

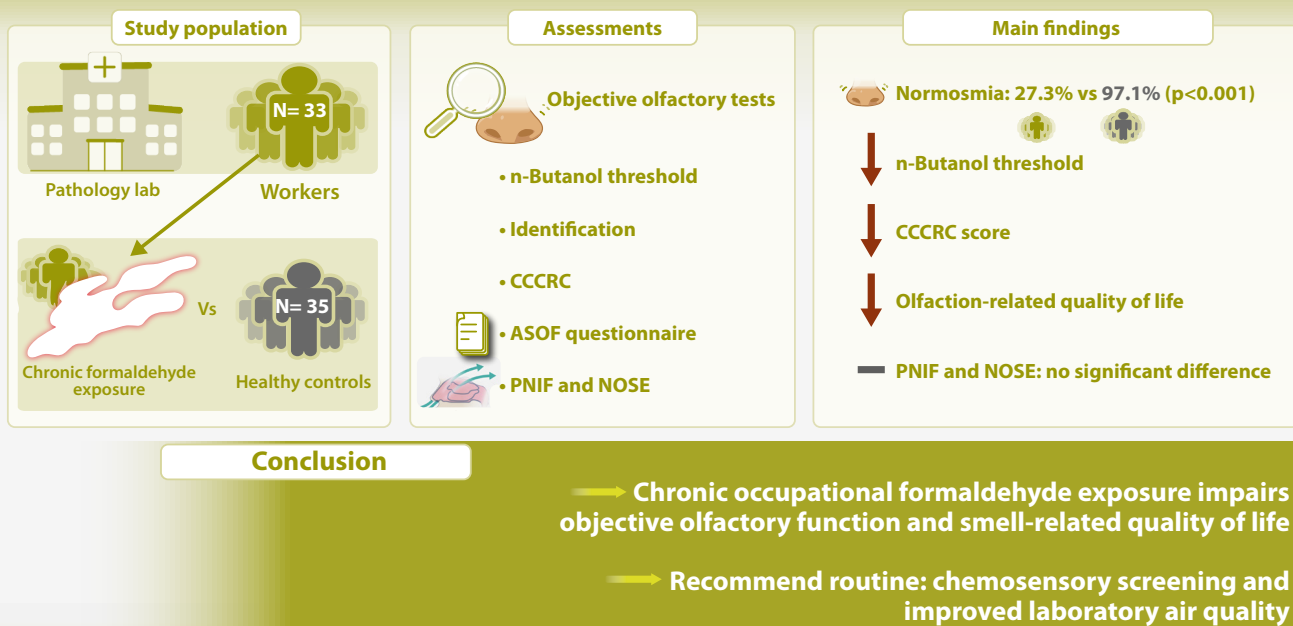
Impact of occupational formaldehyde exposure on objective olfactory thresholds and olfaction-related quality of life

Melih Alpay¹, Fuat Bulut¹, Betül Ağırgöl¹, Hande Özgen², Ahmet Emre Kaymaz¹,
Hakkı Caner İnan¹

Rhinology 64: 6, 0 - 0, 2026

<https://doi.org/10.4193/Rhin26.076>

Impact of occupational formaldehyde exposure on objective olfactory thresholds and olfaction-related quality of life



Alpay M, Bulut F, Ağırgöl B, et al. Rhinology 2026. <https://doi.org/10.4193/Rhin26.076>



RHINOLOGY
Official journal of the European and International Societies

Abstract

Background: Formaldehyde (FA) is essential for tissue fixation, but its chronic effects on the olfactory system are concerning. This study investigated the impact of occupational FA exposure on objective olfactory function, nasal patency, and smell-related quality of life in pathology laboratory workers. **Methods:** This cross-sectional case-control study included 68 participants (33 pathology workers, 35 controls). Assessments included otorhinolaryngological examination, Peak Nasal Inspiratory Flow (PNIF), and the Nasal Obstruction Symptom Evaluation (NOSE) scale. Objective olfactory function was evaluated using n-butanol threshold, identification tests, and the Connecticut Chemosensory Clinical Research Center (CCCRC) battery. Quality of life was measured using the Associated Factors in Olfaction-Related Quality of Life (ASOF) questionnaire. **Results:** Only 27.3% of pathology workers were normosmic, compared to 97.1% of controls. Total occupational FA exposure duration (months) correlated negatively with n-butanol thresholds and CCCRC scores, but not with identification. Weekly FA exposure correlated inversely with Olfaction-Related Quality of Life (ORQ) and positively with Subjective Olfactory Capability (SOC). No significant intergroup differences were found in NOSE or PNIF values. **Conclusion:** Occupational FA exposure significantly impairs objective olfactory thresholds and adversely affects smell-related quality of life. The discrepancy between objective loss and subjective capability highlights the need for regular chemosensory screening and improved air quality standards in laboratories.

Key words: CCCRC, formaldehyde, occupational exposure, olfactory function, quality of life

Introduction

Olfaction begins with the inhalation of volatile airborne molecules and their subsequent interaction with the olfactory epithelium. This complex sense is characterized by various distinct abilities, including odour detection threshold, identification, discrimination, and olfactory memory ⁽¹⁾. The development of olfaction starts in utero, with the fetus beginning to react to olfactory stimuli by the 30th week of life ⁽²⁾. Structurally, the olfactory mucosa serves as a unique neuroimmune interface ⁽³⁾. Beyond its physiological role, odour perception is fundamental to maintaining quality of life; it enables the identification of environmental hazards—such as fire, gas leaks, and volatile chemical risks—while profoundly influencing nutrition, emotional states, memory, and sexuality ^(4,5). Furthermore, recent evidence suggests that olfactory function is even associated with auditory and vestibular performance ⁽⁶⁾.

Formaldehyde (FA, CH₂O) is a colorless, highly reactive, and flammable gas with a pungent, irritating odour ⁽⁷⁾. Due to its high tissue penetration capacity and cost-effectiveness, it remains the most commonly used preservative and chemical fixative in pathology practices ⁽⁸⁾. However, its high reactivity makes it a significant source of occupational health issues among health-care personnel ⁽⁹⁾. Acute FA exposure is associated with irritation of the eyes and the upper/lower respiratory tracts, alongside nausea, headache, contact dermatitis, and neurotoxicity ⁽¹⁰⁾. It is estimated that occupational exposure to toxic agents accounts for approximately 1% to 5% of all olfactory disorders ⁽¹¹⁾. Pathology laboratory workers are at particularly high risk due to the chemical hazards inherent in their working environment ⁽¹²⁾. A previous study highlighted the severity of this risk, reporting that increasing occupational FA exposure from 3 to 8 hours per day elevates the lifetime cancer risk by approximately 2.6 times ⁽⁸⁾. Furthermore, FA inhalation has been shown to cause significant damage to the nasal epithelium, impairing neurotransmission and leading to olfactory dysfunction ⁽¹³⁾. While low-level FA exposure may interfere with olfactory perception, chronic inhalation exposure has been shown to induce morphological changes in the olfactory bulb in rats exposed experimentally to FA released from cotton soaked with 10% formaldehyde for up to 2 months (8 h/day, 6 days/week) ⁽¹⁴⁾. Despite these known risks, a comprehensive literature review reveals a lack of studies objectively demonstrating the impact of FA exposure in pathology laboratory settings on both olfactory function and odour-related quality of life. Therefore, the aim of this study was to investigate the impact of occupational FA exposure on objective olfactory function and odour-specific quality of life. Our findings demonstrate that chronic exposure significantly impairs odour thresholds, confirming the deleterious effects of FA on the human olfactory system.

Materials and methods

Study design

This cross-sectional case-control study was conducted at Bursa Specialised Teaching Hospital between December 12, 2023, and January 31, 2024. The study protocol was approved by the local Ethics Committee (Decision No: 2011-KAEK-25 2023/12-05) and performed in accordance with the principles of the Declaration of Helsinki.

A total of 68 health professionals were enrolled, consisting of 33 pathology laboratory workers (study group) and 35 participants from other hospital personnel with no known FA exposure (control group). The groups were matched for age, gender, educational level, chronic diseases, and tobacco/alcohol consumption. Inclusion required a minimum of one year of employment in the respective department. Exclusion criteria were defined as: history of head trauma, intracranial mass lesions, post-infectious or post-traumatic olfactory loss, and neurodegenerative diseases (Parkinson's, Alzheimer's, or epilepsy).

The pathology laboratory was equipped with local ventilation systems and fume cupboards routinely used during specimen handling and FA-related procedures. Standard pathology biosafety protocols were applied throughout laboratory work. In addition, personnel routinely used personal protective equipment (PPE), including masks, during laboratory procedures. Nevertheless, low-level exposure may still occur in routine practice despite these precautions because of the continuous use of FA in histopathological workflows.

Clinical and occupational assessment

Demographic data, duration of occupational exposure (months), weekly and daily working hours in FA-exposed areas, and "future health concern" levels—measured via a 0–10 Visual Analog Scale (VAS)—were recorded. Exposure assessment was performed using a structured occupational questionnaire administered via face-to-face interviews. Participants reported total duration of employment in pathology laboratories (years/months), average daily hours spent in FA-containing areas, and number of working days per week in such environments. These self-reported data were used to derive proxy measures of exposure duration and intensity. All information was recorded by trained interviewers using a standardized form. Future health concern levels were assessed using a 10-cm visual analogue scale (VAS). Participants were asked to indicate their level of concern regarding potential future health effects related to FA exposure on a horizontal line anchored by "no concern at all" and "extreme concern." The distance from the left anchor point was measured and recorded as the VAS score. This item was designed to capture subjective anticipatory health-related concern associated with occupational exposure.

A comprehensive otorhinolaryngological examination was performed by three ear, nose, and throat (ENT) specialists to exclude

Table 1. Demographic and Clinical Characteristics of the Study and Control groups.

Variable	Pathology workers (n=33)	Control group (n=35)	p-value*
Age (years) , mean $\pm$ SD	37.5 $\pm$ 9.9	37.5 $\pm$ 8.8	0.990
Sex , % (n)			0.959
Male	39.4 (13)	40.0 (14)	
Female	60.6 (20)	60.0 (21)	
Educational level , % (n)			0.233
Associate degree or below	51.5 (17)	37.1 (13)	
High school and above	48.5 (16)	62.9 (22)	
Chronic diseases* , % (n)			0.707
Present	27.3 (9)	31.4 (11)	
Absent	72.7 (24)	68.6 (24)	
Smoking status , % (n)			0.532
Current smoker	27.3 (9)	34.3 (12)	
Former smoker / never smoker	72.7 (24)	65.7 (23)	
Alcohol consumption , % (n)			0.364
Current use	24.2 (8)	34.3 (12)	
Former use / never use	75.8 (25)	65.7 (23)	

*The most frequent chronic conditions were hypertension, diabetes mellitus, and chronic hepatitis B.

confounding factors such as nasal polyps, masses, significant septal deviation, or choanal hypertrophy.

Objective nasal and olfactory evaluation

Peak Nasal Inspiratory Flow (PNIF): Objective nasal patency was assessed using a PNIF meter. Following a forceful expiration, participants were instructed to inhale as rapidly and deeply as possible through the nose with the mouth closed. The highest value of three satisfactory measurements was recorded in L/min (15,16).

Connecticut Chemosensory Clinical Research Center (CCCRC) Test: Olfactory function was quantitatively evaluated using the CCCRC battery, which comprises two components:

1. N-Butanol Threshold Test: Utilizing a 1/3 serial dilution series (9 vials, ranging from 4% to deionized water), the lowest concentration perceivable by the participant was determined. Scores ranged from 0 to 9.
2. Odour Identification Test: Participants were asked to identify seven distinct odourants (e.g. cocoa, coffee, cinnamon, baby powder, peanut butter, soap, mothballs) with closed eyes.

The final CCCRC score was calculated as the arithmetic mean of the threshold (capped at 7) and identification scores. Olfactory function was categorized as: Anosmia (0–1.75), severe hyposmia (2–3.75), moderate hyposmia (4–4.75), mild hyposmia (5–5.75), and normosmia (6–7) ^(17,18).

All olfactory examinations were performed by three independent ENT specialists who were blinded to group allocation. All investigators were trained and calibrated on the CCCRC testing

protocol prior to the study to ensure methodological consistency and minimize inter-observer variability.

Subjective questionnaires

Nasal Obstruction Symptom Evaluation (NOSE): Nasal congestion and its impact on exercise and sleep over the past month were evaluated using the validated Turkish version of the NOSE scale (0–100 points) ⁽¹⁹⁾.

Assessment of Self-reported Olfactory Functioning (ASOF): Olfaction-related quality of life was measured using the ASOF questionnaire, which includes three subscales: Subjective Olfactory Capability (SOC, 0–10 Likert scale), Smell-Related Problems (SRP), and Olfaction-Related Quality of Life (ORQ) ^(20,21).

Statistical analysis

Data were analysed using IBM SPSS Statistics v.25.0. Data distribution was assessed using the Kolmogorov-Smirnov test. Quantitative variables were expressed as mean $\pm$ standard error (S.E.), median, and range. Intergroup comparisons were performed using the Chi-square test for categorical variables, and Student's t-test or Mann-Whitney U test for continuous variables, as appropriate. Correlations between FA exposure duration and olfactory parameters were calculated using Spearman's rank correlation coefficient (rs). To control for potential confounding variables, a multivariable linear regression analysis was performed within the FA-exposed group. The CCCRC score was entered as the dependent variable, while total duration of FA exposure (months), age, sex, and smoking status were included as independent vari-

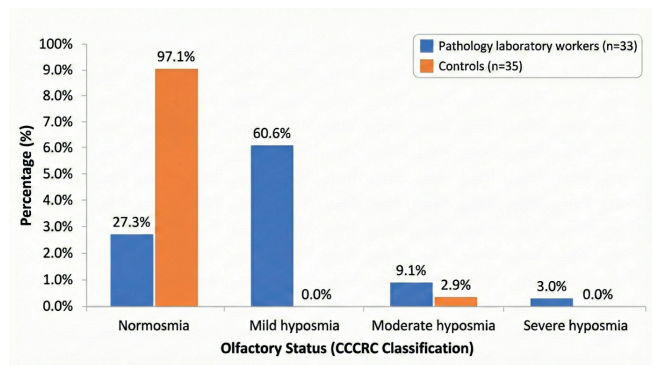


Figure 1. Comparison of olfactory function categories between pathology laboratory workers (n=33) and the control group (n=35). The prevalence of normosmia was markedly lower in the formaldehyde-exposed group (27.3%) compared to controls (97.1%), while mild hyposmia was the most common deficit observed in pathology workers (60.6%). Categories were determined based on the Connecticut Chemosensory Clinical Research Center (CCCCRC) composite scores. Statistical significance between the groups was high ($p < 0.001$).

ables. All variables were entered simultaneously using the enter method. Model assumptions, including linearity, normality of residuals, and homoscedasticity, were assessed prior to analysis. A p-value of <0.05 was considered statistically significant.

Results

Demographic and occupational characteristics

The demographic analysis revealed no significant differences between the pathology laboratory workers and the control group regarding age, sex, educational level, presence of chronic diseases, smoking status, or alcohol consumption ($p > 0.05$) (Table 1). The mean working life was 10.90 ± 1.5 years for the study group and 14.20 ± 1.4 years for the control group; this difference was not statistically significant ($p = 0.11$), confirming that the cohorts were well-matched in terms of professional experience. Analysis of FA exposure profiles in the study group indicated a high occupational burden, with 51.5% (n=17) of workers being exposed to FA throughout their entire weekly working schedule. Notably, the level of concern regarding potential future health risks due to FA exposure was high, with a median VAS score of 8 out of 10 (Table 2).

Olfactory and nasal patency

Objective olfactory assessment revealed that pathology laboratory workers had significantly lower scores in the n-butanol odour threshold test, odour identification test, and the resultant composite CCCRC score compared to the control group ($p < 0.05$).

Regarding nasal patency, no significant differences were observed between the groups in terms of nasal obstruction and airflow, as assessed by NOSE scores and PNIF measurements

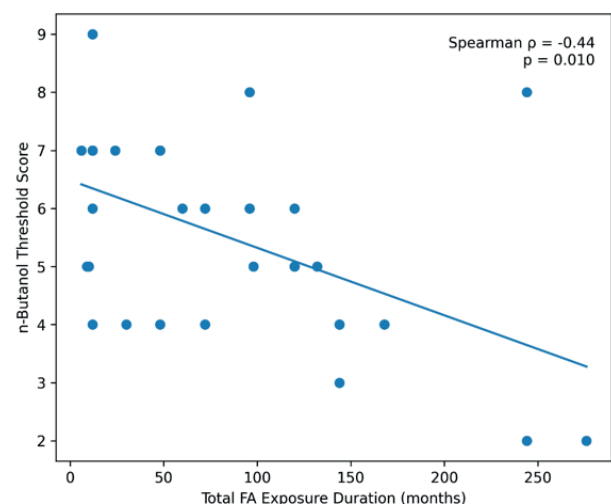


Figure 2. Scatter plot demonstrating the relationship between total formaldehyde exposure duration (months) and n-butanol threshold scores among pathology laboratory workers.

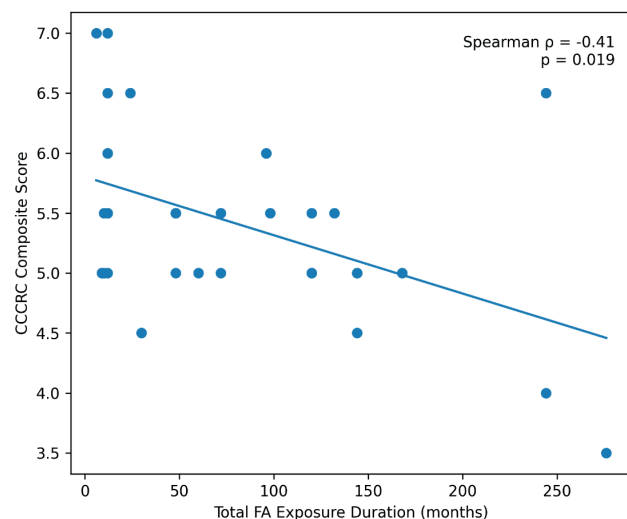


Figure 3. Scatter plot demonstrating the relationship between total formaldehyde exposure duration (months) and CCCRC composite scores among pathology laboratory workers.

($p > 0.05$). This suggests that the observed olfactory deficits in FA-exposed workers are likely neurosensory in origin rather than a result of mechanical nasal airway obstruction. Subjective evaluation via the ASOF questionnaire demonstrated that the intergroup difference reached statistical significance specifically within the SRP subscale (Table 3), while other subjective subscales did not show significant variation.

Olfactory function classification

The most striking finding was observed in the categorical classification of olfactory function based on CCCRC scores. While 97.1% (n=34) of the participants in the control group were classified

Table 2. Occupational formaldehyde (FA) exposure profiles and health concerns of pathology workers (n=33).

Variable	Mean $\pm$ SD	Median (IQR)	Range (Min–Max)
Total FA Exposure (months)	82.9 $\pm$ 76.9	66.0 (24.0 – 120.0)	6.0 – 276.0
Weekly FA Exposure (hours)	28.6 $\pm$ 16.1	40.0 (15.0 – 40.0)	1.0 – 60.0
Future Health Concern (VAS)*	7.1 $\pm$ 3.4	8.0 (5.0 – 10.0)	0.0 – 10.0

Abbreviations: FA, Formaldehyde; SD, Standard Deviation; IQR, Interquartile Range; VAS, Visual Analog Scale. *Measured on a 0–10 scale.

Table 3. Assessment of Self-reported Olfactory Functioning (ASOF) subscale scores, n-Butanol odour threshold test, identification test and CCCRC scores in pathology laboratory workers vs. controls.

Variable	Pathology Workers (n=33)	Control Group (n=35)	p-value*
Subjective Scores (ASOF)			
SOC (Self-reported Capability)	7.9 $\pm$ 0.4 (8.0)	8.4 $\pm$ 0.4 (9.0)	0.476
SRP (Smell-Related Problems)	4.0 $\pm$ 0.2 (4.2)	4.4 $\pm$ 0.1 (4.8)	0.014
ORQ (Quality of Life)	4.2 $\pm$ 0.2 (4.5)	4.2 $\pm$ 0.2 (5.0)	0.169
Objective Tests (CCCR)			
n-Butanol Threshold	5.5 $\pm$ 0.3 (5.0)	6.9 $\pm$ 0.2 (7.0)	< 0.001
Odour Identification	5.5 $\pm$ 0.1 (6.0)	6.5 $\pm$ 0.1 (7.0)	< 0.001
CCCR Composite Score	5.4 $\pm$ 0.1 (5.5)	6.6 $\pm$ 0.1 (6.5)	< 0.001

*The Mann Whitney U test was used

as normosmic, this rate plummeted to only 27.3% (n=9) among pathology laboratory workers. The difference between the two groups was highly significant ($p < 0.001$), indicating a substantial prevalence of olfactory dysfunction in the FA-exposed group (Figure 1 and Figure S1).

Correlation analysis

Spearman's correlation analysis demonstrated a significant relationship between FA exposure metrics and olfactory performance. Total duration of occupational FA exposure (months) showed an inverse, moderate correlation with n-butanol odour threshold scores ($\rho = -0.44$, $p = 0.010$) and composite CCCRC scores ($\rho = -0.41$, $p = 0.019$) (Figure 2 and Figure 3). Notably, no significant correlation was observed between total exposure duration and odour identification scores ($\rho = -0.15$, $p = 0.228$). Regarding short-term exposure, the total FA exposure duration (hours) during the previous week was positively correlated with Subjective Olfactory Capability (SOC) scores ($\rho = 0.38$, $p = 0.03$), while exhibiting a significant negative correlation with Olfaction-Related Quality of Life (ORQ) scores ($\rho = -0.43$, $p = 0.012$).

Multivariable regression analysis

In multivariable linear regression analysis performed within the exposed group, total duration of FA exposure (months) was not significantly associated with CCCRC scores after adjustment for age, sex, and smoking status ($\beta = -0.31$, $p = 0.155$). Although the direction of the association remained negative, consistent with the correlation analysis, it did not reach statistical signifi-

cance after adjustment. None of the covariates, including age ($p = 0.297$), sex ($p = 0.304$), or smoking status ($p = 0.969$), were significantly associated with CCCRC scores. Detailed regression coefficients are presented in Table S1.

Discussion

Pathology laboratory workers occupationally exposed to FA demonstrated significantly worse psychophysical olfactory performance than matched controls, with lower n-butanol odour threshold, odour identification, and composite CCCRC scores. Our most striking finding was that while nearly all controls were normosmic, only 27.3% of pathology workers maintained normal olfactory function, despite no significant differences in nasal patency as measured by PNIF and NOSE scores⁽¹⁷⁾. This discrepancy suggests that FA-induced olfactory impairment is primarily neurosensory or epithelial in origin, rather than a result of mechanical airway obstruction⁽²²⁾.

The relatively high normosmia rate observed in our control group (97.1%) compared with previously published CCCRC normative studies warrants discussion. In the Turkish validation study by Veyseller et al., the proportion of normosmic healthy volunteers was reported as 81.6%, which is lower than that observed in our control cohort⁽¹⁸⁾. We believe this difference may be explained by the specific characteristics of our control group and may partly reflect a possible healthy worker effect. Unlike community-based normative cohorts, our controls

consisted of actively employed hospital staff, predominantly young to middle-aged adults, with relatively preserved general health status and no known occupational chemical exposure. Furthermore, strict exclusion criteria were applied, including the absence of neurodegenerative disease, sinonasal pathology, prior head trauma, and post-infectious olfactory dysfunction. Community-based studies generally include participants with broader age ranges, elderly individuals, and multiple comorbidities, all of which may adversely affect olfactory performance and lower the proportion of normosmic subjects. Therefore, the high normosmia rate in our control cohort may be attributable to the relatively healthy and carefully screened nature of this study population.

The use of the CCCRC olfactory test battery instead of the Sniffin' Sticks TDI test also warrants clarification. Although the Sniffin' Sticks TDI is considered a gold standard in olfactory assessment due to its high reliability and comprehensive evaluation of threshold, discrimination, and identification, the CCCRC test was selected in this study based on both methodological and practical considerations. In particular, FA exposure predominantly affects peripheral olfactory receptor function, making the n-butanol threshold component of the CCCRC test particularly appropriate for detecting early sensory deficits. In addition, the availability of validated Turkish normative data for the CCCRC battery enabled accurate classification of olfactory performance within our population⁽¹⁸⁾. Furthermore, the simplicity, cost-effectiveness, and feasibility of the CCCRC test made it especially suitable for implementation in a busy hospital-based occupational cohort. Taken together, these factors supported the use of the CCCRC battery as an appropriate and clinically relevant tool for the present study.

The selective impairment in n-butanol thresholds, together with their negative correlation with total exposure duration and the relative preservation of identification scores, provides important mechanistic insight. FA acts as a potent irritant and chemical fixative that directly damages the olfactory neuroepithelium and peripheral receptors⁽¹³⁾. Since odour detection thresholds primarily reflect peripheral receptor sensitivity, their significant decline suggests early-stage peripheral damage⁽²³⁾. Conversely, odour identification relies more on central processing and cognitive memory, which may remain resilient during the initial phases of chronic low-level exposure⁽²⁴⁾.

FA exposure is a well-known cause of sensory irritation affecting both the nasal and trigeminal systems. Its pungent and irritative properties may lead to enhanced sensory awareness without necessarily reflecting improved olfactory function. The trigeminal system is highly sensitive to airborne irritants and can contribute to the perception of odour intensity or irritation independent of olfactory receptor activation. This cross-modal interaction may partly explain the observed positive association between FA exposure and Subjective Olfactory Capability (SOC),

although this interpretation remains hypothetical⁽²⁵⁾. Trigeminal chemosensory activation and olfactory–trigeminal interactions have been extensively described in the literature, highlighting that irritant-induced sensations may alter subjective olfactory ratings without corresponding changes in objective olfactory performance⁽²⁶⁾.

In contrast, Olfaction-Related Quality of Life (ORQ) reflects a broader construct encompassing emotional well-being, environmental odor perception, and daily functional impact. Chronic exposure to FA may lead to persistent mucosal irritation, odor annoyance, and discomfort, which can negatively influence hedonic odor perception and overall quality of life. Such effects are consistent with established evidence on indoor air pollutants and their impact on well-being and comfort⁽²⁷⁾.

Taken together, these findings suggest a dissociation between perceptual self-assessment (SOC) and quality-of-life outcomes (ORQ) under chronic irritant exposure. While SOC may be influenced by increased sensory or trigeminal awareness, ORQ more accurately reflects the functional and affective burden of olfactory disturbances. This perceptual–functional dissociation provides a plausible framework for interpreting the divergent associations observed in this study.

The high level of concern regarding future health risks (median VAS: 8/10) among pathology workers further underscores the psychological impact of working in a chemically hazardous environment⁽⁸⁾. Our findings align with previous reports of solvent-related olfactory decrements in other industries, such as paint manufacturing and hairdressing, yet our study is the first to utilize the CCCRC battery to highlight the insidious nature of FA exposure in a clinical pathology setting^(23,28). From a clinical perspective, the fact that many workers were objectively hyposmic but remained unaware of their deficit likely because their identification skills were still functional is a critical warning⁽²⁹⁾. This suggests that routine occupational health screenings should not rely solely on subjective "self-reporting" but must include objective threshold testing like the n-butanol battery⁽³⁰⁾.

In the present study, although a weak-to-moderate but significant association between FA exposure duration and olfactory function was observed in univariate correlation analysis, this relationship did not remain statistically significant after adjustment for potential confounders. This finding suggests that the observed association may be partially influenced by confounding variables or limited statistical power due to the relatively small sample size. Notably, the direction of the association remained consistent after adjustment, indicating a potential underlying relationship between cumulative FA exposure and olfactory impairment that may not have reached statistical significance. Future studies with larger sample sizes and more precise exposure assessment are needed to further clarify this relationship.

Previous studies have shown that pathology and anatomy labo-

ratories represent important occupational settings for chronic FA exposure, particularly during specimen fixation, gross examination, tissue handling, and routine laboratory processing procedures. Although ventilation systems and biosafety precautions are routinely implemented in many pathology laboratories, intermittent airborne FA exposure may still occur during daily laboratory activities because of the continuous and unavoidable use of FA in routine pathology practice⁽³¹⁾. Occupational studies have demonstrated that pathology laboratory workers may experience measurable FA exposure levels and associated biological or health effects despite standard preventive measures⁽³²⁾. Similarly, the pathology laboratory in which our study population worked routinely employed local ventilation systems, fume cupboards, standard pathology biosafety protocols, and personal protective equipment during laboratory procedures. Therefore, the working conditions in our study appear generally comparable to those reported in previous occupational studies evaluating FA exposure among pathology laboratory personnel⁽³¹⁾.

Nevertheless, as emphasized in the literature, chronic low-level FA exposure may persist even in laboratories applying standard preventive measures because of the continuous and unavoidable use of FA in routine pathology practice⁽³¹⁾.

This study is not without limitations. Due to the lack of direct ambient FA concentration measurements, a precise dose-response relationship could not be established. The cross-sectional design and the relatively small sample size from a single center may limit the generalizability of our results. Although controls were selected from healthcare personnel without known FA exposure, unmeasured factors could still confound comparisons. Future studies should incorporate personal exposure monitoring, larger multicenter cohorts, and longitudinal designs to define dose-response relationships.

In parallel, adopting FA-free alternatives such as zinc-based or alcohol-based fixatives, together with more stringent ambient air monitoring in pathology settings, may help reduce occupa-

tional exposure and protect healthcare personnel⁽³³⁾. Current occupational health recommendations emphasize engineering controls as the primary strategy for exposure reduction, with personal protective equipment considered an adjunctive measure. Future preventive strategies may include improved ventilation and enclosed processing systems, real-time air monitoring approaches, and the potential adoption of formaldehyde-free or low-toxicity fixatives to further minimize occupational exposure.

Conclusion

Our findings demonstrate that chronic FA exposure leads to a significant, yet often under-recognized, objective olfactory impairment. Given the discrepancy between objective loss and subjective awareness, we strongly recommend regular psychophysical olfactory screening and enhanced protective measures for pathology laboratory personnel to prevent irreversible chemosensory damage.

Author contributions

MA: Study design, olfactory testing, data collection, quality of life assessments, and interpretation manuscript drafting, supervision, and final approval. FB: Data collection, pathology coordination, and literature review. BA: Methodology, olfactory testing, quality of life assessments and manuscript drafting. HÖ: Statistical analysis and software management, data analysis. AEK: Olfactory testing, data collection, quality of life assessments, and interpretation. HÇ: Critical revision of the manuscript for important intellectual content.

Conflict of interest

The authors declare that they have no conflict of interest related to this study.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

- Mullol J, Alobid I, Mariño-Sánchez F, et al. Furthering the understanding of olfaction, prevalence of loss of smell and risk factors: a population-based survey (OLFACAT study). *BMJ Open* 2012; 2: e001256.
- Sarnat HB, Flores-Sarnat L, Wei XC. Olfactory development, part 1: function, from fetal perception to adult wine-tasting. *J Child Neurol* 2017; 32: 566–578.
- Imamura F, Hasegawa-Ishii S. Environmental toxicants-induced immune responses in the olfactory mucosa. *Front Immunol* 2016; 7: 475.
- Hummel T, Landis BN, Hüttenbrik KB. Smell and taste disorders. *GMS Curr Top Otorhinolaryngol Head Neck Surg* 2011; 10: Doc04.
- Ottaviano G, Zuccarello D, Frasson G, et al. Olfactory sensitivity and sexual desire in young adult and elderly men: an introductory investigation. *Am J Rhinol Allergy* 2013; 27: 157–161.
- Lucas JC, Arambula Z, Arambula AM, et al. Olfactory, auditory, and vestibular performance: multisensory impairment is significantly associated with incident cognitive impairment. *Front Neurol* 2022; 13: 910062.
- Zhou X, Zhang S, Sun X, Zhang J. Alternately airtight/ventilated emission method: a universal experimental method for determining the VOC emission characteristic parameters of building materials. *Build Environ* 2018; 130: 210–218.
- Jalali M, Moghadam SR, Baziar M, et al. Occupational exposure to formaldehyde, lifetime cancer probability, and hazard quotient in pathology lab employees in Iran: a quantitative risk assessment. *Environ Sci Pollut Res Int* 2021; 28: 1878–1888.
- Raja DS, Sultana B. Potential health hazards for students exposed to formaldehyde in the gross anatomy laboratory. *J Environ Health* 2012; 74: 36–40.
- Songur A, Ozen OA, Sarsilmaz M. The toxic effects of formaldehyde on the nervous system. *Rev Environ Contam Toxicol* 2010; 203: 105–118.
- Nordin S, Brämerson A. Complaints of olfactory disorders: epidemiology, assessment and clinical implications. *Curr Opin Allergy*

- Clin Immunol 2008; 8: 10-15.
12. Kundu S, De A, Mitra S. Formaldehyde: Fact sheet reflecting uses, exposure hazards, health effects and toxicological profile- A broad overview for medical professionals and embalmers. *J Clin Exp Res* 2015; 3: 183-196.
 13. Zhang Q, Yan W, Bai Y, Zhu Y, Ma J. Repeated formaldehyde inhalation impaired olfactory function and changed SNAP25 proteins in olfactory bulb. *Int J Occup Environ Health* 2014; 20: 308-312.
 14. Sayed SA, Mahmoud FY, Anwar RI, Abdel-Fatah RM. Effect of formaldehyde inhalation on the olfactory bulb of adult rats. *J Am Sci* 2013; 9: 11-22.
 15. Ottaviano G, Scadding GK, Coles S, et al. Peak nasal inspiratory flow; normal range in adult population. *Rhinology* 2006; 44: 32-35.
 16. Ozkul HM, Balıkcı HH, Gurdal MM, et al. Normal range of peak nasal inspiratory flow and its role in nasal septal surgery. *J Craniofac Surg* 2013; 24: 900-902.
 17. Cain WS, Goodspeed RB, Gent JF, et al. Evaluation of olfactory dysfunction in the Connecticut Chemosensory Clinical Research Center. *Laryngoscope* 1988; 98: 83-88.
 18. Veyseller B, Ozucer B, Karaaltın AB, et al. Connecticut Chemosensory Clinical Research Center (CCCRC) olfactory test: normative values in 426 healthy volunteers. *Indian J Otolaryngol Head Neck Surg* 2014; 66: 31-34.
 19. Onerci Celebi O, Araz Server E, Yigit O, Longur ES. Adaptation and validation of the Turkish version of the Nasal Obstruction Symptom Evaluation scale. *Int Forum Allergy Rhinol* 2018; 8: 72-77.
 20. Pusswald G, Auff E, Lehrner J. Development of a brief self-report inventory to measure olfactory dysfunction and quality of life in patients with problems with the sense of smell. *Chemosens Percept* 2012; 5: 292-299.
 21. Saatçi Ö, Arıcı Düz Ö, Altundağ A. Reliability and validity of the Turkish version of the questionnaire for the assessment of self-reported olfactory functioning and olfaction-related quality of life. *J Acad Res Med* 2020; 10: 277-282.
 22. Holmström M, Wilhelmsson B. Respiratory symptoms and pathophysiological effects of occupational exposure to formaldehyde and wood dust. *Scand J Work Environ Health* 1988; 14: 306-311.
 23. Schwartz BS, Ford DP, Bolla KI, et al. Solvent-associated decrements in olfactory function in paint manufacturing workers. *Am J Ind Med* 1990; 18: 697-706.
 24. Nordin S, Bramerson A, Bende M. Prevalence of self-reported poor odor detection sensitivity: the Skovde population-based study. *Acta Otolaryngol* 2004; 124: 1171-1173.
 25. Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological Profile for Formaldehyde. Atlanta (GA): U.S. Department of Health and Human Services, Public Health Service; 1999.
 26. Hummel T, Livermore A. Intranasal chemosensory function of the trigeminal nerve and aspects of its relation to olfaction. *Int Arch Occup Environ Health* 2002; 75:305-313.
 27. World Health Organization. WHO guidelines for indoor air quality: selected pollutants. Copenhagen: WHO Regional Office for Europe; 2010.
 28. Cabral LB, Miyamoto MA, Lopes NM, Garcia EC, Peixe TS, Fornazieri MA. Evaluation of formaldehyde as a potential cause of olfactory dysfunction in hairdressers. *Occup Dis Environ Med* 2023; 11: 143-149.
 29. Miwa T, Furukawa M, Tsukatani T, Costanzo RM, DiNardo LJ, Reiter ER. Impact of olfactory impairment on quality of life and disability. *Arch Otolaryngol Head Neck Surg* 2001; 127: 497-503.
 30. Denzer MY, Gailer S, Kern DW, et al. Quantitative validation of the n-butanol sniffin' sticks threshold pens. *Chemosens Percept* 2014; 7: 91-101.
 31. d'Ettorre G, Caroli A, Mazzotta M. Minimizing formaldehyde exposure in a hospital pathology laboratory. *Work* 2021;69:209-213.
 32. Costa S, Coelho P, Costa C, et al. Genotoxic damage in pathology anatomy laboratory workers exposed to formaldehyde. *Toxicology* 2008; 252(1-3):40-8.
 33. Zanini C, Gerbaudo E, Ercole E, et al. Evaluation of two commercial and three home-made fixatives for the substitution of formalin: a formaldehyde-free laboratory is possible. *Environ Health* 2012; 11: 59.

Melih Alpay, MD
Department of Otorhinolaryngology
University of Health Sciences
Bursa High Specialty Training and Research Hospital
Bursa
Türkiye

Mobile: +90-5056874829
Fax: +90-2242944246
E-mail: melih_alpay@hotmail.com
Orcid.org/0009-0006-9328-7080

Melih Alpay¹, Fuat Bulut¹, Betül Ağırgöl¹, Hande Özgen², Ahmet Emre Kaymaz¹, Hakkı Caner İnan¹

Rhinology 64: 6, 0 - 0, 2026
<https://doi.org/10.4193/Rhin26.076>

¹ Department of Otorhinolaryngology, University of Health Sciences, Bursa High Specialty Training and Research Hospital, Bursa, Türkiye

² Department of Occupational Health Clinic, University of Health Sciences, Bursa High Specialty Training and Research Hospital, Bursa, Türkiye

Received for publication:
 February 1, 2026

Accepted: June 29, 2026

Associate Editor:
 Basile Landis

This manuscript contains online supplementary material

SUPPLEMENTARY MATERIAL

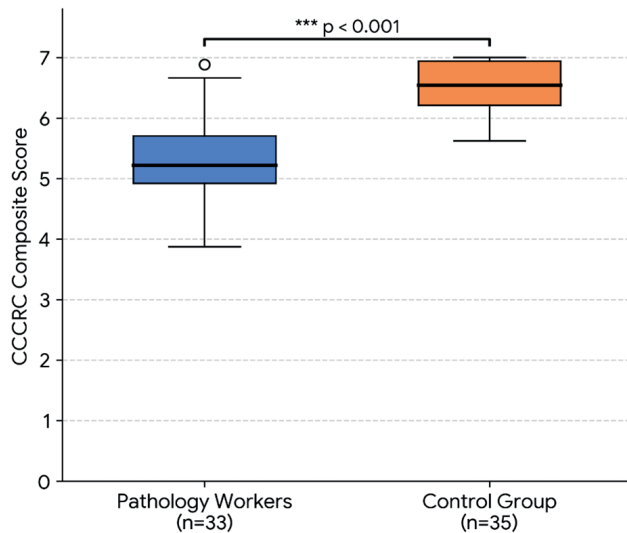


Figure S1. Comparison of objective olfactory function scores between the study groups. The box-and-whisker plot illustrates significantly lower median CCCRC (Connecticut Chemosensory Clinical Research Center) composite scores in pathology laboratory workers (n=33) compared to the control group (n=35). The horizontal black lines within the boxes represent the median values, while the whiskers indicate the range. Statistical significance is indicated by asterisks (***) $p < 0.001$, Mann-Whitney U test). The open circle (o) in the pathology group represents an outlier.

Table S1. Multivariable linear regression analysis of factors associated with CCCRC olfactory scores in the formaldehyde-exposed group.

Variable	B (Unstandardized)	Std. Error	Beta (Standardized)	t	p-value
Constant	6,792	0,776	—	8,757	<0,001
FA exposure Duration (months)	-0,003	0,002	-0,312	-1,462	0,155
Age	-0,018	0,017	-0,227	-1,063	0,297
Sex	-0,286	0,273	-0,183	-1,047	0,304
Smoking status	-0,012	0,305	-0,007	-0,040	0,969

Dependent variable: CCCRC olfactory score. Model assumptions (linearity, normality of residuals, and homoscedasticity) were satisfied prior to analysis.