Scholars Journal of Applied Medical Sciences (SJAMS)
Abbreviated Key Title: Sch. J. App. Med. Sci.
©Scholars Academic and Scientific Publisher
A Unit of Scholars Academic and Scientific Society, India
www.saspublishers.com

ISSN 2320-6691 (Online)
ISSN 2347-954X (Print)

Pulmonary Medicine

Occupational Exposure of Silica and its Immunological Effects at Tertiary Care Hospital

Dr. Sanidhaya Tak[1], Dr. Shweta Choudhary[2*], Dr .Mahesh Gupta[3] , Dr .Gopal Purohit[4], Dr. C.R Choudhary[5], Dr. Sunil Vyas[6], Dr. Hemant Borana[7]

[1]Resident, Department of Pulmonary Medicine, S.N Medical College, Jodhpur, Rajasthan, India
[2]Assistant professor, Department of Pathology, S.N Medical College, Jodhpur, Rajasthan, India
[3] Resident, Department of Pulmonary Medicine, S.N Medical College, Jodhpur, Rajasthan, India
[4] Professor & Head, Department of Pulmonary Medicine S.N Medical College, Jodhpur, Rajasthan, India
[5]Associate Professor, Department of Pulmonary Medicine, S.N Medical College, Jodhpur, Rajasthan, India
[6]Assistant Professor, Department of Pulmonary Medicine, S.N Medical College, Jodhpur, Rajasthan, India
[7]Assistant Professor Department of Pulmonary Medicine, S.N Medical College, Jodhpur, Rajasthan, India

Original Research Article

***Corresponding author**
Dr. Shweta Choudhary

Article History
Received: 08.07.2018
Accepted: 18.07.2018
Published: 30.09.2018

DOI:
10.36347/sjams.2018.v06i09.032

Abstract: Silicosis is an age old occupational disease and remains a major global health problem. It is the most prevalent form of pneumoconiosis, is a preventable, but untreatable, environmental pulmonary disease that can be fatal through the impairment of overall health status.The aim was to evaluate the immunological effects of silica by studying prevalence of autoantibodies Antinuclear Antibody (ANA), Anti Ds DNA, Rheumatoid Factor (RF) and Anti Cyclic Citrullinated Peptide Antibody (Anti CCP) in silica-exposed patients without any known autoimmune disease.The study was done amongst 105 persons engaged in the construction and mining industry exposed to silica attending to tertiary care hospital for respiratory diseases in Western India in two year. Prevalence of ANA, ANTI ds DNA, RF & ANTICCP was studied.In the present study about 64.76% patients were smokers and had history of exposure to silica for more than 10 years. Approx. 70% of the patients had tubercular infection. ANA was positive in 19.04%, Anti ds DNA in 13%, RF in 15% and ANTI CCP in 11% of the patients. Stastistically significant correlation was seen between serum ANA and smoking in silica exposed patients.The present study emphasises that there is increased prevalence of humoral immunologic abnormalities in patients with silicosis. Hence the recognition of autoimmune complications is required in persons exposed to silica.

Keywords: Silica, Silicosis, autoantibodies, autoimmune disease.

INTRODUCTION

Occupational Diseases make an important contribution to the global burden of disease. Silicosis is the most prevalent form of pneumoconiosis, is a preventable, but untreatable. It is irreversible and the disease progresses even when exposure stops. There are large number of workers engaged in sand blasting and chiseling of stones in mines of western Rajasthan. Prevalence of silicosis in Jodhpur Quarry workers is around 9.9% [1].There is a well-established association between inhalational exposure to silica and autoimmune disease, particularly in the context of intense exposure [2]. Silica exposure has also been linked to increased levels of autoantibody production, immune complexes and excess production of immunoglobulin, even in the absence of the full clinical features of a distinct autoimmune disease [2].

There are very few epidemiological studies on immunological effects of silicosis in India, so this study was done in order to ascertain the prevalence of concomitant autoimmune comorbidity in heavily silica-exposed population.

MATERIALS AND METHODS

This study was conducted amongst 105 persons engaged in the sand blasting, cutting, chiselling, drilling and dressing of stones attending to Department of Pulmonary Medicine, Kamla Nehru Chest Hospital, Dr. S.N. Medical College, Jodhpur from 2015 to 2017. This was a hospital based descriptive type of study to study immunological effects of silica. Serum ANA, Anti Ds DNA, Rheumatoid factor, Anti CCP autoantibodies were studied in patients exposed to silica. Information were gathered by the questionnaire and medical records which

included demographic data, occupational history, nature of work, duration of exposure to dust particles, drug use, smoking habits, association with tuberculosis and respiratory symptoms, medical history including joint and skin problems, auto-immune diseases.Informed consent was taken and blood sample was was sent to the Microbiology lab from Patient without known autoimmune disease like SLE, scleroderma, rheumatic arthritis etc. Serum ANA >23.0 IU/ml, Serum Anti Ds DNA >60 IU/ml and Serum ANTI CCP assay >17 µ/ml was considered positive. Significant values of chi square test were seen from probability tables for degree of freedom. P value < 0.05 was considered as significant.

RESULTS

Out of 105 patients, most of the the patients are in the age group of 41-50 years (26.67%) followed by 51-60 yrs (24.76%) and 31-40 yrs (24.76%). Mean age of study population was 50.5 years. .All the patients were male except one female patient. In this study, most of the patients were stone cutter by occupation followed by 6.66% drillers, 1.90% sand blaster and 0.95% was stone dresser. the study revealed that 64.76% were smokers.Majority of the study population is residing in rural area forming 86.67%. Majority of patients had history of exposure to silica of 11-20 years, (60.95%), followed by of 21-30 years, (24.76%). 4.76 % patients were exposed for more than 30 years and 9.53% patients were exposed for less than 10 years. Approx. 70% of the patients had tubercular infection in the past or presently suffering from it. most common presenting complaint was Shortness of breath (88.57%), followed by cough(72.3%) ,chest pain(25.71%) and fever(20%), ANA was positive in 19.04% ,Anti Ds DNA in 13% ,Rheumatoid factor in 15% and Anti CCP in 11% of the patients.(figure no1) there was stastistically significant correlation between detection of serum ANA and smoking in silica exposed patients(p=0.04).No statistically significant correlation was seen between tubercular infection and duration of silica exposure with serum autoantibodies in silica exposed patients.

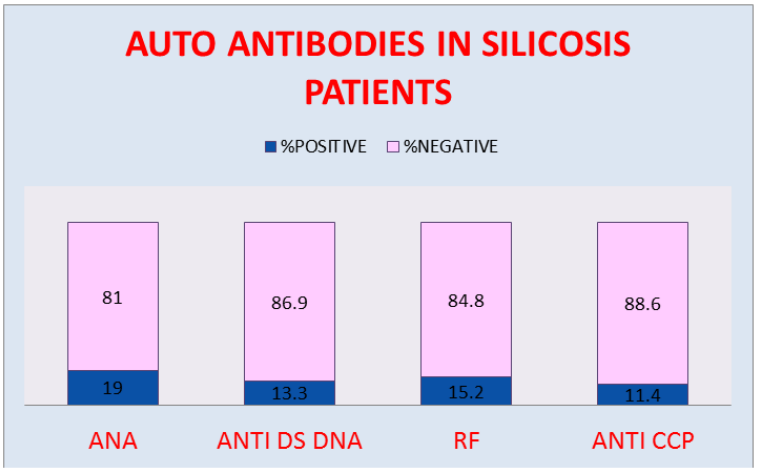

Fig-1

Table-1: Studies on immunological effects of silica

Studies	Year	No of Cases	ANA (%)	Anti-DS DNA(%)	RF (%)	Anti CCP (%)
Kang *et al*. [22]	1973	31	26	-	-	-
Jones *et al*. [23]	1976	39	44	-	-	-
Haslam PL *et al*. [24]	1979	42	43	-	36	-
Doll *et al*. [25]	1981	53	26	0	28	-
Nagoka*et al*. [26]	1993	134	1	-	10.4	-
Julio *et al*. [27]	1993	50	72	-	22	
Subra*et al*.[28]	2001	58	28	6	-	-
Hermano Albuquerque De Castro *et al*. [29]	2004	58	20.6	-	3.4	-
Aminian O *et al*. [30]	2009	78	0	-	2.56	-
Zaghi*et al*. [31]	2010	61	1.6	-	11.4	-
Makol A *et al*. [6]	2011	790	.1	-	4.2	-
O.Shtraichman*et al*. [32]	2015	40	2	-	5	-
PRESENT STUDY	2018	105	19.04	13.33	15.23	11.42

DISCUSSION

A number of epidemiological studies support the association between occupational exposure to respirable crystalline silica dust and development of systemic autoimmune diseases.

There is a well-established association between inhalational exposure to silica and autoimmune disease, particularly in the context of intense exposure. Silica exposure has also been linked to increased levels of autoantibody production, immune complexes and excess production of immunoglobulin, even in the absence of the full clinical features of a distinct autoimmune disease [2]. The association between silica exposure and autoimmune disease was first described by Bramwell in 1914, who observed scleroderma among stone masons [3]. Erasmus also found an increased incidence of systemic sclerosis (SSc) among South African gold miners [4 Caplan described the occurrence of multiple lung nodules in coal miners who also suffered from rheumatoid arthritis (RA), comorbidity known as Caplan's syndrome or rheumatoid pneumoconiosis [5]. Significant risk of developing SSc, RA, systemic lupus erythematosus (SLE), dermatomyositis/polymyositis and anti-neutrophil cytoplasmic antibody (ANCA) - positive vasculitis has been linked to silica exposure in various studies [2, 6, 7].

Adjuvant Effect Silica has long been known to have an adjuvant effect on antibody production [8]. An adjuvant is a substance that nonspecifically enhances or potentiates an immune response to an antigen. Although the mechanism by which silica acts as an adjuvant is not fully understood, it appears to be related to the inflammatory response [9].One theory is that the activation of macrophages at the site of silica deposition may lead to increased antigen processing and accelerated antibody production. Macrophages respond to internalized silica by up regulating cytokine production (including interleukin (IL)-1 and tumor necrosis factor [TNF]) [10, 11], which stimulates other cells and enhances the inflammatory response. IL-1 can activate the T-helper cells that facilitate B-cell production of antibodies. In one study, silica was reported to stimulate the polyclonal (nonspecific) activation of human T cells in vitro, suggesting the potential of silica to act as a superantigen in vivo. Silica may also activate immune processes through the release of reactive oxygen and nitrogen species [12-14].Silicosis increases susceptibility to tuberculosis and other respiratory diseases and silica has recently been categorized by the International Agency for Research on Cancer as a known human carcinogen [15-17].

The present study supports the hypothesis that there is increased prevalence of humoral immunologic abnormalities in patients with silicosis. The detection of autoantibodies in this study is similar to the results of previous studies on patients with silicosis (Table no 1). Patrikstolt and Jonsson*et al.* Shown silica exposure combined with smoking among men is associated with an increased RF [18,19]

In contrast, studies by Aminian O *et al.* and Subra*et al*. could not show any significant increase in RF, ANA, Complements in the serum of silicosis patients [20, 21].Despite the relatively large of the artificial stone-associated silicosis, the absolute number of patients is limited. Therefore, we could not estimate with precision the frequency of different subtypes of concomitant autoimmune diseases.

CONCLUSION

Silicosis is remains a major occupational health problem in India. It is responsible for high morbidity and mortality in industrial workers. The present study supports the hypothesis that there is increased prevalence of humoral immunologic abnormalities in patients with silicosis.Hence recognition of autoimmune complications is required in persons with known silicosis; and also the occupational exposure history in persons presenting with manifestations of autoimmune disease.

REFERENCES

1. Dr. Mathur ML, Ann Nail Acad Med Sci (India) 1996. 32(2): 113-118.
2. Parks CG, Conrad K, Cooper GS. Occupational exposure to crystalline silica and autoimmune disease. Environ Health Perspect. 1999;107(Suppl. 5):793–802
3. Bramwell B. Diffuse sclerodermia: Its frequency; its occurrence in stone-masons; its treatment by fibrolysin—Elevations of temperature due to fibrolysin injections. Edinburgh Medical Journal. 1914 May;12(5):387.
4. Erasmus LD. Scleroderma in Gold-Miners on the Witwatersrand with Particular Reference to Pulmonary Manifestations. South African Journal of Laboratory and Clinical Medicine. 1957;3(3):209-31.
5. Schreiber J, Koschel D, Kekow J, Waldburg N, Goette A, Merget R. Rheumatoid pneumoconiosis (Caplan's syndrome). European journal of internal medicine. 2010 Jun 1;21(3):168-72.
6. Makol A, Reilly MJ, Rosenman KD. Prevalence of connective tissue disease in silicosis (1985–2006)—a report from the state of michigan surveillance system for silicosis. American journal of industrial medicine. 2011 Apr;54(4):255-62.
7. Parks CG, Cooper GS, Nylander-French LA, Sanderson WT, Dement JM, Cohen PL, Dooley MA, Treadwell EL, St. Clair EW, Gilkeson GS, Hoppin JA. Occupational exposure to crystalline silica and risk of systemic lupus erythematosus: A population-based, case–control study in the Southeastern United States. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology. 2002 Jul;46(7):1840-50.
8. Pernis B, Paronetto F. Adjuvant effect of silica (tridymite) on antibody production. Proceedings of the Society for Experimental Biology and Medicine. 1962 Jun;110(2):390-2.
9. Naim JO, van Oss CJ, Wu W, Giese RF, Nickerson PA. Mechanisms of adjuvancy. I: Metal oxides as adjuvants. Vaccine 15:1183-1193(1997).

10. Davis GS, Pfeiffer LM, Hemenway DR. Persistent overexpression of interleukin-1j and tumor necrosis factor-a in murine silicosis. J Environ PatholToxicolOncol. 17:99-114 (1998).
11. Driscoll KE, Carter JM, Hassenbein DG, Howard B. Cytokines and particle-induced inflammatory cell recruitment. Environ Health Perspect. 105 (suppl 5):1159-1164)1997).
12. Ueki A, Yamaguchi M, Ueki H, Watanabe Y, Ohsawa G, Kinugawa K, Kawakami Y, Hyodoh F. Polyclonal human T-cell activation by silicate in vitro. Immunology. 82:332-335(1994).
13. Shoemaker DA, Pretty JR, Ramsey DM, McLaurin JL, Khan A, Teass AW, Castranova V, Pailes WH, Dalal NS, Miles PR. Particle activity and in iwvopulmonary response to freshly milled and aged alphaffuartz. Scan J Work Environ Health 21)suppl 2):15-8 (1995).
14. Vallyathan V, Shi X, Castranova V. Reactive oxygen species: their relation to pneumoconiosis and carcinogenesis. Environmental health perspectives. 1998 Oct; 106(Suppl 5):1151.
15. American Thoracic Society. Adverse Effects on Crystalline Silica Exposure. Am J Crit Care Med. 1997;155:761-5.
16. Silicosis and Silicate Disease Committee. Diseases associated with exposure to silica and nonfibrous silicate minerals. Arch Pathol Lab Med. 1988; 112:673-720.
17. International Agency for Research on Cancer. IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans. Vol. 26. Some antineoplastic and immunosuppressive agents. Distributed for IARC by WHO, Geneva, Switzerland; 1981.
18. Stolt P, Yahya A, Bengtsson C, Källberg H, Rönnelid J, Lundberg I, Klareskog L, Alfredsson L, EIRA Study Group. Silica exposure among male current smokers is associated with a high risk of developing ACPA-positive rheumatoid arthritis. Annals of the rheumatic diseases. 2010 Apr 1:annrheumdis114694.
19. JÓnsson T, Thorsteinsson J, Valdimarsson H. Does smoking stimulate rheumatoid factor production in non-rheumatic individuals?.Apmis. 1998 Jul;106(7-12):970-4.
20. Aminian O, Sharifian S, Mehrdad R, Haghighi K, Mazaheri M. Antinuclear antibody and rheumatoid factor in Silica-Exposed workers. Archives of Industrial Hygiene and Toxicology. 2009 Jun 1;60(2):185-90.
21. Subra JF, Renier G, Reboul P, Tollis F, Boivinet R, Schwartz P, Chevailler A. Lymphopenia in occupational pulmonary silicosis with or without autoimmune disease. Clinical & Experimental Immunology. 2001 Dec; 126(3):540-4.
22. Kang KY, Yagura T, Yamamura Y. Antinuclear factor in pneumoconioses. The New England journal of medicine. 1973 Jan 18; 288(3):164.
23. Jones RN, Turner-Warwick M, Ziskind M, Weill H. High prevalence of antinuclear antibodies in sandblasters' silicosis. American Review of Respiratory Disease. 1976 Mar;113(3):393-5.
24. Haslam PL, Thompson B, Mohammed I, Townsend PJ, Hodson ME, Holborow EJ, Turner-Warwick M. Circulating immune complexes in patients with cryptogenic fibrosingalveolitis. Clinical and experimental immunology. 1979 Sep; 37(3):381.
25. Doll NJ, Stankus RP, Hughes J, Weill H, Gupta RC, Rodriguez M, Jones RN, Alspaugh MA, Salvaggio JE. Immune complexes and autoantibodies in silicosis. Journal of Allergy and Clinical Immunology. 1981 Oct 1;68 (4):281-5.
26. Nagaoka T, Tobata M, Kobayashi K, Okada A. Studies on production of anticollagen antibodies in silicosis. Environ Res. 1993; 60:12-29.
27. Julio Sanchez-Roman, IngeborgWichmann, Javier Salaberri, Jose M Varela, Antonio Nufnez-Roldan. Multiple clinical and biological autoimmune manifestations in 50 workers after occupational exposure to silica. Annals of the Rheumatic Diseases 1993; 52: 534-538
28. Subra JF, Renier G, Reboul P, Tollis F. Lymphopenia in occupational pulmonary silicosis with or without autoimmune disease. ClinExpImmunol. 2001; 126:540-4.
29. Castro HA, Silva CG, Lemle A. Immunoglobulins, complements and autoantibodies in 58 workers exposed to silica. JornalBrasileiro de Pneumologia. 2004 Jun; 30(3):201-6.
30. Aminian O, Sharifian S, Mehrdad R, Haghighi K, Mazaheri M. Antinuclear antibody and rheumatoid factor in Silica-Exposed workers. Archives of Industrial Hygiene and Toxicology. 2009 Jun 1; 60(2):185-90.
31. Zaghi G, Koga F, Nisihara RM, Skare TL, Handar A, Utiyama SR, Silva MB. Autoantibodies in silicosis patients and in silica-exposed individuals. Rheumatology international. 2010 Jun 1; 30(8):1071-5.
32. Shtraichman O, Blanc PD, Ollech JE, Fridel L, Fuks L, Fireman E, Kramer MR. Outbreak of autoimmune disease in silicosis linked to artificial stone. Occupational Medicine. 2015 Jun 12; 65(6):444-50.