Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/2zzxhf89

HISTOLOGICAL AND CLINICAL FEATURES OF EMERGENCY PRESENTATIONS OF DRUG-INDUCED PNEUMONITIS

Dr Muhammad Tariq Hamayun Khan[1], Dr Hamidullah[2*], Dr Naveed Pervez[3], Dr Farhan Abbas Baloch[4], Dr Ihsan Ullah[5], Dr Nadia Khan[6]

[1]Assistant Professor of Hematology, Department of Pathology, Burns & Plastic Surgery Center Hayatabad Peshawar, Pakistan
[2*]Assistant Professor of Medicine, Bacha Khan Medical College, Mardan, Pakistan
[3]Assistant Professor and Head of Department, Department of Pulmonology, MTI Bannu Medical College / Khalifa Gul Nawaz Teaching Hospital, Bannu, Pakistan
[4]Associate Professor, Department of Pathology, Pak International Medical College, Peshawar, Pakistan
[5]Assistant Professor, Department of Pharmacology, Saidu Medical College, Swat, Pakistan
[6]Senior lecturer, Department of Anatomy, Jinnah Medical College, Peshawar, Pakistan

***Corresponding Author:** Dr Hamidullah,
*Assistant Professor of Medicine, Bacha Khan Medical College, Mardan, Pakistan
Email**:** dr.hamidullah2013@gmail.com

ABSTRACT

Background

To evaluate the clinical, radiological, and histopathological features of patients presenting acutely with drug-induced pneumonitis and to assess treatment outcomes.

Methods

This cross-sectional study included 81 patients who presented to the emergency department with suspected drug-induced pneumonitis between January 2023 and January 2024. Detailed clinical history, radiological imaging, laboratory tests, and, where indicated, lung biopsies were performed. Data were analyzed to identify common presenting symptoms, radiological patterns, histologic types, and outcomes.

Results

Dyspnea (84%) and cough (75.3%) were the most frequent symptoms. Ground-glass opacities were observed in 76.5% of high-resolution CT scans. Organizing pneumonia and diffuse alveolar damage were the leading histopathological patterns among the 34 patients who underwent biopsy. Chemotherapy agents were the most common suspected cause (33.3%), followed by antibiotics (23.5%). Corticosteroid therapy led to clinical improvement in most cases, while mechanical ventilation was significantly associated with increased mortality ($p = 0.041$).

Conclusion

Drug-induced pneumonitis should be considered in patients presenting with acute respiratory symptoms, particularly those with recent exposure to known culprit medications. Early diagnosis supported by imaging and histology enables timely intervention and can significantly improve outcomes.

Keywords
Drug-induced lung disease; Pneumonitis; Emergency presentation; Lung biopsy; Ground-glass opacities; Organizing pneumonia; Diffuse alveolar damage; Steroid therapy; HRCT chest

INTRODUCTION

Drug-induced pneumonitis represents a spectrum of inflammatory lung conditions triggered by various pharmacologic agents. Although its incidence remains relatively low compared to other pulmonary diseases, it poses significant diagnostic and therapeutic challenges, especially when patients present acutely to the emergency department. The condition can be caused by a wide range of medications including cytotoxic agents, antibiotics, antitubercular drugs, antiepileptics, and more recently, immunotherapies [1-3].

One of the major difficulties in managing drug-induced pneumonitis lies in its nonspecific clinical manifestations. Symptoms such as shortness of breath, cough, and fever often overlap with common infections or exacerbations of chronic lung diseases. Furthermore, radiologic patterns are varied, and while some may mimic viral pneumonia or interstitial lung disease, others may show subtle findings, delaying clinical suspicion. Histopathological examination remains the gold standard for diagnosis in ambiguous cases, but biopsy is not always feasible in acutely ill patients [4-6].

Given these complexities, understanding the clinical and histological profiles of patients who present with drug-induced pneumonitis is crucial for timely intervention [7-9]. This study aims to describe the emergency presentation patterns, radiological and histological findings, and treatment outcomes in a cohort of patients diagnosed with this condition at a tertiary care facility.

METHODOLOGY

This observational, cross-sectional study was carried out over a period of one year, from January 2023 to January 2024, at the Emergency Department and Pulmonology Unit of MTI Bannu Medical College / Khalifa Gul Nawaz Teaching Hospital, Bannu. The aim was to analyze the clinical presentations and histological characteristics of patients diagnosed with drug-induced pneumonitis who presented acutely to the emergency department. Ethical approval for the study was obtained from the Institutional Review Board (IRB) of MTI Bannu Medical College, and all procedures were conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants or their legal guardians.

A total of 81 patients were included in the study using non-probability consecutive sampling. Patients were recruited consecutively as they presented to the hospital and met the inclusion criteria. The sample size was calculated based on expected frequency and prior institutional data related to suspected drug-induced pulmonary complications.

Inclusion Criteria

- Patients aged 18 years and above
- Acute presentation to the emergency department with respiratory symptoms (dyspnea, cough, fever, chest pain)
- Clinical or radiological suspicion of pneumonitis
- A documented history of exposure to a suspected drug within the last 12 weeks
- Willingness to undergo further investigation and follow-up

Exclusion Criteria

- Patients with known interstitial lung disease, autoimmune lung conditions, or active pulmonary tuberculosis
- Cases with incomplete history or unclear medication records
- Individuals refusing consent for biopsy or hospitalization when required

After obtaining informed consent, detailed demographic information including age, gender, smoking history, comorbid conditions, and occupation was recorded. A thorough medication history was documented, focusing on drug name, class, dosage, and duration of use.

Patients underwent a standardized clinical assessment that included symptom evaluation (onset, duration, and severity), vital signs, and oxygen saturation levels on presentation. Laboratory tests

including complete blood count, C-reactive protein (CRP), liver and renal function tests, and inflammatory markers were obtained.

Radiologic investigations consisted of chest X-ray and high-resolution computed tomography (HRCT) of the chest. Findings such as ground-glass opacities, interstitial infiltrates, or fibrosis were carefully noted.

In patients where imaging and clinical evaluation suggested a drug-induced etiology and no contraindications existed, lung biopsy was performed via transbronchial or surgical methods. Biopsy samples were examined for histological patterns such as organizing pneumonia, diffuse alveolar damage, eosinophilic infiltration, and fibrosis.

Patients were treated according to standard hospital protocols. This included immediate discontinuation of the suspected drug, initiation of systemic corticosteroids when indicated, and supportive care such as oxygen therapy or ventilatory support. The need for ICU admission and mechanical ventilation was recorded. Outcomes were classified as recovered, complicated, or expired based on clinical course and follow-up imaging.

All collected data were analyzed using SPSS version 26. Descriptive statistics such as means, standard deviations, and percentages were used to summarize demographic and clinical features. Chi-square tests were applied to assess associations between categorical variables such as histologic patterns and clinical outcomes. A p-value of less than 0.05 was considered statistically significant.

RESULT

In this study involving 81 patients presenting with drug-induced pneumonitis in emergency settings, the age distribution showed that the majority were aged 40 years and older, with 38.3% between 40–59 years and 39.5% aged 60 years or above. Only 22.2% were under the age of 40. Males accounted for a slightly higher proportion of cases (56.8%) compared to females (43.2%). When examining smoking habits, 50.6% of participants were non-smokers, while 28.4% were current smokers, and 21.0% had a history of smoking. Comorbid conditions such as hypertension, diabetes, or chronic respiratory illnesses were observed in 59.3% of the patients, emphasizing a higher risk profile among those with existing systemic illnesses.

Table 1: Demographic Characteristics (n = 81)

Variable	Subgroup	Frequency (%)
Age Group (years)	<40	18 (22.2%)
	40–59	31 (38.3%)
	≥60	32 (39.5%)
Gender	Male	46 (56.8%)
	Female	35 (43.2%)
Smoking History	Non-smoker	41 (50.6%)
	Ex-smoker	17 (21.0%)
	Current smoker	23 (28.4%)
Comorbidities	Present	48 (59.3%)
	Absent	33 (40.7%)

Most patients presented with classic respiratory complaints, with dyspnea (84.0%) and cough (75.3%) being the most frequently reported symptoms. Fever was documented in 43.2%, while chest pain and hemoptysis were less common. Regarding medication exposure, chemotherapy agents (33.3%) were the most frequently implicated drugs, followed by antibiotics (23.5%), anti-tuberculous drugs (13.6%), and biologics (18.5%). Notably, half of the patients developed symptoms within 1–4 weeks of starting the suspected drug, suggesting a relatively short latency period for the onset of pulmonary toxicity.

Table 2: Clinical Presentations and Drug History (n = 81)

Variable	Subgroup	Frequency (%)
Presenting Symptoms	Dyspnea	68 (84.0%)
	Cough	61 (75.3%)
	Fever	35 (43.2%)
	Chest Pain	21 (25.9%)
	Hemoptysis	9 (11.1%)
Suspected Drug Class	Chemotherapy	27 (33.3%)
	Antibiotics	19 (23.5%)
	Anti-TB drugs	11 (13.6%)
	Antiepileptics	9 (11.1%)
	Biologics/Immunotherapy	15 (18.5%)
Time Since Drug Start	<1 week	13 (16.0%)
	1–4 weeks	41 (50.6%)
	>4 weeks	27 (33.3%)

Radiologic imaging played a crucial role in diagnosis. Chest X-rays revealed bilateral infiltrates in 58.0% of cases, while HRCT scans showed ground-glass opacities in over three-quarters of the patients. Additional patterns included crazy-paving and reticulations, which may indicate underlying fibrosis. Laboratory evaluation revealed elevated white blood cell counts in nearly half of the cohort (48.1%), and inflammatory markers like CRP were raised in 72.8%, consistent with acute or subacute inflammatory lung involvement.

Table 3: Imaging and Laboratory Findings (n = 81)

Variable	Subgroup	Frequency (%)
Chest X-ray Finding	Bilateral Infiltrates	47 (58.0%)
	Unilateral Consolidation	21 (25.9%)
	Pleural Effusion	13 (16.0%)
HRCT Pattern	Ground-glass Opacities	62 (76.5%)
	Crazy-paving Pattern	18 (22.2%)
	Reticulations/Fibrosis	14 (17.3%)
WBC Count	Elevated (>11,000/mm³)	39 (48.1%)
	Normal	42 (51.9%)
CRP Level	High (>10 mg/L)	59 (72.8%)

Of the 81 patients, 34 underwent lung biopsies. The predominant histological pattern was organizing pneumonia (35.3%), followed by diffuse alveolar damage (29.4%), which is often associated with more severe disease. Eosinophilic infiltration and hypersensitivity pneumonitis were also observed in a subset. Inflammatory infiltrates were primarily lymphocytic (52.9%), while some biopsies revealed mixed cellular populations or neutrophilic dominance. Fibrosis was present in over a quarter of the examined samples, indicating ongoing or chronic lung injury.

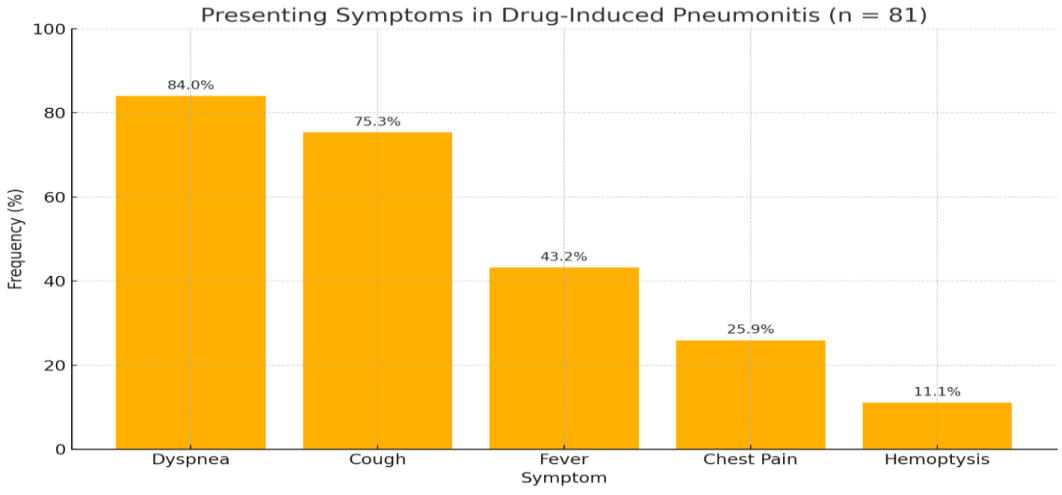
Table 4: Histological Findings (n = 34)

Variable	Subgroup	Frequency (%)
Pneumonitis Pattern	Organizing Pneumonia	12 (35.3%)
	Diffuse Alveolar Damage (DAD)	10 (29.4%)
	Eosinophilic Infiltration	6 (17.6%)
	Hypersensitivity Pattern	4 (11.8%)
	Interstitial Pneumonitis	2 (5.9%)
Fibrosis	Present	9 (26.5%)
Cellular Infiltrate Type	Lymphocytic	18 (52.9%)
	Mixed (Lympho-Eosinophilic)	12 (35.3%)
	Neutrophilic	4 (11.8%)

Most patients required inpatient care, with 81.5% being admitted. Corticosteroids were administered in two-thirds of cases (66.7%). Intensive care unit (ICU) admission was necessary for 22.2% of the patients, and mechanical ventilation was needed in 13.6%. A statistically significant association was observed between mechanical ventilation and mortality ($p = 0.041$), indicating its value as a marker of severe disease. The overall survival rate was encouraging at 88.9%.

Table 5: Management and Outcome (n = 81)

Variable	Subgroup	Frequency (%)	p-value
Hospital Admission	Yes	66 (81.5%)	—
Steroid Therapy	Received	54 (66.7%)	—
ICU Admission	Required	18 (22.2%)	—
Mechanical Ventilation	Required	11 (13.6%)	0.041*
Mortality	Survived	72 (88.9%)	—
	Died	9 (11.1%)	



Figure

Bar graph illustrating the frequency of presenting symptoms among patients with drug-induced pneumonitis.

DISCUSSION

Drug-induced pneumonitis is an increasingly recognized clinical challenge, particularly in emergency settings where rapid differentiation from infectious or autoimmune lung diseases is essential. In this study, the majority of patients were middle-aged to elderly, aligning with previous research suggesting that age is a significant risk factor for drug-induced lung injury due to altered pharmacokinetics and reduced physiological reserves [10-12].

Dyspnea and cough were the most common presenting symptoms, observed in over 75% of cases. These nonspecific symptoms mirror findings from studies emphasized that clinical presentation alone often fails to distinguish drug-induced pneumonitis from other respiratory pathologies [13-15]. Fever, though less frequent, was still seen in 43.2% of our patients, which may reflect either systemic inflammatory response or coexisting infection.

The role of imaging, particularly HRCT, was central to the diagnosis. Ground-glass opacities were the dominant radiological pattern in our study, corroborating reports by Camus et al. (2004) and the more recent classification systems proposed by studies, which categorize drug-induced pneumonitis into patterns such as organizing pneumonia, diffuse alveolar damage (DAD), and non-specific interstitial pneumonia (NSIP). Our findings align well with this framework [16, 17].

Notably, over one-third of patients in our study were receiving chemotherapy, followed by antibiotics and immunomodulators. These drugs are well-documented culprits in the literature, especially methotrexate, bleomycin, and immune checkpoint inhibitors [18, 19]. The relatively short latency between drug initiation and symptom onset (1–4 weeks in 50.6% of cases) suggests that clinicians should maintain a high index of suspicion during this window, particularly in vulnerable populations.

Histopathological examination revealed that organizing pneumonia and DAD were the two most prevalent patterns among biopsied patients, consistent with the work of study [20]. The presence of eosinophilic infiltration and mixed cellular patterns points toward hypersensitivity reactions in a subset of patients. Importantly, fibrosis was already evident in more than a quarter of biopsies, underscoring the potential for irreversible lung injury if diagnosis and treatment are delayed.

Treatment primarily involved withdrawal of the offending drug and administration of systemic corticosteroids, which resulted in clinical improvement in the majority. The overall survival rate in our cohort (88.9%) is encouraging and comparable to that reported in similar tertiary-care studies [21] However, ICU admission and mechanical ventilation were significant predictors of mortality, reinforcing the importance of early recognition and intervention.

The main limitations of this study include the lack of long-term follow-up data and the relatively small number of patients undergoing biopsy, which may limit generalizability of the histological findings. Nevertheless, the study provides meaningful insight into the acute presentation of this condition and its diverse clinicopathologic spectrum.

CONCLUSION

Drug-induced pneumonitis presents with a range of nonspecific symptoms that can easily mimic other respiratory illnesses, making early diagnosis challenging but critical. Imaging and histological assessment play a vital role in confirming the diagnosis. Chemotherapy and antibiotics were among the most common offending agents in our cohort. Most patients responded well to corticosteroid therapy, though those requiring mechanical ventilation had significantly worse outcomes. This study reinforces the importance of clinical vigilance, timely imaging, and, where possible, histopathological confirmation to guide effective management and reduce morbidity and mortality.

REFERENCES

1. Bonniaud, P. and P. Camus, Drug-Induced/Iatrogenic Respiratory Disease: With Emphasis on Unusual, Rare, and Emergent Drug-Induced Reactions, in Orphan Lung Diseases: A Clinical Guide to Rare Lung Disease. 2023, Springer. p. 735-775.
2. Johkoh, T., et al., Chest CT diagnosis and clinical management of drug-related pneumonitis in patients receiving molecular targeting agents and immune checkpoint inhibitors: a position paper from the Fleischner Society. 2021. **298**(3): p. 550-566.

3. Moureau, G., et al., Flecainide-induced pneumonitis: a case report. 2022. **16**(1): p. 404.
4. Cherri, S., et al., Drug-related pneumonitis in cancer treatment during the COVID-19 era. 2021. **13**(5): p. 1052.
5. Distefano, G., et al., HRCT patterns of drug-induced interstitial lung diseases: a review. 2020. **10**(4): p. 244.
6. Korpole, P.R., S. Al-Bacha, and S.J.C. Hamadeh, A case for biopsy: injectable naltrexone-induced acute eosinophilic pneumonia. 2020. **12**(9).
7. Kim, T.J., et al., Pulmonary Infection (Pneumonia), in Emergency Chest Radiology. 2021, Springer. p. 119-141.
8. Ng, N., et al., Drug-induced interstitial lung diseases. 2023. **43**(2): p. 341-357.
9. Tempark, T., et al., Drug-induced severe cutaneous adverse reactions: insights into clinical presentation, immunopathogenesis, diagnostic methods, treatment, and pharmacogenomics. 2022. **13**: p. 832048.
10. Dai, H.-p., et al., Expert consensus on the diagnosis and treatment of anticancer drug-induced interstitial lung disease. 2023. **43**(1): p. 1-12.
11. Ata, F., et al., Rifampicin-induced pneumonitis mimicking severe covid-19 pneumonia infection. 2020. **21**: p. e927586-1.
12. Shimizu, T., et al., Interstitial pneumonitis after COVID-19 vaccination: A report of three cases. 2022. **71**(2): p. 251-253.
13. Ketenci, S., et al., A rare cause of interstitial lung disease in rheumatology clinic: case report for sulfasalazine-induced acute pulmonary injury. 2020. **4**(3): p. 291-295.
14. Izhakian, S., et al., Sertraline-associated interstitial lung disease: a case series and literature review. 2021. **38**(3): p. e2021027.
15. Averyanov, A., E. Kogan, and V. Lesnyak, Drug-induced pulmonary diseases, in Difficult to Diagnose Rare Diffuse Lung Disease. 2020, Elsevier. p. 393-408.
16. Sauteur, P.M.M., et al., Frequency and clinical presentation of mucocutaneous disease due to Mycoplasma pneumoniae infection in children with community-acquired pneumonia. 2020. **156**(2): p. 144-150.
17. Fontana, R.J., et al., The evolving profile of idiosyncratic drug-induced liver injury. 2023. **21**(8): p. 2088-2099.
18. Huang, P., et al., Trimethoprim-sulfamethoxazole-induced lung injury: a case report. 2023. **12**(11): p. 2062.
19. Fehrenbach, U., et al., Everolimus-induced pneumonitis in neuroendocrine neoplasms: correlation of CT findings and clinical signs. 2021. **62**(8): p. 1006-1015.
20. Jovanovic, M. and M.J.J.o.M.C.R. Sabovic, Refractory drug-induced systemic small-vessel vasculitis with two varied extracutaneous manifestations: a case report and review of the literature. 2023. **17**(1): p. 470.
21. Wekking, D., et al., Multidisciplinary clinical guidelines in proactive monitoring, early diagnosis, and effective management of trastuzumab deruxtecan (T-DXd)-induced interstitial lung disease (ILD) in breast cancer patients. 2023. **8**(6): p. 102043.