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Original Research Article

Evaluation of Angiotensin Converting Enzyme in Stone Mine Workers of Rajasthan Region

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Abstract:

Background: Silicosis has been known in industrial workers for millennia. Until recently, clinical evaluation of the respiratory system, pulmonary function tests, and chest radiography were the mainstays of its diagnosis and progression. Several indicators, such as serum angiotensin II, have been identified. The activity of converting enzyme (ACE) has been studied to identify the degree of silicosis.

Objectives: The purpose of this study was to determine the effect of age, gender, duration of silica dust exposure, smoking habit, and pulmonary function status on serum ACE activity in healthy quartz stone miners.

Methods: A cross-sectional study was conducted on 60 stone mine workers and 60 non- mine workers as a control. All the personnel who were being researched had their chests examined. They also measured the pulmonary functions. Blood samples were taken from exposed workers and the controls, centrifuged to separate the serum, and then refrigerated until serum ACE levels could be determined.

Results: The participants' mean age was 35.28 years in mine workers and 38.45 years in non- mine workers. The ACE levels were directly associated with increase in exposure of silica and ACE level (76.45IU/L) was maximum in participants who were exposed to silica for more than 5 years. Males (68.32 IU/L) had higher ACE values compared to females (64.23 IU/L). Participants with smoking habits had values greater than non- smokers.

Conclusion: We found no correlation between serum ACE activity and age, gender but was significant with duration of exposure, smoking behaviours, or pulmonary function status. Increased levels of serum ACE were discovered in cases of silicosis.

Keywords: Mine Workers, Angiotensin Converting Enzymes, Silicosis, Silica Exposure, Pulmonary Function Test.

Introduction

The Rajasthan state of India is noted for having abundant mineral resources and is the location of several mining enterprises. The state possesses a lot of reserves of different minerals, including lead, copper, zinc, limestone, gypsum, rock phosphate, and marble.

In Rajasthan's mining industry, mine workers play important role. They work on the transportation, processing, and extraction of minerals. These personnel are in charge of activities including drilling, blasting, loading, and hauling and frequently work in demanding environments, including deep mines.

Many individuals in Rajasthan have employment chances in the mining industry, especially in rural areas where there may not be many other options for a living. The backgrounds of mine workers are diverse, and they may be employed directly by mining firms or work as.

The peptidyl dipeptide hydrolase angiotensin I-converting enzyme (ACE) is mostly found on the luminal surface of vascular endothelial cells, but it is also present in cells coming from the monocyte-macrophage system. An important enzyme in the renin-angiotensin system, ACE transforms the weak vasopressor angiotensin I into the strong vasopressor angiotensin II while also inactivating the vasodilator bradykinin. [1]

Increased serum ACE activity (SACE) has been observed in pathologies, especially granulomatous illnesses that stimulate the monocytic cell line. Analysing the progress of sarcoidosis and the results of treatment. Additionally, SACE can be elevated in extrathoracic granulomatous pathologies like

Gaucher disease and leprosy, nongranulomatous conditions like hyperthyroidism or cholestasis, and nonsarcoidotic pulmonary granulomatous diseases like silicosis and asbestosis. The assessment of ACE activity in other biological fluids, such as broncho-alveolar and cerebral fluids, in the quest for a locoregional dissemination or dissimulation of the disease, is, however, obviated by the monitoring of sarcoidosis. [2]

Reduced SACE has been documented in endothelium dysfunctions associated to the toxicity of chemotherapy and radiotherapy used in malignancies, leukaemias, and hematopoietic or organ transplantations, as well as in vascular diseases involving an endothelial abnormality, such as deep vein thrombosis. SACE is useful for tracking arterial hypertension that has been treated with particular synthetic ACE inhibitors. [3, 4] The study was aimed to see the effect of age, gender, duration of silica exposure, smoking habits and pulmonary function status on the activity of the angiotensin converting enzyme (ACE) in 60 mine worker compared with 60 control group.

Methodology

It was a cross-sectional controlled study. The study involved 60 employees from mines and 60 employees from other profession (Non- mine workers). The chest X-rays confirmed by high resolution computerised tomography scan (CT) revealed that all the opacities were of the p/p category and of 1/0, 1/1, 1/2, and 2/1 profusion grades small sample size.

Those who had been exposed for an average of 10 years were included. All of them tested negative for silicosis on their chest X-rays and CT scans. None of the exposed employees employed any PPE, such as masks or respirators, while they were working. A control group (with a free chest x-ray) of 60 administrative professionals who have never worked in the mine sector and have an average age of 38.45 years was selected. Each subject's written informed consent attested to his or her voluntary involvement in this study. The participant and the lead researcher both signed the consent form. All employees were questioned and given questionnaires to complete (personal information, smoking habits, thorough present and prior employment histories to uncover work-related complaints, and previous medical histories of chronic illnesses).

The current study did not include participants who had chronic inflammatory disorders such liver disease, rheumatoid arthritis, diabetes, hypertension, or thyroid disease.

All the personnel who were being researched had their chests examined.

3. Plain chest X-ray: All of the study groups underwent full-sized (14" 14") posterior-anterior roentgenograms.

4. The exposed workers had High Resolution CT scans, and the roentgenographic results were categorised in accordance with the pneumoconiosis classification system used by the International Labour Organisation (I.L.O.) [5]

The Swiss company Maker Schiller AG's Spirovit SP-10 was used to measure the pulmonary functions.

At least three valid, reproducible (within 5%), and acceptable spirograms were obtained after the spirometer had been calibrated in accordance with the instructions provided in the catalogue. Records were made of the readings that displayed the greatest value. Utilised were the spirometer's automatic Whites [6] spirometry prediction formulae. According to the International Labour Organisation (I.L.O) classification of pneumoconiosis [7], the spirometric parameters that were recorded comprised percent projected forced vital capacity (% pred FVC), percent predicted forced expiratory volume in 1st second (% pred FEV1), and FVC/FEV1 ratio.

Laboratory investigations: Blood samples were taken from exposed workers and the controls, centrifuged to separate the serum, and then refrigerated until serum ACE levels could be determined.

Using the spectrophotometric technique, the serum ACE activity was assessed. The synthetic tripeptide substrate employed was N-[3-(2-furyl) acryloy]-L phenylalanylglycylglycine (FAPGG). The process is founded on the idea that FAPGG hydrolyzes to form furylacryloylphenylalanine and glycylglycine. The absorbance at 340 nm is decreased by FAPGG hydrolysis. By contrasting the sample reaction rate with that obtained using the ACE calibrator, the ACE activity in the sample is identified [5]. From BEN-Biomedical Enterprise S.r.l. in Milan, Italy, the kit was purchased. Typical ranges (20–70 U/L). [8]

Using the Microsoft Excel data entry and statistical calculations were carried out. 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 participants 60 participants were mine workers and 60 were non- mine workers. Out of them 84 % males and 16% females. The mean age was 35.28 years in mine workers and 38.45 years in non- mine workers. All subjects belong to low socio economic status. Table 1 shows concentration of ACE levels in the mine workers classified on the basis of chest X-

Rays compared with Non- mine workers. The levels were higher in Mine workers (66.27 ± 13.67 IU/L) and the difference was significant. There was no significant difference in the mean serum ACE levels according to age, sex, duration of exposure, smoking habits and pulmonary function tests.

None of the workers used any personal protective devices. Based on spirometric studies (9%) subjects had obstructive, four (3%) had restrictive, and four (3%) had combined pulmonary function impairment; (85.1%) had normal test. In table 2 we compared the mean serum ACE levels in mine workers on the basis of age group, gender, Duration of silica exposure, PFT and also on smoking habits. The mean ± SD serum ACE levels were highest in 41-60 years age group participants followed by 21-40 years and then in <20 years. Grouping on basis of gender the results showed that males (68.32 IU/L) had higher ACE values compared to females (64.23 IU/L). On the exposure duration time the participants were divided into 3 groups (< 1 year, 2-5 years exposure, > 5 years exposure) the ACE levels were directly associated with increase in exposure of silica ACE level (76.45 IU/L) was maximum in participants who were exposed to silica for more than 5 years. The p- value results depicted that the levels were highly significant when compared the results of < 1 year with > 5 years of exposure. Participants smoking habits had values greater than non- smokers. The comparison of variance was highly significant.

The Groups were classified into 3 on the basis of duration of exposure into 1) <1 year silica exposed 2) 2-5 years exposed 3) > 5 years of exposure. The participants were selected 20 participants from each group. The ANOVA test of Variance was performed to compare the effect of duration of silica exposure and Angiotensin Converting enzyme. The ANOVA test revealed that F statistics values were more than F critical value hence the test is significant. (Table 3)

Table 1: Comparison of ACE values in Mine workers and Non- mine workers.

	Group 1 Non- mine workers (Controls) (N=60)			**Group 2 Mine workers (Mine Workers) (N=60)**			**P Values Group 1 & Group 2**
Parameters	Male (N=40)	Female (N=20)	Total (N=60)	Male (N=45)	Female (N=15)	Total (N=60)	
Angiotensin converting Enzymes(ACE) (IU/L)	62.57 ± 13.25	59.02 ± 12.76	60.79 ± 12.87	68.32 ± 12.11	64.23 ± 13.23	66.27 ± 13.67	0.0256 Significant

Table 2: ACE values in Mine workers.

	Serum ACE value (IU/L)		
Parameters	**Mean**	**SD**	**p- value**
Age			---
1) < 20 years (n=12)	65.01	12.23	
2) 21-40 Years (n=31)	67.23	12.76	1& 2 = 0.554
3) 41-60 years (n=17)	69.11	11.23	1& 3 = 0.233
Sex			
Male(n=45)	68.32	11.76	0.136
Female (n=15)	64.23	12.45	
Duration of exposure			
1) < 1 year (n=20)	65.43	11.67	
2) 2-5 years (n=20)	68.76	13.56	1& 2 = 0.412
3) >5 years (n=20)	76.45	12.78	1 &3 = 0.007
PFT status			
Normal (n=30)	63.56	12.23	
Abnormal (n=30)	69.98	11.31	0.0391
Smoking habits			
Non- smoker (n=31)	65.78	13.13	
Smoker (n=29)	75.67	14.32	0.0030

Table 3: Showing ANOVA test results.

ANOVA						
Source of Variation	**SS**	**df**	**MS**	**F**	**P-value**	**F crit**
Between Groups	1548.508	2	774.2542	485.4347	1.59E-36	3.158843
Within Groups	90.91334	57	1.594971			
Total	1639.422	59				

SS	Sum of Squares, quantifies the variability between or within groups.	
df	Degree of freedom (within Groups) = Number fo groups -1	
MS	Mean Square means average variation between groups and within groups	
F	F statistics MS (between groups)/MS (within groups)	
	F statistics > F critical value	Test is significant

Discussion

In fibrotic lung conditions, serum levels of ACE are increased. They can be employed not only in the diagnosis of silicosis but also as possible biomarkers of exposure. In order to implement preventive measures, silicosis must be detected in both overt and covert cases.

A helpful biomarker to track lung damage brought on by exposure to crystalline silica is serum ACE. The increase in serum ACE activity caused by hypertension may be ruled out because the workers' blood pressure readings were normal. Studies on humans have yielded conflicting results. In the Gwalior region, stoneworkers exposed to silica dust showed elevated serum ACE levels [9]. Serum ACE activities were found to be higher in silicosis patients compared to controls, but these activities did not correlate with the severity of the disease as determined by changes in chest x-rays and respiratory function tests, and they provided no additional insight into the course of the disease [10, 11].

Serum ACE activity was shown to be higher in coal workers with pneumoconiosis (CWP) compared to control subjects. There was no association between the disease's progression and the control participants. [12] Other research, however, supported the notion that patients with silicosis had elevated serum ACE activity. They discovered a connection between the serum ACE activity and the fibrosis severity as seen on roentgenograms.

The current study's results, which showed a significant increase in ACE levels compared to controls and higher mean serum ACE levels in silicotic workers than in non-silicotics and smokers, respectively, supported the hypothesis that silica dust exposure played a significant role in the rise in ACE levels. This rise is a reflection of the disease's severity as seen by changes in chest x-rays and pulmonary function tests. Serum ACE levels were higher in people with abnormal pulmonary function and silicosis than in people with abnormal pulmonary function but no silicosis when pulmonary function status was taken into account. These results agreed with those of Bucca et al. [11] and Tiwari et al. [13].

Only 14 women were involved in this study, and none of them had respiratory morbidities. This can be explained by the much smaller length of exposure. Furthermore, these women worked in process units with reduced dust output; therefore their overall exposure was lower than men's. Men had greater mean serum ACE levels than women among those without respiratory morbid diseases, albeit the difference was not statistically significant. This is consistent with the findings of Gronhagen-Riska, who discovered that ACE activity was independent of gender in healthy subjects. [10]

We discovered a considerable increase in ACE levels among those exposed for more than a year. This can be related to workers' greater cumulative exposure to silica. One of the two participants with respiratory disease who had been exposed for more than 5 year had silicosis and a blood ACE level of 82 IU/L. [14]

In terms of pulmonary function status, serum ACE levels were greater in individuals with abnormal pulmonary function than in those with normal pulmonary function in those with no respiratory diseases based on their chest x-ray. Similarly, those with abnormal PFT had greater serum ACE levels than those without disease, while the difference was statistically significant. This could be related to the obstructive kind of pulmonary impairment caused by smoking and chronic bronchitis, in which the airways are more impacted than the lung parenchymal tissue. This discovery is also consistent with previous observations. [11]

According to Romano et al.'s explanation [15], increased serum ACE levels are caused by the fibrotic involvement of lung tissue, which includes capillaries since they contain a lot of angiotensin-1-converting enzyme in their endothelial cells.

The mononuclear phagocyte cell line is thought to be the main source of serum ACE in sarcoidosis, and human AM are also known to carry ACE [16]. It appears that a key factor in the emergence of silicosis is the cytotoxic impact of silica particles on macrophages, which causes their rupture and loss of cytoplasmic contents [17]. The accumulation and accelerated destruction of macrophages are likely reflected in the serum ACE level in silicosis, at least in part. This suggests that macrophages may be a source of serum ACE in silicosis.

There is mounting proof that AM is crucial in the local and systemic inflammatory reactions brought on by exposure to ambient particulate matter (PM). In the lung, AM interacts with other lung cells such bronchial epithelial cells and dendritic cells in an effort to process and eliminate the PM from the lung, which affects the size and character of the inflammatory response. Recent investigations

support the idea that these systemic mediators translocate from the lung tissues into the circulation since these macrophages also produce the mediators linked to the systemic inflammatory response brought on by PM exposure [18]. The NLRP3 inflammasome, which spreads the local inflammatory response by interacting with resident dendritic cells present within or close to the epithelium and starting and maintaining an adaptive immune response, is responsible for the increased IL-1 production.

Similarly, whereas smokers had higher serum ACE levels than nonsmokers in both study groups—those with and without respiratory morbidity—the difference was not statistically significant. This could be because smoking causes chronic bronchitis rather than lung parenchyma, and hence does not alter mononuclear cell activity, which is thought to be the source of elevated serum ACE levels in silicosis patients

We discovered a highly significant positive connection between employment length and ACE. This can be attributable to the fact that workers have been exposed to silica dust more frequently overall. This result contrasts with that of Tiwari et al. [13], who found no connection between serum ACE activity and exposure time.

Silicosis can be prevented to some extent by improving industrial hygiene, employing methods like wet drilling, fully enclosed systems, mechanisation, and efficient ventilation systems (artificial, natural, local, and exhaust ventilation). To best treat this disease, the issue of respirable dust exposure-linked lung fibrosis should be addressed through a medico-socio-engineering strategy. It makes sense to assume that treating the local and systemic inflammatory reactions of AMs brought on by exposure to PM would help lessen the harmful clinical pulmonary effects of air pollution. The relatively limited sample size of the current study is a drawback that has to be addressed by more future studies.

Conclusion

There was no link found between serum ACE activity and age, gender, whereas association was found in duration of exposure, smoking behaviours, or pulmonary function status. Increased levels of serum ACE gradually was seen in increased time of exposure and were discovered in cases of silicosis.

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References

1. Cvariani F, Carneiro AP, Leonori R, Bedini L, Quercia A, Forastiere F Silica in ceramic industry: exposition and pulmonary diseases. Med Lav Ergon. 2005; 27: 300–302.
2. Porter DW, Hubbs AF, Mercer R, et al. Progression of lung inflammation and damage in rats after cessation of silica inhalation. Toxicol Sci. 2004; 79:370–380.
3. Tiwari RR, Sharma YK, Saiyed HN Peak Expiratory Flow and associated epidemiological factors: A study among silica exposed workers of Chhotaudepur, India. Indian J Occup Environ Med. 2004; 8:7-10.
4. Vanhée D, Gosset P, Boitelle A, Wallaert B, Tonnel AB Cytokines and cytokine network in silicosis and coal workers' pneumoconiosis. Eur Respir J. 1995; 8:834-842.
5. Gaensler EA, Carrington CB Open biopsy for chronic diffuse infiltrative lung disease: clinical, roentgenographic, and physiological correlations in 502 patients. Ann Thorac Surg. 1980; 30:411-426.
6. Knudson RJ, Slatin RC, Lebowitz MD, Burrows B The maximal expiratory flow-volume curve normal standards, variability, and effect of age. Am Rev Respir Dis. 1976; 113:589–590.
7. 18 International Labor Office (ILO). Guidelines for the use of the ILO International Classification of Radiographs of Pneumoconiosis. Revised Ed. 2000 (Occupational Safety and Health Series, No. 22). Geneva, 2002.
8. Holmquist B, Bunning P, Riordan JF A continuous spectrophotometric assay for angiotensin converting enzyme. Anal Biochem. 1979; 95:540-548.
9. Raghuvanshi S, Shrivastava S, Johri S, Shukla S Therapeutic associated with occupational exposure to silica. J Trace Elem Med Biol. 2012; 8:205-209.
10. Gronhagen-Riska C Angiotensin-converting enzyme. I. Activity and correlation with serum lysozyme in sarcoidosis, other chest or lymph node diseases and healthy persons. Scand J Respir Dis. 1979; 60:83-93.
11. Bucca C, Veglio F, Rolla G, Cacciabue M, Cicconi C, Ossola M, Nuzzi A, Avolio G, Angeli, ASerum angiotensin converting enzyme (ACE) in silicosis. Eur J Respir Dis. 1984; 65:477–480.
12. 26 Wallaert B, Deflandre J, Ramon P, Voisin C Serum angiotensin-converting enzyme in coal

worker's pneumoconiosis. Chest. 1985; 87:844–845.
13. Tiwari RR. Karnik AB, Sharma YK Silica Exposure and Serum Angiotensin Converting Enzyme Activity. Indian J Occup Environ Med. 2010; 1:21-28.
14. Milne DB Trace elements In:Teitz Textbook of Clinical Chemistry. Burtis CA, Ashwood ER (Eds.)3rd edn. PA: WB Saunders Co., Philadephia, pp 1999: 482-484.
15. Romano C, Sulotto F, Peruccio G, Pavan I, Parola S Serum angiotensin-converting enzyme level in silicosis. Med Lav. 1985; 76:366-370.
16. Silverstein E, Friedland J, Ackerman T Elevation of granulomatous lymph-node and serum lysozyme in sarcoidosis and correlation with angiotensin-converting enzyme. Am J Clin Pathol. 1977; 68:219-224.
17. Ziskind M, Jones RN, Weill H Silicosis. Am Rev Respir Dis. 1976; 113:643-665.
18. Hiraiwa K, van Eeden SF. Contribution of lung macrophages to the inflammatory responses induced by exposure to air pollutants. Mediators Inflamm. 2013.