Original Article

Silica Exposure and Serum Angiotensin Converting Enzyme Activity

RR Tiwari,[1] AB Karnik,[2] YK Sharma[3]

Abstract

Background: Silicosis is known in industrial workers for centuries. Till recently, the mainstay of its diagnosis and progress was clinical examination of the respiratory system, pulmonary function test and chest radiography. Several biomarkers such as serum angiotensin converting enzyme (ACE) activity have been examined to determine the extent of silicosis.

Objective: To elucidate the effect of age, gender, duration of exposure to silica dust, smoking habit, and pulmonary function status on the serum ACE activity among quartz stone workers without disease.

Methods: A cross-sectional study was carried out on 134 (111 men and 14 women) workers of quartz stone crushing units were studied. Standard diagnostic criteria were used for diagnosing silicosis and tuberculosis. Pulmonary functions of the participants were also assessed.

Results: The mean±SD age for participants was 26.1±6.3 years (26.6±6.3 for men and 21.9±4.3 for women). The mean±SD duration of exposure was 1.1±1.9 years. In the present study, only one case of silicosis and eight cases of tuberculosis were found. The mean±SD serum ACE levels for those with and without respiratory disease were 68.44±11.61, and 66.9±14.4 IU/L, respectively (p>0.05).

Conclusion: We could not observe any association between serum ACE activity and age, gender, duration of exposure, smoking habits and pulmonary function status. However, elevated levels of serum ACE was found in a solitary case of silicosis.

[1]Scientist C
[2]Ex-Deputy Director
[3]Scientist E
National Institute of Occupational Health, Meghani Nagar, Ahmedabad 380016, Gujarat, India

Keywords

Angiotensin converting enzyme; Peptidyl-dipeptidase A; ACE protein, Human; Respiratory function tests, Silicosis, India

Introduction

The dust hazard known as pneumoconiosis in industrial workers has existed for centuries. Various physical properties and chemical components of dust produce different changes in the lungs. But the silica dust, which is ubiquitous in the atmosphere, still outnumbers the other types of dust, thus making silicosis the most frequently occurring pneumoconiosis.[1-4] Improvement in industrial hygiene, techniques such as wet drilling, efficient ventilation systems and personal protective devices, have prevented silicosis to some extent. In India, however, small-scale industries do not have such preventive measures.

Correspondence to
Dr. Rajnarayan R Tiwari,
Occupational Medicine Division,
National Institute of Occupational Health,
Meghani Nagar,
Ahmedabad 380016
E-mail: drrajtiwarinioh@rediffmail.com

TAKE-HOME MESSAGE

- This study was conducted to determine the effect of age, gender, duration of exposure to silica dust, concentration of silica dust in the working environment, smoking habit, and pulmonary function status on the serum ACE activity among quartz stone workers without any diseases.
- There was no significant difference in the mean serum ACE level in various categories of age, gender, duration of exposure, smoking habits and pulmonary function status.

Quartz stone grinders who are involved in crushing quartz stone into powder, which is then used as a precursor for glass manufacturing industry, are exposed to excess risk of silicosis as the stone contains approximately 100% free silica and the process liberates huge amount of silica dust into the working environment. In Godhara region of Gujarat itself, about 10 000 workers work as contract laborer in these quartz crushing units.

Till recently, the diagnosis of silicosis was mainly made on clinical examination with special emphasis on the respiratory system, assessment of pulmonary function tests, particularly lung volumes and grading of profusion according to the International Labour Organization classification of pneumoconiosis. After Lieberman[5] who in 1975 first reported the elevation of serum angiotensin converting enzyme (ACE) in sarcoidosis, several investigators have confirmed that the serum ACE activity is increased in a large proportion of patients with granulomatous diseases like sarcoidosis and silicosis.

Angiotensin I converting enzyme (peptidyl-dipeptidase A, EC 3.4.15.1) is a membrane-bound glycoprotein, which converts angiotensin 1 to angiotensin 2 and participates in bradykinin degradation.[6] ACE is bound to the luminal membranes of endothelial cells and its action takes place mainly in the pulmonary circulation.[7,8] The serum activity of ACE in pulmonary diseases is of interest for its principal localization in the large capillary bed of the lungs. Furthermore, it helps in distinguishing between silicosis and sarcoidosis; the possibility of silicotuberculosis must be also considered when high serum ACE levels are encountered.[9] There are, however, scarce and conflicting[10-12] data on the association between serum ACE and silica exposure in workers without any diseases. Moreover, the effect of age, gender, duration of exposure to silica dust, smoking habit, and pulmonary function status on the serum ACE activity is a matter of debate in several articles published, particularly from India. This study was therefore, carried out to determine the effect of age, gender, duration of exposure to silica dust, concentration of silica dust in the working environment, smoking habit, and pulmonary function status on the serum ACE activity among quartz stone workers without any diseases.

Patients and Methods

The present cross-sectional study was carried out in 2002 in Godhara, Gujarat, India. Godhara usually has a hot weather with an average temperature of 32 °C and very scanty rainfall. There were 18 functional units where 181 workers were working. We asked all the workers to participate in the study, out of whom 134 (74%) agreed to give blood sample for measurement of serum ACE and thus were includ-

Table 1: Distribution of serum ACE values (IU/L) in quartz stone workers free from disease.

Study variable		n	Mean±SD	p value
Age group (yrs)	<25	77	67.09±13.46	
	25–29	30	66.2±13.13	
	≥30	27	67.41±17.49	0.94
Sex	Male	120	67.22±13.94	
	Female	14	64.64±16.44	0.52
Duration of exposure	<1 yr	102	66.9±15.0	
	≥1 yr	32	67.12±11.36	0.93
PFT status	Abnormal	20	67.5±18.31	
	Normal	114	66.86±13.42	0.85
Smoking habit	Non smoker	64	66.03±14.58	
	Smoker	56	68.59±13.18	0.31

ed in the analysis. An informed consent was obtained from each participant after the nature of the procedures had been fully explained. Through an interview, demographic and occupational details of participants were recorded on a data collection sheet. The participants were also asked whether they used any protective devices and if yes what type of it.

In the present study, those who have ceased smoking since last year were categorized as "ex-smokers." For analyzing the effect of smoking habit on the pulmonary function test (PFT) parameters, the ex-smokers were included in the "non-smokers" group as they were very few in number and most of them had smoked occasionally when they were smokers. Furthermore, women were excluded while analyzing the effect of smoking as no woman was smoker and inclusion of them might have diluted the effect.

Standard diagnostic criteria were used for diagnosing silicosis and silico-tuberculosis.[13] The pulmonary functions of participants were assessed using a Spirovit SP-10 spirometer (Maker Schiller AG, Switzerland). After calibrating the spirometer according to the manufacturer's guide, three readings of each ventilatory function of each subject were taken. The highest recorded values, considering that the subject has cooperated at his/her best, were used for further analysis.

Blood samples were collected from the subjects and centrifuged for the separation

Table 2: Distribution of serum ACE levels (IU/L) of quartz workers with and without respiratory disease.

Parameters		Respiratory morbidity				p value
		Present		Absent		
		n	Mean±SD ACE levels	n	Mean±SD ACE levels	
Age group (yrs)	<25	4	79.00±9.2	73	66.44±13.39	0.016
	25–29	3	59.33±2.9	27	66.96±13.62	
	≥30	2	61.00	25	67.92±18.1	
Gender	Male	9	68.44±11.6	111	67.13±14.2	0.545
	Female	0	—	14	64.64±16.4	
Duration of exposure	<1 yr	7	66.57±9.8	95	66.93±15.4	0.914
	≥1 yr	2	75.00	30	66.6±10.9	
PFT status	Abnormal	2	69.00	18	67.33±19.1	
	Normal	7	68.29±12.4	107	66.77±13.5	0.878
Smoking habit	Non-smoker	4	68.25±14.6	51	65.88±14.7	
	Smoker	5	68.60±10.5	60	68.59±13.5	0.32

of serum which was kept frozen until analyzed. The serum ACE activity was measured by the spectrophotometric method; the synthetic tripeptide substrate used was N-[3-(2-furyl) acryloy]-L-phenylalanylglycylglycine (FAPGG). The method is based on the principle of hydrolysis of FAPGG to furylacryloylphenylalanine and glycylglycine.[14] Hydrolysis of FAPGG results in a decrease in the absorbance at 340 nm. The ACE activity in the sample is determined by comparing the sample reaction rate to that obtained with the ACE calibrator.

Statistical analyses were carried out us-

ing EpiInfo 5 (World Health Organization, Geneva). One-way analysis of variance (ANOVA) and *Student's t* test for independent samples were used for comparing means among the study groups.

Results

The present cross-sectional study included 120 (89.5%) men and 14 (10.5%) women making a total of 134 participants. The majority of the subjects (47.0%) aged <25 years. The mean±SD age of participants was 26.6±6.3 years (26.6±6.3 for men and 21.9±4.3 for women). The mean±SD duration of exposure was 1.1±1.9 years. Most of the subjects belonged to the "lower socio-economic strata," according to modified Kuppuswamy's socio-economic classification.[15]

Table 1 shows distribution of serum ACE level among the quartz stone workers who were found normal according to their chest roentgenogram. There was no significant difference in the mean serum ACE level in various categories of age, gender, duration of exposure, smoking habits and pulmonary function status.

None of the workers used any personal protective devices. Based on spirometric studies 12 (9%) subjects had obstructive, four (3%) had restrictive, and four (3%) had combined pulmonary function impairment; 114 (85.1%) had normal test.

In Table 2, we compared the mean serum ACE level in those workers with and without disease. In the present study, only one patient with silicosis and eight with tuberculosis were found. The mean serum ACE level for those with and without respiratory disease was 68.44±11.61 and 66.85±14.38 IU/L, respectively (p>0.05).

Discussion

Among the workers without respira-

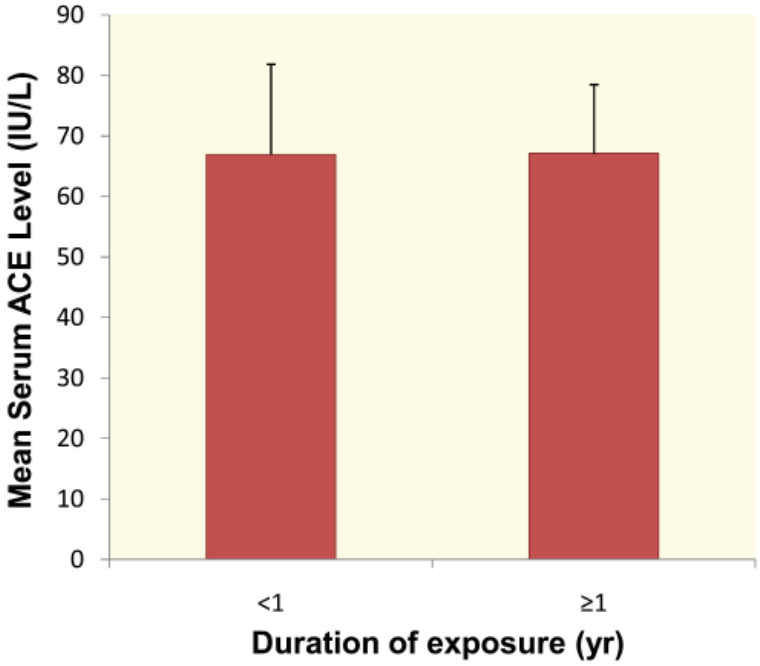

Figure 1: Mean serum ACE level in two groups with different durations of exposure. The error bar represents SD.

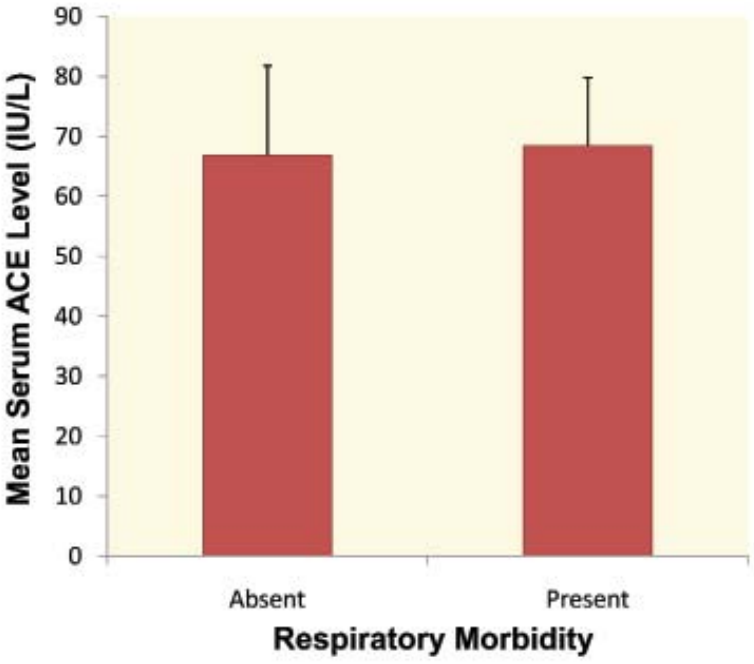

Figure 2: Mean serum ACE level in those with and without respiratory morbid conditions. The error bar represents SD.

tory disease, the mean serum ACE level was higher in those aged ≥30 (n=27) than in those <30 (n=107) years of age. The difference, however was not statistically significant. This is in agreement with the earlier observations.[16-18] Nonetheless, few studies claimed age dependence in healthy controls.[5,19] When serum ACE level was compared between the group with and without respiratory morbidity, the levels was significantly higher in those aged <25 years who had respiratory morbidity than those aged <25 but were free from respiratory morbidity (Table 2). This might be due to the case of silicosis belonging to this age group. For other age groups, the difference between the two groups, *i.e.*, those with and without respiratory morbidity, was not statistically significant.

In the present study, only 14 women were included; none had respiratory morbid conditions. This can be attributed to the significantly lower duration of exposure. Furthermore, these women were working in those process units where production of dust is less, and thus their overall exposure was lower than men. Among those free from respiratory morbid conditions, the mean serum ACE level was higher in men than women, though the difference was not statistically significant. This is in keeping with the findings of Grønhagen-Riska who showed that in healthy subjects the ACE activity was independent of gender.[20]

We found a significant increase in the ACE level among those exposed for more than one year. This can be attributed to the increased cumulative exposure of workers to the silica. Out of the two subjects with respiratory disease who were exposed more than one year, one had silicosis and had a serum ACE level of 82 IU/L (Fig. 1).

The source of increased serum ACE level in silicosis remains hypothetical. The endothelial cells in the capillary bed have high contents of ACE.[7,8,21,22] Fibrosis of tissues may give rise to release of ACE. Human alveolar macrophages are also known to contain ACE, and the mononuclear phagocyte cell line is considered the primary source of serum ACE in sarcoidosis.[23] The cytotoxic effect of silica particles on macrophages leading to their rupture and loss of the cytoplasmic contents, seem to be crucial in the development of silicosis.[24] It is likely that the serum ACE level in silicosis, at least partly, reflects the accumulation and the increased degradation of macrophages; this indicates that macrophages may be a source of serum ACE in silicosis. Among those free from respiratory diseases, the workers exposed to silica dust for less than one year had a significantly lower serum ACE level than those exposed for one year or more. This could be attributed to the very small sample size in that particular group. Bucca, *et al,* also reported similar findings.[25]

Considering the pulmonary function status, serum ACE level, though not statistically significant, was higher in those with abnormal pulmonary function than those with normal pulmonary function in those who had no respiratory disorders based on their chest x-ray. Similarly, the serum ACE level was higher among those with respiratory disorders than those free from disease, although the difference was not statistically significant (Fig. 2). This might be attributed to the obstructive type of pulmonary impairment due to smoking and chronic bronchitis where airways are more affected than the lung parenchymal tissue. This finding is also in concordance with earlier observations.[25]

Similarly, though the smokers had more serum ACE level than non-smokers for the

both studied groups—*i.e.*, those with and without respiratory morbidity—the difference was not statistically significant. This might due to the fact that smoking is mostly responsible for chronic bronchitis rather than affecting lung parenchyma, and thus it does not affect the mononuclear cell activity, which is supposed to be the source of increased serum ACE level among patients with silicosis.

We could not observe any association between serum ACE activity and age, gender, duration of exposure, smoking habits and pulmonary function status. However, elevated levels of serum ACE was found in a solitary case of silicosis.

Conflict of Interest: None declared

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