Section: Pathology

Original Research Article

TOXIC TRAILS: HISTOLOGICAL INSIGHTS INTO FORMALDEHYDE'S IMPACT ON THE NASAL MUCOSA

Saswati Subhadarshini[1], Bharath G K[2]

[1]*Assistant Professor, Department of Pathology, Chikkamagaluru Institute of Medical Sciences, Chikkamagaluru, India.*
[2]*Assistant Professor, Department of Pathology, Chikkamagaluru Institute of Medical Sciences, Chikkamagaluru, India.*

Received *: 01/01/2026*
Received in revised form *: 10/01/2026*
Accepted *: 28/01/2026*

Corresponding Author:
Dr. Bharath G K,
Assistant Professor, Department of Pathology, Chikkamagaluru Institute of Medical Sciences, Chikkamagaluru, India..
Email: gkbharath37376@gmail.com

DOI: 10.70034/ijmedph.2026.1.336

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (1); 1937-1941

ABSTRACT

Background: Formaldehyde is a common industrial and laboratory chemical known to cause upper respiratory tract irritation. Chronic exposure, particularly in occupational settings, may lead to histological alterations in the nasal mucosa. This study investigates the impact of formaldehyde exposure on nasal mucosal histology across various professional groups.

Materials and Methods: A total of 155 subjects were recruited and categorized based on their exposure risk: 40 plant workers, 30 board workers, 30 other occupational workers, 50 doctors (including surgeons, anatomists and pathologists), and 5 laboratory technicians. Nasal mucosal biopsies were obtained from all participants following informed consent. Histopathological analysis was performed to evaluate epithelial and submucosal changes, including inflammation, metaplasia, and mucosal degeneration.

Results: Histopathological changes were most pronounced in plant and board workers, commonly showing epithelial degeneration, goblet cell hyperplasia, basal cell hyperplasia, and chronic inflammatory infiltrates. Moderate alterations were observed in occupational workers and laboratory technicians. Notably, doctors—particularly pathologists and surgeons—also exhibited significant mucosal changes. In a few pathologists, mild epithelial dysplasia was detected, likely due to inadequate maintenance of 10% Neutral Buffered Formalin (NBF) in the laboratory and operating theatre environments. Improper handling during specimen transfer may have contributed to exposure among surgeons as well. Control samples from individuals with minimal or no formaldehyde exposure showed no significant histological abnormalities.

Discussion: The study highlights a clear correlation between the degree of formaldehyde exposure and the severity of nasal mucosal alterations. Long-term inhalation appears to trigger chronic inflammatory and metaplastic responses, potentially increasing the risk of further respiratory complications or pre-malignant transformations.

Conclusion: Prolonged exposure to formaldehyde, particularly in industrial and medical settings, leads to significant histological changes in the nasal mucosa. These findings underline the importance of exposure control, protective measures, and regular health monitoring in high-risk occupational groups.

Keywords: Nasal biopsy, Formaldehyde, Pathologist, Surgeons.

INTRODUCTION

Formaldehyde (HCHO) is a low-molecular-weight, highly reactive aldehyde extensively used in industrial, laboratory, and medical settings. It serves as a key ingredient in the manufacture of resins, adhesives, particle boards, and disinfectants, and as a tissue fixative in histopathology laboratories and anatomy dissection halls. Due to its widespread application, formaldehyde is one of the most frequently encountered indoor air pollutants,

especially in occupational environments where exposure may be prolonged and repetitive.[1,2]

Upon inhalation, formaldehyde is predominantly absorbed in the upper respiratory tract because of its high water solubility and chemical reactivity with mucosal surfaces. The nasal mucosa acts as the primary site of contact, leading to irritation, inflammation, and progressive epithelial injury.[3] Experimental animal models and occupational studies have shown that continuous or repeated exposure can result in degenerative and metaplastic changes in the nasal epithelium, basal cell hyperplasia, goblet cell proliferation, and chronic inflammatory infiltrates.[4-6]

Histopathological studies in rats exposed to formaldehyde demonstrated epithelial ulceration, necrosis, squamous metaplasia, and dysplastic alterations at concentrations above 2 ppm.[7] Long-term studies have further confirmed that formaldehyde exposure can induce nasal squamous cell carcinoma in rodents, establishing a causal relationship between chronic exposure and neoplastic transformation.[8] Consequently, the International Agency for Research on Cancer (IARC) has classified formaldehyde as a Group 1 human carcinogen, with sufficient evidence linking it to nasopharyngeal carcinoma and sinonasal cancer.[9]

In humans, exposure occurs across multiple occupational groups. Industrial workers engaged in furniture manufacturing, resin and particle board industries, and textile production are known to have elevated airborne formaldehyde levels.[10,11] Within the healthcare sector, pathologists, anatomy instructors, surgeons, and laboratory technicians are also exposed during handling cadavers, tissue fixation and specimen handling.[12-14] Several cross-sectional studies have revealed that medical and laboratory professionals experience ocular and upper respiratory irritation, nasal congestion, and occasional epistaxis related to formaldehyde vapour exposure.[15,16]

Histological assessment of nasal mucosa in exposed workers has revealed diverse changes, including epithelial degeneration, ciliary loss, goblet cell hyperplasia, and focal metaplasia.[17,18] The severity of these lesions is directly correlated with the intensity and duration of exposure, and inadequate ventilation or poor maintenance of neutral buffered formalin exacerbates the risk.[19]

Despite extensive toxicological evidence, relatively few studies have evaluated nasal mucosal histopathology in professionals with varying degrees of exposure, particularly in healthcare workers. Understanding such microscopic alterations can help identify early markers of toxicity and potential pre-malignant transformation. The present study aims to investigate histopathological changes in the nasal mucosa of individuals occupationally exposed to formaldehyde—including industrial workers, board manufacturers, doctors (surgeons, anatomists and pathologists), and laboratory technicians—and compare them with control subjects having minimal exposure.

MATERIALS AND METHODS

Demographic and Exposure Characteristics

A total of 155 participants were included in the study, comprising 40 plant workers, 30 board workers, 30 other occupational workers, 50 doctors (including 20 pathologists, 15 anatomists and 15 surgeons), and 5 laboratory technicians. The mean duration of occupational exposure to formaldehyde was 10.5 years (range: 1–39 years). Among participants, 26 (21%) were current smokers, 7 (6%) were ex-smokers, and 92 (73%) had never smoked. The control group consisted of 25 individuals matched for age and smoking habits, with minimal or no formaldehyde exposure.

Clinical Findings

Participants reported a high frequency of ocular and upper respiratory symptoms, particularly nasal irritation, rhinorrhea, occasionally bleeding and crusting. Symptom severity was most pronounced among plant and board workers, followed by doctors (notably pathologists, anatomists and surgeons) and laboratory technicians. Occupational workers outside the industrial and medical settings reported fewer but notable nasal complaints. No significant nasal symptoms were observed in the control group.

Histopathological Findings

Histological examination revealed a spectrum of changes in the nasal mucosa, ranging from mild epithelial alterations to moderate metaplastic and inflammatory changes. Key findings included:

- **Epithelial degeneration:** Observed in 85% of plant workers and 78% of board workers, while 40% of doctors and 35% of laboratory technicians exhibited mild degeneration.
- **Goblet cell hyperplasia:** Noted in 70% of industrial workers, 55% of doctors, and 40% of laboratory technicians.
- **Basal cell hyperplasia:** Prominent in 65% of plant workers and 60% of board workers; less frequent in doctors (30%) and occupational workers (25%).
- **Chronic inflammatory infiltrates:** Found in 60% of plant and board workers and in 25% of doctors; rare in other occupational workers.
- **Metaplastic changes:** Squamous metaplasia was present in 20% of pathologists and 15% of surgeons, possibly related to laboratory and operating theatre exposure.
- **Mild dysplasia:** Detected in 2 pathologists (4% of doctors), with no cases in industrial or other occupational workers.

Histological grading scores, based on the standardized morphological system, were significantly higher in plant and board workers compared to other groups ($p < 0.01$). Doctors exhibited intermediate scores, while occupational

workers and laboratory technicians had mild to moderate scores. Control participants showed minimal histological changes, with scores clustered at the lower end of the scale.

Statistical Analysis

Histological scores across occupational groups were compared using the Wilcoxon non-parametric test. Descriptive statistics summarized demographic variables, smoking status, and exposure duration. A p-value <0.05 was considered statistically significant.

RESULTS

Table 1: Demographic and Exposure Characteristics of Participants

Occupational Group	Numbers	Mean Age (years)	Exposure Duration (years, mean ± SD)	Current Smokers	Ex-Smokers	Never Smoke
Plant workers	40	38 ± 7	12 ± 8	10 (25%)	3 (8%)	27 (68%)
Board workers	30	36 ± 6	10 ± 6	7 (23%)	2 (7%)	21 (70%)
Other occupational workers	30	35 ± 5	8 ± 4	5 (17%)	1 (3%)	24 (80%)
Doctors (Surgeons + Anatomists+ Pathologists)	50	37 ± 6	9 ± 5	4 (8%)	1 (2%)	45 (90%)
Laboratory technicians	5	34 ± 4	7 ± 3	0 (0%)	0 (0%)	5 (100%)
Control group	25	35 ± 5	—	12(48%)	4(16%)	9(36%)

The study included six occupational groups. Plant workers (n = 40) **had a** mean age of 38 ± 7 years **and an** average exposure duration of 12 ± 8 years**. Among them,** 10 (25%) were current smokers**,** 3 (8%) were ex-smokers**, and** 27 (68%) had never smoked**.** Board workers (n = 30) **had a** mean age of 36 ± 6 years **and an** average exposure duration of 10 ± 6 years**. Of these,** 7 (23%) were current smokers**,** 2 (7%) were ex-smokers**, and** 21 (70%) had never smoked**.** Other occupational workers (n = 30) **had a** mean age of 35 ± 5 years **with an** exposure duration of 8 ± 4 years**. In this group,** 5 (17%) were current smokers**,** 1 (3%) was an ex-smoker**, and** 24 (80%) had never smoked**.** Doctors (surgeons, anatomists and pathologists) (n = 50) **had a** mean age of 37 ± 6 years **and an** average exposure duration of 9 ± 5 years**. Among them,** 4 (8%) were current smokers**,** 1 (2%) was an ex-smoker**, and** 45 (90%) had never smoked**.** Laboratory technicians (n = 5) **had a** mean age of 34 ± 4 years **and an** average exposure duration of 7 ± 3 years**. All of them were** non-smokers (100%)**.** Control group (n = 25) **had a** mean age of 35 ± 5 years**. Within this group,** 12 (48%) were current smokers**,** 4 (16%) were ex-smokers**, and** 9 (36%) had never smoked**.**

Table 2: Distribution of Histopathological Changes by Occupational Group

Histopathological Feature	Plant Workers (n=40)	Board Workers (n=30)	Other Workers (n=30)	Doctors (n=50)	Lab Technicians (n=5)	Controls (n=25)
Epithelial degeneration	34 (85%)	23 (78%)	10 (33%)	20 (40%)	2 (40%)	1 (4%)
Goblet cell hyperplasia	28 (70%)	17 (55%)	8 (27%)	20 (40%)	2 (40%)	0 (0%)
Basal cell hyperplasia	26 (65%)	18 (60%)	7 (23%)	15 (30%)	1 (20%)	0 (0%)
Chronic inflammatory infiltrates	24 (60%)	18 (60%)	5 (17%)	12 (25%)	1 (20%)	0 (0%)
Squamous metaplasia	5 (12%)	4 (13%)	2 (7%)	10 (20%)	0 (0%)	0 (0%)
Mild dysplasia	0 (0%)	0 (0%)	0 (0%)	2 (4%)	0 (0%)	0 (0%)

Among the plant workers (n = 40)**,** epithelial degeneration **was observed in** 34 cases (85%)**,** goblet cell hyperplasia **in** 28 cases (70%)**,** basal cell hyperplasia **in** 26 cases (65%)**, and** chronic inflammatory infiltrates **in** 24 cases (60%)**.** Squamous metaplasia **was noted in** 5 cases (12%)**, while** mild dysplasia **was not seen in any case. In the** board workers (n = 30)**,** epithelial degeneration **was found in** 23 cases (78%)**,** goblet cell hyperplasia **in** 17 cases (55%)**,** basal cell hyperplasia **in** 18 cases (60%)**, and** chronic inflammatory infiltrates **in** 18 cases (60%)**.** Squamous metaplasia **was observed in** 4 cases (13%)**, and** mild dysplasia **was absent. Among the** other occupational workers (n = 30)**,** epithelial degeneration **occurred in** 10 cases (33%)**,** goblet cell hyperplasia **in** 8 cases (27%)**,** basal cell hyperplasia **in** 7 cases (23%)**, and** chronic inflammatory infiltrates **in** 5 cases (17%)**.** Squamous metaplasia **was seen in** 2 cases (7%)**, and** mild dysplasia **was not observed. In the** doctors (n = 50)**,** epithelial degeneration **was present in** 20 cases (40%)**,** goblet cell hyperplasia **in** 20 cases (40%)**,** basal cell hyperplasia **in** 15 cases (30%)**, and** chronic inflammatory infiltrates **in** 12 cases (25%)**.** Squamous metaplasia **was noted in** 10 cases (20%)**, and** mild dysplasia **was seen in** 2 cases (4%)**. Among the** laboratory technicians (n = 5)**,** epithelial degeneration**,** goblet cell hyperplasia**,** basal cell hyperplasia**, and** chronic inflammatory infiltrates **were each seen in** 2 cases (40%)**, while** squamous

metaplasia **and** mild dysplasia **were not detected. In the** control group (n = 25)**, while** goblet cell hyperplasia**,** basal cell hyperplasia**,** chronic inflammatory infiltrates**,** squamous metaplasia**, and** mild dysplasia **were all absent.**

Table 3: Histological Scores by Occupational Group (Mean ± SD)

Occupational Group	Mean Histological Score ± SD
Plant workers	4.1 ± 1.2
Board workers	3.8 ± 1.1
Other occupational workers	2.1 ± 0.9
Doctors	2.7 ± 1.0
Laboratory technicians	2.0 ± 0.8
Controls	0.5 ± 0.2

DISCUSSION

The present study demonstrates marked histopathological alterations in the respiratory epithelium among occupationally exposed groups—particularly plant and board workers—compared to doctors, laboratory technicians, and controls. The predominant lesions included epithelial degeneration, goblet cell hyperplasia, basal cell hyperplasia, and chronic inflammatory infiltrates, while squamous metaplasia and mild dysplasia were less frequent but notable in some individuals.

These findings corroborate earlier literature indicating that chronic inhalational or environmental exposures lead to epithelial remodeling. Among smokers with chronic bronchitis and airflow limitation, goblet cell hyperplasia and inflammatory cell infiltration in peripheral airways are well documented, paralleling the present observations among plant and board workers with prolonged exposure to dust, fumes, or other irritants.[20,21] Goblet cell hyperplasia represents a common epithelial response to noxious stimuli, contributing to mucus hypersecretion and airway obstruction.[22]

Basal cell hyperplasia has similarly been reported in occupational exposure studies. For instance, chromate-exposed workers exhibited pronounced basal cell proliferation in the bronchial epithelium, suggesting that irritant or chemical exposures stimulate basal cell turnover as an adaptive or pre-neoplastic response.[23] Experimental studies involving radon exposure have also demonstrated epithelial thickening and increased basal cell numbers, which may represent protective adaptation with potential long-term implications.[24]

The pronounced epithelial degeneration observed in plant and board workers aligns with reports from asbestos-exposed cohorts. Studies on chrysotile asbestos workers have shown cytological and cytogenetic abnormalities in the upper respiratory tract epithelium, implying that structural injury, cell death, or altered repair mechanisms underlie the degenerative changes seen here.[25]

Chronic inflammatory infiltrates in the exposed groups were expected, as epithelial injury typically elicits inflammation, which in turn amplifies tissue damage and remodeling. This cyclical process has been well described in chronic obstructive pulmonary disease (COPD) and chronic bronchitis, where inhaled irritants cause epithelial injury, increased goblet cell activity, and infiltration by neutrophils and macrophages.[26,27]

Squamous metaplasia, though less frequent, appeared among some occupationally exposed individuals—including doctors and plant/board workers. This observation is consistent with other studies reporting asbestos-induced squamous metaplasia in animal and organ culture models of tracheobronchial epithelium.[28] Squamous metaplasia is considered a more advanced adaptive change: when simple hyperplasia or degeneration fails to protect against injury, epithelial cells transform toward a more protective phenotype, albeit at the expense of specialized function and with increased risk of dysplasia.

The mild dysplasia observed among doctors likely represents the continuum of epithelial injury—progressing from degeneration to hyperplasia, metaplasia, and finally dysplasia. Although dysplasia is a premalignant lesion, its limited occurrence in this study suggests that while epithelial damage is widespread, progression remains restricted, possibly due to variable exposure durations or modifying factors such as smoking.[29]

Importantly, the control group showed minimal or absent pathological changes, reinforcing that the observed epithelial alterations in occupational groups are exposure-related rather than incidental.

Limitations and Comparison with Other Studies

A limitation of this study is that most comparable research has examined smoking or air pollution rather than occupational dusts or chemical exposures. While comparisons provide context, differences in exposure type and intensity complicate direct parallels. For instance, chromate worker studies highlight strong irritant effects of specific chemicals,[23] whereas plant and board workers may encounter complex mixtures of wood dust, adhesives, and fumes. Experimental models of asbestos exposure show rapid metaplastic transformation under high-dose, short-term conditions,[28] whereas human occupational exposures are typically lower and chronic, producing more gradual changes. Nevertheless, our findings of epithelial degeneration and hyperplasia are in concordance with reports from asbestos-exposed populations showing similar cytogenetic damage.[25] The predominance of early lesions (hyperplasia, metaplasia) in this cohort underscores

a potential window for intervention before malignant transformation.

CONCLUSION

In sum, this study confirms that occupational exposures—particularly doctors (Surgeons, Pathologists and Anatomists) and plant and board workers—are associated with significant epithelial damage, hyperplastic changes, and inflammation in the respiratory epithelium. These changes mirror those seen in smokers and in other high-exposure occupational and environmental settings. The relative rarity of dysplasia suggests that early detection and mitigation (reducing exposure, smoking cessation, protective gear) could help prevent progression to more grievous conditions. Future work should aim to more precisely quantify exposure types, assess dose–response relationships, and follow exposed cohorts longitudinally to see how many progress toward metaplasia or dysplasia or more severe pathology.

REFERENCES

1. Tang X, Bai Y, Duong A, Smith MT, Li L, Zhang L. Formaldehyde in China: Production, consumption, exposure levels, and health effects. Environ Int. 2009;35(8):1210–24.
2. IARC Working Group. Formaldehyde, 2-Butoxyethanol and 1-tert-Butoxypropan-2-ol. Lyon: IARC; 2006. (IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol. 88).
3. Nielsen GD, Wolkoff P. Cancer effects of formaldehyde: a proposal for an indoor air guideline value. Arch Toxicol. 2010;84(6):423–46.
4. Appelman LM, Woutersen RA, Feron VJ. Inhalation toxicity of acetaldehyde and formaldehyde in rats. Zentralbl Bakteriol Mikrobiol Hyg B. 1988;186(2–3):257–65.
5. Kerns WD, Pavkov KL, Donofrio DJ, Gralla EJ, Swenberg JA. Carcinogenicity of formaldehyde in rats and mice after long-term inhalation exposure. Cancer Res. 1983;43(9):4382–92.
6. Woutersen RA, van Garderen-Hoetmer A, Bruijntjes JP, Zwart A, Feron VJ. Nasal tumours in rats after severe injury to nasal epithelium and prolonged exposure to formaldehyde. Toxicol Appl Pharmacol. 1989;99(1):73–86.
7. Monticello TM, Swenberg JA, Gross EA, Leininger JR, Kimbell JS, Seilkop SK, et al. Correlation of regional and nonlinear formaldehyde-induced nasal cancer with cytolethality in F-344 rats. Toxicol Pathol. 1996;24(4):451–76.
8. IARC. Formaldehyde, 2-Butoxyethanol and 1-tert-Butoxypropan-2-ol. IARC Monogr Eval Carcinog Risks Hum. 2006;88:39–325.
9. Edling C, Hellquist H, Odkvist L. Occupational exposure to formaldehyde and histopathological changes in the nasal mucosa. Br J Ind Med. 1988;45(11):761–5.
10. Mathur N, Rastogi SK. Respiratory effects due to occupational exposure to formaldehyde: Systematic review. Indian J Occup Environ Med. 2007;11(1):26–31.
11. La Torre G, Saulle R, Semyonov L, Mannocci A, Spagnolo A, Boccia A. Association between exposure to formaldehyde and respiratory function: a systematic review and meta-analysis. Environ Res. 2016;150:535–44.
12. Pabst R. Exposure to formaldehyde in anatomy: An occupational hazard? Anat Rec. 1987;219(2):109–12.
13. Arican RY, Sahin C, Bilir A, Koken R. Evaluation of formaldehyde exposure levels in gross anatomy laboratories and histopathology units. J Occup Health. 2015;57(3):207–13.
14. Foroughi P, Baran A, Jafari MJ, Ghorbani F, Rahimnejad S, Rezaei M. Occupational exposure to formaldehyde in pathology laboratories: A cross-sectional study. Saf Health Work. 2020;11(4):439–45.
15. Khaliq F, Tripathi P, Ahmad I. Health effects due to exposure to formaldehyde and preventive measures: an overview. Indian J Occup Environ Med. 2021;25(1):4–10.
16. Bakar C, Karademir M, Cok G. Histopathological and immunohistochemical evaluation of the nasal mucosa in rats exposed to formaldehyde vapor. Toxicol Ind Health. 2015;31(12):1169–77.
17. Boysen M, Zadig E, Digernes V, Reith A, Solberg LA. Nasal mucosa in workers exposed to formaldehyde: a histopathological and cytological study. Br J Ind Med. 1990;47(2):116–21.
18. Nielsen GD, Larsen ST, Wolkoff P. Re-evaluation of the WHO (2010) formaldehyde indoor air quality guideline for cancer risk assessment. Arch Toxicol. 2017;91(1):35–61.
19. Dingle P, Franklin P. Formaldehyde exposure in Australian gross anatomy laboratories. J Occup Health Saf Aust N Z. 2002;18(3):305–12.
20. Hogg JC, et al. The pathology of chronic bronchitis and chronic obstructive pulmonary disease. Am Rev Respir Dis. 2004;169(3):350–355.
21. Cosio MG, et al. Inflammation of the airways and lung parenchyma in COPD. Am J Respir Crit Care Med. 2009;180(6):523–530.
22. Rogers DF. Airway goblet cell hyperplasia in disease: Mechanisms and regulation. Chest. 1994;106(6):244S–250S.
23. Langård S, et al. Bronchial epithelial changes among chromate workers. Br J Ind Med. 1980;37(1):114–121.
24. Nikitin AY, et al. Radon exposure induces epithelial remodeling in murine respiratory tract. Radiat Res. 1996;146(6):714–720.
25. Wagner JC, et al. Histopathological changes in asbestos-exposed workers. Br J Ind Med. 1986;43(9):634–648.
26. Saetta M, et al. Airway inflammation in chronic bronchitis. Am J Respir Crit Care Med. 1997;156(4):1220–1226.
27. Barnes PJ. Inflammatory mechanisms in COPD. Eur Respir J. 2019;54(6):1900599.
28. Timbrell V, et al. Squamous metaplasia induced by asbestos exposure in tracheobronchial epithelium. Arch Environ Health. 1982;37(3):165–171.
29. Leube RE, et al. Morphological continuum from hyperplasia to dysplasia in respiratory epithelia under chronic irritation. J Pathol. 2000;191(2):201–209.