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Smoking Related Interstitial Lung Diseases in The Local Population of Sahiwal; An Autopsy Study

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ABSTRACT

Background: Smoking-related interstitial lung diseases (SR-ILDs) are a heterogeneous group of diseases with major clinical significance. **Objective:** To study the effect of cigarette smoking in causing interstitial lung diseases in cadavers. **Study Design:** Retrospective descriptive study. **Settings:** Department of Pathology at Sahiwal Medical College in collaboration with the Department of Forensic Medicine and Toxicology at Sahiwal Teaching Hospital, Sahiwal Pakistan. **Duration:** January, 2016 till October, 2019. **Methods:** Lungs from 30 autopsies, 20 of those whose cause of death was related to pulmonary diseases due to smoking, and 10 from the control group who had never smoked, were collected from males between 50 – 80 years of age. Tissue sections from different segments of each lung were obtained, processed and stained with hematoxylin and eosin to examine changes indicating interstitial fibrosis. Interstitial fibrosis was arbitrarily graded between 0-1 to observe its spread in the lung tissues under the light microscope. **Results:** Out of 20 autopsies of smokers, interstitial fibrosis was present in 17 cases bilaterally. None of the cases from the control group showed any signs of interstitial fibrosis (grade 0). From the smokers' group, 3 cases had no signs of intersitial fibrosis (grade 0), 2 showed mild changes (grade 1), 4 had moderate changes (grade 2), severe changes (grade 3) were observed in 8 cases, whereas complete obliteration of the lung tissue was seen in 3 cases (grade 4). **Conclusion:** Smoking is significantly associated with interstitial lung diseases. Thus, it is established that interstitial lung diseases are present in Pakistani population who are chronic smokers. As the hidden iceberg of diseases linked with smoking is unveiled, there is a need for incorporation of patient education and primary prevention measures in our health care delivery system.

Keywords: Interstitial lung disease, Smoking, H and E stains, Autopsy, Lung specimen.

INTRODUCTION

Interstitial lung disease (ILD) is an umbrella term used for a large group of diseases that cause fibrosis of the lungs. These are somewhat complex and assorted group of diffuse lung parenchymal disorders of either known or unknown cause, reflected clinically by dyspnea, cough, impaired gas exchange, restrictive pulmonary function, and radiologically by lung infiltrates.[1]

Some of them are occupation related (asbestosis, silicosis, hypersensitivity pneumonitis), treatment related (chemotherapy, radiation therapy, some medications) and sarcoidosis.[2] The scarring causes stiffness in the lungs which makes it difficult to breathe and get oxygen to the bloodstream. Lung damage from ILDs is often irreversible and gets worse over time.[3] Many things can increase the risk of or cause ILDs including genetics, certain viral infections including covid -19, or they may be idiopathic.[4] Exposure to hazardous materials has been linked to ILDs such as asbestosis and hypersensitivity pneumonia.[5] It is interesting to know that Covid-19 has the same clinical manifestation as interstitial lung disease.[4] Over the last two decades, an increasing list of ILDs have been linked with smoking.[6] Cigarette smoking

induces many inflammatory changes in the respiratory system and alsoenables the recruitment of macrophages, neutrophils, and Langerhans' cells.[6] Cigarette smoking has recently been documented as a significant cause of interstitial lung diseases and fibrosis.

This study was planned to document the presence and categorization of smoking related interstitial fibrosis and other smoking related interstitial lung diseases in our study population by doing a morphological study of lungs removed at autopsies in smokers and comparing the findings with non-smokers. This so far had not been studied and reported in Pakistan.

METHODS

This retrospective descriptive study was conducted in the Department of Pathology at Sahiwal Medical College in collaboration with the Department of Forensic Medicine and Toxicology at Sahiwal Teaching Hospital, Sahiwal. It was completed in 3 years, starting in January, 2016 till October, 2019, after obtaining approval from the ethical review committee. Autopsies of smokers (who had at least smoked 10 pack years) and non-smokers (who never smoked) of adult age group, between 50 to 80 years, males, were included in the study. Lungs from 20 autopsies, 10 of those whose cause of death was related to pulmonary diseases due to smoking, and 10 from the control group who had never smoked, were collected after taking written consent from the nearest available relative of the deceased. Among the 30 samples obtained, 20 were those of smokers allocated to group A and 10 were of non-smokers allocated to group B. Socio-demographic information (name, age, sex & history of smoking) was obtained from the nearest relative available at the time of autopsy. All the information was collected on specially designed proforma.

Both the lungs of each cadaver were obtained and inspected carefully. They were inflated with 10% formalin solution and air-dried. Macroscopic features including color, consistency, contraction of lobes and pleural adhesions were noticed with the help of hand lens. Tissue sections from different segments of each lung were obtained. All tissues were subjected to automated histology tissue processor and later stained with hematoxylin and eosin to examine changes indicating interstitial fibrosis. Interstitial fibrosis was labelled as presence of hyalinized, eosinophilic collagen deposition that variously thickened alveolar septae or obliterated the septae eventually leading to enlarged airspaces.

Data was analyzed with the help of SPSS version 20. Independent Samples T-test and One-way ANOVA followed by Fisher's exact test was applied. A p-value of 0.05 was considered statistically significant.

RESULTS

The relationship between history of smoking and gross features like color, consistency, contraction of lobes and pleural adhesions was sought. A statistically significant association was found between smoking history and all of these gross features using Fisher's exact test.

On gross examination in the smokers' group, the color of lungs was pinkish in 3 (15 %) of cases, grayish in 8 (40 %) cases and grayish-black in 9 (45 %) cases and. Over all, in all 30 cases, 16 (53 %) cases had consistency of lungs soft and spongy, while in 14 (46 %) cases it was firm and in 1 (3.3 %) case it was firm to hard. On gross examination of lungs contraction of lobes and pleural adhesions was examined using a hand lens and found to be present in 60 % of the cases respectively. Macroscopic features like contraction of lobes, emphysema and pleural adhesions were significantly associated with the history of smoking.

Interstitial fibrosis was arbitrarily graded as follows[7]:

- Grade 0: Near normal lung
- Grade 1: Mild fibrosis (mild thickening of alveolar septal walls)
- Grade 2: Moderate fibrosis (moderate thickening of alveolar septal walls)
- Grade 3: Severe fibrosis (severe thickening of alveolar septal walls)
- Grade 4: Total obliteration of alveolar spaces by fibrosis

Out of 20 autopsies of smokers, interstitial fibrosis was present in 17 cases bilaterally. In case of nonsmokers, out of 10 autopsies, none of the cases had interstitial fibrosis.

Table 1: Grading of interstitial fibrosis in smokers' group

Grade	Fibrosis	No. of cases	Percentage
Grade 0	Near normal	3	15 %
Grade 1	Mild	2	10 %
Grade 2	Moderate	4	20 %
Grade 3	Severe	8*	40 %*
Grade 4	Complete obliteration	3	15 %
	Total	20	100%

None of the cases from the control group showed any signs of interstitial fibrosis (grade 0). From the smokers' group, 3 cases had no signs of intersitial fibrosis (grade 0), 2 showed mild changes (grade 1), 4 had moderate changes (grade 2), severe changes (grade 3) were observed in 8 cases, whereas complete obliteration of the lung tissue was seen in 3 cases (grade 4). Association between history of smoking and interstitial fibrosis was significant ($p < 0.001$*). The number of 'pack years smoked' positively correlated with the grade of interstitial fibrosis ($p < 0.001$).

Figure 1: Photomicrograph of near normal lung, showing normal texture of interalveolar septae (H&E, 4x)

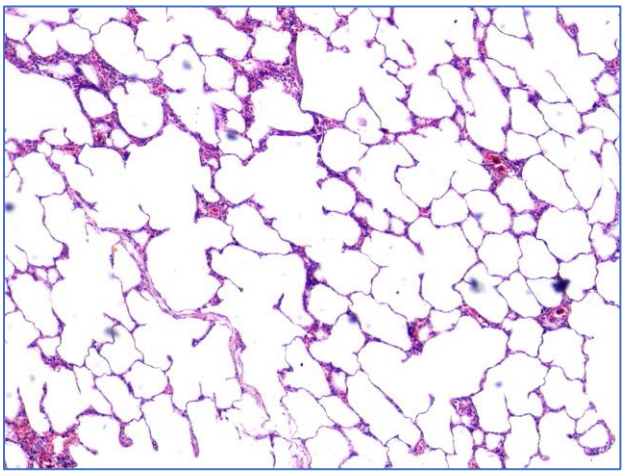


Figure 2: Photomicrograph of grade 1 interstitial fibrosis, showing mild thickening of alveolar septae (H&E, 4x)

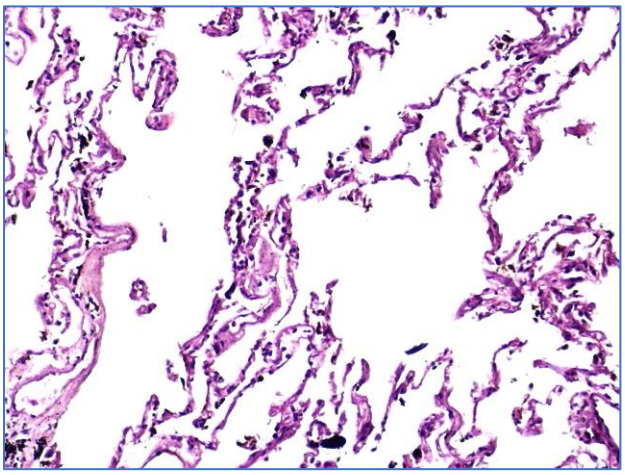


Figure 3: Photomicrograph of grade 2 interstitial fibrosis, showing moderate thickening of alveolar septae (H&E, 4x)

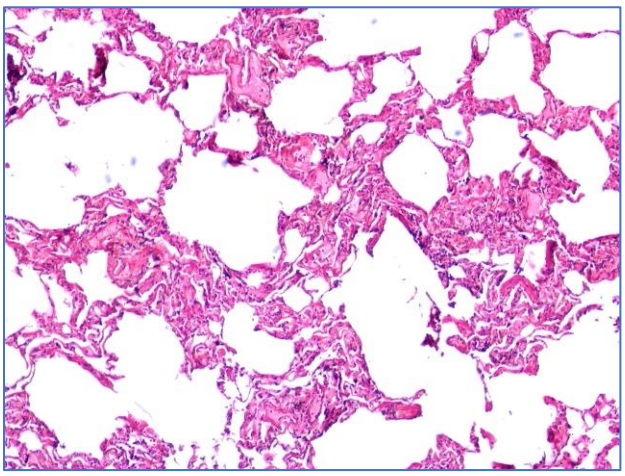


Figure 4: Photomicrograph of grade 3 interstitial fibrosis showing severe thickening of alveolar septal walls (H&E, 4x)

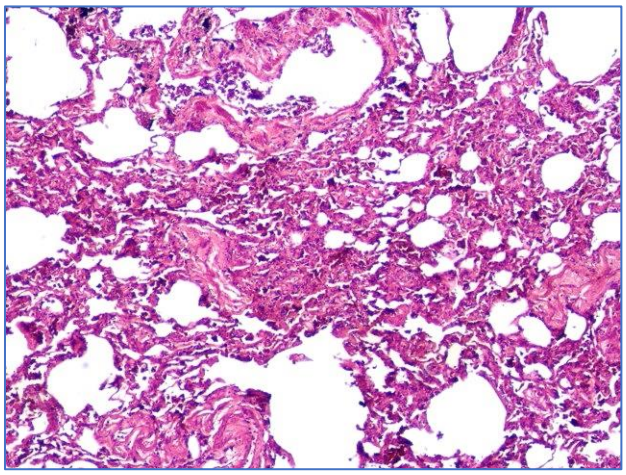
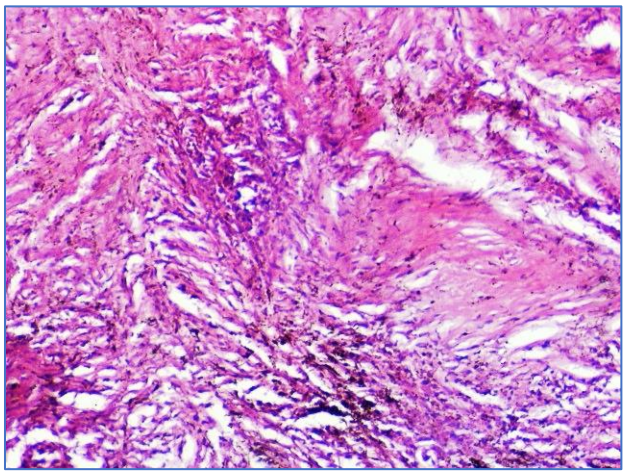


Figure 5: Photomicrograph of grade 4 interstitial fibrosis showing complete obliteration of alveolar septal walls and alveoli (H&E, 4x)



DISCUSSION

Data on prevalence of ILD is limited in our country and death certificate-based mortality data are neither accurate nor sensitive to estimate the occurrence of ILDs. This study is the first of its kind to be carried out on cadavers instead of live subjects. More patients of ILD can be identified by evaluating the patients at risk by the use of bronchoalveolar lavage, extensive physiological testing and high-resolution computer tomography at an earlier stage of disease.[8]

Usual lung diseases associated with smoking range from chronic obstructive pulmonary disease (COPD) to pulmonary carcinoma. Cigarette smoking is associated with a various non-neoplastic histological and radiological changes in the lung parenchyma.[9] In some smoker's various patterns of smoking induced injury can be seen in the same patient.[9] Cause and effect relationship

has been established between smoking and interstitial lung disease.[10]

Epidemiological and clinical evidence for association between smoking and ILD is stronger than experimental confirmation. This relationship is almost wholly confirmed by clinical and epidemiological studies while experimental research data fails to suggest a direct link between ILDs and smoking. Smoking is well known to cause inflammation of lung parenchyma and air channels.[11] A classical study in long term smoking dogs testified the presence of interstitial fibrosis and emphysema in lungs.[12]

Another study evaluating pulmonary fibrosis using an electron microscope in smoking dogs reported alveolar septal thickening due to collagen, presence of large numbers of macrophages occurring singly, in clumps, and in granulomas with the presence of a unique content in their cytoplasm of these macrophages.[13] Nevertheless, these investigations had confounding parameters and they can't be compared with humans.

CONCLUSION

Smoking is significantly associated with interstitial lung diseases. Thus, it is established that interstitial lung diseases are present in Pakistani population who are chronic smokers. As the hidden iceberg of diseases linked with smoking is unveiled, there is a need for incorporation of patient education and primary prevention measures in our health care delivery system.

LIMITATIONS

In this study sample size was small and study was based on only one center so only reflects the results from one center.

SUGGESTIONS / RECOMMENDATIONS

Further studies should be conducted with larger sample size.

CONFLICT OF INTEREST / DISCLOSURE

There is no conflict of interest.

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