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Effects of the Silica Dust on the Nasal Mucosa of Ceramic Workers

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Abstract: Background. Adverse health effects due to occupational exposures are a global public health concern and have been studied for many years. Ceramic workers are occupationally exposed to a wide range of toxic substances as they manage clay (silico-aluminous feldspar mixed with sodium, potassium salts and iron oxide). The objective of this study was to assess the presence of any inflammation or alteration of the nasal mucosa of ceramic workers by nasal cytology. **Materials and methods.** Twenty-eight ceramic workers from Caltagirone (Italy) were enrolled. Nasal symptoms, atopy, health habits and workplace features were assessed by a special questionnaire, and nasal mucosa health was evaluated by nasal cytology. **Results.** The cytological study of the nasal mucosa revealed the constant presence of abundant, thick and filamentous mucus, as well as a reorganization of the nasal cellularity with a prevalence of muciparous hyperplasia and metaplasia in the study group, and only in a lesser extent for the subjects with some protective environmental measures. **Conclusions.** The ceramic workers showed chronic inflammatory rhinitis on nasal cytology, with a remodelling of the nasal mucosa and thick mucus. Nasal cytology may be a helpful tool either for the health surveillance of the ceramic workers, or for the screening of any pathology of the upper airways.

Keywords: nasal cytology; ceramic workers; silicosis; upper airways; inflammation; occupational rhinitis; occupational health; quality of life; social health

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1. Background

Adverse health effects due to occupational exposures are a global public health concern and have been studied for many years. A high incidence of silicosis and other pulmonary diseases in the ceramic working population has been reported from Japanese researchers in the early decades of the last century [1,2]. It is well documented that workers engaged in pottery-related industries are at great risk for pulmonary diseases, lead and other metal poisoning, as well as other toxic reactions caused by occupational exposure to clays, glazes and furnace emissions [3]. Some reports indicate that 1.7 million workers in the United States [4] and over 3 million workers in Europe [5] are exposed to crystalline silica.

Silicosis is a well-known consequence of exposure to silica dust, and long-term exposure to crystalline silica has also been associated with the risk of developing lung cancer, pulmonary tuberculosis and other airway diseases [6–8]. On the other hand, glaze or crystallinity, enamel and colours randomly used for decorations, may play a direct irritating action on airway epithelial cells. Since 1997, crystalline silica has been classified as a human carcinogen by the International Agency for Research on Cancer (IARC) [9], and a worldwide series of risk assessments has been conducted for respirable silica dust exposure, especially for low levels of exposure [10–13]. Although advances in occupational safety make this disorder quite avoidable, silicosis remains the most prevalent occupational disease in both developed and developing countries [14].

Health surveillance is provided to workers regularly exposed to respirable silica exclusively for lung diseases. In practice, the assessment for workers at high risk for occupational exposures, would include any respiratory questionnaire, lung function testing and a baseline chest X-ray for comparison with future chest X-rays [15–17]. However, there is evidence that chronic inflammatory changes in the upper airways may precede the development of lung injuries even in the absence of radiological signs or symptoms [18,19], and early screening of any changes in the normal functioning of the mucosa of the upper airways may be beneficial for the implementation of adequate preventive measures and amelioration of worker health and quality of life.

A recent Finnish review revealed that the surveillance spirometry in absence of respiratory symptoms was not beneficial for any diagnosis of occupational asthma. On the other hand, the authors reported that eight per cent of the patients presented exclusively nasal symptoms at the beginning of the valuation, and that later developed occupational asthma [20]. The temporal relation between the occupational rhinitis and the onset of asthma has been documented in several studies [21]. These data suggest the importance of evaluating nasal symptoms in the occupationally exposed workers.

The aim of our study was to assess whether silica exposure correlated with specific inflammatory patterns of the nasal mucosa, and nasal cytology was used as a diagnostic tool for sampling of the nasal mucosa.

2. Materials and Methods

Ceramic workers from the city of Caltagirone were invited to participate in the study, as per inclusion criteria of the study. Caltagirone is an Italian centre that is well-renowned for its long handcrafted-ceramic tradition. Forty-five ceramic workers volunteered, and twenty-eight of them were selected to participate in the study according to the exclusion criteria. The inclusion criteria were: (a) workers from the hand-crafted ceramic sector; and (b) workers with a minimal duration of employment of 1 year. The exclusion criteria were: (a) pregnancy and lactation; (b) presence of any malignancy and diseases of the immune system; (c) acute and subacute infections of the airways, chronic lung diseases, chronic rhinosinusitis with or without nasal polyposis; and (d) therapies affecting the health of nasal mucosa (nasal sprays with corticosteroids and/or antihistamines, oral antihistamines, NSAIDs). The study was approved by the ethical committee of AIAS di Afragola, and written consent was obtained from all the participants.

The participants were administered a self-report questionnaire to investigate the presence of nasal symptoms (nasal obstruction, rhinorrhoea, itching and sneezing), presence of atopy and previous nasal interventions, cigarette smoking history, climate of the areas of residence and work, and workplace habits (years of exposure, type of clay and techniques of clay processing, use of plaster moulding, methods of drying and firing the pieces, use of glaze, enamels or colours and techniques of decoration).

Nasal cytology: Cytologic sampling was carried out by a scraping technique, i.e., by crawling a cytology plastic curette (IR Medical, Lugo, Italy), 2–3 times on the mucous surface of the central area of the inferior turbinate. The nasal mucosal cells were placed on an electrostatically charged cytology slide (Superfrost Plus Menzel-Gläser, Thermo Scientific, Milan, Italy). The cells were then stained according to the panoptic method (3 min in pure May-Grunwald dye (Carlo Erba, Milan, Italy), 6 min in 50% May-Grunwald dye, 1 min in bidistilled water (Carlo Erba, Milan, Italy) and 30 min in Giemsa solution (Carlo Erba, Milan, Italy) diluted 1:10 v/v). The slide was observed under an optical microscope (Nikon Eclipse 50i, Nikon Instruments Inc., Melville, NY, USA) at 1000× oil-immersion enlargement, over fifty observational fields. The images were recorded using a Nikon DS1 camera and digitized using a NIS-D elements computer support. Samples were observed at microscope by the same investigator who assessed according to a 0–4 score

(0 = none, 1 = rare, 2 = some, 3 = easily visible and 4 = many) the presence and number of goblet cells, neutrophils, eosinophils, mast cells, bacteria and fungi [22].

The study was conducted in accordance with the International Conference on Harmonisation Good Clinical Practice, the Declaration of Helsinki and all applicable laws and regulations.

Statistical analysis: Non-parametric analysis was performed. Values are reported as a mean (range) or a number (percentage), except where explicitly stated. A Spearman Rank correlation analysis was conducted between nasal cytology results and demographics (age, gender), patient medical history (allergy, previous surgery) and smoking habits, values are reported as r_s. Cohen's standards were used to evaluate the strength of relationship (small effect size: $0.10 < r_s < 0.29$; moderate effect size: $0.30 < r_s < 0.49$; large effect size $r_s > 0.50$). A value of $p < 0.05$ was considered to be statistically significant. The entire analysis was performed Statistica 12 software (Statsof).

3. Results

Twenty-eight ceramic workers (4 females and 24 males) aged between 19 and 64 years old (mean age 46.28 years old) participated in the study. All of them resided in the town of Caltagirone characterized by a humid climate. The average duration of the ceramic working period was 27.82 years (range from 4 to 35 years). The working setting consisted of minor industries located in homes or small factories (Table 1).

Table 1. Baseline characteristics of the study participants.

Characteristics	N (%)
Male:Female	24 (85):4 (15)
Mean Age (years) (range)	46.28 (19–64)
Years of exposure (range)	27.28 (4–35)
Smoking status, current:ex:never	9 (32.14):5 (17.85):14 (50)
Allergics	8 (28.57)
Mites	1 (3.57)
Grass	3 (10.71)
Parietaria	2 (7.14)
Alternaria	1 (3.57)
Mites and Grass	1 (3.57)
Previous upper airways surgeries:	3 (10.71)
Adenoidectomy	2 (7.14)
Septoplasty	1 (3.57)
Nasal congestion	28 (100)
Sneezing	17 (60.7)
Itching	10 (35.7)

Of the 28 subjects, 8 (28.57%) were allergic (3 to grasses, 1 to mites, 2 to parietaria, 1 to alternaria, 1 to grass and mites), 3 (10.71%) had previous upper airway surgery (2 adenoidectomy, 1 septoplasty), 9 (32.14%) were smokers and 5 (17.85%) were former smokers. Nasal symptoms were reported by all the participants. Nasal congestion was the main symptom, followed by sneezing and itching of the nasal mucosa. In particular, the subjects who reported sneezing referred it as immediately as they entered their workplaces or during contact with the glazes and crystalline materials.

All of them worked the refined clay by hand. A total of 89, 28 % of the study population (25 subjects) reported that either the process of clay modelling, or its drying and firing, took place in the same environment, while 3 of them (10.71%) made use of an electric kiln for the firing process, placed in a separate room from the workroom.

Room air extractors were present only in five cases (17.85%): located inside of the laboratory for two subjects, and for the other three, the air extractors were placed where the electric kiln was situated. Only six participants (21.42%) did not make use of plaster moulding.

For the decoration techniques, 18 subjects (64.28%) used hand painting, while the other 10 (35.71%) made use of spray decoration. Two subjects (7.14%) made exclusive use of watery colours; otherwise, the other twenty-six (92.85%) used crystalline metal oxides, and enamels.

The cytological study of the nasal mucosa revealed the constant presence of abundant, thick and filamentous mucus, generally tending to be basic (Figure 1). The mucus was detected in a lower quantity only in the samples of three subjects (10.7%), the ones with the oven in a separate room. In 10 participants (35.71%), precipitates and dust were documented free in the background (Figures 2 and 3).

From a strictly cytological point of view, there was a reorganization of the nasal mucosa structure with a prevalence of muciparous hyperplasia and metaplasia of the goblet cells (Figure 4) and numerous polynucleations of the epithelial cells (Figure 3) and an almost total absence of ciliated cells of the nasal epithelium, for rather all the subjects, 26 out of 28% or 92.85%.

Regarding the presence of inflammatory cells, 10 participants (35.71%) presented a majority of neutrophilic granulocytes (Figure 1). Of the eight allergic patients, nasal samples from five of them showed very rare neutrophils, and many lymphocytes and eosinophils were found only in a single rhinocytogram. None of the subjects presented mast cells, bacteria or fungi on the rhinocytogram (Table 2).

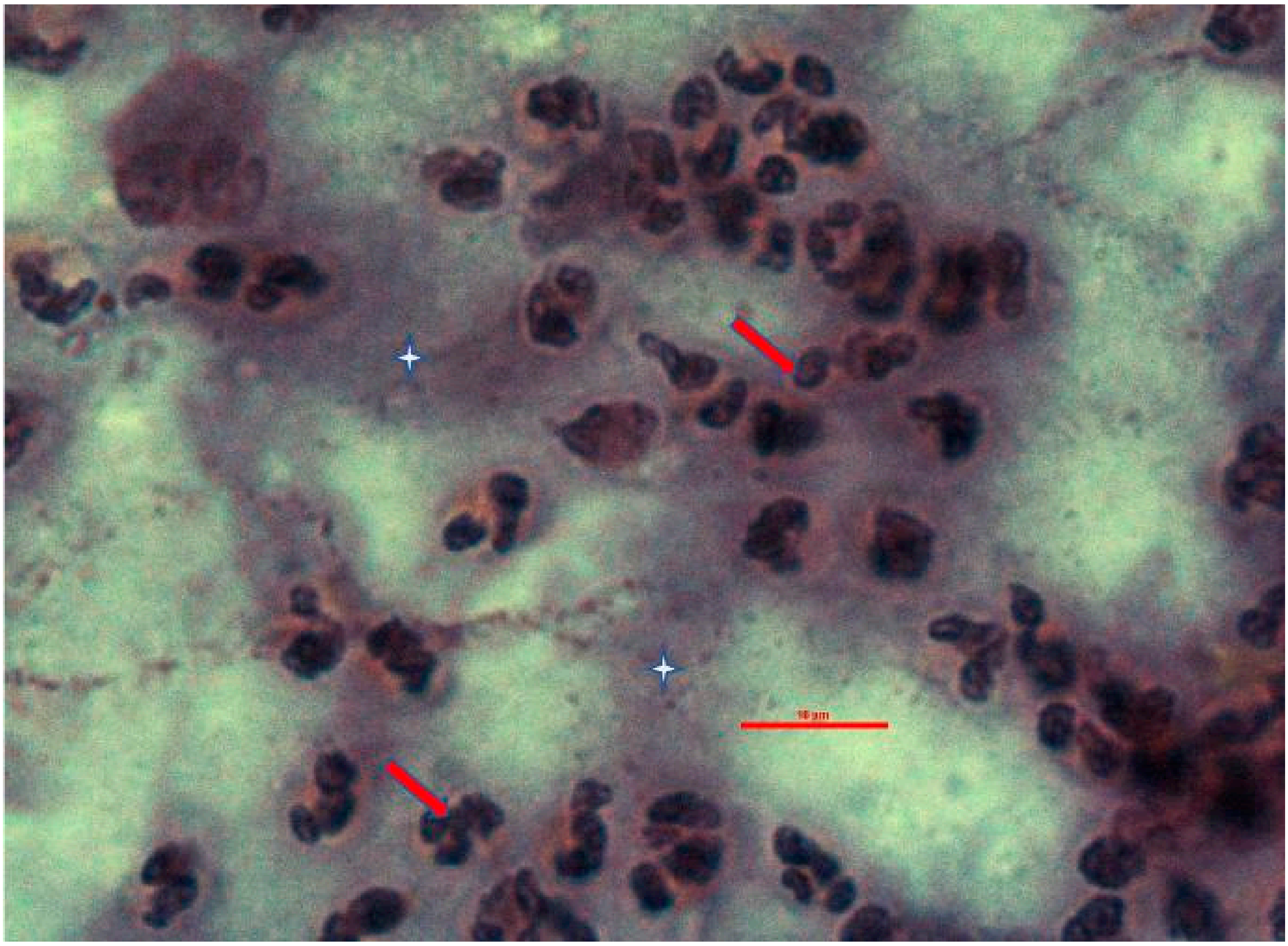

Figure 1. Numerous neutrophils (arrow) in heavily blue coloured (cross) smear because of the mucus. Observation by optical microscope. Magnification at 1000 X oil immersion. Col. MGG.

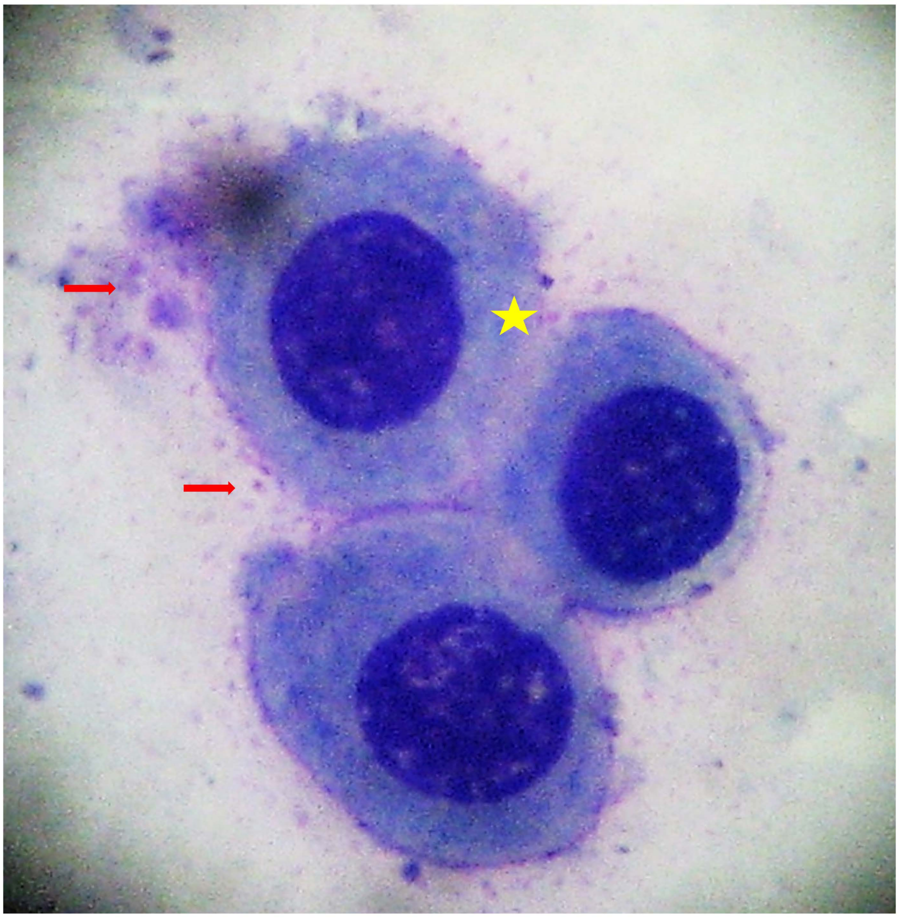

Figure 2. Lymphocytes (star) and dust precipitates (arrow). Observation by optical microscope. Magnification at 1000 X oil immersion. Col. MGG (part).

Figure 3. Polynucleation of the epithelial cell (cross) and dust precipitates (arrow). Observation by optical microscope. Magnification at 1000 X oil immersion. Col. MGG (part).

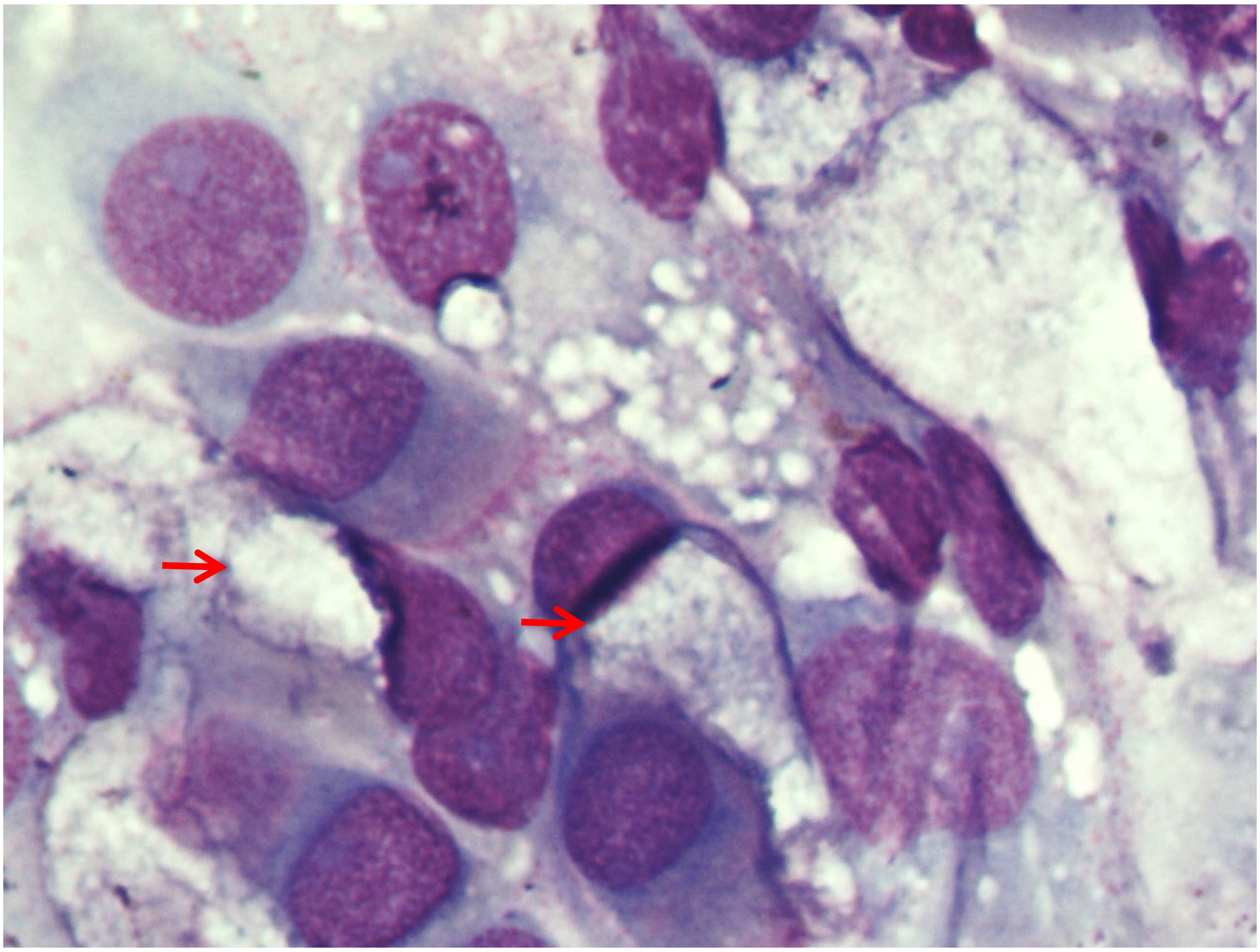

Figure 4. Muciparous hyperplasia and metaplasia of the goblet cells (arrow). Observation by optical microscope. Magnification at 1000 X oil immersion. Col. MGG.

Table 2. Nasal cytology results of ceramic workers.

Type of Cells	N of Subjects (%)
Thick mucus	26 (92.85)
Ciliated	2 (7.14)
Muciparous hyperplasia and metaplasia	25 (89.28)
Ratio Ciliated/Muciparous < 5	28 (100)
Polynucleated ciliated cell	20 (71.42)
Dust (precipitation)	10 (35.7)
Bacteria/fungi	0 (0)
Neutrophils	10 (35.7)
Eosinophils	1 (3.57)
Lymphocytes	1 (3.57)
Mast cells	0 (0)

Spearman Rank correlation analysis showed only a significant negative correlation between the location of the oven (kiln) and the concomitant utilization of watery colours, and nasal cytology ($r_s = -0.75$, $p < 0.01$). Correlation between nasal cytology and smoking ($r_s = 0.54$, $p > 0.05$), or former smoking ($r_s = 0.41$, $p > 0.05$) were not significant. Moreover, sex ($r_s = 0.12$, $p > 0.05$), age ($r_s = 0.23$, $p > 0.05$) and atopy ($r_s = 0.48$, $p > 0.05$) showed no significant correlation with the nasal cytology results.

4. Discussion

The principal components of ceramic and enamel mixtures consist of crystalline silica particles (an average of 35–38% for vitreous China and 22–26% enamel) and other minerals such as Al, Fe and FeCrNi alloys [23]. Occupational exposure to silica dust is well-known to be related to a higher risk of many malignant and other respiratory diseases [18,24,25]. As a result, it is a legal obligation to provide health surveillance for the occupationally exposed workers in presence of a reasonable risk to develop silicosis [15].

The development of occupational diseases is highly conditioned by work environment characteristics [26] and the application of prevention measures, as predicted by the current legislation [27,28]. Studies have indicated that workers of small ceramic factories present a poorer health-related quality of life and a higher incidence of silicosis-related airway diseases, due to poor environmental conditions, irregular working hours and a high proportion of older employees [29,30]. Our data were consistent with these studies, as the majority of the participants reported that the different ceramic working processes took place in the same environment lacking protective measures: only 10.71% of our subjects made use of an electric oven placed in a separate area from the workroom, and 17.85% used an aspiration system. The only participants with a smaller quantity of mucus and inflammatory cells were those (2 out of 28) who made exclusive use of tempera colours and had a separate area provided with aspiration systems for the firing phase. Furthermore, the age of the majority of our subjects was over 60 years old.

The primary aim of this study was to assess whether silica exposure correlated with specific inflammatory patterns of the nasal mucosa. In our sample, quite all of the subjects reported nasal congestion with itching and sneezing. It is difficult to assess whether these data are in accordance with the results of other studies. There is a lack of data about the epidemiology of nasal symptoms due to the occupational exposure of ceramic workers, as the majority of studies have focused on lower airway silica-related diseases.

The nasal mucosa is the first target that comes into contact with airborne pollutants and the initial site of injury induced by them [31]. Microscopically, the nasal mucosa of healthy individuals is organized by four types of cells (ciliate, muciparous, striate and basalis) with rarely some neutrophils. The normal ratio between ciliate and muciparous cells is 5:1. The detection of cells different from these, or in any different ratio or shape, is a sign of possible pathology [31,32].

The mucous layer on the nasal mucosa surface has an important function in relation to the conditioning of inhaled air and provides an adhesive surface for the deposition of inhaled particles [32]. Studies have demonstrated the potential value of nasal epithelial cells for the prediction of lung cancer risk [33]. As widely demonstrated, nasal epithelial cells, sampled either by brushing or scraping, allow the detection of toxic and inflammatory effects of airborne pollutants such as tobacco smoking, environmental carcinogens and silica [34–36].

To rule out the influence of any pollen on the nasal mucosa, nasal cytology took place in November when no pollen was detected, in accordance with the data of the pollinic calendar of the area.

On nasal cytology, the majority of the ceramic workers presented a rearrangement of the respiratory epithelium of the nasal mucosa, a total absence of ciliated cells and a significant increase in the goblet (mucous) cell number. This pattern is described as mucous hyperplasia and metaplasia [32]. Remodelling of the nasal mucosa has important consequences, as the diminution of ciliated cells and the increase in goblet cells cause hypersecretion of mucus, reduced mucociliary transport and subsequent sinonasal mucus stagnation [31,32,34]. Reduced mucociliary transport is a major factor in the pathogenesis of rhinitis, sinusitis and other airway pathologies [37]. The presence of dust precipitates and inflammatory cells such as neutrophils and lymphocytes, is consistent with a picture of chronic inflammatory rhinitis [31]. These inflammatory changes in the nasal mucosa would have been undetected in a routinely performed health surveillance.

We suggest that silica dust may act as a mucous membrane irritant, activating an inflammatory response. Since the turnover of ciliated cells is approximately 21 days, persistent inflammation may prevent the recovery of the nasal mucosa to a healthy epithelium. As a consequence, nasal obstruction, rhinorrhoea or sneezing occur with an important impact on workers' quality of life [38]. Smoking has not achieved a statistically significant correlation with the cytologic data, such as to discriminate between smoking or former smoking effects, and occupational exposure. The only significant correlation of the nasal cytology results was with the location of the oven (kiln) and the concomitant utilization of watery colours ($r_s = -0.75$, $p < 0.01$); that is, in the presence of protective systems and using watery colours, muciparous hyperplasia and metaplasia does not occur and the ciliate cells appear healthy. The better cytologic outcome of the workers using watery colours and separate spaces for the different ceramic procedures, suggest that the implementation of protective measures has important effects on the workers' health. Recent studies about the impact of the occupational levels for the silica exposure on workers mortality, demonstrated that even less restrictive policies have still a substantial risk reduction in the mortality from lung malignancies [39].

A strong limitation of the current study is the limited sample size and the absence of a control group. A further limitation of the study was the lack of exposure data; thus, it was not possible to perform any correlation of it with the inflammatory pattern presented in the nasal mucosa.

A strength of our study is that the presence of any inflammatory pattern was analysed in the mucosa of the upper airways, rather than in peripheral blood cells or in the bronchial mucosa. In fact, the nasal mucosa is a target tissue of airborne pollutants, and its sampling can be achieved by minimally invasive methods, e.g., nasal scraping. The principal advantages of nasal scraping consist of being economical, noninvasive and easy to perform in an outpatient situation (we performed nasal scraping at the workplaces of the participants, and the smears were easier to handle than other kinds of samplings). Other studies have confirmed the reliability of nasal cytology as a screening tool for chronic inflammatory rhinitis [34,36] and have suggested the utilization as part of the health surveillance programmes of workers exposed to pathological noxae [40].

5. Conclusions

A pattern of chronic inflammatory rhinitis, with remodelling of the nasal mucosa and thick mucus, was found in silica -exposed ceramic workers. Nasal cytology may be a very helpful tool for the screening of early pathologic changes in the nasal mucosa in workers occupationally exposed to crystalline silica.

Further investigations in larger populations are required to assess the relation of the exposure levels of silica to the inflammatory changes in the nasal mucosa and how the implementation of adequate protective measures (environmental and/or personal) could improve the workers' health.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Ethics Committee of AIAS Afragola, Naples, Italy (protocol code n.1, 15 January 2015).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of Interest: The authors declare no conflict of interest.

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