 2002; **12**: 285-287.
19. American Thoracic Society. Adverse effects of crystalline silica exposure. *Am J Respir Crit Care Med* 1997; **155**: 761-768.
20. Guha N, Straif K, Benbrahim-Tallaa L. The IARC monograph on the carcinogenicity of crystalline silica. *Med Lav* 2011; **102** (4): 310-320.
21. Ross MH, Murray J. Occupational respiratory disease in mining. *Occup Med* 2004; **54**: 304-310.
22. Osim EE, Tandayi M, Chinyanga HM, Matarira HT, Mudambo KK, Musabayane CT. Lung function, blood gases, pH and serum electrolytes of small scale miners exposed to chrome ore dust on the great Dyke in Zimbabwe. *Tropical Medicine and International Health* 1999 ; **4** (9) : 621-628.
23. Calvert GM, Rice FL, Boano JM, Sheehy JW, Sanderson WT. Occupational silica exposure and risk of various diseases: an analysis using death certificates from 27 states of the United States. *Occup Environm Med* 2003 ; **60** (2) : 122-129.
24.Cowie RL. The epidemiology of tuberculosis in gold miners with silicosis. *Am J Respir Crit Care Med* 1994; **150**: 1460–1462.
25. Chong S, Lee KS, Chung MJ, Han J, Kwon OJ, Kim TS. Pneumoconiosis: comparison of imaging and pathologic findings. *RadioGraphics* 2006; **26**:59–77.
26. Steen TW, Gyi KM, White NW *et al*. Prevalence of occupational lung diseases among Botswana men formerly employed in South African mining industry. *Occup Environm Med* 1997; **54** (1): 19-26.
27. Milovanovic A, Nowak D, Milovanovic A, Hering KG, Kline JN, Kovalevskiy E *et al*. Silicotuber-culosis and silicosis as occupational diseases: Report of two cases. *Srp Arh Celok Lek* 2011; **139** (7-8): 536-539.
28. Finkelstein MM. Silica, silicosis, and lung cancer: a risk assessment. *AM J Ind Med* 2000; **38** (1): 8:18.

29. Mitchell BC, dehkharghani S. Imaging of intracranial infectious diseases in adults. Applied Radiology; February 2004. Available from: http://cdn.agilitycms.com/applied-radiology/PDFs/AR_02-14_Dehkharghani-Mitchell.pdf
30. Rieder HL, Snider DE Jr, Cauthen GM. Extrapulmonary tuberculosis in the United States. *Am Rev Respir Dis* 1990; **141**: 347-351.
31. Centers for Disease Control and Prevention (CDC). Extrapulmonary tuberculosis cases and percentages by site of disease: reporting areas. CDC report 2005. Available from: www.cdc.gov/tb/surv/surv2005/PDF/table27.pdf
32. Phypers M, Harris T, Power C. CNS tuberculosis: a longitudinal analysis of epidemiological and clinical features. *Int J Tuberc Lung Dis* 2006; **10**: 99-103.
33. Fujimura N. Pathology and pathophysiology of pneumoconiosis. *Curr Opin Pulm Med* 2000; **6**: 140–144.
34.Green FHY, Vallyathan V, Hahn FF. Comparative pathology of environmental lung disease. *Toxicologic Pathology* 2007; **35**: 136–147.
35.Gupta M, Lobo FD, Adiga DSA, Gupta A. A histomorphological pattern analysis of pulmonary tuberculosis in lung autopsy and surgically resected specimens. Pathology Research International 2016; Accessed 15 May 2016. http://dx.doi.org/10.1155/2016/8132741.
36. Barboza CEG, Winter DH, Seiscento M, Santos UP, Terra Filho M. Tuberculosis and silicosis: epidemiology, diagnosis and chemoprophylaxis.J *Bras Pneumol* 2008; **34** (11): 961-968
37. Hnizdo E, Murray J. Risk of pulmonary tuberculosis relative to silicosis and exposure to silica dust in South African gold miners. *Occup Environ Med* 1998; **5**(7): 496-502. Erratum in: *Occup Environ Med* 1999; **56** (3):215-216.
38. Hong Kong Chest Service/Tuberculosis Research Centre, Madras/British Medical Research Council. A double-blind placebo-controlled clinical trial of three antituberculosis chemoprophylaxis regimens in patients with silicosis in Hong Kong. *Am Rev Respir Dis* 1992; **145**(1):36-41
39. Pasula R, Wright JR, Kachel DL, Martin WJ 2nd. Surfactant protein A suppresses reactive nitrogen intermediates by alveolar macrophages in response to *Mycobacterium tuberculosis*. *J Clin Invest* 1999; **103** (4):483-490
40. Gold JA, Hoshino Y, Tanaka N, Rom WN, Raju B, Condos R, *et al*. Surfactant protein A modulates the inflammatory response in macrophages during tuberculosis. *Infect Immun* 2004; **72** (2):645-650.
41. Rees D, Murray J. Silica, silicosis and tuberculosis. *Int J Tuberc Lung Dis* 2007; **11**(5): 474-484.
42. Stuckler D, Basu S, McKee M, Lurie M. Mining and risk of tuberculosis in Sub-Saharan Africa. *Am J Public Health* 2011; **101**(3): 524-530.