

# Bronchoalveolar lavage as a tool for assessing potential occupational exposure: a retrospective study

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## ABSTRACT

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**Introduction:** Bronchoalveolar lavage (BAL) is a fundamental diagnostic procedure for evaluating diffuse parenchymal lung diseases (DPLDs). However, its diagnostic precision is critically dependent on the integration of a detailed occupational history. Occupational exposures are frequently overlooked in clinical practice, leading to potential misdiagnosis.

**Methods:** We conducted a retrospective analysis of 210 BAL samples from 207 patients over one calendar year at a tertiary referral hospital in Attica, Greece. Data regarding demographics, smoking status, and occupational history (classified via ISCO-08) were correlated with BAL cytology using descriptive statistics,  $\chi^2$  tests, t-tests, and one-way ANOVA with post-hoc comparisons. Missing data were supplemented through extensive record review and patient interviews.

**Results:** Occupational history was absent in 79.5% of initial clinician referrals. Upon data completion, 23.3% of patients were identified as active workers. Workers in the agricultural and forestry sector (ISCO-08 Group 6) showed significantly higher total BAL cell counts ( $P=0.025$ ) and specific cytological patterns, including increased macrophages and mast cells. While smoking significantly altered differential counts, it did not influence the total cell count.

**Conclusion:** Specific BAL profiles are associated with certain occupational groups, yet a significant gap in history-taking persists. Systematic occupational assessment is mandatory to improve the diagnostic utility of BAL in respiratory medicine. These findings suggest that BAL can serve as a valuable 'sentinel tool' for occupational surveillance in respiratory medicine.

**Keywords:** Bronchoalveolar lavage, occupational exposure, ISCO-08, agricultural workers, lung diseases

## Introduction

The diagnosis of diffuse parenchymal lung diseases (DPLDs) remains one of the most challenging areas in respiratory medicine. These conditions encompass a wide array of interstitial disorders, many of which are directly or indirectly caused by prolonged inhalation of hazardous environmental and occupational agents.<sup>1,2</sup> According to the Global Burden of Disease study, occupational exposures to organic and inorganic

dusts, chemical fumes, and bioaerosols contribute significantly to the global prevalence of chronic respiratory morbidity and mortality.<sup>3</sup>

Bronchoalveolar lavage (BAL) has established itself as a cornerstone of the diagnostic workup of these diseases, offering a safe, minimally invasive method for sampling the distal airways and alveolar spaces.<sup>4</sup> By analyzing the cellular and

non-cellular components of the epithelial lining fluid, clinicians can gain valuable insights into the inflammatory and immunological processes occurring within the lung parenchyma. However, BAL findings are rarely pathognomonic and must be interpreted in the appropriate clinical context. For instance, a lymphocytic predominant pattern can be found in sarcoidosis, hypersensitivity pneumonitis, or certain drug-induced lung diseases.<sup>5</sup>

The clinical "gold standard" for interpreting BAL results is the integration of cytological data with a meticulous clinical and occupational history. In the absence of such history, specific findings—such as the presence of mast cells or certain inorganic particles—may be overlooked or misinterpreted, leading to the erroneous classification of occupational diseases as "idiopathic".<sup>6</sup> Despite the critical importance of this information, occupational history-taking is often neglected in the fast-paced environment of tertiary care hospitals.

This study seeks to address this gap by quantifying the extent of underreporting of occupational data in a specialized respiratory setting in Greece. Furthermore, by utilizing the International Standard Classification of Occupations (ISCO-08), we aimed to investigate whether specific labor sectors exhibit characteristic "BAL signatures" that could assist in the early identification of work-related lung injury, even when clinical symptoms are non-specific.

## Methods

We conducted a retrospective analysis of all patients who underwent BAL for diagnostic purposes at a tertiary general hospital in the Attica region over a continuous 12-month period. The hospital serves as a major referral center for complex respiratory cases in Greece. A total of 210 BAL samples were collected from 207 patients. The study received ethical approval from the Institutional Review Board, and all data were anonymized to protect patient confidentiality. The study and the telephone interview protocol were

approved by the Scientific Council of the General Hospital of Attica (Approval No. 31 HΔ/25, 2025).

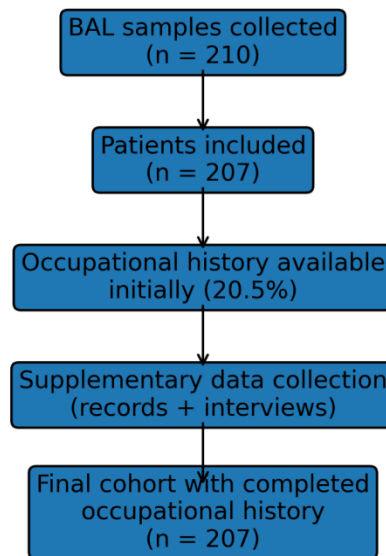
Recognizing the limitations of existing medical records, a comprehensive data retrieval protocol was implemented:

1. **Laboratory Archives:** Retrieval of the primary cytological reports, including total nucleated cell counts (TNCC) and differential cell counts.
2. **Clinical Referrals:** Examination of the original request forms submitted by the referring pulmonologists.
3. **Medical Records:** Review of inpatient and outpatient files, including discharge summaries and admission notes.
4. **Confirmatory Interviews:** When occupational or smoking data were missing or ambiguous (which was the case for the majority of the cohort), telephone interviews were conducted with the patients or their primary caregivers using a structured questionnaire focusing on lifetime work history and environmental exposures. Missing occupational data were supplemented through 173 confirmatory telephone interviews. Verbal informed consent was obtained from all participants after explaining the study's scope. BAL recovery was considered adequate if >40% of the instilled volume was retrieved with minimal bronchial epithelial contamination (<5%). The structured questionnaire used for the telephone interviews was developed specifically for this study and included standardized questions regarding current occupation, longest-held occupation, duration of employment, and potential exposure to organic, inorganic, and chemical agents throughout the patient's working life.

To ensure international comparability, occupations were classified using the ISCO-08 system. This hierarchical structure allowed us to group patients based on the nature of their work and potential exposure profiles. We focused on the "Major Groups" of the ISCO-08 to maintain statistical power. Patients who had retired many

years prior but had a significant lifetime exposure in a specific sector were classified based on their primary long-term occupation.

Figure 1 illustrates the flow of BAL sample collection, patient inclusion, and completion of occupational history data.



**Figure 1:** Study flow diagram and occupational data completion process

BAL was performed by instilling sterile saline (typically 3 X 50 mL) into a wedge position of a segmental bronchus. The fluid was recovered by gentle suction. Total nucleated cell counts were determined using a hemocytometer. Differential cell counts (macrophages, lymphocytes, neutrophils, eosinophils, and mast cells) were performed on Cytospin preparations stained with May-Grünwald-Giemsa, with at least 500 cells counted per slide. The presence of specialized cells (e.g., siderophages, foamy cells) and foreign particles (e.g., asbestos fibers) was also documented.

**Results**

The most striking initial result was the lack of documentation. On the initial clinician referral forms, occupational history was completely absent in 79.5% of cases. Even when records were searched, the information was often vague (e.g., "worker" or "private employee"). Through our supplemental retrieval process, we successfully classified the occupations of 100% of the cohort. Following the supplemental retrieval strategy and confirmatory interviews, the occupational

Data were analyzed using SPSS (version 24.0). Descriptive statistics were used for demographic variables. Continuous variables were expressed as mean ± standard deviation (SD). Differences between occupational groups were assessed using independent-samples t-tests and a one-way ANOVA with post hoc Tukey tests for multiple comparisons. Categorical variables were compared using the x<sup>2</sup> test. A P-value of <0.05 was considered statistically significant.

classification success rate reached 100% for the study cohort.

The cohort comprised 207 patients, with a mean age of 64.9 ± 14.08 years. Regarding their status at the time of the procedure, 23.3% were active workers, 40.0% were retired, 12.4% were engaged in domestic work, and 4.3% were unemployed. The distribution across ISCO-08 groups is detailed in Table 1.

A significant association was found between occupational category and BAL cellularity.

Group 6 (Agricultural and Forestry workers) emerged as a distinct subgroup with the highest inflammatory markers in the lung.

**Table 1:** Detailed Distribution of Patients by ISCO-08 Occupational Category (N=207)

ISCO-08 Group	Occupational Description	N	Percentage (%)
1 & 4	Managers and Clerical Support	14	6.7%
2	Professionals (Engineers, Scientists, Doctors)	30	14.3%
3	Technicians and Associate Professionals	14	6.7%
5	Service and Sales Workers	26	12.4%
6	Agricultural, Livestock, Forestry, and Fishery	18	8.6%
7	Craft and Related Trades Workers	14	6.7%
8	Plant and Machine Operators, Assemblers	20	9.5%
9	Elementary Occupations (Unskilled Laborers)	19	9.0%
N/A	Domestic Work / Retired / Unemployed	52	26.1%

**Table 2:** Comparison of Total BAL Cell Counts (TNCC) across Occupational Groups

Comparison: Group 6 (Agriculture) vs.	Mean Difference in TNCC (10 <sup>6</sup> cells)	P-value
Group 2 (Professionals)	Higher in Group 6	0.025
Group 5 (Service Workers)	Higher in Group 6	0.008
Group 7 (Craft/Trades)	Higher in Group 6	0.002
Group 8 (Machine Operators)	Higher in Group 6	0.026
Group 9 (Elementary Occ.)	Higher in Group 6	0.035

As shown in Figure 2, the mean total BAL cell count differed across ISCO-08 major occupational groups, with the highest values observed in Group 6 (Agriculture).

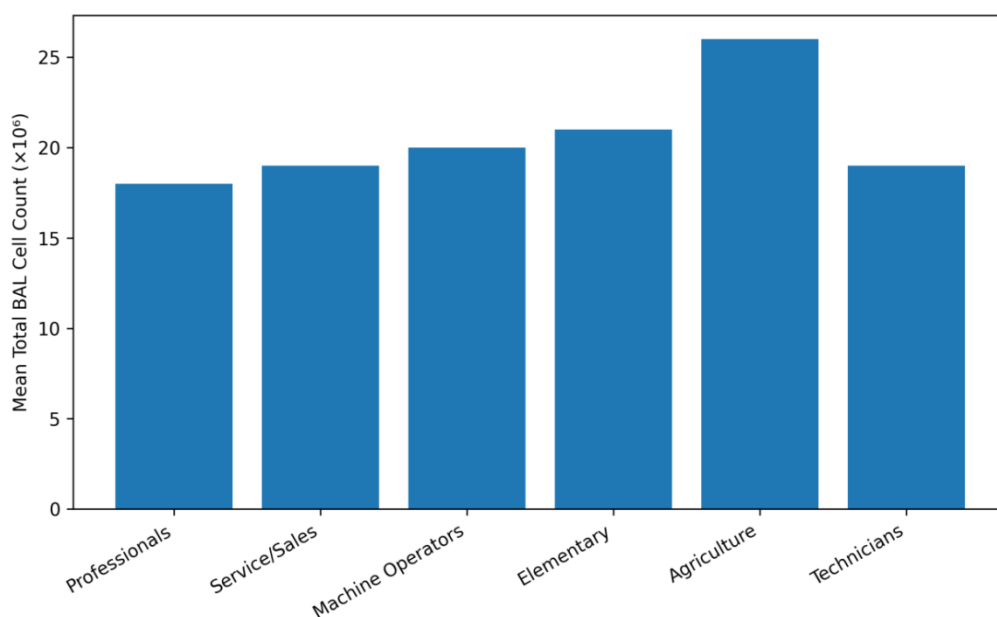
In addition to the total cell count, the differential analysis showed that agricultural workers had a unique combination of elevated macrophages and mast cells. Specifically, the presence of mast cells—often a marker of hypersensitivity

reactions to organic dusts—was significantly more frequent in this group compared to the "cleaner" professional environments of Group 2. Agricultural workers (Group 6) exhibited higher mast cell percentages and greater total BAL cellularity than other occupational groups, suggesting a distinct inflammatory pattern in this sector.

Given the high prevalence of smoking in the Greek population, we analyzed its impact. Active smokers (24.8%) and former smokers (22.4%) showed distinct patterns: smokers had higher macrophage counts, while former smokers showed neutrophil predominance.

Interestingly, while Group 6 workers were among the heaviest smokers (highest mean pack-years), there was no statistical correlation between smoking status and the total cell count.

This suggests that the increased total cellularity in agricultural workers is a direct result of occupational exposure rather than tobacco use. Pearson correlation analysis showed no significant association between smoking pack-years and total nucleated cell count ( $r = 0.12, P = 0.45$ ), indicating that occupational exposure, rather than smoking, was the primary driver of TNCC elevation in Group 6.



### Discussion

The results of this study highlight a profound systemic weakness in the diagnostic workup of respiratory diseases: the neglect of occupational history. Similar occupational health challenges have been documented across different industries worldwide, including aquaculture and food processing sectors.<sup>6,7</sup> In nearly 80% of our cases, the clinician failed to record the patient's occupation, effectively "blinding" the cytologist. This persistent underreporting of occupational history—evidenced by the 79.5% rate of missing data in the initial referrals—likely reflects practical constraints in routine clinical practice, including time constraints during

patient consultations and limited training of clinicians in occupational risk assessment. This finding is consistent with international literature suggesting that occupational history is the most frequently omitted part of the medical record.<sup>8,9</sup> These findings should be interpreted as exploratory and hypothesis-generating, rather than as evidence of causal relationships or individual-level exposure assessment.

The diagnostic consequences of this omission are significant. Our findings demonstrate that different occupations lead to different "biological footprints" in the lungs. The Agricultural and

Forestry group (ISCO-08 Group 6) showed a consistent pattern of high cellularity and increased mast cells. This cytological signature is strongly associated with chronic exposure to organic dusts, endotoxins, and fungal spores—common in livestock farming and agriculture.<sup>10</sup> The elevated mast cell count in agricultural workers likely reflects an immune response to organic dust and fungal antigens, such as *Saccharopolyspora rectivirgula*, which are known to trigger hypersensitivity pathways.<sup>10</sup> Such patients are at high risk for conditions like "Farmer's Lung" or Organic Dust Toxic Syndrome (ODTS). Without an occupational context, a high cell count might be dismissed as non-specific inflammation or attributed solely to smoking.<sup>11</sup> Although Group 6 exhibited the most pronounced cytological alterations, modest increases in total cellularity were also observed in Groups 7 (Craft and Related Trades Workers) and 8 (Plant and Machine Operators), suggesting that industrial and mechanical occupational environments may also contribute to inflammatory BAL profiles, albeit to a lesser extent.

Our data, however, suggest that the total BAL cell count may serve as an independent indicator of occupational exposure. While smoking shifts the *proportions* of cells (more macrophages or neutrophils), the *absolute volume* of cellular infiltration appears to be driven by the work environment. This is a critical distinction for the clinician. If a patient presents with a very high total cell count, the suspicion for an occupational etiology should be high, regardless of their smoking status.

Furthermore, we identified inorganic particles (such as asbestos) in a small but significant percentage of patients (1.67%). In these cases, the BAL provided definitive evidence of exposure that was not initially reported by the patient. These findings underscore the potential role of BAL not only as a diagnostic procedure but also as a sentinel tool for occupational health surveillance.<sup>12</sup>

The integration of the ISCO-08 system proved to be an effective framework for this analysis. By standardizing the way we categorize work, we can begin to build a database of "normal" and "pathological" BAL ranges for specific industries. This would move BAL interpretation from a subjective assessment to a more data-driven, objective diagnostic process.

Future prospective studies with larger occupational subgroups are required to validate these associations using multivariable analytical approaches. From a practical standpoint, the implementation of a short structured occupational checklist within referral forms—mandating documentation of current occupation, longest-held occupation, and classification according to ISCO-08 major groups—could substantially reduce underreporting and enhance the diagnostic interpretation of BAL findings.

As a retrospective study, we were limited by the quality of the original records, although our 173 confirmatory telephone interviews mitigated this significantly. However, the retrospective design precludes definitive causal inferences, and potential recall bias from these interviews must be acknowledged. Additionally, the sample size in certain ISCO-08 groups was small, which may have limited our ability to detect more subtle cytological differences between industrial sectors or to perform robust multivariable regression models. Given the limited number of participants within individual ISCO-08 major groups, formal multivariable regression modeling was not statistically appropriate and could have resulted in model overfitting. Future prospective studies are needed to further control for non-occupational confounders and validate these exploratory findings. Additionally, as a single-center study conducted in a specific regional population (Attica, Greece), the generalizability of these findings to other healthcare systems or industrial settings may be limited. Other potential confounders, including age-related inflammatory changes, comorbidities, and non-occupational

environmental exposures, were not systematically adjusted for due to the retrospective design.

## Conclusion

Occupational history is a critical but often missing piece of the diagnostic puzzle in respiratory medicine. Our study suggests that specific occupational groups—particularly those in agriculture and forestry—are associated with unique BAL cytological profiles characterized by high total cell counts and specific inflammatory markers. The current 80% underreporting rate highlights a significant clinical gap that may lead to the underdiagnosis of work-related lung

diseases. We recommend that a structured, ISCO-08 based occupational history become a mandatory component of the referral process for all patients undergoing bronchoalveolar lavage.

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