Background: The adverse health effects of silica are still a major concern in some industries. The purpose of this study was to evaluate pulmonary function in a group of sub-radiological silicotic workers after 11 years of silica dust exposure.

Methods: The study sample consisted of 381 exposed and 254 non-exposed workers. The history of pulmonary function parameters was obtained from workers' medical records. The data were collected through interviews with employees and completing questionnaires on demographic variables, detailed occupational and medical history, and respiratory symptoms. Workers' exposure to silica dust was also determined.

Results: The mean frequency of workers' exposure to silica dust was 6.3 times greater than its exposure limit. All pulmonary function parameters were significantly lower in the silica-exposed workers, and the difference between the two groups was still statistically significant after adjusting the potential confounding variables. FEV1 showed the greatest reduction, and FVC and FEV1 showed a significant decreasing trend. Also, the prevalence of respiratory symptoms was significantly higher in smokers than in nonsmokers among silica-exposed workers.

Conclusions: Even in the absence of radiographic evidence of silicosis, exposure to high levels of silica dust is associated with reductions in pulmonary function. In the absence of radiological evidence of silicosis, progressive deterioration of FEV1 over time most likely indicates sub-radiological silicosis. The effects were associated with the severity and duration of exposure. Exposure to sub-TLV levels of silica dust may not affect pulmonary function. Smoking appears to have a synergistic effect in relatively high silica exposures.

1. Introduction

The ceramic tile industry is one of the main workplaces where workers are exposed to silica and, thereby, a higher risk of developing pulmonary diseases. In various parts of the world, a large number of workers are exposed to silica [1, 2, 3, 4, 5]. Unfortunately, despite improved industrial hygiene standards and stricter occupational exposure limits (OELs), many workers in both developed and developing countries are diagnosed with silicosis, a disease there is currently no cure for [6, 7]. As a result, more studies are needed to determine the best way of screening silica-exposed workers. The diagnosis of silicosis currently may require several medical procedures and examinations, including review of medical and occupational history, review of symptoms and their onset time, a chest X-ray, a lung function test, and a sputum test.

Although spirometry is not specific to the diagnosis of silicosis, it can be a screening tool for identifying silica-exposed workers. Spirometric findings may not be compromised in the early stages of silicosis. However, as the disease progresses, obstruction, restriction, or a mixed ventilatory disorder may develop [8]. In addition, assessment of pulmonary function parameters is a good option to monitor the progress and prognosis of the disease [9].

Some studies have investigated the longitudinal changes in the pulmonary function of silica-exposed workers [10, 11, 12, 13, 14, 15, 16]. For instance, the mean reduction in forced expiratory volume in the first second/forced vital capacity (FEV1/FVC) has been reported to be 2.75% in silica-exposed workers [10]. Malmberg et al. also reported a significant reduction in FEV1 (~4.6%) and FEV1/VC (~5.4%) in granite workers exposed to silica dust [14]. The severity of the effects can be influenced...
by the intensity, frequency, and duration of silica exposure. Furthermore, smoking has been shown to have a synergistic effect on silica dust pulmonotoxicity [17, 18, 19]. Workers are exposed to silica for a longer time in extended work schedules (more than 8 h per day, 40 h per week). The application of OELs, such as threshold limit values (TLVs), to such work schedules necessitates careful consideration in order to provide these workers with the same level of protection as workers on traditional work shifts [6].

This study aims to assess respiratory impairments in a group of workers exposed to various levels of silica dust. This study also seeks an answer to the question whether the synergistic effects of smoking on the pulmonotoxicity of silica dust depend on the severity of the exposure.

2. Materials and methods

2.1. Participants and study design

This historical cohort study was conducted in a ceramic tile factory in Iran. The study sample consisted of 419 male silica-exposed workers who had no radiological evidence of silicosis. In addition, 254 male non-exposed workers were randomly selected from a nearby gas power plant to form the control group. All participants signed an informed consent before the beginning of the study, and the research protocol was approved by the Ethics Committee of Shiraz University of Medical Sciences [IR.SUMS.REC.1399.1205]. Moreover, the study was conducted in accordance with the Helsinki Declaration of 1964, as revised in 2000. The data were collected in three ways: review of participants’ medical records, interviews with participants by an occupational health physician (the second author) and occupational health practitioners, and completion of questionnaires on demographic variables, smoking habits, detailed occupational history, history of pulmonotoxic chemical exposure in previous jobs, if any, or leisure time activities, and specific questions about all jobs held before employment in the studied industry, particularly those associated with the risk of pulmonotoxicity. Participants with asthma, a history of respiratory illness or any other chest operations or injuries, a history of exposure to other pulmonotoxic chemicals other than silica, or radiographic evidence of silicosis were all excluded from the study.

2.2. Exposure assessment

To estimate workers’ exposure to silica dust, a comprehensive exposure assessment program was designed and implemented [20, 21]. Briefly, 381 silica-exposed workers were divided into 14 similar exposure groups (SEGs) with 9–45 members each. A total of 48 workers were chosen randomly from the SEGs to collect personal air samples. The samples were then analyzed using NIOSH method 7601 [22]. The time-weighted average (TWA) exposure of the workers was then calculated according to the following equation:

$$\text{TWA} = \frac{C_1T_1 + C_2T_2 + \ldots + C_nT_n}{T}$$

where, $C_i$ is the silica concentration in each air sample, $T_i$ denotes the time over which measurement took place, and $T$ represents the duration of the work shift [23, 24]. Workers worked 12-hour shifts for two weeks in a row, four days and five days a week. The model developed by the University of Montreal and the Institute de Recherche en Sante et en Securite du Travail (IRSSST) was used to adjust the TLV-TWA of silica [25]. According to the model, the adjustment factor will be $\frac{40}{54} = 0.74$. Therefore, the adjusted OEL becomes $0.74 \times 0.025 \, \text{mg/m}^2 = 0.019 \, \text{mg/m}^2$.

The vast majority of workers wore no protective equipment. To protect themselves from silica dust, some workers in more polluted areas of the factory wore simple fabric masks. We were not permitted to examine the silica content of the raw material used in the production of ceramic tiles because the factory considered it confidential. However, in the air monitoring, we measured the silica content of ceramic dust specifically, as described above.

2.3. Pulmonary function parameters

Parameters of pulmonary function from 2009 to 2019 (2009, 2011, 2013, 2015, and 2019) were extracted from the medical records of silica-exposed workers. Since there was no history of pulmonary function tests available for participants in the control group, spirometric tests were performed using a portable calibrated Vitalograph spirometer (Vitalograph-COMPACT, Buckingham-England) in the workplace. All spirometric tests were performed by qualified practitioners in occupational medicine clinics. In addition, the occupational health physician reviewed all spirometric results (the second author). The following pulmonary function parameters (percentage predicted) were obtained: forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), FEV1/FVC, and peak expiratory flow (PEF). Pulmonary function tests were performed in occupational medicine clinics where the studied silica-exposed workers were examined, according to American Thoracic Society guidelines (ATS). The following was the reference range for pulmonary function: FEV1: greater than 80% predicted; FVC: greater than 80% predicted; FEV1/FVC ratio: greater than 70% predicted.

2.4. Respiratory symptoms

The Farsi version of the European community respiratory health survey (ECRHS) questionnaire, Cronbach’s alpha = 0.854 [26], with some modifications, was employed to assess respiratory symptoms among the participants. The questionnaire asks about respiratory symptoms such as wheezing, shortness of breath, chest tightness, coughing, and phlegm. Trained practitioners conducted face-to-face interviews with participants to complete the questionnaire.

2.5. Statistical analysis

Data were analyzed using version 21.0 of the SPSS software. The student’s-t test and the χ2 or Fisher’s exact test were used where applicable. Linear regression analyses were employed to assess the adjusted associations between exposure to silica dust and pulmonary function parameters. In addition, repeated measure ANOVA was used to determine the statistical significance of differences in pulmonary function parameters during the exposure period. A p-value of less than 0.05 was considered significant in all statistical tests.

3. Results

There were no silicosis diagnoses among the silica-exposed participants. According to the inclusion and exclusion criteria, 38 of the 419 silica-exposed participants were excluded (13 workers with a current or a history of lung diseases, 18 workers with a family history of lung diseases, and seven workers with a history of chest surgery). The silica-exposed participants had a mean TWA exposure of 0.12 mg/m³ (range from 0.01 to 0.29 mg/m³), about 6.3 times higher than the adjusted TLV-TWA of 0.019 mg/m³ for the studied work shift. The majority of workers (77.70%) had exposures greater than the adjusted TLV-TWA, and only one SEG (85 workers (22.30%)) had low silica dust exposure (TWA<0.019 mg/m³). Personal air samples collected from participants in the non-exposed group revealed no detectable levels of silica. The demographic characteristics of participants are shown in Table 1. There was a significant difference between the two groups of participants only in age, working hours per day, and body mass index (BMI). Table 2 compares the pulmonary function of silica-exposed workers (values at the end of the study) to that of the control group. All pulmonary parameters had significantly lower values in silica-exposed workers. Linear regression analysis was used to adjust the effects of potential confounding variables (Table 3). All studied pulmonary function parameters had
Table 1. Demographic characteristics of the studied subjects.

| Characteristics | Exposed group (n = 381) Mean ± SD | Non-exposed group (n = 254) Mean ± SD | p-value |
|-----------------|-----------------------------------|--------------------------------------|---------|
| Age (year)*     | 36.2 ± 7.2                       | 39.8 ± 8.3                           | <0.001  |
| BMI (kg/m²)*    | 24.7 ± 3.6                       | 25.3 ± 3.1                           | 0.03    |
| Job tenure (year)| 9.8 ± 7.0                        | 10.0 ± 6.7                           | 0.14    |
| Working hours per day*   | 11.9 ± 0.5                       | 8.7 ± 1.3                            | <0.001  |
| Duration of Cigarette smoking (year) | 1.6 ± 4.8 | 1.7 ± 4.7                           | 0.67    |
| Duration of Ghalyan (year)     | 0.2 ± 1.8                        | 0.1 ± 0.9                            | 0.41    |

BMI: body mass index; Ghalyan: a traditional type of smoking * Independent sample t-test; **Chi-square test; Significantly different from its corresponding values for the non-exposed group.

Table 2. The comparison of pulmonary function parameters of the exposed and non-exposed groups.

| Parameters          | Exposed group (mean ± SD) | Non-exposed group (mean ± SD) | p-value |
|---------------------|---------------------------|-------------------------------|---------|
| FVC                 | 93.22 ± 7.47              | 96.52 ± 7.18                 | <0.001  |
| FEV1                | 91.65 ± 8.05              | 96.99 ± 8.03                 | <0.001  |
| FEV1/FVC            | 98.46 ± 6.28              | 100.62 ± 6.81                | 0.001   |
| PEF                 | 98.39 ± 9.41              | 101 ± 10.77                  | 0.001   |

* Independent Samples t-test.
** Data of the last year of the study (2019).
† Significantly different from its corresponding values for the non-exposed group.
‡ Forced vital capacity; FEV1: forced expiratory volume in the first second; PEF: peak expiratory flow.

Table 3. The adjusted associations between exposure to silica dust and the pulmonary function.

| Parameters | Crude β | CI (95%) | p-value | Adjusted β | CI (95%) | p-value |
|------------|---------|----------|---------|------------|----------|---------|
| FVC        | -4.72   | -9.1 to -0.3 | 0.037 | -4.10 | -8.3 to -0.2 | 0.049 |
| FEV1       | -10.40  | -15.3 to -5.5 | -0.001 | -8.64 | -13.4 to -3.7 | 0.001 |
| FEV1/FVC   | -6.27   | -10.1 to -2.4 | 0.002 | -5.22 | -9.1 to -1.2 | 0.009 |
| PEF        | -9.14   | -14.5 to -3.8 | 0.001 | -8.41 | -13.7 to -1.3 | 0.002 |

* Multiple linear regression analysis adjusted for age, BMI, job tenure, smoking, and duration of cigarette and Ghalyan smoking. CI: confidence interval; FVC: forced vital capacity; FEV1: forced expiratory volume in the first second; PEF: peak expiratory flow.

statistically significant adjusted associations with silica dust exposure. FEV1, PEF, and FEV1/FVC showed stronger patterns of association, respectively. FVC showed a small but clear signal, with a reduction of 4.10 (p = 0.049) for a one-unit increase in silica dust exposure level.

The mean difference between lung function parameters in different years and the pre-employment year in silica-exposed workers is shown in Table 4. FVC, FEV1, and PEF means were lower in 2013 and later than in the pre-employment year. This reduction was significant for FVC in 2019 (mean d. = −7.3, p = 0.02) and for FEV1 in all years from 2013 to 2019 (mean d. = −2.1, p = 0.03 in 2013 to mean d. = −8.5, p < 0.001 in 2019). On the other hand, FEV1/FVC (mean d. = −1.6, p = 0.004) and PEF (mean d. = −2.7, p = 0.02) slightly reduced in 2011 and 2013, respectively. As can be seen, the deviation of FVC and FEV1 from pre-employment values increased with exposure duration, with the greatest reductions in 2019 (mean d. of −7.3 and −8.5, respectively) after 11 years of exposure.

Figure 1 presents a repeated measure ANOVA comparison of the means of pulmonary function parameters in different years. The decreasing trend in FVC and FEV1 was statistically significant during the study period. The mean of FVC and FEV1 reduced from 99.51 ± 12.90 and 99.62 ± 12.66 to 93.22 ± 7.47 and 91.65 ± 8.05, respectively. The greatest reductions occurred in 2013, after five years of silica dust exposure, and continued with a milder slope until 2019. FEV1/FVC and PEF showed no significant trends. Similar results were obtained for the silica-exposed workers with TWA exposure greater than the 12-hour TLV-TWA of 0.019 mg/m².

Table 5 compares the pre-employment and current pulmonary function parameters of silica-exposed workers with different severities of exposure. The workers in Group 1 showed no significant reduction. By contrast, the reduction in FVC and FEV1 was statistically significant in groups 2 and 3. The prevalence of respiratory symptoms was significantly higher in Group 3 than in other groups (data not shown).

Table 6 further assesses the studied parameters based on the severity of exposure among the smoker and nonsmoker silica-exposed workers. There was no significant difference in the mean of the pulmonary parameters between smokers and nonsmokers in Group 2. However, a significant difference in FEV1 and FEV1/FVC was observed between smokers and nonsmokers in Group 3.

4. Discussion

Even in the absence of radiographic evidence of silicosis, high silica exposure was associated with decreased pulmonary function. There was no significant difference between the groups in the number of smokers or smoking history. High exposure to silica dust, combined with working 12-hour shifts, puts workers at a higher risk of pulmonary toxicity, including silicosis, in the following years. Several studies reported the association between occupational exposures to silica and decreased pulmonary function parameters in workers with [8] and without radiographic evidence of silicosis [10, 11, 12, 14, 16]. In general, pulmonary functions are slightly affected in these studies and, while statistically significant, were of questionable clinical significance. In this study, the current pulmonary function of silica-exposed workers (values at the end of the study) was significantly lower (Table 2). After controlling for potential confounding variables of age, BMI, job tenure, and smoking, these differences remained significant (Table 3). Exposure to silica dust resulted in a reduction of 4.10, 8.64, 5.22, and 8.41 units in the levels of FVC, FEV1, FEV1/FVC, and PEF, with FEV1 experiencing the greatest reduction. These findings are consistent with those of some previous studies [10, 11, 12, 14, 16]. Meijer et al., for example, reported a statistically significant 2.2% decrease in FEV1/FVC among concrete industry workers [16]. Similarly, Mohner et al. showed a statistically significant 2.75% decrease in FEV1/FVC in a cohort of uranium miners with cumulative exposure to 1 mg/m³-year [10]. A significant small loss of pulmonary function has been also reported in concrete workers exposed to low levels of silica dust, independent of other risk factors such as smoking and a history of allergic symptoms [16].

According to international recommendations, the OELs for crystalline silica range between 0.025 and 0.05 mg/m³ [6, 27]. In this study, workers were exposed to high concentrations of silica dust (TWA = 0.12 mg/m³, in a range of 0.01–0.29 mg/m³). Some studies have found that the mean silica exposure of less than 0.1–0.16 mg/m³ negatively impacted pulmonary function [14, 16, 28]. Myers and Cowell reported a clear effect on FVC and FEV1 in 268 brick workers exposed to extremely high concentrations of silica dust [29]. In contrast, Graham et al.
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Table 4. Mean difference (mean d.) between lung function parameters in different years and the pre-employment year.

| Years | FVC Mean ± SD | Mean d. | p-value* | FEV1 Mean ± SD | Mean d. | p-value* | FEV1/FVC Mean ± SD | Mean d. | p-value* | PEF Mean ± SD | Mean d. | p-value* |
|-------|-------------|---------|---------|--------------|---------|---------|-------------------|---------|---------|-------------|---------|---------|
| 2009** | 99.51 ± 12.90 | 99.62 ± 12.66 | 100.3 ± 8.1 | 101.3 ± 16.6 | 101.42 ± 12.33 | 3.2 ± 0.9 | 0.001 | 100.42 ± 12.71 | 1.9 ± 0.8 | 0.02 | 99.13 ± 6.74 | −1.6 ± 0.5 | 0.004 | 100.30 ± 14.71 | −0.8 ± 1.1 | 0.48 |
| 2013 | 96.41 ± 12.14 | −1.5 ± 1.1 | 0.1 | 97.14 ± 11.31 | −2.1 ± 0.9 | 0.03 | 100.92 ± 6.15 | −0.7 ± 0.5 | 0.1 | 99.37 ± 13.82 | −2.7 ± 1.2 | 0.02 |
| 2015 | 95.54 ± 14.27 | −2.3 ± 1.4 | 0.1 | 95.55 ± 12.95 | −3.2 ± 1.2 | 0.008 | 100.41 ± 7.49 | −0.9 ± 0.7 | 0.1 | 100.77 ± 16.45 | 0.6 ± 1.3 | 0.6 |
| 2019 | 93.22 ± 7.47 | −7.3 ± 2.2 | 0.002 | 91.65 ± 8.05 | −8.5 ± 1.9 | <0.001 | 98.45 ± 6.28 | −1.8 ± 1.5 | 0.2 | 98.33 ± 9.41 | −4.2 ± 2.8 | 0.1 |

* Paired t-test.
** Pre-employment year. FVC: forced vital capacity; FEV1: forced expiratory volume in the first second; PEF: peak expiratory flow.

Figure 1. Trends in the parameters of pulmonary function in all silica workers (A) and those with silica exposure higher than the 12-h TLV-TWA (B).

conducted a longitudinal study on 711 granite workers and found no statistically significant association between the loss of FVC or FEV1 with the duration of employment at mean exposure of 0.06 mg/m³ [30], approximately 20% of the exposure level in this study. When silica-exposed workers were divided into groups based on the severity of their exposure, it was observed that, despite their longer duration of exposure than the other groups, there was no significant difference in pre-employment and current pulmonary function parameters in Group 1 (sub-OEL exposure) (Table 5). This is consistent with the findings of other studies [30] that reported no significant differences in FVC or FEV1 levels...
Table 5. Comparison of the pre-employment and current pulmonary functions of the silica-exposed workers with different severity of exposure.

| Parameters | Intensity of exposure* | Group 1 Exposure > TLV-TWA (n = 85) | p-value | Group 2 TLV-TWA < Exposure ≤ 5 TLV-TWA (n = 102) | p-value | Group 3 Exposure < 5 TLV-TWA (n = 194) | p-value |
|------------|------------------------|-------------------------------------|---------|-----------------------------------------------|---------|-------------------------------------|---------|
|            |                        | Pre-employment (2009) | Current (2019) | Pre-employment (2009) | Current (2019) | Pre-employment (2009) | Current (2019) |
| FVC        | 96.52 ± 7.18           | 100.3 ± 12.1               | 93.8 ± 6.9   | 0.3                                           | 99.3 ± 13.4 | 92.5 ± 7.5               | 0.007   |
| FEV1       | 96.99 ± 8.03           | 100.3 ± 11.2               | 92.2 ± 8.1   | 0.5                                           | 100.5 ± 12.4 | 92.4 ± 7.2               | 0.006   |
| FEV1/FVC   | 100.62 ± 6.81          | 100.4 ± 8.3                | 98.4 ± 6.3   | 0.1                                           | 101.4 ± 5.9 | 100.1 ± 5.9              | 0.7     |
| PEF        | 101.5 ± 10.77          | 103.6 ± 16.2               | 99.4 ± 8.4   | 0.7                                           | 102.2 ± 12.2 | 99.8 ± 8.9               | 0.1     |

* Based on the TWA exposure: group 1: 0.01 mg/m³ (0.01–0.019), group 2: 0.089 mg/m³ (0.02–0.095), group 3: 0.24 mg/m³ (0.10–0.29). Durations of exposure: group 1: 11.81 ± 6.84, group 2: 9.87 ± 6.39, group 3: 6.54 ± 5.18 years.

Table 6. Comparison of the pre-employment and current pulmonary functions of the smoker and nonsmoker silica-exposed workers with different severity of exposure.

| Parameters | Intensity of exposure | Group 2 TLV-TWA < Exposure ≤ 5 TLV-TWA (n = 102) | Group 3 Exposure < 5 TLV-TWA (n = 194) | p-value |
|------------|-----------------------|-------------------------------------------------|-------------------------------------|---------|
|            | Smoking               | No 81 (%)                                       | Yes† 22 (%)                         | p-value† |
|            | Smoking               | No 161 (%)                                      | Yes‡ 34 (%)                         | p-value‡ |
| FVC        | 92.6 ± 7.5            | 92.3 ± 8.1                                      | 93.3 ± 8.1                          | 0.87    |
| FEV1       | 92.5 ± 7.5            | 92.3 ± 6.3                                      | 94.2 ± 9.2                          | 0.92    |
| FEV1/FVC   | 100.0 ± 6.1           | 100.2 ± 5.6                                     | 101.1 ± 8.0                         | 0.89    |
| PEF        | 100.6 ± 9.1           | 96.5 ± 7.5                                      | 96.9 ± 7.5                          | 0.14    |

* Independent t-test.
† Smoking history; group 2: 11.0 ± 6.6 years; group 3: 10.45 ± 7.4 years. Age: group 2 = 41.7 ± 6.6 years, group 3 = 35.8 ± 7.6 years.
‡ significantly lower than those of nonsmokers. FVC: forced vital capacity; FEV1: forced expiratory volume in the first second; PEF: peak expiratory flow. TLV-TWA: threshold limit value-time weighted average for silica dust proposed by the ACGIH.

In this study, slight increases were observed in the pulmonary parameters two years after silica exposure (2011), which can be attributed to the body's response to the physical demands of industry work [32]. However, the studied parameters began to decrease two years later, in 2013 (Figure 1A and Table 4). FVC and FEV1 showed significant decreasing trends during the study period. These parameters decreased with steep slopes from 2011 to 2013 and then continued with milder slopes until 2019. While the means of FVC from 2013 to 2019 were lower than the pre-employment value, the difference was only significant in 2019 (mean d. = −7.3, p = 0.02). On the other hand, the mean of FEV1 in all years from 2013 to 2019 was significantly lower than the pre-employment value, with the highest reduction in 2019 (mean d. = −8.5, p < 0.001). These findings are consistent with the results of Malmberg et al. who reported a significant reduction in FEV1 of granite crushers with TWA exposure of 0.2 mg/m³ (about eight times the current TLV of silica dust) for 12 years [14]. As can be seen, the deviation of FVC and FEV1 from pre-employment values increased with the duration of silica dust exposure, with the greatest reductions in 2019 (mean d. of −7.3 and −8.5, respectively). In contrast, no significant trend was observed for FEV1/FVC and PEF. FEV1/FVC (mean d. = −1.6, p = 0.004) and PEF (mean d. = −2.7, p = 0.02) showed slight reductions only in 2011 and 2013, respectively. Similar trends were observed in the sub-group of the silica-exposed workers with TWA exposure higher than the TLV-TWA: threshold limit value-time weighted average for silica dust proposed by the ACGIH.

Chronic silicosis can be either a restrictive, obstructive, or mixed lung disease [9, 35, 36]. The findings of this study were more consistent with restrictive ventilatory disorders. The prevalence of respiratory symptoms, however, was not significantly different between the silica-exposed workers and the non-exposed group, and the difference remained non-significant when the silica-exposed workers' sub-groups were compared based on the severity of the exposure. In contrast, the prevalence was differed significantly between smokers and nonsmoker silica-exposed workers. Chronic silicosis develops slowly, typically presenting 10–30 years after initial exposure, and workers are frequently asymptomatic in the early stages [37]. The mean duration of exposure to silica dust in this study was 9.82 ± 7.04 years. However, some studies have reported a high prevalence of respiratory symptoms in silica-exposed workers [38, 39, 40]. This discrepancy can be partially attributed to differences in the severity of exposure, duration of exposure, and some methodological flaws in different studies. For example, Souza et al. reported a high prevalence of respiratory symptoms in artisanal mine workers with a mean silica exposure of 1.6 mg/m³ [38]. The severity and...
duration of exposure in their study were about 9 and 2.3 times higher than those in this study, respectively. Moreover, they did not use a non-exposed control group to compare the prevalence of respiratory symptoms.

Some major strengths of this study are as follows: first, the non-exposed group had similar job tenure, a number of smokers, and a history of smoking to minimize selection bias. Second, the pulmonary function and respiratory symptoms were investigated in sub-radiological silicotic workers. Third, pulmonary function and respiratory symptoms were assessed in silica-exposed workers with a wide range of exposure from < TLV-TWA to >5 TLV-TWA. Fourth, the possible synergistic effect of smoking on pulmonotoxicity in silica-exposed workers was assessed. On the other hand, an important limitation of this study was the lack of a history of pulmonary function parameters of the non-exposed workers for the same period as the silica-exposed workers. In addition, the spirometric data were obtained through periodic medical examinations at various medical facilities throughout the study period. Therefore, the inherent limitations of historical cohorts made it impossible to guarantee the consistency of spirometry test conditions over time. Furthermore, the structural damage to the lungs was not assessed in this study because it required measuring appropriate biomarkers such as serum club cell protein 16 (CC16).

This study investigated the pulmonary function of a group of sub-radiological silicotic workers. Radiologically speaking, there was no evidence of silicosis, and significant decreasing trends were observed in the lung function parameters of the silica-exposed workers during the study period. This should be considered in the workers’ health management because there is a high risk that these sub-radiological silicotic workers will become future silicotic subjects. Aside from deterioration of lung function, they are at risk of silico-tuberculosis and require periodic screening for early detection of it. Unfortunately, silicosis was diagnosed in some retired workers in the studied industry. This indicates that workers in the industry are at risk of developing silicosis in the coming years, and respiratory symptoms such as bronchitis and dyspnea are possible. To reduce workers’ exposure, it is recommended to establish an industrial hygiene control hierarchy, including engineering control measures (e.g., replacing old machines with new ones, work rotation, and installation of local exhaust ventilation systems), safe work practices, administrative control, and the use of appropriate respirators. Additionally, silica-exposed workers should be instructed to stop smoking. Serum CC16 has recently been identified as a biomarker for the early detection of silicosis. The measurement of CC16 and pulmonary function can be used as a periodic screening tool for the early detection and secondary prevention of silicosis [41].

5. Conclusions

Prolonged exposure to high levels of silica dust is associated with reduction in the parameters of pulmonary function with a pattern consistent with restrictive ventilatory disorders. This can be a source of concern because the exposed participants were young and the exposure lasted for only a short period. The gradual decline in FEV1 over time among silica-exposed workers without radiological signs of silicosis suggests that they are likely sub-radiologically silicotic. The severity and duration of silica dust exposure are related to lowered pulmonary function. Exposure to sub-TLV levels of silica may not affect pulmonary function. Moreover, the synergistic effect of smoking on the pulmonary function of the silica-exposed workers was shown to be dependent on the severity of the exposure. Although spirometry is not specifically to diagnose silicosis, it can be considered a tool for screening sub-radiological silicotic workers, especially in those with high exposure to silica dust.

Declarations

Author contribution statement

Younes Sohrabi; Fatemeh Rahimian: Performed the experiments.

Sobhan Sabet: Conceived and designed the experiments; Analyzed and interpreted the data.

Saeed Yousefnejad: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data.

Mohammad Aryaie: Analyzed and interpreted the data.

Esmaeel Soleimani: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Saeed Jafari: Conceived and designed the experiments.

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Data availability statement

The authors do not have permission to share data.

Declaration of interest statement

The authors declare no conflict of interest.

Additional information

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