Journal of Air Pollution and Health (Autumn 2022); 7(4): 341-346

Original Article

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Urinary levels of amorphous urate crystals as a biological marker for occupational exposure to crystalline free silica

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ARTICLE INFORMATION

Article Chronology:
Received 03 August 2022
Revised 07 September 2022
Accepted 20 November 2022
Published 30 December 2022

Keywords:
Crystalline free silica; Amorphous urate; Biological marker

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ABSTRACT

Introduction: Due to the obvious adverse effects of exposure to free crystalline silica and the high exposure level in silica-related occupations, the present study aimed at the investigation of renal symptoms in cement factory workers.

Materials and methods: For this reason, 128 workers who were working cement factory with a determined occupational exposure to crystalline-free silica were selected as the case group, and 143 workers who were working in the Hamedan Province Rural Water and Wastewater company without being exposed to crystalline free silica were selected as controls. Various kidney-related parameters were evaluated and compared between the selected case and control groups.

Results: The results of urine analysis between cases and control showed that there was a statistical difference between the cases and controls regarding Red Blood Cell (RBC), epithelial count, and bacteria ($p<0.05$). Moreover, the percentage of amorphous urate crystals of the exposed workers (cases) and control were 80.7% and 38.3%, respectively ($p<0.001$). The results of adjusted results showed that the odd presence of amorphous urate crystals among cases was 7.65 times of the control group ($p<0.001$).

Conclusion: Our findings clearly showed that the level of urinary levels of amorphous urate crystals in silica-exposed individuals is higher than that of non-exposed individuals. Therefore, the presence of urinary amorphous urate crystals in exposed workers may be used as a cheap, non-invasive, and efficient method and urine biological maker for detecting silica exposure in silica-related industries.

Introduction

After carbon, silica is the most abundant substance on earth and is found in crystalline and non-crystalline (amorphous) types [1]. Amorphous silica is divided into natural and synthetic types [2]. Silica, or SiO_2, is found in both crystalline and amorphous forms. The different forms of crystalline silica include α-quartz, β-quartz, α-tridymite, β-tridymite, α-cristobalite,

Please cite this article as: Poormohammadi A, Ayubi E, Barati N, Motavallihaghi S, Mir Moeini ES, Mehri F. Urinary levels of amorphous urate crystals as a biological marker for occupational exposure to crystalline free silica. Journal of Air Pollution and Health. 2022;7(4): 341-346.

β-cristobalite, keatite, coesite, stishovite, and moganite. Among them, α-quartz is the most abundant form of silica.The quartz term is used as a general term of crystalline silica [3, 4]. Man-made silica is generally amorphous and produced in tonnage quantities for commercial applications [5]. Chronic occupational exposure to high levels of crystalline silica dust may have carcinogenic effects, and hence it has been classified as a carcinogen by the International Agency for Research on Cancer (IARC) [6, 7]. With the rapid increase in the application of crystalline silica and its release in the air of the workplace, especially in developing countries, there is a growing concern regarding the toxicity of crystalline silica particles and its inhalation has historically increased with the sharp rise in respiratory diseases such as silicosis. Silicosis is a spectrum of pulmonary diseases known as alveolar proteinosis and fine nodular fibrosis [2]. Although silica-dependent diseases are preventable, they remain a common problem, especially in developing countries [8]. Different types of clinical and pathological silicosis include acute, accelerated, chronic, and conglomerate silicosis (advanced progressive silicosis or complex silicosis). The progression of different types of silicosis depends on the duration of exposure and the concentration of silica particles. Inhalation of free crystalline silica in occupational exposure can also cause glomerulonephritis, liver disorders, spleen, and immune system [9].

A toxicological review of crystalline silica conducted by the World Health Organization (WHO) has shown that environmental exposure to quartz dust can occur during natural, industrial and agricultural activities. Chronic exposure to free crystalline silica dust occurs mainly in industries where the industrial resources of free crystalline silica include any commercial and industrial use of sand, quartz, mining, and crushing. Mining, stone cutting, employment in abrasive industries such as cement, glass, pottery, and stone factories, foundry, silica powder packaging, and stone extraction industries, especially granite, are among the major occupations with high exposure to free crystalline silica [10]. Among them, cement plant industries have a high exposure level to free crystalline silica [11].

More than 90 years ago, hypotheses were made about the effect of free crystalline silica dust on the human kidney. The pathological renal changes identified are similar to the effects of heavy metal-induced nephropathy in the form of dose-dependent nephropathy, leading to degenerative changes in tubular epithelium and interstitial inflammation, bone nephrosis, glomerulonephritis, and systemic vasculitis. In addition, it has been shown that workers exposed to free crystalline silica can experience distinct histological changes in the kidney in the glomerular and proximal tubes [12]. It has been shown that various urinary biomarkers are useful in determining defects in certain parts of the nephron and can detect early renal changes due to exposure to nephrotoxins [13].

Given the obvious effects of exposure to free crystalline silica and the high exposure level in silica-related occupations, the present study aimed the investigation of subclinical nephropathy in cement factory workers. The main idea of this study was based on experimental observations of the results of a clinical test of personnel, which showed a high level of amorphous urate crystals in workers with higher exposure compared to non-exposed individuals.

Materials and methods

The research methods were approved by the Research Ethics Committee of Hamadan University of Medical Sciences, Hamadan, Iran. In this study, a total of 128 workers who were working cement factory were selected as the study population, and 143 workers who were working in the Hamedan Province Rural Water and Wastewater company without being exposed to crystalline-free silica were selected as controls. Before the annual occupational examinations, it was coordinated with one of the laboratories to include the required parameters including the color of urine, appearance changes, gravity, pH, protein, ketone, Billy Rubin, nitrate, White Blood Cells (WBC), Red Blood Cell (RBC), epithelial cell, amorphous urate crystals, urea, creatinine, and uric acid. Due to the previous view towards the amorphous urate crystals in the exposed workers, its level was mainly evaluated.

The registered information of the occupational groups in the health network of Hamadan province was also used to obtain the exposure level to free crystalline silica in cement workers employed in the cement plant. In the clinical laboratory, a random morning urine sample was collected in acid-washed plastic containers and transported to the laboratory under appropriate conditions.

The urine samples of the workers were taken in a clinical laboratory under the occupational annual health checkup of employees in Iran. In the laboratory, the urine sample was first centrifuged for 10 min, and then 15 mL of the top of the sample was stored at – 20 ° C. The samples were then transferred to the clinical laboratory for laboratory tests and the relevant additional analyses were performed. According to related studies, in this study, changes in the parameters of urine analysis, especially urinary crystals, and their differences with a control group were also investigated. For this purpose, a job group with a relatively similar statistical population without any exposure to free crystalline silica or any chemical compounds that may induce similar effects was selected. The inclusion criteria included being employed in the studied cement factory, consenting to participate in the study, not having kidney disorders, and taking drugs concerning urinary crystal excretion (e.g. diuretics, Human Immunodeficiency Virus (HIV) treatments, antiseizure medications, and calcium-based antacids).

The studied variables according to the study groups were presented as numbers (%) and tested using the chi-square test. The effect of type of occupation on urinary levels of amorphous urate was evaluated using the logistic regression method in two models of univariate and multivariable models. The statistical significance level was set as $p<0.05$. All statistical analyses were performed using Stata Software (version 14).

Results and discussion

Occupational exposure to free crystalline silica is associated with distinct histological changes in the kidney in the glomerular and proximal tubes. It has been also reported that various urinary biomarkers are useful in determining defects in certain parts of the nephron and can detect early renal changes due to exposure to nephrotoxins. In this regard, subclinical nephropathy results of 128 workers who were working in a cement factory that was compared with a control group. As mentioned earlier, an occupational group with the same conditions but without any exposure to crystalline-free silica was selected as a control group. The results of urine analysis between cases and control are shown in Table 1. As can be seen here, a total of 128 cases and 143 controls were included in the analysis. As shown, the mean (SD) of age in the cases and controls were 38.66 (5.54) and 43.02 (7.30), respectively ($p<0.001$). There was a statistical difference between the cases and controls regarding RBC counts, epithelial count, and bacteria ($p<0.05$). These results showed that the RBC and epithelial counts in the silica-exposed workers are significantly lower than that of the non-exposed workers. As reported, the mean age of the controls was significantly higher than the cases, and the higher counts of RBC and epithelial cells in the controls can be attributed to the prostate inflammation that was positively associated with increased age [14].

Table 1. Comparison of urine analysis between case and controls

Variables	Case	Control	*p*
Age (year)			
<35	36 (28.8)	21 (18.1)	
35 - 45	76 (60.8)	52 (44.8)	<0.001
>45	13 (10.4)	43 (37.1)	
Specific gravidity	1.03 (0.3)	1.02 (0.01)	0.06
PH	5.31 (0.77)	5.28 (0.73)	0.76
Appearance			
Clear	116 (90.6)	102 (71.3)	<0.001
Semiclear	9 (7)	31 (21.7)	
Other	3 (2.3)	10 (7)	
Protein (yes)	2 (1.6)	0	0.05*
Glucose (yes)	4 (3.1)	0	0.05*
WBC			
0-1	6 (4.7)	10 (7)	0.11
1-2	100 (78.1)	120 (83.9)	
>2	22 (17.2)	13 (9.1)	
RBC			
0-1	127 (99.2)	132 (92.3)	0.04
1-2	1 (0.8)	8 (5.6)	
2-3	0	1 (0.7)	
4-6	0	1 (0.7)	
Many	0	1 (0.7)	
Epithelial			
0-1	4 (3.1)	6 (4.2)	
1-2	80 (62.5)	106 (74.1)	
2-4	40 (31.2)	21 (14.7)	
4-6	3 (2.3)	4 (2.8)	
6-8	1 (0.8)	3 (2.1)	0.02
8-10	0	2 (1.4)	
10-12	0	1 (0.7)	
Bacteria			
>few and over	122 (95.3)	37 (25.9)	<0.001
<rare and no	6 (4.7)	106 4.1)	

*according to fisher exact test

Table 2. Number (%) of amorphous urate crystals between cases and control and corresponding odds ratios and confidence intervals

Group	Amorphous urate crystals Yes	No	Crude OR (95% CI)	*P*-value	Adjusted* OR (95% CI)	*p*
Case	46 (80.7)	82 (38.3)	6.73 (3.29, 13.76)	<0.001	7.65 (3.35, 17.47)	<0.001
Control	11 (19.3)	132 (61.7)				

* adjusted for age

OR: Odds ratio, CI: Confidence interval

The results indicated that the percent of amorphous urate crystals in cases and control were 80.7% vs. 38.3% with p<0.001 (Table 2). As shown, in the silica-exposed group, of 128 workers, 46 individuals (35.9%) had amorphous urate crystals in their urine samples. While in the non-exposed group (controls) only 11 workers showed amorphous urate crystals in their urine samples. Due to the average age difference between the silica-exposed and non-silica-exposed groups, the results were adjusted and their significance level was evaluated. The results of adjusted results showed that the odd presence of amorphous urate crystals among cases was 7.65 times of the control group. This indicated that the amorphous urate crystals are higher among silica-exposed workers compared to the controls. It has been previously reported that silicon-containing compounds as being particularly damaging to the renal system, particularly for individuals who experience intense and prolonged exposure (e.g., miners, sandblasters, glassmakers, brick and grain workers) [15, 16]. For example, a previous study reported that silica-exposed workers, particularly in foundries, brick making, or sandblasting, were more likely to have rental disorders compared with non-exposed individuals, and an increased risk of end-stage renal disease was observed with increasing silica exposure levels in the exposed workers [17, 18]. These results are consistent with our results and indicate renal disorders associated with exposure to silica. Our findings demonstrated a strong relationship between occupational exposure to free crystalline silica and high level of amorphous urate crystals. However, further studies are required to tightly confirm this association.

Conclusion

Our findings clearly showed that the level of urinary amorphous urate crystals in silica-exposed individuals was higher than that of non-exposed individuals. Therefore, the presence of urinary levels of amorphous urate crystals in exposed workers can be used as a cheap, non-invasive, and efficient method and urine biological maker for detecting silica exposure in silica-related industries. However, further studies are required to investigate the effect of interfering factors and their dose-response effect on silica exposure, especially in animal models.

Financial supports
This research was supported by the Hamadan University of Medical Sciences (with No. 140011059141).

Acknowledgements
The authors would like to gratefully acknowledge Hakim laboratory for collaborating in this research. This research and its protocol (with No. 140011059141) were approved by the Research Ethics Committee of Hamadan University of Medical Sciences (Ethical code: IR.UMSHA.REC.1400.804).

Ethical considerations
The protocol of this research was approved by

the Research Ethics Committee of Hamadan University of Medical Sciences (Ethical code: IR.UMSHA.REC.1400.804)

Competing interests

The authors declare no conflict of interest regarding this research

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