

Occupational Exposure to Formaldehyde and Xylene and Associated Respiratory and Haematological Health Outcomes among Laboratory Personnel: A Systematic Review

Baijnath Das^{1*}, Sushil Pal², Hemant Kumar³, Sharad Kumar⁴

¹College of Allied and Healthcare Sciences, Teerthanker Mahaveer University, Moradabad, U.P. India.

Email ID: baijnathadasbiochemaiims@gmail.com

²Charak Institute of Allied and Healthcare Studies Lucknow, Uttar Pradesh, India.

Email.ID: upsushilpal1999@gmail.com

³College of Allied and Healthcare Sciences, Teerthanker Mahaveer University, Moradabad, U.P. India.

Email ID : hemantkurmi53498@gmail.com

⁴School of Health and Paramedical Sciences, Vivek University, Bijnor, Uttar Pradesh, India.

Email.id sharadkumar6788@gmail.com

Correspondence Author:

Baijnath Das

College of Allied and Healthcare Sciences, Teerthanker Mahaveer University, Moradabad, U.P. India

Email: baijnathadasbiochemaiims@gmail.com

ABSTRACT

Background/Objective: Formaldehyde and xylene are routinely used in histopathology, but reports of chemical exposure do not always include clinical measurements. The evidence linking these agents with respiratory complaints and changes in blood counts among laboratory personnel requires careful interpretation. To examine freely available original studies published during 2020–2026 that assessed formaldehyde or xylene exposure and respiratory or haematological outcomes in laboratory workers.

Methodology: A PRISMA 2020-based search strategy was developed for PubMed, Scopus and Web of Science. Publicly accessible original papers were checked against prespecified population, exposure and outcome criteria. Complete subscription-database screening, duplicate reconciliation and independent assessment remain outstanding; this manuscript therefore presents an evidence-verified synthesis rather than a completed systematic search.

Results: Four relevant open-access investigations were verified. Two pathology-laboratory studies described respiratory complaints in relation to formaldehyde exposure. One investigation of university laboratory staff found selected blood-count differences among workers assigned formaldehyde exposure, while another study, including an anatomic-pathology subgroup, reported more irritation and allergic symptoms but no significant differences in pulmonary function or complete blood counts. The verified studies did not isolate the effects of xylene on either outcome.

Conclusions: Recent evidence is more consistent for irritant and upper-airway symptoms during formaldehyde exposure than for persistent impairment of lung function or haematological toxicity. Xylene-specific effects cannot be estimated from the verified outcome studies. A complete systematic search and documented appraisal are necessary before journal submission.

Keywords: Biological monitoring; Blood cell count; Cross-sectional studies; Environmental monitoring; Respiratory function tests; Volatile organic compounds

INTRODUCTION

Formaldehyde remains central to tissue fixation because it preserves cellular structure during specimen processing. Employees in surgical pathology, histopathology and anatomy departments may inhale formaldehyde vapour while receiving specimens, opening containers, trimming tissues and disposing of fixative. Xylene is used at later stages of tissue preparation, including clearing and slide handling. These are distinct exposures, but employees may encounter both within the same workday. A comparative investigation in Malaysia documented higher formaldehyde concentrations in histopathology rooms than in administrative offices and a greater frequency of several irritation-related complaints among exposed

staff.¹

The extent of exposure depends on how work is organised. In a study of four hospital pathology laboratories in Iran, formaldehyde was measured in the breathing zones of staff and respiratory complaints were assessed using a standard questionnaire. The findings drew attention to the exposure experienced by technicians and pathologists, although the cross-sectional design did not establish that formaldehyde caused the reported symptoms.² An investigation of health-care workers in Türkiye has also documented volatile organic compounds, including xylene, in pathology-related work areas, showing why the chemical environment should be considered rather than a single reagent in isolation.³

Interpretation of effects on blood cells is less straightforward. Chemical exposure varies between laboratories and different groups of workers; full blood count results are also influenced by age, illness, medication and other occupational factors. A large Italian occupational health investigation identified several differences in haematological indices among research-laboratory workers, including a subgroup assigned formaldehyde exposure.⁴ In contrast, a Taiwanese study of lower-level formaldehyde exposure found no meaningful group differences in routine blood counts or measured lung function, despite more irritation and allergic symptoms among exposed workers.⁵

The present review examines the extent to which recent, freely available original investigations address these two clinical domains in laboratory personnel. Respiratory symptoms, pulmonary function and haematological indices are considered separately; information derived from formaldehyde exposure is not treated as proof of an effect from xylene.

MATERIALS & METHODS

The review question and planned reporting approach were framed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.⁶ The intended publication window was 1 January 2020 to 3 October 2026, and the specified sources were PubMed/MEDLINE, Scopus and Web of Science; the reproducible search concept was (formaldehyde OR formalin OR xylene OR xylenes) AND (histopathology OR pathology OR anatomy OR laboratory OR laboratories OR laboratory personnel OR technician*) AND (respiratory OR cough OR wheeze OR spirometry OR pulmonary function OR haematolog* OR hematolog* OR complete blood count OR haemoglobin OR leukocyte* OR platelet*), restricted to English-language human original research with freely accessible full text.

The accessible verification underlying this draft used public PubMed records, PubMed Central and journal/publisher pages; comprehensive executions in subscription Scopus and Web of Science, complete deduplication and dual-reviewer screening have not been documented. Eligible outcome evidence required occupational exposure relevant to laboratory personnel and direct measurement or ascertainment of respiratory symptoms, pulmonary function, or routine haematological parameters; reviews, animal studies, conference abstracts, studies limited to environmental concentrations or genotoxicity alone, and investigations confined to non-laboratory workers were not counted as outcome evidence. Relevant study characteristics and numerical findings were transcribed from verified full-text articles and compared narratively, with attention to exposure ascertainment, comparison groups, confounding and outcome definition. No pooled effect was calculated because the samples, exposure classifications and outcome measures were not sufficiently comparable. A final PRISMA flow diagram, independent risk-of-bias assessment and registration identifier require the authors' completed search and screening record before submission.

RESULTS

Overview of the verified evidence

Four freely accessible original investigations directly addressed at least one specified outcome in a laboratory population or an identifiable pathology-laboratory subgroup: a Malaysian comparison of histopathology and administrative workers,¹ an Iranian survey of hospital pathology personnel,² an Italian occupational blood-count investigation involving research laboratories,⁴ and a Taiwanese occupational study that separately identified employees from an anatomic-pathology department.⁵ These are verified reports, not a documented final total of eligible studies from all three bibliographic databases. The studies differed materially in exposure measurement, use of a comparison group and clinical outcomes.

Table 1. Summary of outcome-relevant, accessible primary investigations verified for this draft. Numbers refer to study participants or subgroups as specified in the published articles; they should not be added across studies because the populations and exposures differ.

Study and population	Exposure and endpoints	Main reported results
Ramli et al., 2023 [1] Malaysia; 41 histopathology workers, 164 administrative staff	Area formaldehyde; symptom questionnaire	8-h mean: 0.113 versus 0.031 ppm; cough 24.4% versus 3.0%; sore/dry throat 39.0% versus 7.9%. No blood-count or spirometry assessment.
Foroughi et al., 2024 [2] Iran; 57 pathology-department personnel	Personal formaldehyde sampling; respiratory questionnaire	Reported prevalence: cough 58.39%, wheeze 52.38%, phlegm 70%, breathlessness 80%; no non-exposed comparison group. No blood counts.
La Torre et al., 2024 [4] Italy; 1,402 exposed laboratory workers and 3,121 donors; 47 classified as formaldehyde exposed	Assigned chemical-risk category; full blood count	In formaldehyde subgroup: monocytes 0.51 vs 0.37 $\times 10^3/\mu\text{l}$; haematocrit 40.82% vs 43.05%; haemoglobin and total WBC not significantly different.
Fan et al., 2025 [5] Taiwan; 242 exposed and 172 controls; 57 higher-exposure pathology staff	Air formaldehyde; symptoms, spirometry and full blood count	More allergic rhinitis/irritation; no significant between-group differences in routine blood counts or spirometry. High-exposure pathology subgroup differed in symptom frequency.

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Respiratory symptoms and measured lung function

In the Malaysian comparative study, average 8-hour formaldehyde concentrations were higher in the histopathology laboratory than in the administrative area (0.113 versus 0.031 parts per million). Cough was reported by 24.4 per cent of histopathology workers compared with 3.0 per cent of administrative staff; sore or dry throat occurred in 39.0 versus 7.9 per cent. The study also reported a higher frequency of eye irritation, rhinorrhoea and sneezing. These comparisons support an association between workplace assignment and irritation-related complaints, but the study cannot fully separate formaldehyde from other laboratory conditions.¹

The Iranian pathology-laboratory investigation used personal air sampling and a respiratory questionnaire in 57 employees. The authors reported cough in 58.39 per cent, wheezing in 52.38 per cent, phlegm in 70 per cent and shortness of breath in 80 per cent. These percentages describe symptoms in the examined sample; they should not be read as incident disease or as attributable risks. The absence of an independent unexposed group, reliance on self-report and restriction to selected departments limit causal interpretation.²

The Taiwanese study provides a useful contrast. Among 414 workers, 242 were classified as formaldehyde exposed, including 57 workers from anatomic pathology with higher exposure, and 172 were controls. Irritation-related complaints and history of allergic rhinitis were more frequent among exposed workers. The adjusted association for allergic rhinitis versus the unexposed group was reported as an odds ratio of 16.78 (95% confidence interval 4.00–70.55), with substantial uncertainty around its size. Nonetheless, comparisons of forced expiratory volume in one second, forced vital

capacity and their ratio did not show significant differences. Symptoms and objective lung-function impairment should therefore not be treated as interchangeable outcomes.⁵

Haematological parameters

The Italian investigation compared university laboratory workers assigned various chemical-risk categories with healthy blood donors. Of the laboratory workers, 47 were reported in the formaldehyde exposure subgroup. The published subgroup comparisons showed higher monocyte counts (0.51 versus 0.37 $\times 10^3/\mu\text{l}$), higher mean platelet volume (8.72 versus 7.85 femtolitres) and lower haematocrit (40.82 versus 43.05 per cent). Total white-cell count and haemoglobin did not differ significantly in that subgroup. Because exposure categories were assigned in a mixed chemical environment and blood donors served as controls, the study cannot establish isolated formaldehyde-induced blood toxicity.⁴

The Taiwanese study assessed routine complete blood counts, including haemoglobin, haematocrit, red-cell indices, leukocytes and platelets. It did not identify significant differences between exposed and unexposed workers or between its higher- and lower-exposure categories. These findings differ from the selected haematological associations reported in the Italian study and indicate that any effects on routinely measured blood indices remain uncertain in the occupational populations examined.⁵

Evidence relating specifically to xylene

Neither the verified respiratory-outcome studies nor the verified full-blood-count studies provided a comparison capable of estimating the independent effect of xylene. Xylene was measured in the pathology work environment in another open-access study of healthcare workers, but that investigation assessed genotoxicity and oxidative-stress indicators rather than the primary respiratory and routine blood-count outcomes considered here.³ It is therefore inappropriate to assign the respiratory or haematological findings above to xylene, or to infer that the available data demonstrate the absence of xylene toxicity.

Discussion

The recent, directly relevant occupational studies show a pattern of irritation and upper-airway complaints among workers handling formaldehyde-containing fixatives. The consistency is greatest for symptoms such as cough, sore throat, eye irritation and rhinitis. By contrast, the evidence for sustained impairment of pulmonary function is limited: symptoms were measured more often than spirometry, and the study with objective lung-function measurements did not find a significant between-group difference. An association with irritation does not necessarily imply chronic lung disease.^{1,2,5}

Findings for haematological outcomes were less consistent. The Italian study reported selected changes in monocytes, haematocrit and mean platelet volume in a formaldehyde-classified subgroup, whereas the Taiwanese investigation showed no significant change in routine haematology measures. The studies did not employ comparable exposure definitions, control groups or occupational settings. Particularly in the Italian study, a donor-based comparison and exposure to other chemical agents may have influenced observed differences. Neither

paper provides enough evidence to conclude that formaldehyde exposure at the investigated levels produced clinically important bone-marrow impairment.^{4,5}

The central limitation for assessing xylene is the difference between identifying exposure and measuring an outcome attributable to that exposure. Although formaldehyde and xylene can be handled by the same personnel, their sources, time patterns and physical properties are not identical. Monitoring studies of pathology units can establish where and when xylene vapour is encountered, but studies without respiratory measurements or blood-count data cannot answer the present clinical questions. The reported association with mixed volatile organic compound exposure in pathology workplaces should not be presented as a xylene-specific effect.³

Several features also constrain the overall interpretation. Most observations were cross-sectional, reducing the ability to establish temporal sequence; questionnaires may be affected by symptom recall; selection of workers with sufficient service, absence of illness, or participation in occupational medical examinations can alter estimates; and air sampling at one period may poorly represent earlier years of exposure. Moreover, the evidence-verification process for this manuscript did not provide a completed multi-database search log or independently verified risk-of-bias ratings. The available reports therefore support a cautious descriptive synthesis, not a pooled risk estimate or a definitive assessment of long-term effects.

For routine laboratory practice, findings support attention to specimen-handling procedures and exposure control. Local exhaust ventilation during grossing, appropriately covered fixative containers, inspection of clearing stations, prompt management of spills and task-specific instruction are sensible measures in workplaces where these chemicals are used. Future investigations would be more informative if they assessed formaldehyde and xylene separately, recorded personal exposure over time, used a well-defined comparison group, and measured standardised respiratory symptoms, pre- and post-shift spirometry and complete blood counts with appropriate adjustment for smoking, prior disease and co-exposures.

Conclusion

The verified open-access studies published during 2020–2026 report associations between formaldehyde exposure in laboratory settings and irritation-related respiratory complaints, while evidence of persistent lung-function impairment is limited. Findings for routine

haematological parameters are inconsistent, and the independent contribution of xylene to either outcome is not established by these reports. Better controlled and longitudinal studies are needed. Completion of the planned Scopus and Web of Science searches, duplicate reconciliation, independent screening, risk-of-bias appraisal and a traceable PRISMA flow diagram is required before this text can be submitted as a completed systematic review.

Declarations

Ethical approval: No new human participants, clinical samples or individual-level patient records were involved in preparing this literature synthesis.

Funding and competing interests: Not Applicable

Data availability: Numerical findings discussed in this manuscript were drawn from the cited publicly accessible reports

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