

## Health Risk Assessment of Occupational Exposure to BTEX Compounds in the Industrial Offset Printing Sector: A Combined Environmental and Biological Monitoring Approach

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### ABSTRACT

**Introduction:** Occupational exposure to the BTEX compounds (Benzene, Toluene, Ethylbenzene, and Xylene) in the printing industry is a major health concern due to their established carcinogenic and non-carcinogenic toxicity. This study aimed to quantify respiratory exposure, assess the internal biological dose, and determine the associated carcinogenic and non-carcinogenic health risks using the US-EPA methodology.

**Methods:** This cross-sectional study monitored 23 occupationally exposed printing workers and 23 unexposed administrative staff (control group). Personal respiratory air sampling was conducted for BTEX (NIOSH 1501/GC), and end-of-shift urine samples were collected for biological monitoring of t,t-MA (Benzene metabolite) and Hippuric Acid (Toluene metabolite) using HPLC. Health risks were calculated using the EPA guidelines for the Hazard Quotient (HQ) and Lifetime Cancer Risk (LCR).

**Results:** The Mean BTEX concentrations were high, notably toluene (47.17±52.03 ppm) and xylene (45.12±68.41 ppm) were markedly elevated. Biological monitoring revealed statistically significant differences between the groups ( $p < 0.001$ ); the mean t,t-MA level in the exposed group was 51,809.37 µg/g creatinine compared to 265.75 µg/g creatinine in the control group. Risk assessment indicated critical non-carcinogenic risks, with HQs for Xylene (230.06), Benzene (16.43), and Toluene (8.35) far exceeding the safety threshold of 1. The mean LCR for Benzene was  $7.8 \times 10^{-3}$ , significantly surpassing the EPA acceptable limit of  $10^{-6}$ .

**Conclusion:** Chronic BTEX exposure in this printing facility significantly exceeded the permissible occupational limits, resulting in substantial non-carcinogenic and carcinogenic risks. Immediate intervention through engineering controls and comprehensive revision of safety standards is urgently required to protect worker health.

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### Introduction

Occupational exposure to volatile organic

compounds (VOCs), particularly the BTEX group (Benzene, Toluene, Ethylbenzene, and Xylene),

remains a critical global health concern in solvent-based industries such as printing<sup>1,2</sup>.

These compounds are classified as hazardous air pollutants due to their diverse toxicity profiles, including the Group 1 carcinogenicity of benzene and the neurotoxic effects associated with toluene, ethylbenzene, and xylene.<sup>3-10</sup> In the printing industry, heating or spraying solvent-based inks frequently releases substantial concentrations of BTEX into the breathing zone<sup>11, 12</sup>. Systematic risk assessment, as defined by the National Research Council (NRC), is essential for quantifying these hazards and informing regulatory control measures<sup>13-17</sup>. While modern printing employs various methods like offset and lithography, studies consistently identify benzene and toluene as the predominant airborne contaminants<sup>12, 18</sup>. Notably, recent research indicates that even when BTEX concentrations fall below occupational exposure limits (OELs), the associated Hazard Quotients (HQ) and Lifetime Cancer Risk (LCR) can still exceed acceptable international thresholds, such as those set by the EPA and WHO<sup>19</sup>. This disparity underscores the urgent need for comprehensive monitoring and risk characterization to protect workers from cumulative health outcomes. Similarly, a study by Shi et al. in 2022 found that over 60% of job groups were in the high-risk category, and approximately 20% were in the high carcinogenic risk category, especially in the printing and gluing departments, which often lack adequate local ventilation. Among the models used, the EPA model was particularly important because it allowed for the simultaneous calculation of non-carcinogenic (HQ) and carcinogenic (LCR) risks. The findings showed that in some groups, the HQ value exceeded 1, indicating a probability of non-carcinogenic outcomes, while the LCR values for benzene were often estimated to be beyond the acceptable range ( $10^{-6}$  to  $10^{-4}$ ), clearly highlighting an increased risk of cancer over a working lifetime<sup>20</sup>. While previous studies have documented BTEX exposure in printing environments<sup>19, 21</sup>, a distinct gap persists regarding high exposure scenarios. Recent literature predominantly focuses on digital

printing centers or facilities with modern ventilation systems, often reporting concentrations near or below the occupational limits. There is a paucity of data integrating comprehensive EPA-based risk assessment with biological monitoring in legacy offset printing facilities in developing regions, where engineering controls are often inadequate. This study aimed to bridge this gap by quantifying the worst-case exposure scenarios.

## Materials and Methods

This cross-sectional study with an exposed cohort and a control group was conducted in 2025 to determine the health risks for workers occupationally exposed to BTEX pollutants in a printing industry in Tehran province using the US-EPA method. The facility utilized offset printing with mechanical ventilation. Oil-based inks and organic solvents containing BTEX compounds were used to thin the ink, maintain proper flow, and clean the machinery. The workers used N95 masks during their tasks.

### Participants

Participants were eligible if they had at least one year of work experience, provided informed consent, and were in good health. Those participants with acute illness, chronic liver or kidney disorders, alcohol use, relevant medication or supplement use, or a second BTEX-related job were excluded. The same inclusion and exclusion criteria were applied to both the exposed and control groups to ensure their comparability.

### Sample Size Determination

The sample size was estimated as 46 participants (23 exposed and 23 controls) based on NIOSH guidelines for the top 10% of workers at highest exposure risk with 90% confidence, and respiratory air sampling was conducted accordingly<sup>22</sup>.

### Biological Monitoring (Urine Sampling)

Urinary trans,trans-muconic acid (t,t-MA) and hippuric acid were selected as biological exposure indices for benzene and toluene, respectively, and were analyzed using validated HPLC methods.<sup>23, 24</sup> At the start of the work shift, study objectives were

explained to participants and informed consent was obtained. Demographic and occupational information was collected using a questionnaire. End-of-shift urine samples were collected in labeled containers, transported under cooled conditions, and stored at  $-20^{\circ}\text{C}$  until analysis. Urinary t,t-MA was determined using the Boogaard and Van Sittert method, and creatinine levels were measured by the colorimetric Jaffe method<sup>25, 26</sup>. Samples were analyzed by HPLC using a C18 column and UV detection at 230 nm.

### Respiratory Monitoring

Personal air sampling for BTEX was performed in the workers' breathing zone according to NIOSH Method 1501 using activated charcoal tubes at a flow rate of 100 mL/min for 4 h<sup>27</sup>. Samples were sealed, kept cooled, and transported to the laboratory for analysis by gas chromatography with a flame ionization detector (GC-FID).

### Quality control

Standard QA/QC procedures (calibration, blanks, and duplicate samples) were implemented to verify the analytical accuracy and precision.

### Health Risk Assessment

Among the BTEX compounds, benzene is recognized by the IARC and EPA as a definitive human carcinogen; therefore, the Lifetime Cancer Risk (LCR) index was used. The non-carcinogenic Hazard Quotient (HQ) was also used for all BTEX compounds. Risk assessment for carcinogenicity and non-carcinogenicity was performed using the method provided by the US Environmental Protection Agency<sup>28</sup>.

### Non-cancerous Hazard Quotient (HQ)

This index represents the ratio of the actual absorbed dose to the reference dose (RfD) or reference concentration (RfC).

$$\text{HQ} = \text{EC}/\text{RfC} \quad (1)$$

EC was calculated using the following equation:

$$\text{EC} = (\text{C} \times \text{ET} \times \text{ED} \times \text{EF})/\text{AT} \quad (2)$$

Where:

C = Pollutant concentration ( $\text{mg}/\text{m}^3$ ) from personal air samples

ET = Exposure time (hr/day)

EF = Exposure frequency (days/year)

ED = Exposure duration (years)

AT = Averaging time (hours)

The RfC is an estimate of inhalation exposure concentration to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. RfC is reported in mg of pollutant per cubic meter of air ( $\text{mg}/\text{m}^3$ ).

$$\text{HQ} = \text{EC}/(\text{RfC} \times 1000\mu\text{g}/\text{mg}) \quad (3)$$

- $\text{HQ} < 1$ : Exposure is within a safe range, and the probability of non-carcinogenic effects is low.
- $\text{HQ} \geq 1$ : Exposure is above the safe limit; there is a probability of non-carcinogenic effects, and control measures or exposure reduction are required.

### Lifetime Cancer Risk (LCR)

LCR is an index that indicates the probability of developing cancer over a lifetime (typically 70 years) due to chronic exposure to a carcinogenic chemical.

The value of this index was calculated using the following formula:

$$\text{LCR} = \text{IUR} \times \text{EC} \quad (4)$$

Where:

- IUR = Inhalation Unit Risk (per  $\mu\text{g}/\text{m}^3$ )
- EC = Exposure Concentration obtained from Equation-2 ( $\mu\text{g}/\text{m}^3$ )

An LCR greater than  $10^{-4}$  is considered a definite risk, an LCR between  $10^{-4}$  and  $10^{-5}$  is a probable risk, an LCR between  $10^{-5}$  and  $10^{-6}$  is a possible risk, and an LCR less than  $10^{-6}$  is considered a negligible risk. The input parameters and toxicological reference values used in this study are consolidated in Table 1.

**Table 1:** Variables and Values Used for Health Risk Assessment

Parameter	Symbol	Value	Unit	Source
Exposure Time	ET	8	hours/day	Site Data
Exposure Frequency	EF	300	days/year	Site Data
Exposure Duration	ED	30	years	Assumption
Averaging Time (Non-Cancer)	AT	ED×365×8	hours	EPA
Averaging Time (Cancer)	AT	70×365×8	hours	EPA
Reference Values				
Benzene RfC	RfCB	0.03	mg/m <sup>3</sup>	EPA IRIS
Toluene RfC	RfCT	5	mg/m <sup>3</sup>	EPA IRIS
Ethylbenzene RfC	RfCE	1	mg/m <sup>3</sup>	EPA IRIS
Xylene RfC	RfCX	0.1	mg/m <sup>3</sup>	EPA IRIS
Benzene Inhalation Unit Risk	IUR	7.8 × 10 <sup>-6</sup>	(μg/m <sup>3</sup> ) <sup>-1</sup>	EPA IRIS

### Statistical Analysis

Statistical analyses were performed using SPSS (version 27), with appropriate parametric or non-parametric tests applied based on data distribution.

### Results

A total of 46 individuals, including 23 in the exposed group and 23 in the control group, were monitored for exposure to BTEX compounds, urinary hippuric acid (a metabolite of toluene exposure), and trans,trans-muconic acid (a metabolite of benzene exposure). Employees in the administrative section of the same industry were considered the control group (without BTEX exposure).

### Demographic Information of the Study Population

The study population comprised 46 male participants, equally divided into exposed and non-exposed groups (n=23 per group). Both cohorts were statistically comparable ( $p > 0.05$ ) regarding age ( $42.71 \pm 4.58$  vs.  $41.65 \pm 6.08$  years), body weight ( $81.48 \pm 9.03$  vs.  $79.69 \pm 7.42$  kg), and work experience ( $14.04 \pm 8.48$  vs.  $16.13 \pm 6.74$  years). Smoking status was perfectly balanced, with 26.1% smokers in each group, eliminating it as a potential confounder. While educational distribution varied-with the non-exposed group showing a higher concentration of bachelor's degrees (69.6%) compared to the more diverse educational backgrounds in the exposed group-the baseline homogeneity across key physiological and professional metrics ensures a robust foundation

for comparative exposure analysis.

### Results of Biological Monitoring for t,t-Muconic Acid and Hippuric Acid

Urinary biomarker analysis revealed a profound disparity between the study groups. The exposed cohort exhibited significantly elevated t,t-muconic acid levels (Median: 2,272.73 vs. 97.00 μg/g creatinine), with high variance (SD = 165,754.58) indicating substantial inter-individual variability and the presence of influential exposure outliers. Similarly, hippuric acid concentrations in the exposed group were markedly higher and more consistently distributed compared to the control group ( $48.10 \pm 14.89$  vs.  $1.46 \pm 0.46$  mg/g creatinine;  $p < 0.001$ ). These findings objectively confirm an intense internal dose resulting from occupational BTEX inhalation.

### Results of Personal Monitoring of BTEX Concentrations

Airborne VOC monitoring identified toluene ( $47.17 \pm 52.03$  ppm) and xylene ( $45.13 \pm 68.41$  ppm) as the primary contaminants, followed by lower concentrations of ethylbenzene ( $17.50 \pm 29.62$  ppm) and benzene ( $2.69 \pm 4.41$  ppm). The recording of peak levels reaching 146.99 ppm (toluene) and 170.00 ppm (xylene) underscores the occurrence of extreme, episodic exposure events. Due to the pronounced right-skewed distribution-evidenced by standard deviations exceeding mean values-median concentrations provide a more robust representation of typical occupational exposure in this setting.

**Comparison of BTEX Concentrations in Different Sections**

Inter-departmental analysis revealed significant variability in toluene, ethylbenzene, and xylene concentrations across the four operational units (Kruskal-Wallis,  $p < 0.05$ , Table 3). In contrast,

benzene levels remained statistically uniform ( $p = 0.081$ ), although Flatbed Printing was identified as a critical exposure hotspot with the highest mean concentration (6.16 ppm) compared to the Roll Offset unit (0.51 ppm).

**Table 3:** Comparison of BTEX Concentrations (ppm) in Different Sections

Work Section	Number of sample	Benzene Mean (ppm) (ANOVA)	Toluene Mean Rank (Kruskal-Wallis)	Ethylbenzene Mean Rank (Kruskal-Wallis)	Xylene Mean Rank (Kruskal-Wallis)
Sheetfed Offset	8	1.63	11	15	16.5
12-Color Offset	4	0.89	11.25	4.38	3.5
Web Offset (Roll)	4	0.51	2.75	8.38	6.5
Flatbed Printing	7	6.16	18.86	15	14.86
Test Statistic	-	F = 2.618	H = 14.818	H = 9.138	H = 13.677
P-value	-	0.081	0.002	0.028	0.003

Non-parametric analysis of departmental exposure identified Flatbed Printing and Sheetfed Offset as the highest exposure zones for toluene, ethylbenzene, and xylene. Conversely, the Roll Offset and 12-Color Offset units consistently recorded the lowest relative exposure ranks across all monitored compounds. These results pinpoint specific operational areas where solvent evaporation and inadequate localized control measures exacerbate airborne pollutant accumulation.

Biomonitoring confirmed a significant occupationally-induced body burden, with urinary metabolite levels strongly correlating with airborne concentrations—specifically for benzene/t,t-MA (Spearman’s  $\rho=0.503$ ,  $p=0.015$ ) and toluene/HA (Pearson’s  $r=0.897$ ,  $p<0.001$ ). Comparative analysis revealed a profound disparity in HA concentrations between the exposed and control groups (48.10 vs. 1.45 mg/g creatinine;  $p<0.001$ ), a trend further supported by significantly elevated t,t-MA levels ( $U=130$ ,  $p=0.003$ ). While demographic factors and smoking status exerted no statistical influence ( $p>0.05$ ), a borderline significant trend ( $p=0.051$ ) suggested higher HA accumulation among workers with intermediate educational backgrounds, likely reflecting

increased exposure within specific technical job roles.

Statistical analysis confirmed that urinary metabolite distributions were independent of smoking status, work section, and educational level within the exposed cohort. Specifically, the Kruskal-Wallis H test showed no significant influence of educational attainment on t,t-MA concentrations ( $H = 1.68$ ,  $p = 0.794$ ), ruling out these demographic variables as potential confounders for benzene metabolism in the study population.

**Health Risk Assessment Results**

Health risk assessment for BTEX exposure was calculated in two parts: cancer risk (LCR) and non-cancer risk using the Hazard Quotient (HQ). Carcinogenic risk assessment was calculated for benzene (Table 4), and non-carcinogenic risk was calculated for all pollutants (Table 5).

**Benzene Cancer Risk (LCR)**

Since the other BTEX compounds are not classified as definitive carcinogens, the cancer risk was calculated only for benzene. The results showed that the LCR for benzene was higher than the maximum acceptable level of 1 in 1,000,000 proposed by the US-EPA <sup>29</sup>.

**Table 4:** Lifetime Cancer Risk (LCR) for Benzene

Metric	Number (N)	Mean	Median	Standard Deviation	Maximum Value
Carcinogenic Risk (LCR)	23	0.00787	0.00404	0.01289	0.0489

**Non-Cancer Risk (HQ)**

Based on the RfC values from the IRIS database for benzene, ethylbenzene, toluene, and xylene

(0.03, 1, 5, and 0.1 mg/m<sup>3</sup>, respectively), the HQ index was calculated. The acceptable value is less than 1<sup>30</sup>.

**Table 5:** Non-Cancer Hazard Quotient (HQ) for BTEX Compounds

Compound	Number (N)	Risk Metric	Mean	Median	Standard Deviation	Maximum Value
Benzene	23	HQ	16.429	13.754	15.09	70.02
Ethylbenzene	23	HQ	8.924	1.07	15.101	44.866
Toluene	23	HQ	8.348	7.739	2.632	13.008
Xylene	23	HQ	230.055	15.447	348.759	866.685

The estimated lifetime cancer risk (LCR) for benzene had a mean of  $7.87 \times 10^{-3}$  (Table 4), far exceeding the commonly accepted risk level of  $1 \times 10^{-6}$ . For non-cancer risk, all BTEX compounds had mean HQs well above 1 (benzene 16.43, xylene 230.06, etc.; Table 5), indicating the potential for adverse health effects. These results underscore the serious risk levels.

**Discussion**

The results showed that BTEX exposure in offset printing workshops was significantly higher than permissible limits and was accompanied by increased urinary metabolites; moreover, the HQ and LCR indices clearly exceeded safe thresholds. Differences between printing processes (offset, gravure, and flexo) also lead to different emission patterns; for instance, worker exposure levels in offset printing have been reported to be higher than those in digital printing owing to the extensive use of cleaning solvents and IPA<sup>31</sup>.

In addition to primary emission sources, environmental conditions play a decisive role in the accumulation of BTEX pollutants in printing houses. The primary factor was inadequate ventilation. In many printing units, general and local ventilation systems lack the necessary efficiency, and the air exchange rate is below the standard, leading to the accumulation of volatile compounds from inks, solvents, and adhesives. The enclosed and indoor spaces of printing halls exacerbate this problem, as in the absence of

natural airflow, volatile compounds cannot be quickly diluted or removed and remain in the workers' breathing zone<sup>19, 32</sup>. These findings suggest that insufficient ventilation played a major role in the accumulation of BTEX, highlighting the urgent need for improved air exchange systems in this facility.

Consistent with the high consumption of organic solvents in this facility, all monitored BTEX compounds exceeded the ACGIH limits, indicating a high-risk respiratory environment. The mean benzene concentration (2.69 ppm) was more than 100 times the ACGIH limit (0.02 ppm), clearly indicating an unsafe and hazardous exposure level. Similarly, the mean toluene concentration (47.17 ppm) was higher than the ACGIH limit (20 ppm). This level of contamination in the workplace can cause not only short-term effects (such as dizziness, headache, and eye and throat irritation) but also increase the risk of chronic damage, such as neurotoxicity, liver and kidney damage, and especially carcinogenicity<sup>33</sup>.

In the studied offset facility, intensive solvent use for cleaning rollers, blankets, and print heads—exacerbated by high production volumes—was identified as the primary driver of BTEX emissions, aligning with previous findings in similar industrial settings<sup>34</sup>. A critical toxicological insight from this study is the lack of correlation between individual factors (e.g., smoking, BMI) and urinary metabolites. This suggests a 'saturation effect' or 'masking effect',

where the magnitude of occupational inhalation is so severe that it overrides subtle physiological and lifestyle variations. Consequently, the internal dose in this cohort is driven almost exclusively by workplace ambient concentrations, reinforcing the conclusion that the observed body burden is a direct consequence of inadequate industrial hygiene rather than personal habits.

In contrast to our results, Rostami et al.<sup>19</sup> reported BTEX levels below OELs in laser-printing shops. This discrepancy likely reflects differences in printing processes and ventilation; offset printing (our study) uses more organic solvents in enclosed spaces than laser printing. This difference is mainly due to the type of printing process (offset vs. laser/inkjet), the use of organic solvents, the enclosed space, and inadequate ventilation in the studied printing houses. In contrast, in the Ardabil printing houses, due to the less use of organic solvents and better ventilation systems, BTEX concentrations were at a safer level<sup>19</sup>.

The health risk indices calculated in this study reach critical thresholds, far exceeding established safety limits. The Hazard Quotient (HQ) for benzene (16.43) and xylene (230) significantly surpass the EPA unity threshold (HQ > 1), signaling an alarming risk for chronic non-carcinogenic effects. Furthermore, the Lifetime Cancer Risk (LCR) for benzene ( $4.04 \times 10^{-3}$ ) falls into the 'definite risk' category, necessitating immediate regulatory intervention<sup>35</sup>. These findings align with previous reports of elevated risk in offset printing environments, where high solvent consumption and inadequate ventilation drive TVOC levels beyond international standards<sup>19, 34</sup>. Specifically, the practice of cleaning print heads with VOC-laden solvents, coupled with deficient localized exhaust systems, appears to be the primary driver of these unprecedented risk levels, reinforcing the need for urgent engineering controls.

The biological monitoring findings confirmed respiratory exposure. The significant increase in t,t-MA in the exposed group, with a mean of 51809.36  $\mu\text{g/g}$  creatinine, which is much higher

than the ACGIH recommended limit of 500  $\mu\text{g/g}$  creatinine, indicates the real and biological absorption of benzene. In contrast, the mean concentration in the control group was 447.52  $\mu\text{g/g}$  creatinine. In other words, a more than 103-fold increase in this biomarker is strong evidence of the direct impact of occupational exposure on individuals. Urinary hippuric acid (a toluene metabolite) was significantly higher in exposed workers (~48 mg/g creatinine) than in controls (~0.46 mg/g), confirming a substantial toluene absorption. The permissible index for hippuric acid is 1.6 g/g creatinine, according to the ACGIH<sup>36</sup>.

Furthermore, concurrent high-level exposure to a mixture of BTEX compounds raises concerns regarding metabolic competition and synergistic toxicity, which standard risk assessment models (such as the Hazard Quotient) may not fully capture. Since Benzene and Toluene share similar metabolic pathways involving the cytochrome P450 (specifically CYP2E1) enzyme system, the extremely high concentrations of Toluene observed in this study (mean 47.17 ppm) could potentially inhibit the metabolism of Benzene, thereby altering the toxicokinetic profile and potentially extending the half-life of unmetabolized Benzene in the blood. While the calculation of separate HQs indicates severe risk (particularly for Xylene with an HQ exceeding 230), the combined neurotoxic impact of this solvent mixture on the central nervous system is likely greater than the sum of its parts. This highlights the necessity of viewing the cumulative Hazard Index (HI) not just as a mathematical summation, but as an indicator of a profound systemic chemical assault on the workers' physiology.

As the results of this study showed, the Pearson correlation test, given the normal distribution of the two variables, indicated a strong correlation between hippuric acid and toluene in the participants (p-value < 0.001). This correlation was also replicated in a study by Ukai et al., where the reason for this correlation was the high concentration of toluene in the inhaled air of the workers<sup>37</sup>.

The current study found no significant

correlation between individual factors (education, BMI, smoking) and urinary t, t-MA (benzene) and Hippuric Acid (toluene) levels. This contradicts the findings of other studies, such as that of Scherer<sup>38</sup>. and a comparative study by Taheri<sup>39</sup>. This discrepancy is likely rooted in the magnitude of environmental exposure in the studied industry:

1- Masking Effect of Severe Exposure: In this study, the high concentration of Benzene and Toluene in the workplace environment likely overshadowed the influence of individual factors such as BMI or education. External environmental exposure was the dominant determinant of metabolite concentration, rendering minor biological or lifestyle effects statistically insignificant. 2- Sensitivity of Factors to Exposure Level: A comparative study by Taheri suggests that individual factors such as BMI, diet, and smoking are only likely to show a significant effect in environments with low compound concentrations. In such low-exposure settings, minor individual differences can influence the total body burden; however, this effect is lost under conditions of severe occupational exposure. 3. Metabolic Variability: Individual differences in metabolism further complicate the analysis by increasing data dispersion. This wide scatter in metabolite levels can hide potential subtle correlations with the individual factors.

The calculated risk indices forecast severe clinical implications for the workforce. The Hazard Quotient (HQ) for xylene exceeded safety thresholds by over 230-fold, signaling a critical risk of cumulative neurotoxicity, hepatotoxicity, and renal impairment. This elevated HQ—driven by the low RfC (0.1 mg/m<sup>3</sup>) and high ambient concentrations—suggests a high probability of long-term neurological disorders. Furthermore, the Lifetime Cancer Risk (LCR) for benzene reached the 'definite risk' category ( $7-8 \times 10^{-3}$ ), implying an unacceptable incidence of hematopoietic malignancies, such as Acute Myeloid Leukemia (AML). Such significant risk magnitudes render current exposure conditions ethically and legally indefensible, necessitating immediate structural and regulatory interventions.

A primary strength of this study is the integrated application of environmental air monitoring, biological surveillance, and the US-EPA health risk assessment framework, providing a robust multifaceted evaluation of occupational BTEX exposure. The documented direct correlation between airborne concentrations and urinary biomarkers (t,t-MA and HA) reinforces the validity of the exposure-internal dose relationship in this setting. However, certain limitations must be acknowledged. Financial constraints limited the sample size and precluded longitudinal or repeated sampling. Additionally, the exclusively male cohort and the cross-sectional design in a single facility may limit the generalizability of the findings across genders and different industrial environments. While potential confounders like diet and smoking were monitored, their complete isolation remains challenging in field studies. Future research should prioritize larger, multi-center longitudinal cohorts to further elucidate causal pathways and seasonal variations in exposure.

This study identifies a 'masking effect' in high-exposure printing environments, where extreme occupational BTEX levels override individual physiological and lifestyle confounders (e.g., BMI, smoking). This phenomenon necessitates a shift from individual-centric monitoring to source-oriented engineering controls, specifically local exhaust ventilation (LEV) and solvent substitution. Given the documented overexposure, a revision of national occupational limits and the implementation of targeted medical surveillance—focusing on hematological and organ function—are imperative to mitigate long-term health risks in this sector.

## Conclusion

This study conclusively demonstrates that offset-printing facility workers are exposed to BTEX compounds, with levels (particularly Benzene and Toluene) found to be significantly above the established occupational limits, especially near printing machinery. This substantial environmental exposure translated directly into an increased internal dose, confirmed

by the significantly elevated urinary metabolites (t,t-MA for Benzene and Hippuric Acid for Toluene) observed in the exposed group compared to the controls. The subsequent health risk assessment, conducted using the US EPA framework, determined that both non-cancer risk (HQ) and carcinogenic risk (LCR) indices were at unprecedented and significant levels, placing the workers in an unfavorable health situation. The significant internal dose and elevated environmental levels observed necessitate immediate corrective actions, specifically prioritizing local exhaust ventilation and the use of low-VOC alternatives to safeguard worker health.

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### Conflict of Interest

The authors declare no conflicts of interest.

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### Ethical Considerations

This study was conducted in strict adherence to ethical guidelines for research involving human participants. Prior to participation, informed consent was obtained from all subjects after a detailed explanation of the study's objectives, procedures, and the voluntary nature of their involvement. All collected sample data were handled with the utmost confidentiality and anonymized to ensure the privacy of the participants and the industrial facilities.

### Ethical approval

This study was approved by the Research Ethics Committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran

### Code of Ethics

(IR.SBMU.PHNS.REC.1403.195).

### Authors' Contributions

Methodology: A.Ansari, D.Panahi Data curation: Z.Khodoumi, A.Ansari Formal Analysis: A.Ansari, D.Panahi Writing original draft: A.Ansari Writing review & editing: D. Panahi, S. Farhang Dehghan Supervision: D.Panahi

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