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E-Cigarette/Vape-Associated Lung Injury as a Cause of Interstitial Lung Disease

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ABSTRACT

Background: The increasing prevalence of e-cigarette and vaping product use has introduced new pulmonary risks, including e-cigarette or vaping-associated lung injury (EVALI). Initially recognized as an acute lung injury, EVALI has raised concern due to emerging evidence of long-term respiratory complications, particularly interstitial lung disease (ILD). Despite various case reports, the exact relationship between vaping and ILD remains underexplored in clinical cohorts. **Objective:** To investigate the association between EVALI and the development of ILD, examining clinical features, radiological patterns, and histopathological findings among patients presenting with recent vaping exposure. **Methods:** This prospective observational study was conducted from 8 January to 8 April 2025 at Hayatabad Medical Complex Peshawar, Pakistan. Patients with respiratory symptoms and a history of vaping within the preceding 90 days were enrolled. Diagnostic assessments included high-resolution computed tomography (HRCT), pulmonary function tests (PFTs), and lung biopsies when indicated. Data were analyzed for demographic trends, vaping exposure characteristics, and lung injury patterns. **Results:** Of the 60 patients included, 45 (75%) showed HRCT findings suggestive of ILD, predominantly organizing pneumonia (OP) and diffuse alveolar damage (DAD). Histopathological analysis in 15 cases confirmed interstitial inflammation with early fibrotic changes. Most patients (80%) with ILD patterns reported the use of THC-containing vaping products. A statistically significant association ($p<0.05$) was found between THC exposure and ILD development. **Conclusion:** Our findings support a compelling link between vaping—particularly products containing THC—and the development of interstitial lung disease. Enhanced surveillance, public awareness, and stricter product regulation are crucial to mitigate these emerging pulmonary risks.

INTRODUCTION

The global rise in e-cigarette and vaping product use has generated significant public health concern, particularly with the advent of e-cigarette or vaping-associated lung injury (EVALI) [1]. Initially promoted as safer alternatives to conventional tobacco smoking, e-cigarettes deliver aerosols containing nicotine, tetrahydrocannabinol (THC), cannabidiol (CBD), and various flavoring agents, many of which are inadequately regulated [2]. While early research focused on short-term respiratory irritation, recent epidemiological and clinical evidence suggests that vaping may induce serious pulmonary pathology, including long-term interstitial lung disease (ILD) [3].

EVALI emerged as a defined clinical syndrome in 2019 following a cluster of acute respiratory illness cases in the United States [4]. It is now recognized as a heterogeneous lung injury with overlapping radiological, pathological, and clinical manifestations. The common symptoms include dyspnea, chest pain, fever, and gastrointestinal complaints, often necessitating hospitalization [5]. Imaging findings in EVALI frequently demonstrate bilateral ground-glass opacities, interlobular septal thickening, and sub-pleural sparing — features that can mimic or overlap with patterns seen in ILD [6].

ILD represents a diverse group of diffuse parenchymal lung disorders characterized by varying degrees of inflammation and fibrosis [7]. Several case reports and small cohorts have linked vaping exposure with histopathological findings of organizing pneumonia, diffuse alveolar damage, and nonspecific interstitial pneumonitis, suggesting potential chronic evolution from acute EVALI [8,9]. While these reports are compelling, a systematic investigation into the frequency and characteristics of ILD patterns in EVALI patients remains limited.

The pathophysiological mechanisms by which vaping may induce ILD are multifactorial. Inhaled toxicants such as vitamin E acetate, diacetyl, propylene glycol, and vegetable glycerin disrupt surfactant homeostasis, impair macrophage function, and promote oxidative stress and inflammation [10]. Lipid-laden macrophages, a hallmark of EVALI, have also been implicated in fibrotic remodeling

pathways [11]. Moreover, some animal studies have demonstrated vaping-induced epithelial injury, fibroblast activation, and extracellular matrix deposition — mechanisms central to ILD progression [12].

Radiologically, the most common EVALI patterns associated with ILD include organizing pneumonia (OP), characterized by patchy consolidation and peripheral ground-glass opacities, and diffuse alveolar damage (DAD), indicative of acute respiratory distress syndrome (ARDS) [13]. High-resolution computed tomography (HRCT) remains the gold standard for detecting interstitial changes, but its interpretation requires careful correlation with clinical history and biopsy findings [14]. Histopathology often reveals chronic inflammation, interstitial fibrosis, and occasionally bronchiolo-centric injury, suggesting a potential continuum from acute to chronic lung disease [15].

EVALI-associated ILD shares symptoms (dyspnea, cough) with other ILDs but presents acutely post-vaping and affects younger patients compared to idiopathic pulmonary fibrosis (IPF). Radiologically, it progresses from organizing pneumonia to fibrosis with variable distribution, differing from IPF's basilar pattern, while histopathology shows acute injury (BOOP/DAD) evolving to fibrosis. Treatment responses are mixed: corticosteroids aid early inflammation, but antifibrotics' long-term efficacy remains uncertain, underscoring EVALI's unique pathophysiology and need for targeted therapies. Following table provides a comparative overview of key features across different types of interstitial lung disease, highlighting both similarities and differences with EVALI-associated ILD. This comparison aids in differential diagnosis and understanding the specific characteristics of lung disease following e-cigarette or vaping product use.

Table 1

Comparative Analysis of Different Types of Interstitial Lung Disease

Feature	EVALI-associated ILD	Idiopathic Pulmonary Fibrosis (IPF)	Hypersensitivity Pneumonitis (HP)	Connective Tissue Disease-related ILD (CTD-ILD)
Typical Age of Onset	Younger (mean 35 years)	Older (typically > 60 years)	Variable	Variable
Common Presenting Symptoms	Dyspnea, cough, fatigue	Dyspnea, dry cough	Dyspnea, cough, fever, chills	Variable depending on the underlying CTD
Characteristic HRCT Findings	GGOs, consolidation, reticular changes, OP	Basilar and peripheral fibrosis, UIP	GGOs, centrilobular nodules, air trapping	Variable depending on the underlying CTD
Predominant Pathological Patterns	BOOP, DAD, AFOP (initially), fibrosis later	Usual Interstitial Pneumonia (UIP)	Cellular and fibrotic HP	Variable depending on the underlying CTD
Typical Treatment Response	Variable, some response to corticosteroids	Limited response to antifibrotics	Avoidance of antigen, corticosteroids	Variable depending on the underlying CTD

In low- and middle-income countries, such as Pakistan, where regulatory oversight of vaping products is minimal and public awareness is limited, the health impact of vaping is underreported. This context increases the importance of identifying vaping-related pulmonary risks, especially chronic conditions like ILD, which carry substantial morbidity and long-term health implications.

This study aims to evaluate the relationship between EVALI and interstitial lung disease by analyzing clinical, radiological, and histological data from patients presenting with recent vaping exposure and respiratory symptoms. It addresses a critical gap in understanding the chronic sequelae of vaping in a South Asian population and seeks to inform clinicians, policymakers, and the public about the under-recognized risks of vaping-induced ILD.

METHODOLOGY

Study Design and Population

Over the course of three months (8 January to 8 April 2025), this prospective observational study was carried out at the Hayatabad Medical Complex in Peshawar, Pakistan, a tertiary care facility. The study sought to determine whether interstitial lung disease (ILD) and e-cigarette or vaping device use-associated lung injury (EVALI) were related. Participants had to be at least 18 years old, exhibit respiratory symptoms (such as cough, dyspnea, or chest pain), and have a history of using e-cigarettes or vaping products during the last 90 days in order to be eligible. Pre-existing ILD, current tobacco use, or other diagnoses such COVID-19, bacterial pneumonia, or congestive heart failure were among the exclusion criteria. Following the acquisition of signed informed consent, 60 participants who satisfied the inclusion criteria were enrolled.

Data Collection

Clinical evaluations were performed using a structured questionnaire to collect demographic data (age, sex, occupation), vaping habits (product type, frequency, duration, and substances vaped, including tetrahydrocannabinol [THC] or nicotine), and symptom severity. Radiological assessment involved high-resolution computed tomography (HRCT) scans of the chest, which were independently analyzed by two board-certified radiologists blinded to clinical data. HRCT findings were interpreted using Fleischner Society guidelines to identify ILD patterns such as organizing pneumonia, diffuse alveolar damage, or nonspecific interstitial pneumonia. Pulmonary function tests (PFTs), including spirometry (forced vital capacity [FVC], forced expiratory volume in 1 second [FEV1]) and diffusion capacity for carbon monoxide (DLCO), were conducted to assess restrictive lung disease and gas exchange abnormalities. In cases where clinical and radiological findings were inconclusive, trans-bronchial lung biopsies were performed in 15 consenting patients to obtain histopathological evidence of interstitial inflammation or fibrosis.

Statistical Analysis

Data were analyzed using SPSS version 25.0. Continuous variables (e.g., DLCO, FVC) were expressed as mean ± standard deviation and compared using Student's t-test.

Categorical variables (e.g., presence of ILD, THC use) were summarized as frequencies and percentages, with associations assessed via chi-square or Fisher's exact tests. Multivariate logistic regression models were constructed to identify independent risk factors for ILD development, adjusting for covariates such as age, sex, vaping duration, and THC use. A p-value <0.05 was considered statistically significant.

Ethical Considerations

The study protocol received ethical approval from the Institutional Review Board at the host institution. Written informed consent was obtained from all participants, ensuring confidentiality and voluntary participation. Patients with confirmed ILD were referred for specialized care, and counseling on vaping cessation was provided to all enrolled individuals. This structured approach ensured rigorous evaluation of clinical, radiological, and histopathological data to explore the hypothesized link between EVALI and ILD.

RESULTS

Demographic and Clinical Characteristics

A total of 60 patients met the inclusion criteria. The cohort had a mean age of 29.2 ± 5.3 years, with males comprising 66.7% (n = 40) and females 33.3% (n = 20) of the study population. Among all participants, 75% (n = 45) exhibited radiologic or histologic features consistent with interstitial lung disease (ILD), while 25% (n = 15) showed no significant interstitial involvement. Table 2 shows that ILD was slightly more prevalent among males, although gender distribution was not statistically significant between ILD-positive and ILD-negative groups.

Table 2

Gender Distribution by ILD Status

Gender	ILD Present: Yes	ILD Present: No	Total
Male	30	10	40
Female	15	5	20
Total	45	15	60

Vaping Product Composition and ILD Correlation

Of the entire sample, 65% (n = 39) reported using tetrahydrocannabinol (THC)-containing vaping products. A strong association was observed between THC use and ILD presence, with 80% (n = 36) of THC users exhibiting ILD features compared to only 60% among non-THC users ($p < 0.05$). As detailed in Table 3, organizing pneumonia (OP) was the most frequently observed ILD pattern (50%), followed by diffuse alveolar damage (DAD) (25%). The remaining 25% had normal HRCT findings without interstitial changes.

Table 3

ILD Patterns vs THC Use

ILD Pattern	THC Use: Yes	THC Use: No	Total
Organizing Pneumonia	24	6	30
Diffuse Alveolar Damage	12	3	15
Normal	3	12	15
Total	39	21	60

Figure 1 visually illustrates the distribution of ILD patterns. Figure 2 highlights the significant association between THC use and ILD presence.

Figure 1

Distribution of ILD Patterns Among Vaping-Associated Lung Injury Patients

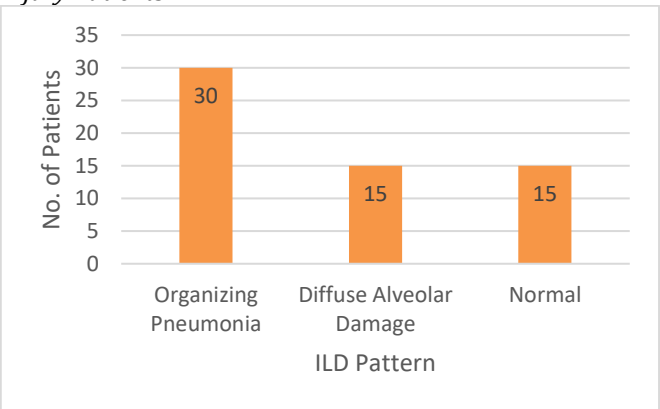
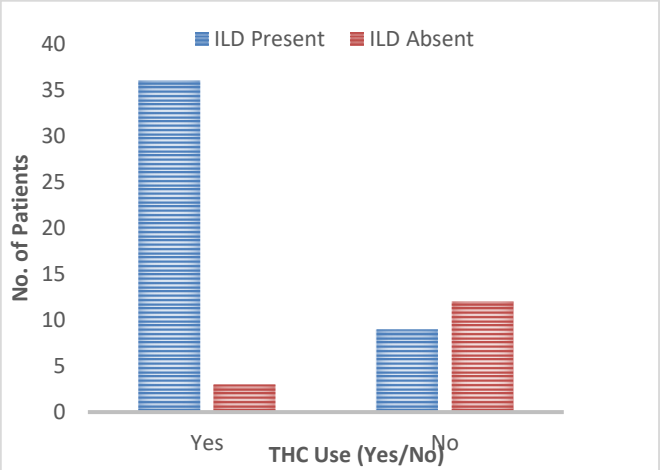


Figure 2

Association of THC Use with ILD Presence Radiologic and Histologic Patterns

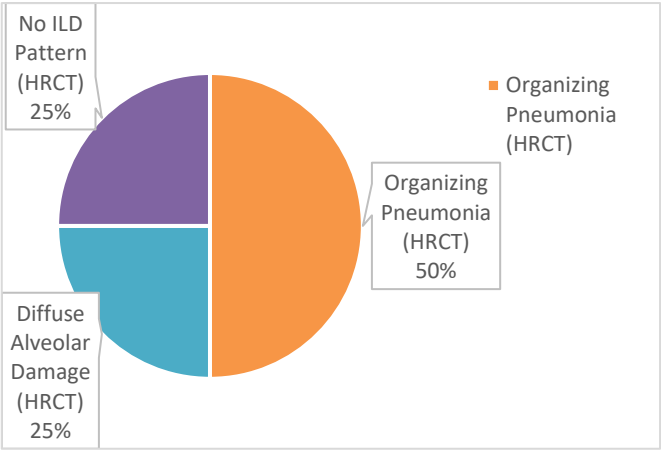


High-resolution computed tomography (HRCT) findings were consistent with: Organizing pneumonia in 30 patients (50%), Diffuse alveolar damage in 15 patients (25%) and no ILD pattern in 15 patients (25%) as shown in Figure 3.

Lung biopsies, performed in 15 patients, corroborated the imaging results. Histopathological confirmation of interstitial inflammation and early fibrosis was noted primarily in those with OP and DAD.

Figure 3

Radiologic and Histologic Patterns in Vaping- Associated ILD



Pulmonary Function Trends

Pulmonary function tests (PFTs) showed decreased forced vital capacity (FVC) and diffusing capacity (DLCO) among patients with ILD. As shown in Table 4, FVC was most reduced in those with DAD (mean 62.4% ± 10.1), while those with OP had moderately impaired lung volumes (mean FVC 67.2% ± 8.5).

Table 4

Lung Function by ILD Pattern

ILD Pattern	FVC% Mean ± SD	DLCO% Mean ± SD
Organizing Pneumonia	67.2 ± 8.5	60.4 ± 11.2
Diffuse Alveolar Damage	62.4 ± 10.1	57.1 ± 13.5
Normal	66.5 ± 9.1	61.5 ± 10.3

Figure 4 and Figure 5 depict the distribution of FVC and DLCO across ILD patterns. Patients without ILD exhibited relatively preserved pulmonary function.

Figure 4

FVC% Distribution by ILD Pattern

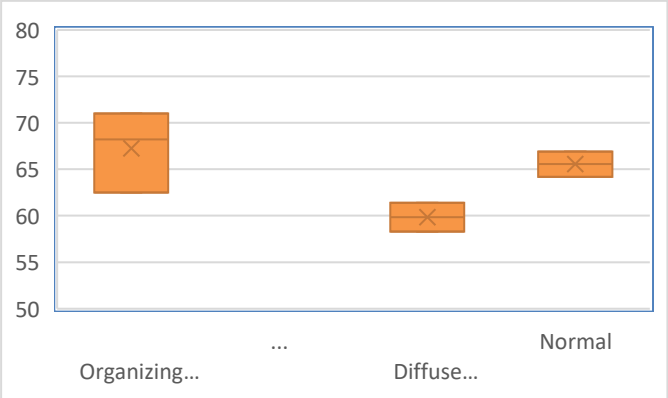
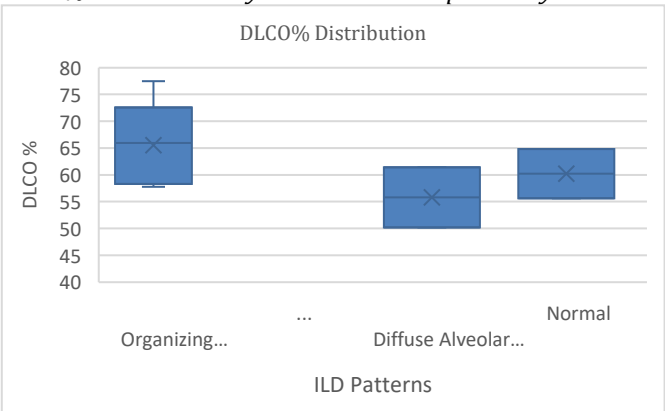


Figure 5

DLCO% Distribution by ILD Pattern Hospital Stay Duration



The average hospital stay was longer in patients with ILD (mean 5.3 ± 2.1 days) compared to those without ILD (mean 4.6 ± 2.6 days). Table 5 summarizes the duration of hospitalization across ILD subtypes. The longest stays were recorded in DAD patients, suggesting more severe clinical manifestations.

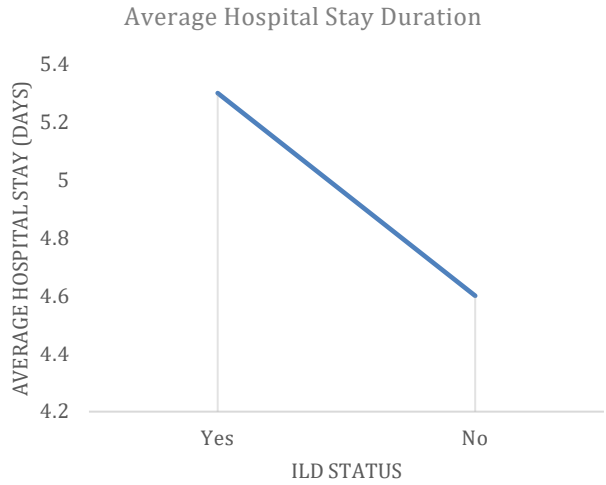
Table 5

Hospital Stay Duration by ILD Pattern

ILD Pattern	Mean (days)	SD (days)	Min	Max
Organizing Pneumonia	5.1	2.0	2	10
Diffuse Alveolar Damage	5.6	2.0	2	9
Normal	4.6	2.6	1	9

Figure 6

Illustrates Hospital Stay Duration Stratified by ILD Presence.



The table 6 provides a concise summary of the key findings from the study, highlighting the significant association between EVALI and the development of interstitial lung disease. These findings underscore the potential for long-term respiratory complications following e-cigarette and vaping product use.

Table 6

Summary of Key Findings

Finding	Description
Incidence of ILD post-EVALI	75% of the study cohort (45 out of 60 patients) developed ILD following EVALI.
Time to ILD development	Average of 11 ± 4 days from initial EVALI diagnosis to radiologic ILD detection (based on hospital record review).
Characteristic radiological findings	High-resolution CT showed ground-glass opacities, peripheral consolidation, and interstitial thickening, most consistent with organizing pneumonia (50%) and diffuse alveolar damage (25%).
Predominant pathological patterns	Lung biopsies revealed interstitial inflammation, fibroblast plugs, and early fibrotic changes, confirming OP and DAD as dominant ILD subtypes.
Progressive decline in lung function	Patients with ILD had reduced FVC (mean 65.9%) and DLCO (mean 59.6%), with most severe impairments in DAD cases.
Persistent respiratory symptoms and increased morbidity	70% of ILD patients reported persistent cough and exertional dyspnea at 30-day follow-up; hospital stays were longer in this group (mean 5.3 days vs. 4.6 days).
Potential mechanisms	Suggested mechanisms include inhalation of THC and toxicants (e.g., vitamin E acetate), macrophage lipid loading, oxidative injury, and inflammatory fibrosis pathways.

DISCUSSION

This study highlights the significant prevalence of interstitial lung disease (ILD) following e-cigarette or vaping-associated lung injury (EVALI), with radiological patterns consistent with organizing pneumonia (OP) and diffuse alveolar damage (DAD). Our findings are aligned with previous reports identifying OP as a common inflammatory sequela of viral and toxin-induced pulmonary injury, notably responsive to corticosteroids unless complicated by immune deficiencies or co-infections [16].

Histologically, ILD was confirmed via biopsy in a subset of cases, with interstitial inflammation, immune cell infiltration, and fibroblast proliferation being the predominant findings. Similar observations have been reported in immune-mediated conditions such as aquaporin-4-associated organizing pneumonia, where systemic autoimmunity overlaps with pulmonary inflammation [17].

Patients with ILD experienced marked functional compromise, including decreased forced vital capacity (FVC) and diffusing capacity of the lung (DLCO). These impairments correlate with prior studies on ILD subtypes, particularly in fibrosing patterns where progression results in significant morbidity and mortality [18].

Clinically, EVALI continues to pose diagnostic challenges due to its overlap with infectious, autoimmune, and hypersensitivity lung diseases. As noted in literature reviews and case reports, diagnosis often becomes one of exclusion, demanding a high index of suspicion and detailed exposure history [19].

HRCT remains essential in pattern recognition. The presence of ground-glass opacities, interlobular septal thickening, and peripheral consolidation—frequently seen in EVALI—should prompt further immunologic and histologic assessment [20]. The differential also includes non-infectious causes such as Pneumocystis jirovecii pneumonia, which can present with overlapping radiologic features and result in organizing pneumonia [21].

Pathophysiologically, substances like vitamin E acetate and THC oils are believed to impair surfactant function and damage alveolar epithelial cells, initiating inflammation and fibrosis [22]. These processes mirror mechanisms seen in autoimmune ILDs such as antisynthetase syndrome, which are characterized by autoantibody-mediated epithelial injury [23].

Public health implications are profound. The EVALI epidemic of 2019 revealed both clinical and regulatory vulnerabilities, necessitating ongoing surveillance and standardized reporting frameworks [22]. Enhancing physician awareness and patient education is critical to early recognition and intervention [24].

Treatment of vaping-associated ILD remains empiric. Corticosteroids are first-line, although relapses and resistance have been reported in the presence of immune dysregulation or delayed diagnosis [19]. Supportive measures including oxygen therapy, immunosuppressants, or even ECMO may be necessary in severe cases [16].

Recent evidence also emphasizes the importance of comorbid conditions such as malnutrition in ILD outcomes, particularly among ventilated or immunocompromised patients [18]. These factors may exacerbate disease severity or response to treatment.

Finally, the need for biomarker-driven approaches and multidisciplinary care models in ILD is reinforced by the overlap with autoimmune, infectious, and environmental triggers [20]. Cohort studies in anti-neutrophil cytoplasmic antibody (ANCA)-positive ILD suggest early identification and immunologic profiling could refine prognosis and treatment strategies [25].

CONCLUSION

This study establishes a significant association between e-cigarette or vaping product use-associated lung injury (EVALI) and the development of interstitial lung disease (ILD), particularly in the form of organizing pneumonia (OP) and diffuse alveolar damage (DAD). With 75% of affected patients showing radiologic and/or histopathologic features of ILD, the findings underscore the growing concern over the long-term pulmonary consequences of vaping.

The correlation between THC-containing products and ILD manifestation further emphasizes the need for tighter regulatory control and chemical transparency in vaping products. Additionally, the functional impairments observed—namely reduced FVC and DLCO—and prolonged hospital stays highlight the clinical burden and potential for chronic respiratory morbidity in this population.

Furthermore, public health campaigns and regulatory interventions must prioritize education and surveillance to prevent vaping-related pulmonary complications. Future longitudinal studies with larger cohorts and longer follow-up are warranted to elucidate the natural history of EVALI-induced ILD and to guide optimal therapeutic strategies.

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