# SERUM COPPER LEVELS AMONG QUARTZ STONE CRUSHING WORKERS: A CROSS SECTIONAL STUDY

## RAJNARAYAN R. TIWARI\*, NATTUBHAI G. SATHWARA<sup>2</sup> AND HABIBULLAH N. SAIYED<sup>3</sup>

National Institute of Occupational Health, Meghani Nagar, Ahmedabad – 380 016

#### (Received on February 15, 2004)

Abstract : The present cross sectional study was carried out among 134 workers of quartz stone crushing units to assess the serum Cu activity among quartz stone workers without disease. Demographic and occupational details of the subjects were recorded on the predesigned proforma. Standard diagnostic criteria were used for diagnosing silicosis and tuberculosis. The pulmonary functions of the subjects were measured using Spirovit SP-10. The mean age for male was found to be 26.63±6.28 years while that for female was 21.93±4.29 years and for the whole group was 26.13±6.26 years. In the present study only one case of silicosis and seven cases of tuberculosis were found. The mean serum Cu levels of those having respiratory disease was found to be 91.5±19.8 µg/dl while mean serum Cu level of those free from respiratory disease was 86.8±21.3 µg/dl The difference was found to be statistically non-significant (t = 0.64, df = 1, P>0.05). Thus, in the present study, though the elevated level of serum Cu was found in solitary case of silicosis, no association could be established between the silica exposure and serum copper levels as suggested by nonsignificant effect of duration of exposure (P = 0.53).

Key words : serum Cu silica exposure quartz stone worker

## INTRODUCTION

Silicosis, one of the oldest occupational diseases, still kills thousands of people every year, all over in the world (1–3). It is an incurable lung disease caused by the inhalation of dust containing free crystalline silica. It is irreversible and, moreover, the disease progresses even when exposure stops. Extremely high exposure are associated with much shorter latency and more rapid disease progression. Silica dust is released during operations in which rocks, sand, concrete and some ores are crushed or broken. Work in mines, quarries, foundries, and construction sites, in the manufacture of glass, ceramics, and abrasive powders, and in masonry workshops is particularly risky. Stone quartz grinders who are involved in crushing quartz stone into powder from are exposed to excess risk of silicosis as the stone contains approximately 100% free silica and the process liberates huge amount

<sup>\*\*</sup>Address for Corresponding: E-mail: rajtiwari2810@yahoo.co.in

of silica dust in the working environment. In Godhara region of Gujarat itself about 10,000 workers work as contract labourer in these quartz crushing units.

The diagnosis of silicosis was mainly based of clinical examination of the subjects with special emphasis of respiratory system, measurement of pulmonary function specially lung volumes and grading of profusion according to the International Labour Organization classification of Penumoconiosis, But after Lieberman (4) in 1975 first reported the elevation of serum Angiotensin Converting Enzyme in sarcoidosis, several investigators have tried various biomarkers for the early diagnosis of silicosis. One such possible biomarkers could be serum Cu levels as it is reported in the literature that Cu has a fibrogenic property (5) and as the primary pathogenic changes in silicosis include fibrosis and the proliferation of collagen tissue in the lungs there could be possible association with raised levels of serum Cu. Though the mechanism of increase in serum Cu is still not understood, it has been suggested that an increase in ceruloplasmin levels in silicotics, which contains eight Cu atoms may be responsible for such an increase (6). Moreover, other studies have also reported elevated levels of serum Cu in silicotics (7-9).

However, there is a need to develop a biomarker of exposure rather than developing a biomarker of effect for silicosis because of irreversible nature of the disease. But no data on the association between serum Cu levels and silica exposure in workers without disease and particularly the effect of age, sex, duration of exposure to silica dust, smoking habit, and pulmonary function status on the serum Cu activity, is available, particularly from India. Thus, this study was carried out to elucidate the effect of epidemiological factors such as age, sex, duration of exposure to silica dust, smoking habit, and pulmonary function status on the serum Cu activity among quartz stone workers without disease.

## METHODS

The present study was designed as a cross sectional study. 134 present quartz workers working in the different quartz crushing units of Godhara were included in the current study. The consent was obtained from each person after the nature of the procedures had been fully explained. Using interview technique as a tool for data collection demographic and occupational details of the subjects were recorded on the predesigned proforma. In the present study those who have left smoking since last one year were categorized as ex-smokers. For analyzing the effect of smoking habit on PFT values, the ex-smokers were included in the non-smokers group as they were very few in number and most of them smoked occasionally when they were smokers. Also the females were excluded while analyzing the effect of smoking as no female was smoker and inclusion of female might have diluted the effect. Standard diagnostic criteria were used for diagnosing silicosis and silico-tuberculosis. The pulmonary functions of the subjects were measured using Spirovit SP-10 (Maker Schiller AG, Switzerland). After calibrating the spirometer according to the procedure given in the catalog, three readings of each ventilatory function of each subject were

taken. The readings showing the highest value were recorded considering that the subject has co-operated at his/her best and used for further analysis. Blood samples were collected from the subjects and centrifuged for the separation of serum, which was kept frozen until analyzed. The serum Cu levels were estimated using flame Atomic Absorption Spectrophotometer (M/s Perkin Elmer, USA, Model No. 3100). Statistical analysis was carried out using statistical software package "Epi Info 5" (World Health Organization, Geneva) and included calculation of proportion and percentages and application of tests of significance such as two-way ANOVA and student's t-test.

#### RESULTS

The present cross sectional study included 120 (89.5%) males and 14 (10.5%) females making a total of 134 subjects. Majority of the subjects were in the age group <25 years (47.0%). The mean age for male was found to be 26.63±6.28 years while that for female was 21.93±4.29 years and for the whole group was 26.13±6.26 years. Socio-economic status revealed that most of the subjects belonged to lower socioeconomic strata according to modified Kuppuswamy's social-economic classification (9). It is a three-pronged scale used to assess the socio-economic status in India. It takes into consideration the occupation of the head of the family, educational status of the head of the family and per capita income into consideration while categorizing a family into one of the five socio-economic strata which include upper, upper middle, lower middle, upper lower and lower strata.

TABLE I: Distribution of mean serum Cu values ( $\mu g/dl$ ) according to different study variables in the subjects free from disease.

Study	v variable	No.	<i>Mean±SD</i>	P value
Age g	roup (in yrs)			
	<25	63	$86.9 \pm 19.4$	
	25-30	32	$84.0 \pm 16.4$	
	≥30	39	$88.7 \pm 27.1$	0.53
Sex				
	Male	120	$87.0 \pm 21.2$	
	Female	14	$87.4 \pm 22.3$	0.94
Durat	ion of exposure			
	6 months	95	$88.3 \pm 23.5$	
	6 months-1 yr	2	$73.5 \pm 14.8$	
	≥1 yr	37	$84.7 \pm 14.5$	0.53
PFT s	status			
	Abnormal	20	$89.2 \pm 18.2$	
	Normal	114	$86.7 \pm 21.8$	0.64
Smok	ing habit#			
	Non smoker	64	$79.6 \pm 15.4$	
	Smoker	56	$95.6 \pm 23.8$	0.0001*

\* Significant

<sup>#</sup>Includes only male subjects as no female was smoker.

Table I shows distribution of means serum Cu levels according to various study parameters among the quartz stone workers unadjusted for respiratory morbidity. The differences in the means serum Cu levels were found to be statistically non-significant according to various categories of age (P>0.05), sex (P>0.05), duration of exposure (P>0.01) and pulmonary function status (P>0.05). However, smokers had significantly higher levels of serum Cu as compared to non-smokers (P<0.001).

Table II shows the comparison of the mean serum Cu levels of the workers free from disease with those having disease. In the present study only one case of silicosis and seven cases of tuberculosis were found. The mean serum Cu levels of those having

	Mean serum Cu levels						
Study variable	Respiratory morbidity		Respiratory morbidity absent				
	No.	Mean serum Cu levels	No.	Mean serum Cu levels	P value		
Age group (in yrs)							
<25	3	$106.7 \pm 4.6$	60	$86.0 \pm 19.3$	< 0.05*		
25-30	3	$84.3 \pm 27.7$	29	$83.9 \pm 15.6$	>0.05		
≥30	2	$79.5 \pm 4.9$	37	$90.3 \pm 27.7$	>0.05		
Sex							
Male	8	$91.5 \pm 19.8$	112	$86.7 \pm 21.4$	>0.05		
Female	0	-	14	$87.4 \pm 22.3$	-		
Duration of exposure							
6 months	6	$84.0 \pm 16.6$	89	$88.6 \pm 23.9$	>0.05		
6 months-1 yr	0	_	2	$73.5 \pm 14.8$	_		
≥1 yr	2	$114.0 \pm 2.8$	35	$83.0 \pm 12.9$	< 0.05*		
PFT status							
Abnormal	2	$93.5 \pm 14.8$	18	$88.7 \pm 18.8$	>0.05		
Normal	6	$90.8 \pm 22.4$	108	$86.5 \pm 21.8$	>0.05		
Smoking habit <sup>#</sup>							
Non smoker	4	$91.3 \pm 26.6$	60	$78.8 \pm 14.4$	>0.05		
Smoker	4	$91.8 \pm 14.4$	52	$95.8 \pm 24.4$	>0.05		

TABLE II: Distribution of mean Cu levels  $(\mu g/dl)$  of quartz workers with and without respiratory disease.

\* Significant

<sup>#</sup>Includes only male subjects as no female was smoker.

respiratory disease was found to be  $91.5\pm19.8 \ \mu g/dl$  while mean serum Cu level of those free from respiratory disease was  $86.8\pm21.3 \ \mu g/dl$ . The difference was found to be statistically non-significant (t = 0.64, df = 1, P>0.05).

## DISCUSSION

The present study was carried out among the workers of quartz stone crushing units of Godhara, Gujarat, India and analyzed the effect of age, sex, duration of exposure to silica dust, smoking habit, and pulmonary function status on the serum Cu activity among quartz stone workers without disease.

The mean serum Cu levels were found

to be higher in those aged <25 years having disease as compared to those ≥25 years of age free from disease and the difference was statistically significant. However, when adjusted for age, this difference was found to be non-significant according to the presence or absence of respiratory disease. This could be attributed to very small sample of the subjects developing disease. However, the serum Cu levels among workers free from disease but only exposed to free silica, the levels in different age groups varied nonsignificantly.

In the present study only 14 females study subjects were included and none was having respiratory morbid condition. This can be attributed to significantly low duration of exposure and also these females work in those processes in the quartz crushing units where the dust generation is less thereby the overall exposure is lower as compared to males. Among those free from respiratory morbid conditions the mean serum Cu levels of males were lower than females and the difference was statistically non-significant. Similarly the mean serum Cu level of males having disease was found to be statistically non-significantly higher than the males free from disease.

When the mean serum Cu levels were compared according to duration of exposure, no significant difference was found among different categories. However, when further categorization according to presence or absence of respiratory disease was done, those having respiratory disease and exposed for  $\geq 1$  year were found to have significantly more levels of serum Cu as compared to those having similar duration of exposure but free from disease. This may be attributed to the high levels of serum Cu in the solitary case of silicosis which had a exposure of >1 year and had serum Cu levels of 104  $\mu$ g/dl. This suggests that with increasing exposure the chances for developing silicosis increases and thus higher levels of serum Cu may be noticed. Though the mechanism of increase in serum Cu is still not understood, it has been suggested that an increase in ceruloplasmin levels in silicotics, which contains eight Cu atoms may be responsible for such an increase (6). However, no significant difference was found in the means serum Cu level of the workers exposed <6 months and 6 months-1 year. Also the serum Cu levels varied non-significantly among different duration of exposure categories.

When compared according to the pulmonary function status, mean serum Cu levels were statistically non-significantly higher in those having abnormal pulmonary function as compared to those with normal pulmonary function among the subjects. Similarly, when pulmonary function tests were categorized according to respiratory morbidity, the serum Cu levels were higher among those having respiratory disorders as compared to those free from disease though the difference was statistically nonsignificant. This can partly 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, thus making fibrosis a much later pathology.

In the present study, on unadjusted analysis, the smokers had significantly higher serum Cu levels as compared to nonsmokers. Even after adjustment for the age and duration of exposure by carrying out two-way ANOVA, the smokers had significantly higher values of serum Cu as compared to non-smokers. However, the difference in serum Cu levels between smokers and non-smokers was found to be statistically non-significant when adjusted for respiratory morbidity. Thus it can be attributed to smoking per se rather than to age, duration of exposure or respiratory morbidity. In the earlier studies also conflicting results were reported regarding the relationship between serum Cu and smoking habits (11-15).

The limitation of the study included the non-comparison with the suitable control group. However, by internal comparison efforts have been made to Thus, in the present study, though the elevated level of serum Cu in solitary case of silicosis are similar as the findings of earlier studies (6, 7, 16), it was found to be unaffected by the silica exposure as suggested by non-significant effect of duration of exposure. Further, the epidemiological factors such as age, sex, smoking habits and pulmonary function status were also found to be non-significantly associated. This can be attributed to small sample size of the study.

### ACKNOWLEDGEMENTS

The authors are grateful to Mr. A.M. Suthar, and Mr. H.H. Patel for their help during the field study in collecting the blood samples and to Mr. R.A. Rathod in carrying out serum Cu analysis.

#### REFERENCES

- 1. Elmes PC. Inorganic dusts. In Hunter's Diseases of Occupations ed. Raffle PAB, Adams PH, Baxter PJ and Lee WR. Edward Arnold Publications (London) 1994: 421-428.
- A Gordon Leitch. Functions of lungs. In Anthony Seaton, Douglas Seaton and A. Gordon Leitch. Crofton and Douglas's Respiratory disease, 5th edition, Blackwell Science Ltd., Oxford. Vol. 1, 2000: 43-46.
- 3. Mittleman RE and Welti CV: The fatal café coronary. JAMA 247: 1285-1288 (1982).
- Lieberman J. Elevation of serum Angiotensinconverting-enzyme (ACE) level in sarcoidosis. Am J Med 1975; 59: 365-372.
- 5. Kolev K, Burkova T. Histochemical mechanisms in etiology of pulmonary fibrosis after short-term exposure to a mixture of dust and quartz from copper mine. *Probl Khig* 1982; 7: 88–97.
- Ren ML, Jiang XL. Detection of coalsilicosis by radioimmunoassay used for ceruloplasmin. *Chinese J Ind Hyg Occup Dis* 1993; 11: 145–146. (in Chinese with English abstract).
- 7. Niculescu T, Dumitru R, Burnea D. Changes of copper, iron and zinc in the serum of patients with silicosis, silico-tuberculosis and active lung tuberculosis. *Environ Res* 1981; 25(2): 260–268.
- Bai Y, Wang JJ, Wei SC, Hao DQ. Changes of trace element copper and zinc in sera of cases with silicosis. *Chinese J Ind Hyg Occup Dis* 1993; 11: 280. (in Chinese with English abstract).

- Konishi A, Iguchi H, Ochi J, Kinoshita R, Miura K, Uchino H. Increased lysyl oxidase activity in culture medium of non-parenchymal cells from fibrotic levers. *Gastroenterology* 1985; 89: 709–715.
- Mahajan BK, Gupta MC. Textbook of Preventive and Social Medicine, 2nd edition, 1995, Jaypee Publishers, New Delhi, 135-136.
- Kim SH, Kim JS, Shin HS, Keen CL. Influence of smoking on markers of oxidative stress and serum mineral concentrations in teenage girls in Korea. *Nutrition* 2003; 19(3): 240–243.
- Faruque MO, Khan MR, Rahman MM, Ahmed F. Relationship between smoking and antioxidant nutrient status. Br J Nutr 1995; 73(4): 625-632.
- Schuhmacher M, Domingo JL, Corbella J. Zinc and copper levels in serum and urine: relationship to biological, habitual and environmental factors. *Sci Total Environ* 1984; 148(1): 67–72.
- Davidoff GN, Votaw ML, Coon WW, Hultquist DE, Filter BJ, Wexler SA. Elevations in serum copper, erythrocyte copper and ceruloplasmin concentration in smokers. *Am J Clin Pathol* 1978; 70(5): 790–792.
- Marcheggiani F, Stella F, Battistelli S, Stocchi O, Troccoli R. Serum levels of Cd, Pb, Cu and Zn in cigarette smokers. *Boll Soc Ital Biol Sper* 1990; 66(10): 921–928. [English abstract of Italian article]
- Wang W, Wang L, Yiwen L. Serum concentrations of copper and Zinc in patients with silicosis. *J Occup Health* 1998; 40: 230-231.