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Natural carcinogenic fiber and pleural plaques assessment in a general population: A cross-sectional study

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ABSTRACT

Natural carcinogenic fibers are asbestos and asbestiform fibers present as a natural component of soils or rocks. These fibers are released into the environment resulting in exposure of the general population. Environmental contamination by fibers are those cases occurred in: rural regions of Turkey, in Mediterranean countries and in other sites of the world, including northern Europe, USA and China.

Fluoro-edenite(FE) is a natural mineral species first isolated in Biancavilla, Sicily. The fibers are similar in size and morphology to some amphibolic asbestos fibers, whose inhalation can cause chronic inflammation and cancer.

The aim of the current study is to assess the presence and features of pleural plaques (PPs) in Biancavilla's general population exposed to FE through a retrospective cross-sectional study. All High-Resolution Computed Tomography (HRCT) chest scans carried out between June 2009 and June 2015 in Biancavilla municipality hospital site (exposed subjects) were reviewed. The exposed groups were 1:1 subjects, matched according to age and sex distributions, with unexposed subjects (n.1.240) randomly selected among HRCT chest scans carried out in a Hospital 30 km away from Biancavilla. Subjects from Biancavilla with PPs were significantly more numerous than the control group ones (218 *vs* 38). Average age of either group was >60 years; the age of exposed subjects was significantly ($p=0.0312$) lesser than the unexposed group. In exposed subjects, in most PPs thickness ranged between 2 and 4.9 cm(38%, n=83); while in unexposed ones PPs thickness was less than 2 cm (55%, n=21). As to the size of PPs in exposed subjects, in most cases it ranged between 1 cm and 24% of chest wall (53%, n=116); while in unexposed ones the size of PPs was lesser than 1 cm (23%, n=58). Among exposed subjects, 36 cases (17%) PPs were detected with calcification, whereas in unexposed ones only three (8%) presented calcification. 137 lung parenchymal abnormalities were observed in exposed group; whereas, 12 lung parenchymal involvement were registered in unexposed subjects. The RR for PPs is 6,74 CI 95% (4,47–9,58) $p<0,0001$ in the exposed population. These findings, suggested the urge to extend the screening on the possible involvement of the respiratory tract to all Biancavilla's population, particularly in those aged more than 30. Besides, it seems essential to start indoor monitoring Biancavilla's municipality.

1. Introduction

Occupational and/or environmental exposure to various types of asbestos fibers is associated with an increase in the incidence of both malignant and non-malignant respiratory diseases (Alberg and Samet, 2003; LaDou, 2004; Fujimoto et al., 2015). Lung cancer

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and malignant mesothelioma (MM) are the main malignant diseases (Prazakova et al., 2014). Non-malignant effects of exposure to asbestiform fibers include lung function impairment, pleural plaques (PPs), pleural effusions, diffuse pleural thickening and parenchymal fibrosis (Hillerdal, 1981; Guidotti et al., 2004; Cugell and Kamp 2004; Gevenois et al., 1998).

PPs can occur even after relatively low exposure to asbestiform fibers and are the most common among non-malignant effects (Clin et al., 2011; Laurent et al., 2014; Maxim et al., 2015; Kim et al., 2015).

Environmental exposure to asbestiform fibers has been described in several areas of the world, including Greece, Turkey, Cyprus, Corsica, New Caledonia, Afghanistan, Russia, Montana (USA) and Italy (Constantopoulos, 2008; Voisin et al., 1994; Schüz et al., 2013; Sullivan, 2007; Szychlinska et al., 2014; Paoletti et al., 2000).

In Italy, a 10-year study of mortality from MM (1988–1997) highlighted an unexpected cluster in Biancavilla, Sicily (Paoletti et al., 2000; Comba et al., 2003) that was confirmed by later studies (Bruno et al., 2014). The high mortality rate was attributed to exposure to a fibrous amphibole, identified as fluoro-edenite (FE) (Gianfagna and Oberti, 2001), which is chemically similar to tremolite, except that its OH groups are replaced by fluorine. FE fibers were found in inert materials, such as sand and rubble, extracted from a stone quarry in Mt. Calvario, on the outskirts of the town (South-East) and in sheep lymph nodes (Fazzo et al., 2014; Ledda et al., 2016; Rapisarda et al., 2005).

This material had been employed locally in construction work for about 50 years (Paoletti et al., 2000; Comba et al., (2003). The quarry was shut down in 1998 (Miozzi et al., 2016).

On the basis of *in vivo*, *in vitro* and epidemiological surveys (Ballan et al., 2014; DeNardo et al., 2004; Loreto et al., 2008; Martinez et al., 2006; Soffritti et al., 2004) the International Agency for Research on Cancer (IARC; Lyon, France) classified FE as carcinogenic to humans (Grosse et al., 2014).

A study conducted on Biancavilla's general population also showed a higher incidence of chronic obstructive lung disease (Biggeri et al., 2004).

Recently, an excess of non-malignant pleural lesions has been described by Rapisarda et al. (2015a, 2015b) in subjects occupationally exposed to FE.

The aim of the current study is to assess the presence and features of PPs in Biancavilla's general population exposed to FE through a cross-sectional study.

2. Methods

2.1. Study design

The study was performed in accordance with the Declaration of Helsinki of the World Medical Association with the approval of Institutional Ethics Committee of Hospital of the University of Catania (ref. no.: 768/2014). In this retrospective study we reviewed all High-Resolution Computed Tomography (HRCT) chest scans carried out between June 2009 and June 2015 in Biancavilla municipality hospital site (exposed subjects).

Data collection included also personal data (age, domicile, etc.) and was stratified by gender and age.

The exposed groups were 1:1 subjects, matched according to age and sex distributions, with unexposed subjects randomly selected among HRCT chest scans carried out in a Hospital 30 km away from Biancavilla.

Inclusion criteria for exposed population were to have been born and living in Biancavilla's municipality. Exclusion criteria were not to have been born and living in Biancavilla's municipality. For unexposed group the inclusion criteria were to have been born and living at least 30 km away from Biancavilla. Exclusion criteria were to have been born and living in Biancavilla's municipality.

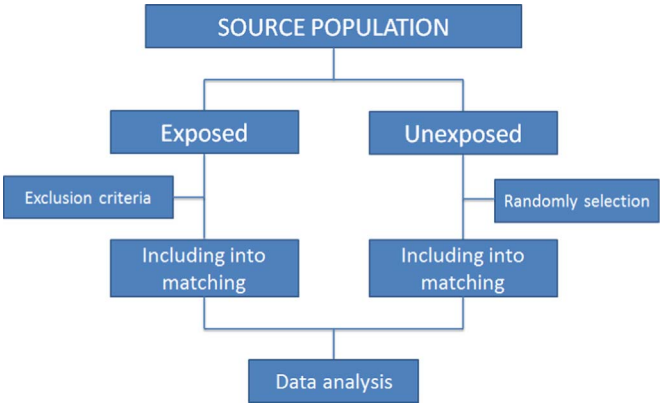

Fig. 1. Schematic flow diagram of enrollment and matching process.

In both groups, patients who had undergone more than one HRCT test were considered only once (the first scan). Fig. 1 schematizes the enrollment and matching process of source population.

HRCT scan tests that did not comply with the requirements stated by Clin et al. (2011) were rejected. Briefly, here follow the technical faults that classified the test as *"insufficient"*: inappropriate slice thickness preventing correct analysis of the parenchyma; failure to produce sections in the prone position in the case of suspected interstitial abnormalities observed in images in the decubitus position; prominent motion artifacts due to insufficient apnea.

2.2. Assessment of PPs

All available HRCT were submitted for randomized, independent, double reading (and triple reading in the case of disagreement) focused on benign asbestos-related abnormalities. Radiologists also received specific training in the interpretation of HRCT scans by experienced chest radiologists and occupational physicians.

HRCT scanning tests done in Biancavilla were performed using a General Electric Healthcare CT Scan (GE Healthcare, Fairfield, CT, USA).

HRCT scanning tests done in control hospital were performed using a Philips Healthcare Brilliance iCT (Koninklijke Philips Electronics N.V., The Netherlands, EU).

PPs were considered to be present on each hemithorax when either a single focal pleural abnormality with typical characteristics of a PP (circumscribed quadrangular pleural elevations with sharp borders and soft tissue density, possibly calcified, in typical postero-lateral and antero-lateral locations) or multiple bilateral less typical images with a typical location was detected. When associated with rounded atelectasis or parenchymal bands, pleural thickenings were considered to correspond with diffuse pleural thickening (fibrosis of visceral pleura) (Gevenois et al., 1998).

Thickness and extent of PPs were classified as proposed by Clin et al. (2011). The thickness was evaluated by classifying the most thickened plaque into four categories: <2/mm, 2–5/mm, 5–10/mm and >10/mm. The extent of PPs was assessed using a semi-quantitative method. The cumulative extent of PPs detected on each section was calculated and expressed as the percentage of the lateral chest contour as measured on a single axial section at the level of the carina.

This cumulative extent was graded according to four categories: less than 1 cm; between 1 cm and less than 25% of the