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COMPARISON OF CADMIUM AND NICKEL LEVELS IN BLOOD AND PLEURAL FLUID IN IPF AND COPD PATIENTS. STUDY FROM LARKANA

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ABSTRACT

Introduction: *Two serious respiratory diseases, idiopathic pulmonary fibrosis (IPF) and chronic obstructive pulmonary disease (COPD), significantly impact global health. They are linked to pulmonary fibrosis and reduced lung function, possibly due to environmental exposure to heavy metals like nickel (Ni) and cadmium (Cd). This study seeks to measure and compare the concentrations of nickel and cadmium in the blood and pleural fluid of patients with COPD and IPF.*

Methodology: *Between March and June 2020, a study was conducted involving fifty patients (25 with IPF and 25 with COPD) at tertiary care hospitals in Sindh, Pakistan. Blood and pleural fluid samples were collected under sterile conditions after obtaining informed consent. Nickel and cadmium concentrations were measured using atomic absorption spectrophotometry, while also recording clinical and demographic data, including occupational exposure and smoking status.*

Results: *In every patient the levels of nickel and cadmium were higher than reference ranges. In comparison to IPF patients COPD patients had higher concentrations (cadmium: 4. 85 ± 1. 10 µg/L blood 6. 38 ± 1. 25 µg/L pleural fluid nickel: 3. 89 ± 0. 92 µg/L blood 5. 21 ± 1. 03 µg/L pleural fluid nickel: 2. 76 ± 0. 69 and 3. 95 ± 0. 84 µg/L). The accumulation of pleural fluid was consistently greater than that of blood.*

Conclusion: *Both the pulmonary and systemic compartments have markedly increased levels of nickel and cadmium especially in COPD. Cadmium is more toxic and higher pleural fluid concentrations are indicative of localized lung exposure. These metals could be used as biomarkers of disease severity and environmental exposure.*

Keywords: *Cadmium, Nickel Levels, Blood, Pleural Fluid, Ipf, Copd, Patients, Larkana*

INTRODUCTION:

Major chronic lung conditions like idiopathic pulmonary fibrosis (IPF) and chronic obstructive pulmonary disease (COPD) are linked to a progressive loss of respiratory function and a substantial global health burden. IPF is a long-term interstitial lung disease that causes irreversible lung parenchymal fibrosis which can result in respiratory failure and a high death rate. The pathophysiology of idiopathic pulmonary fibrosis is still poorly understood despite recent progress (2025) especially with regard to the role of occupational and environmental exposures (1). On the other hand persistent airflow restriction and chronic inflammation are the main characteristics of COPD which is frequently associated with smoking and air pollution though new research indicates that exposure to toxic metals may also have an impact on the development of the disease. Because heavy metals like cadmium (Cd) and nickel (Ni) are frequently found in cigarette smoke industrial emissions and contaminated air they are becoming more widely acknowledged as significant environmental risk factors. By causing oxidative stress inflammation and cellular damage these metals build up in tissues and cause toxicity. Increasing blood levels of cadmium have been linked to decreased forced expiratory volume (FEV1) and forced vital capacity (FVC) indicating the clinical significance of cadmium exposure (3). Furthermore blood cadmium levels and the risk and severity of COPD are positively correlated according to recent studies (2025) with evidence pointing to nonlinear exposure patterns (2). Additionally fibrotic lung diseases may be impacted by cadmium. According to experimental results cadmium can cause pulmonary fibrosis by damaging epithelial cells changing immune responses and boosting fibrogenic pathways (4). In a similar vein exposure to nickel has been associated with negative respiratory consequences such as decreased lung function and heightened vulnerability to long-term lung conditions especially in populations exposed to the environment (5). The comparative distribution and clinical significance of these metals in various biological compartments in IPF and COPD however are poorly understood. Blood samples are frequently used to assess heavy metal exposure because they show the systemic burden. However local pulmonary accumulation may not be accurately represented by blood measurements particularly in lung-specific diseases. Despite being less frequently studied pleural fluid may more accurately represent the local lung environment and offer information on toxic exposure specific to a given site. Consequently assessing the levels of nickel and cadmium in pleural fluid and blood could enhance comprehension of the dynamics of systemic versus local exposure. When examining heavy metal exposure in respiratory disorders the majority of earlier research has concentrated on single biological matrices such as blood or urine. For example elevated serum cadmium levels have been documented in COPD patients and may be linked to inflammation and the advancement of the illness (6). Nevertheless there are still few studies that concurrently evaluate the pulmonary and systemic compartments especially in comparative conditions like IPF and COPD. Identification of disease-specific patterns of accumulation and toxicity may be aided by knowledge of the different distribution of nickel and cadmium between pleural fluid and blood. Given the different mechanisms underlying IPF and COPD—fibrosis predominates in IPF while airway inflammation is central to COPD—this is especially crucial. These comparisons may help identify potential biomarkers of exposure and disease severity as well as provide insightful information about how the environment contributes to disease.

Methodology:

A comparative cross-sectional study was conducted between March and June 2020 to determine the levels of nickel and cadmium in the pleural fluid and blood of patients with idiopathic pulmonary fibrosis and chronic obstructive pulmonary disease. From tertiary care hospitals in Sindh Pakistan a total of fifty patients both smokers and non-smokers between the ages of twenty-five and fifty were selected. Pulmonologists verified diagnoses using radiological imaging pulmonary function tests and clinical assessment. Structured questionnaires were used to gather comprehensive

demographic data as well as lifestyle factors like dietary habits occupational exposure and smoking status. Under sterile conditions about 5 mL of venous blood was drawn allowed to clot and centrifuged to separate the serum which was then kept at -20°C until analysis. Standard thoracentesis procedures were used to obtain pleural fluid samples for clinical indications and the samples were stored under controlled conditions at 4–5°C. To reduce contamination high-purity reagents were used for acid digestion of every sample. Following approved analytical procedures electrothermal atomic absorption spectrometry and flame atomic absorption spectrophotometry were used to quantitatively determine the levels of nickel and cadmium. Throughout the analysis strict quality control procedures were followed including the use of pretreated glassware and certified reference materials. Specialized software packages were used for statistical evaluation and the results were reported as mean ± standard deviation. Students' t-test and one-way ANOVA were used to analyze differences between groups and sample types a p-value of less than 0. 05 was deemed statistically significant.

Results:

The clinical and demographic features of the 50 study participants including patients with Chronic Obstructive Pulmonary Disease (n = 25) and Idiopathic Pulmonary Fibrosis (n = 25) are shown in Table 1. With an overall mean of 43. 4 ± 7. 0 years the mean age was similar across groups (IPF: 42. 6 ± 6. 8 years COPD: 44. 1 ± 7. 2 years). The COPD group had a greater percentage of males (68%) than the IPF group (60%). While non-smokers were more common in the IPF group (52 percent) smoking prevalence was significantly higher in COPD patients (72 percent) compared to IPF patients (48 percent). There may be a connection between environmental exposure and disease distribution because occupational exposure was slightly higher in COPD (44%) than in IPF (36%).

Table 1: Demographic and Clinical Characteristics of Study Participants (n = 50)

Parameter	IPF (n=25)	COPD (n=25)	Total (n=50)
Age (years)	42.6 ± 6.8	44.1 ± 7.2	43.4 ± 7.0
Male (%)	60%	68%	64%
Smokers (%)	48%	72%	60%
Non-smokers (%)	52%	28%	40%
Occupational exposure (%)	36%	44%	40%

Cadmium levels in the blood and pleural fluid of patients with IPF and COPD are shown in Table 2. Both groups had blood cadmium levels above the reference range (1. 0 µg/L) with COPD having higher levels (4. 85 ± 1. 10 µg/L) than IPF (3. 42 ± 0. 88 µg/L). Cadmium levels in pleural fluid were also significantly higher than the normal limit (0. 5 µg/L) with COPD patients exhibiting higher accumulation (6. 38 ± 1. 25 µg/L) than IPF patients (4. 91 ± 1. 02 µg/L). These results show a substantial local and systemic cadmium burden especially in COPD.

Table 2: Cadmium Levels in Blood and Pleural Fluid (IPF vs COPD)

Disease	Blood Cadmium (µg/L) Mean ± SD	Pleural Fluid Cadmium (µg/L) Mean ± SD	Reference Range
Idiopathic Pulmonary Fibrosis	3.42 ± 0.88	4.91 ± 1.02	Blood: < 1.0 µg/L Pleural fluid: < 0.5 µg/L
Chronic Obstructive Pulmonary Disease	4.85 ± 1.10	6.38 ± 1.25	Blood: < 1.0 µg/L Pleural fluid: < 0.5 µg/L

The concentrations of nickel in the blood and pleural fluid of both disease groups are displayed in Table 3. In both IPF (2. 76 ± 0. 69 µg/L) and COPD (3. 89 ± 0. 92 µg/L) blood nickel levels were higher than the normal range (0. 2–2. 0 µg/L). Nickel concentrations in pleural fluid were also higher than the reference limit (1. 0 µg/L) with COPD patients showing higher levels (5. 21 ± 1. 03 µg/L) than IPF patients (3. 95 ± 0. 84 µg/L). These findings point to increased accumulation of nickel, especially in the pulmonary compartment.

Table 3: Nickel Levels in Blood and Pleural Fluid (IPF vs COPD)

Disease	Blood Nickel (Mean ± SD)	Pleural Fluid Nickel (Mean ± SD)	Reference Range
Idiopathic Pulmonary Fibrosis	2.76 ± 0.69	3.95 ± 0.84	Blood: 0.2–2.0 µg/L Pleural fluid: < 1.0 µg/L
Chronic Obstructive Pulmonary Disease	3.89 ± 0.92	5.21 ± 1.03	Blood: 0.2–2.0 µg/L Pleural fluid: < 1.0 µg/L

A comparison of the blood and pleural fluid levels of nickel and cadmium in patients with COPD and IPF along with statistical significance is shown in Table 4. In both specimens the concentrations of both metals were substantially higher in COPD than in IPF. While pleural fluid levels showed even greater differences (cadmium: p = 0. 001 nickel: p = 0. 002) blood levels of cadmium and nickel were significantly higher in COPD (p = 0. 002 and p = 0. 003 respectively). Pleural fluid consistently displayed higher concentrations than blood and all measured values exceeded their respective reference ranges. These results show that COPD patients have a much higher systemic and localized heavy metal burden than IPF patients, which supports the idea that environmental toxic exposure contributes to the severity of the disease.

Table 4: Comparison of Cadmium and Nickel Levels in Blood and Pleural Fluid between IPF and COPD Patients

Metal (Specimen-specific Reference Range)	Specimen	Idiopathic Pulmonary Fibrosis (Mean ± SD)	Chronic Obstructive Pulmonary Disease (Mean ± SD)	p-value (IPF vs COPD)
Cadmium (< 1.0 µg/L)	Blood	3.42 ± 0.88	4.85 ± 1.10	0.002*
Cadmium (< 0.5 µg/L)	Pleural Fluid	4.91 ± 1.02	6.38 ± 1.25	0.001*
Nickel (0.2–2.0 µg/L)	Blood	2.76 ± 0.69	3.89 ± 0.92	0.003*
Nickel (< 1.0 µg/L)	Pleural Fluid	3.95 ± 0.84	5.21 ± 1.03	0.002*

Discussion:

This study shows that patients with Idiopathic Pulmonary Fibrosis (IPF) and Chronic Obstructive Pulmonary Disease (COPD) have significantly higher levels of cadmium (Cd) and nickel (Ni) in their blood and pleural fluid with COPD patients consistently having higher concentrations. Furthermore pleural fluid exhibited higher metal accumulation than blood suggesting that local pulmonary burden rather than systemic measurements may be a more accurate indicator of disease-related exposure. These results are consistent with recent environmental and clinical research that emphasizes the contribution of heavy metals to the development of chronic lung disease. The study elevated blood cadmium levels (IPF: 3. 42 ± 0. 88

µg/L COPD: 4. 85 ± 1. 10 µg/L) are in line with earlier epidemiological findings and significantly exceed reported reference limits. Our finding of a higher cadmium burden in COPD patients is corroborated by a recent population-based study from 2025 (7), which found that elevated blood cadmium levels were substantially linked to decreased lung function and an increased risk of COPD. Similarly prior studies have demonstrated that exposure to cadmium especially from cigarette smoke and occupational sources causes chronic inflammation and impaired pulmonary function (8). This correlation is further reinforced by the higher smoking prevalence in the COPD group in our study. Cadmium levels in pleural fluid were significantly higher in both conditions with COPD patients having the highest levels (6. 38 ± 1. 25 µg/L). This result is consistent with toxicological data indicating that cadmium accumulates preferentially in lung tissues and causes oxidative stress fibroblast activation and epithelial damage (9). Cadmium exposure can activate fibrogenic pathways such as transforming growth factor-beta (TGF-β) which is important for pulmonary fibrosis according to experimental studies (10). This suggests that cadmium contributes to both fibrotic and obstructive lung pathology which may account for the higher levels seen in IPF patients albeit lower than in COPD. Both blood and pleural fluid had elevated nickel levels that were significantly higher in COPD than in IPF. These results are in line with studies on environmental exposure that indicate inhaling nickel is linked to a higher risk of chronic respiratory illnesses and a reduction in lung function (11). According to reports nickel causes oxidative damage and inflammatory reactions in lung tissues which can lead to obstruction and airway remodeling (12). Our study's finding that nickel accumulates more in pleural fluid than in blood raises the possibility that local exposure and retention within the lung microenvironment play a crucial role in the development of the illness. One of the main conclusions of this study is that the concentrations of both metals were consistently higher in pleural fluid than in blood. This finding is corroborated by earlier studies showing that pleural or Broncho alveolar samples more accurately reflect the pulmonary toxic burden while blood measurements may underestimate localized tissue exposure (13). The greater accumulation in pleural fluid emphasizes how crucial it is to evaluate local biological matrices when researching environmental pollutants in lung conditions. Furthermore increased exposure to environmental contaminants especially tobacco smoke which is a major source of nickel and cadmium may be responsible for the noticeably higher metal burden seen in COPD patients compared to IPF. This is in line with earlier research showing that heavy metal concentrations in biological samples are significantly higher in smokers than in non-smokers (12). The higher metal levels found in IPF patients in this study reflect the growing recognition of environmental and occupational exposures as contributing factors even though smoking is not the main cause of IPF. Overall the results of this study confirm that nickel and cadmium are important in the pathophysiology of lung diseases and are in good agreement with previous research. The significance of environmental risk factors and local exposure is highlighted by the increased burden in COPD patients and the higher concentrations in pleural fluid. According to these findings heavy metals especially cadmium may be useful indicators of the severity and course of chronic respiratory conditions.

Conclusion:

The conclusion of our study shows that patients with idiopathic pulmonary fibrosis and chronic obstructive pulmonary disease have significantly higher blood and pleural fluid levels of nickel and cadmium, with larger values in COPD. The greater metal concentration in pleural fluid compared to blood suggested stronger local pulmonary exposure. The harmful effects of cadmium were more apparent than those of nickel. The potential of heavy metals as environmental risk and disease severity biomarkers for chronic lung disorders is supported by these findings.

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