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RESEARCH ARTICLE

Occupational exposure to formaldehyde, lifetime cancer probability, and hazard quotient in pathology lab employees in Iran: a quantitative risk assessment

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Abstract

Formaldehyde is a colorless and highly irritating substance that is used as a preservative and chemical fixative in tissue processing in pathological laboratories. Formaldehyde is mutagenic and is classified by the IARC as the definitive carcinogen (A1 group). This cross-sectional descriptive-analytical study was performed to determine the respiratory exposure of 60 employees of pathology labs with formaldehyde and to estimate carcinogenic and non-carcinogenic risk in Iran in 2018–2019. Occupational exposure to formaldehyde was assessed in summer season using the NIOSH 3500 method and a personal sampler with flow of 1 l/min connected to two Glass Midget Impingers containing 20 ml of 1% sodium bisulfate solution. The respiratory symptoms questionnaire provided by the American Thoracic Society was used to assess the health effects of formaldehyde exposure. The carcinogenic and non-carcinogenic risk assessment of inhaled exposure to formaldehyde was also performed using the USA Environmental Protection Agency (OEHHA) method. The mean respiratory exposure of employees to formaldehyde was 0.64 mg/m^3 (range: 0.1474 to 1.3757). Occupational exposure in 28.3% ($n = 17$) of employees was above the OSHA recommended range. Wheezing (24%), burning eyes (25%), and cough (21.7%) were the most prevalent health problems. The mean ± SD of the carcinogenic risk among the employees was $3.45 \times 10^{-4} \pm 2.27 \times 10^{-4}$. The highest mean of carcinogenic risk was found in lab workers (4.44×10^{-4}). Given the high level of carcinogenic and non-carcinogenic risk of respiratory exposure to formaldehyde in pathological employees, especially lab worker, the use of management controls, engineering controls, and respiratory protection equipment to reduce exposure levels of all workers to less than the allowed exposure limits seems necessary.

Keywords Formaldehyde · Health risk assessment · Hospital pathology department · Occupational exposure.

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Introduction

People in their workplace routinely deal with a range of occupational harmful factors including chemicals (dust, gases, and vapors), physical hazards (noise, ionizing radiation, and inappropriate weather conditions), and psychologic and ergonomic factors (stress and high mental workload). Exposure to these factors can cause a variety of occupational complications and diseases such as respiratory diseases, musculoskeletal disorders, physiological disorders, and cancer (Aliabadi 2017; Aliabadi et al. 2018; Fazlzade et al. 2012; Jahangiri et al. 2015; Jalali et al. 2014; Jalali et al. 2016; Mohammadpour et al. 2018; Mohammadyan et al. 2019; Negahban et al. 2014).

Formaldehyde is a colorless gas with a nasty odor and strong irritation produced by the oxidation of methanol gas (Ghasemkhani et al. 2005; Naya and Nakanishi 2005). This

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compound has various uses as a disinfectant and preservative, production of resins and binders usable in the wood, pulp and paper industries, production of plastics, paints, and in the textile industry (Nielsen et al. 2017). Formaldehyde belongs to the aldehyde group but has different properties. The difference between formaldehyde and other aldehydes is that it does not have an alkyl group which causes its high reactivity compared with other aldehydes (Orsiere et al. 2006). Formaldehyde exposure has been reported in various industries such as plastic, paper, textile, melamine containers, and in pathology laboratories and operating rooms. Despite exposure to formaldehyde in various industries, exposure to vapors may occasionally occur at home due to the release of formaldehyde from chipboard or MDF sheets used in decoration and furniture or urea formaldehyde foams (Nielsen et al. 2017).

Formaldehyde has a nasty odor at low concentrations, and its vapors and solutions stimulate the respiratory system, skin, and eye (Arts et al. 2006). Common effects of formaldehyde exposure are caused by irritation of the eyes and the upper airways (Pala et al. 2008). Exposure to this substance at very low concentrations (0.1 ppm) may cause eye burns, tears, and irritation of the upper respiratory tract and at high concentrations (10–20 ppm) may cause cough, chest compression, increased heart rate, and feeling pressure on the head. Exposure to a concentration of 50–100 ppm of formaldehyde vapors may cause pulmonary edema, pneumonitis, or death (Nielsen et al. 2017; Orsiere et al. 2006). Formaldehyde is a mutagenic substance and, due to its high toxicity and carcinogenicity, is very dangerous to human health and can cause cancer of the sinonasal, lung, pancreas, prostate, and colon. Exposure to formaldehyde also increases the risk of myeloid leukemia (Nielsen et al. 2017; Rumchev et al. 2002; Zhang et al. 2010). Hence, this compound was classified in the A1 group as the definitive carcinogen by the IARC and in the A2 group by the ACGIH (Binetti et al. 2006).

The use of formaldehyde in the healthcare system is one of its most important applications. Formaldehyde is used in many hospitals and related laboratories, such as the pathology laboratory. It is also used as a dead body preservative in the hospital's anatomy department. It is also widely used in pathology laboratories as a tissue preservative and stabilizer. Other uses include the use of formaldehyde for floor and equipment disinfection (Ghasemkhani et al. 2005). Studies show exposure to formaldehyde in different wards of hospitals, and the highest concentration has been reported in pathology departments and operating rooms. The results of these studies indicate the exposure of hospital staff to formaldehyde in the range of 0.1–1.75 ppm that have exceeded the occupational exposure limits in some cases (Alizadeh et al. 2003; Cope et al. 2011; Ochs et al. 2012; Tang et al. 2009). Environmental concentrations of formaldehyde in some Iranian hospitals have also been reported in the range of 0.25 to 1.67 ppm (Alizadeh et al. 2003; Assari et al. 2017).

So far, some studies in Iran have investigated the exposure of hospital staff to formaldehyde (Azari et al. 2012; Ghasemkhani et al. 2005; Mosafer et al. 2017). But few studies have quantified the exposure of formaldehyde in pathology lab staff. However, many international organizations, including the World Health Organization (WHO), the US Environmental Protection Agency (US EPA), and the US Food and Drug Administration (US FDA), have considered the use of quantitative risk assessment (QRA) as the basis for regulation of chemical substances, and only the determination of exposure level to the compounds is considered inadequate (US EPA 1996). Most studies of formaldehyde occupational exposure in Iran have only provided occupational exposure levels to these compounds, and few studies have quantitatively estimated the carcinogenic and non-carcinogenic risk of these workers in Iran (Alizadeh et al. 2003; Assari et al. 2017; Ghasemkhani et al. 2005; Neghab et al. 2010; Vahhabi et al. 2016).

To our knowledge, this paper is the first study to concurrently evaluate individual exposure to formaldehyde, determine the effects of exposure, and estimate the carcinogenic and non-carcinogenic risk of exposure in Iran. According to the abovementioned and inadequate studies of carcinogenic and non-carcinogenic risk estimation in hospital staff, especially in pathology laboratories, the present study was performed to (1) determine the personal exposure of pathology lab staff to formaldehyde as time-weighted average, (2) determine respiratory stimulatory effects and eye effects caused by formaldehyde exposure, and (3) assess carcinogenic and non-carcinogenic risk due to occupational exposure to formaldehyde.

Materials and methods

Study design

This descriptive cross-sectional study was conducted to evaluate the health risk of occupational exposure to formaldehyde in employees of pathology labs of several hospitals in Iran in summer season 2019. Sample size was determined by census method according to inclusion criteria. Inclusion criteria consisted of work experience of 1 year and more in pathology laboratories, no smoking, presence in the pathology laboratory for 1 h a day and more, and lack of respiratory diseases in the employees. Employees who had the flu during the study and data collection were also excluded. As a result, from 70 people working in pathology laboratories in study population, 60 were finally selected. The present study was approved by the Ethics Committee of the Birjand University of Medical Sciences. Prior to the evaluations, the consent form for

participating in the study was prepared and distributed among the employees. All subjects completed and signed the consent form.

Demographics

A researcher-made checklist was used to collect demographic and occupational data of the surveyed employees, and variables including age, height, weight, gender, work experience, type of work, daily working hours in the pathology laboratory, and exposure patterns were collected through interviews as well as observation of working cycles.

Inhalation exposure assessment

NIOSH 3500 method was used to determine the level of personal exposure of employees to formaldehyde. This method has a good and acceptable sensitivity for decomposition of formaldehyde in peripheral samples due to the detection limit of 0.5 μg and the stability of the samples for 30 days at 25 °C (Niosh Manual of Analytical Methods (NMAM) 1994). The SKC AirChek TOUCH sampling pump was used for this purpose. To collect air samples, two Glass Midget Impingers containing 20 ml of 1% sodium bisulfate solution and a trap bottle were serially connected to each other via tigon tubes and were set with a sampling pump at a flow rate of 1 l/min (Fig. 1). The collected samples were then transferred to the laboratory by polyethylene bottles. To prepare the samples, in the first step, 0.1 ml of 1% chromotropic acid and 6 ml of 98% sulfuric acid were added to the samples, and then these were placed at 95 °C for 15 min. The samples were finally placed at room temperature for 2–3 h.

To draw the calibration curve, standard stock solution of formaldehyde was prepared from 37% formalin solution at a concentration of 1.26 mg/ml, and then standard solutions were made at concentrations of 0.25–5 μg/ml by diluting standard solution using 1% sodium bisulfite. Then, the absorbance was read using a UV-Vis Spectrophotometer (DR 5000) at 580 nm. Finally, the concentration of formaldehyde in unknown samples was calculated by comparing the absorbance of standard samples.

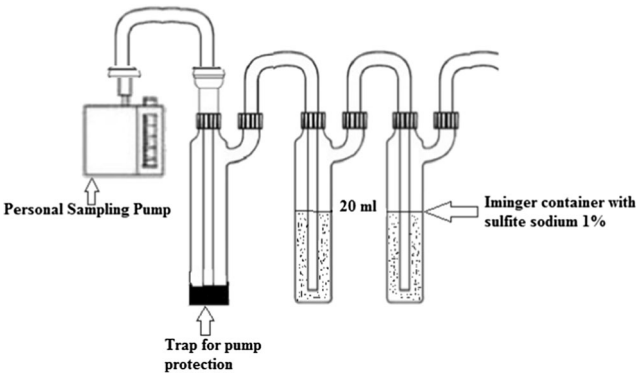

Fig. 1 Sampling set

Determination of respiratory complaints

The respiratory symptoms questionnaire provided by the American Thoracic Society (ATS) was used to assess the health effects of formaldehyde exposure (Ferris 1978). The questionnaire included questions about respiratory status (cough, sputum, sputum cough, wheezing, shortness of breath, chest compression) and nasal and eye symptoms (eye irritation, tears, burning sensation in nose and throat). Data were collected through face-to-face interviews with surveyed employees.

Carcinogenic and non-carcinogen risk estimation

Risk assessment of exposure of pathology lab employees to formaldehyde was carried out by carcinogenic risk assessment and non-carcinogenic health risk assessment of formaldehyde. Carcinogenic risk estimation was performed by estimating the increased probability of developing cancer due to continuous exposure to formaldehyde over several years of activity in the occupation and by means of lifetime cancer probability (LCP) index proposed by EPA (Mehralipour et al. 2018; US EPA 1996). The following equation (Eq. 1) was used to determine the excess LCP:

$$R_{FA} = C_{FA} \times IUR_{FA} \times L_{worker} \quad (1)$$

where RFA is the excess LCP for formaldehyde (FA), CFA is the concentration in μg/m^3 of formaldehyde, IURFA is the IUR factor for formaldehyde (1 μg/m^3)$^{-1}$, and L_{worker} is the adjustment factor for the ratio of the workplace time to 70 years.

The IUR estimates are defined as the individual lifetime excess risk because of a chronic lifetime exposure to one unit of pollutant concentrations (1 μg/m^3) (California Environmental Protection Agency (CalEPA) 2009).

In this study, the CFA was represented by the average 8-h formaldehyde exposure during working time. Unit risk is the simplification of the dose-response data used in regulatory risk assessment procedures, which is derived from many toxicological and epidemiologic studies based on a maximum likelihood estimation of dose-response data and the single numerical value obtained from the California Environmental Protection Agency whose inhalation unit risk of formaldehyde is 6×10^{-6} (California Environmental Protection Agency (CalEPA) n.d.); California Environmental Protection Agency (CalEPA) 2009).

The L_{worker} in this study was calculated assuming that the lab staff and laboratory reception staff work 8 h per day and servants work 3 h per day in pathology labs, 5.5 days per

week, 44 weeks per year, and 30 years at the same location over a 70-year time period (Wu et al. 2003).

As a result (Eq. 2), for lab staff and laboratory reception staff, it would be:

$$L_{worker} = \left({}_{30_y} \times \frac{8_h}{24_h} \times \frac{5.5_d}{7_d} \times \frac{44_w}{52_w} \right) \Big/ {}_{70_y} = 0.095 \qquad (2)$$

And for service workers, it would be:

$$L_{worker} = \left({}_{30_y} \times \frac{3_h}{24_h} \times \frac{5.5_d}{7_d} \times \frac{44_w}{52_w} \right) \Big/ {}_{70_y} = 0.0356$$

According to the literature, the risk of carcinogenesis accepted by the World Health Organization (WHO) for the general public is 10^{-5}, and higher risks indicate an unacceptable risk of carcinogenicity (International Programme on Chemical Safety (IPCS) 2010). The acceptable amount of risk presented by the US Environmental Protection Agency for the general public is 10^{-6} (US EPA 1996). In the present study, since the target group were employees, the results of the carcinogenic risk were compared with the recommended limits of carcinogenic risk in the labor societies, and risk values of less than 10^{-4} were considered as acceptable risk, while levels greater than that were considered as unacceptable (Gratt 1996).

For non-cancer health risks, the hazard quotient (HQ) is a measure of the relative significance of the exposure to a chemical and is estimated by dividing the exposure level by a reference concentration (RfC). The RfC for chronic non-cancer effects is defined as the long-term exposure to toxic compounds in μg/m^3, without any adverse effects (Dourson and Stara 1983). This index is usually compared with 1, which is interpreted as the level at which health effects are not expected to occur (Gratt 1996).

The HI of chronic non-carcinogenic effects is calculated from Eq. 3:

$$HQ_{FA} = C_{FA}/RfC_{FA} \qquad (3)$$

where the RfC_{FA} is the inhalation reference exposure level for chronic non-cancer health effects of formaldehyde, which is 3.6 μg/m^3 for general population (California Environmental Protection Agency (CalEPA) 2009).

Since 3.6 μg/m^3 has been provided for the general population and population of this study were employees, therefore, the HQ using the standard value provided by OSHA (PEL) was also calculated. Finally, the HQ results for the general population and occupational population were compared. The PEL value for formaldehyde is 0.75 ppm or 922 μg/m^3 (Occupational Safety and Health Administration 2002).

Statistical analysis

Data were analyzed using SPSS (Chicago, IL, USA). The distribution of data was examined with Kolmogorov-Smirnov Normality test. Mann-Whitney *U* test was conducted to compare mean of rank personal exposure to formaldehyde in people with respiratory and ocular problems and in people without respiratory and ocular problems. Also, one-way ANOVA test and Tukey post hoc test were used to compare mean of exposure to formaldehyde in occupational groups. In all tests, the level of significance was set at $P < 0.05$.

Results

The demographic and occupational characteristics of the employees studied in pathobiology laboratories were presented in Table 1 based on gender. Thirty-one (51.7%) of the employees were female, and 29 (48.3%) were male. The mean of age, height, weight, and body mass index of the employees were 34.58 years, 74.98 kg, 168.77 cm, and 26.35, respectively. The mean of work experience was 4.86 years.

The results of formaldehyde measurement in respiratory air of employees based on occupational groups and comparison of mean individual exposure between groups were presented in Table 2. The mean (SD) of exposure of employees to formaldehyde was 0.64 mg/m^3 (0.36), which was below the exposure limit provided by the OSHA (PEL = 0.922 mg/m^3) and above the exposure limit recommended by the NIOSH (REL = 0.019 mg/m^3) and Iran's national occupational exposure ceiling limit (OEL-Ceiling = 0.37 mg/m^3). The results showed that the highest mean individual exposure was related to lab workers (0.78 mg/m^3) and then to lab reception staff (0.61 mg/m^3). The lowest mean occupational exposure was also determined for servants (0.28 mg/m^3). Results of one-way ANOVA test showed that there was a statistically significant difference between the mean of individual exposure to formaldehyde among the group employees (P value <0.001). Results of Tukey post hoc test showed that there was a statistically significant difference regarding the mean individual exposure to formaldehyde between the lab workers with lab reception staff (P value <0.001) and lab workers with servants (P value = 0.029). But there was no statistically significant difference regarding the mean individual exposure to formaldehyde between the lab reception staff and servants (P value = 0.211).

Comparative results of employees' exposure level with allowed limits of occupational exposure and comparison of mean concentration of individual exposure to formaldehyde in pathobiology employees in this study and studies performed in other countries were presented in Figs. 2 and 3, respectively. The results presented in Fig. 2 show that the exposure of studied employees to formaldehyde was generally

Table 1 Occupational and demographic characteristics of pathology lab employees by gender

Variable	Sex	Number	Percentage	Mean	Std. deviation	Minimum	Maximum
Age (year)	Man	29	48.3%	35.7241	4.54263	28.00	46.00
	Woman	31	51.7%	33.5161	3.06454	28.00	39.00
	Total	60	100.0%	34.5833	3.97574	28.00	46.00
Weight (kg)	Man	29	48.3%	80.1724	4.48863	70.00	90.00
	Woman	31	51.7%	70.1290	6.75644	59.00	85.00
	Total	60	100.0%	74.9833	7.64131	59.00	90.00
Height (cm)	Man	29	48.3%	176.83	4.83	169	186
	Woman	31	51.7%	161.23	3.83	152	169
	Total	60	100.0%	168.77	8.96	152	186
Work experience (year)	Man	29	48.3%	5.5862	3.67926	1.00	14.00
	Woman	31	51.7%	4.1935	2.56150	1.00	10.00
	Total	60	100.0%	4.8667	3.20205	1.00	14.00
Body mass index	Man	29	48.3%	25.6597	1.44121	22.64	28.08
	Woman	31	51.7%	27.0067	2.72325	22.21	32.05
	Total	60	100.0%	26.3557	2.28417	22.21	32.05

unacceptable compared with the NIOSH standard (REL = 0.019 mg/m^3). Compared with Iran's occupational exposure ceiling limit (OEL-Ceiling = 0.37 mg/m^3), the exposure level was at allowed level only in 31.6% of the investigated employees. While compared with the exposure limit provided by the OSHA (PEL = 0.922 mg/m^3), exposure level was unacceptable only in 17 (28.3%) of the employees. The results presented in Fig. 3 also show that the mean exposure of pathobiology lab employees in the present study was higher than that in the studies conducted in the USA (Lee et al. 2017), Italy (Vimercati et al. 2010), France (Orsiere et al. 2006), and Portugal (Viegas et al. 2010) and lower than the levels expressed in the studies performed in Brazil (Ochs et al. 2012), China (Fan et al. 2006), Hungary (Jakab et al. 2010), Turkey (Burgaz et al. 2002), and UAE (HH et al. 2015).

The health problems associated with exposure to formaldehyde and its relation to exposure rate were presented in Table 3. Wheezing (24%), burning eyes (25%), and cough (21.7%) were the most prevalent health problems. The results showed that the mean concentration of formaldehyde in respiratory air of employees with cough, wheezing, burning eyes, lachrymation, and nasal burning had statistical significant difference with those without these symptoms (P value <0.05).

The results of carcinogenic and non-carcinogenic risk assessment of individual exposure to formaldehyde in the studied population were presented in Table 4. The results showed that the mean (SD) of the carcinogenic risk in the employees was 3.45×10^{-4} (2.27×10^{-4}). The highest mean carcinogenic risk was found in lab workers (4.44×10^{-4}). The lowest carcinogenic risk belonged to the servants (6.16×10^{-5}).

In general, the mean carcinogenic risk among employees according to the risk acceptance criterion in labor societies (reference value: 10^{-4}) was 3.45 times higher than the reference value, and only 18.3% of the employees were at acceptable risk level. Hence, the carcinogenic risk was in an unacceptable level in 81.7% of employees.

The results of the mean non-carcinogenic risk in the surveyed employees showed that when the risk was calculated for the general population ($gRfC_{FA} = 3.6$ μg/m^3), the mean hazard quotient (HQ) was 178.49. But when the non-carcinogenic risk was calculated for labor societies ($wRfC_{FA} = 922$ μg/m^3), the mean hazard quotient was determined 0.69. As a result, according to the HQ of the general population, the non-carcinogenic risk for all subjects was higher than the reference level (HQ = 1). But according to

Table 2 Personal exposure assessment to formaldehyde (mg/m^3) among the pathology lab employees and statistical differences between occupational groups

Job group	N (percent)	Mean	Std. deviation	Minimum	Maximum	P value
Lab workers	34 (56.7%)	0.780307	0.3408588	0.1474	1.3757	
Lab reception staff	14 (23.3%)	0.611499	0.3429055	0.1842	1.1668	< 0.001
Servants	12 (20.0%)	0.288642	0.1209698	0.1474	0.5527	
Total	60 (100.0%)	0.642586	0.3609168	0.1474	1.3757	–

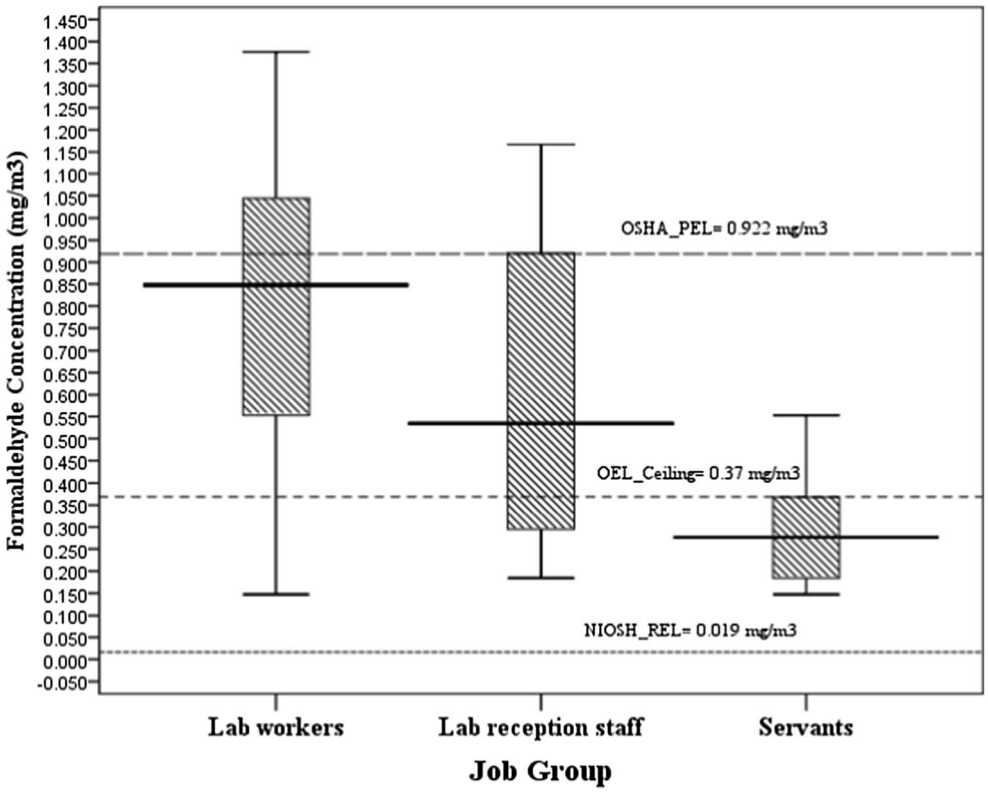

Fig. 2 Comparative results of exposure level of employees to formaldehyde with the allowed occupational exposure limits provided by different organizations

HQ of labor societies, non-carcinogenic risk in 33.3% of employees was at unacceptable level (HQ > 1) and in 66.7% of employees was at acceptable level (HQ < 1).

Discussion

This study was conducted to determine the personal exposure of pathology lab employees to formaldehyde and to estimate the carcinogenic and non-carcinogenic risk due to occupational exposure to formaldehyde. To our knowledge, this was the first study to evaluate the carcinogenic and non-carcinogenic risk of exposure to formaldehyde in employees of pathobiology laboratories in Iran. The results of this study showed the high exposure of employees to formaldehyde through inhalation in lab workers and lab reception staff. Carcinogenic and non-carcinogenic risk was also at high level in these workers.

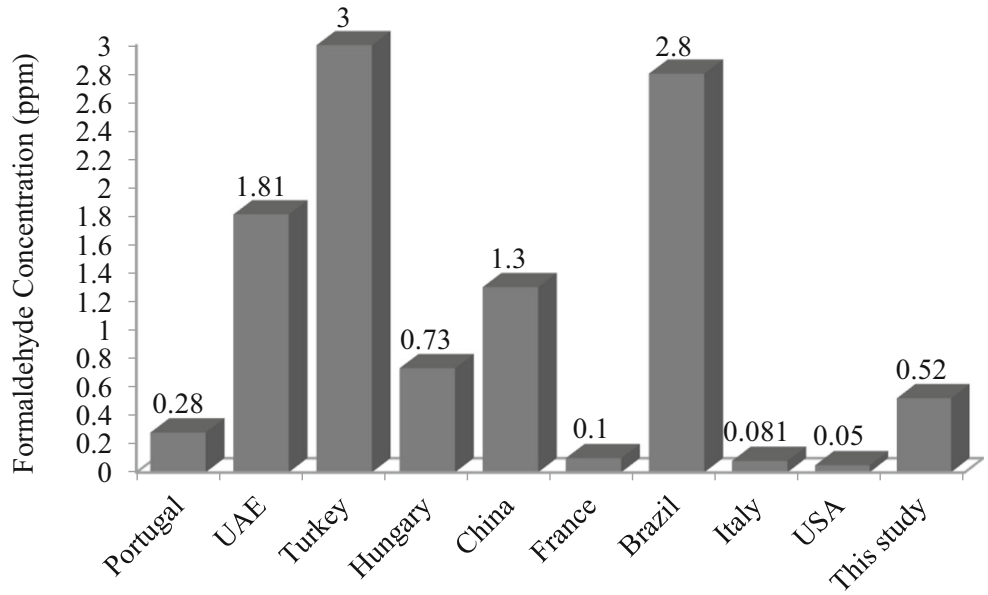

Fig. 3 Comparative results of mean concentration of individual exposure to formaldehyde in pathobiology employees between this study and studies performed in other countries

Table 3 Frequency of health problems among employees and comparison of formaldehyde concentration in respiratory air in people with and without health symptoms

Health problems	Group	*N* (percent)	Mean ± SD	Mean rank	*P* value*
Cough	Yes	13 (21.7%)	0.909 ± 0.360	42.27	*0.006*
	No	47 (78.3%)	0.568 ± 0.327	27.24	
Phlegm	Yes	7 (11.7%)	0.800 ± 0.428	36.79	0.311
	No	53 (88.3%)	0.621 ± 0.317	29.67	
Cough-phlegm	Yes	5 (8.3%)	0.876 ± 0.448	39.10	0.250
	No	55 (91.7%)	0.621 ± 0.349	29.72	
Wheezing	Yes	24 (40%)	0.733 ± 0.338	35.18	*0.011*
	No	36 (60%)	0.505 ± 0.350	23.48	
Dyspnea	Yes	6 (10%)	0.548 ± 0.389	25.08	0.423
	No	54 (90%)	0.653 ± 0.359	31.10	
Chest compression	Yes	6 (10%)	0.523 ± 0.287	31.64	0.811
	No	54 (90%)	0.593 ± 0.318	30.24	
Burning eyes	Yes	15 (25%)	0.836 ± 0.336	41.23	*0.006*
	No	45 (75%)	0.562 ± 0.337	26.92	
Lachrymation	Yes	10 (16.7%)	0.902 ± 0.345	42.85	*0.014*
	No	50 (83.3%)	0.590 ± 0.313	28.03	
Nasal burning	Yes	10 (16.7%)	0.962 ± 0.390	44.80	*0.005*
	No	50 (83.3%)	0.578 ± 0.322	27.64	
Throat burning	Yes	10 (16.7%)	0.813 ± 0.452	38.45	0.115
	No	50 (83.3%)	0.678 ± 0.324	28.91	

Italics values are statisticaly significant

*Mann-Whitney *U* test

The mean respiratory exposure of employees to formaldehyde was 0.64 mg/m^3, less than the OSHA exposure allowed limit (PEL = 0.922 mg/m^3) and above the NIOSH recommended exposure limit (REL = 0.019 mg/m^3) and Iran's occupational exposure ceiling limit (OEL-Ceiling = 0.37 mg/m^3). The results of this study showed that occupational exposure of 28.3% (n = 17) of the surveyed employees was above the recommended occupational exposure limit provided by the OSHA (PEL = 0.922 mg/m^3). Of these workers, 44% (n = 15) belonged to the lab worker, and 14% (n = 2) were from the staff of lab reception. Occupational exposure of none of the servants was above the recommended limit. Jakab et al. reported a mean respiratory exposure of pathobiology lab staff with formaldehyde equal to 0.9 mg/m^3 (Jakab et al. 2010). In the study of Vimercati et al., in Italy, it was found that the mean respiratory exposure of pathobiology lab staff with formaldehyde was 0.1 mg/m^3 (Vimercati et al. 2010). Lee et al. also determined the mean respiratory exposure of pathologists to formaldehyde equal to 0.061 mg/m^3 (Lee et al. 2017). According to the study of Azari et al., in Iran, the mean respiratory exposure of pathologists to formaldehyde was 0.857 mg/m^3 (Azari et al. 2012). The mean occupational exposure to formaldehyde in the present study was lower than studies of Jakab and Azari and higher than studies conducted by Vimercati and Lee.

Comparative results of mean respiratory exposure of pathobiology employees between present study and other countries

Table 4 Lifetime cancer risk (LCR) and hazard quotient (HQ) formaldehyde in pathology lab employees

Job group		LCR	HQ (for general)*	HQ (for worker)**
Lab workers	Mean	4.44×10^{-4}	216.75	0.84
	Std. deviation	1.94×10^{-4}	94.68	0.36
Lab reception staff	Mean	3.48×10^{-4}	169.86	0.66
	Std. deviation	1.95×10^{-4}	95.25	0.37
Servants	Mean	6.16×10^{-5}	80.17	0.31
	Std. deviation	2.58×10^{-5}	33.60	0.13
Total	Mean	3.45×10^{-4}	178.49	0.69
	Std. deviation	2.27×10^{-4}	100.25	0.39

*$gRfC_{FA}$ = 3.6 μg/m^3

**$wRfC_{FA}$ = 922 μg/m^3

showed that the mean exposure of pathobiology employees in the present study was higher than that of the USA (Lee et al. 2017), Italy (Vimercati et al. 2010), France (Orsiere et al. 2006), and Portugal (Viegas et al. 2010) and lower than that of Brazil (Ochs et al. 2012), China (Fan et al. 2006), Hungary (Jakab et al. 2010), Turkey (Burgaz et al. 2002), and UAE (HH et al. 2015). The differences observed in the results of different studies may be due to differences in job duties, the amount of formaldehyde used in pathobiology laboratories, variation in ventilation and control systems, as well as differences in sampling methods and sampling air volume.

The difference in mean individual exposure between occupational groups can also be attributed to occupational duties and duration of exposure. Lab workers have a variety of tasks including sample passage, tissue processing, molding and cutting, and slide preparation in the lab, some of which cause direct exposure to formaldehyde. The most important step in tissue processing is fixation of sample, which uses formaldehyde as a fixator. The lab worker group has the highest exposure to formaldehyde during the sample passage and fixation phase (Ganjali and Ganjali 2013; Mosafer et al. 2017). Low exposure of servants to formaldehyde was also due to the low time of presence in the pathobiology laboratory (4 h per day), while lab worker and lab reception staff had 8 h of presence in lab. These results are in contrast to the results of Karami et al.'s study, which showed no significant difference in mean respiratory exposure to formaldehyde among workers of different occupational groups (Mosafer et al. 2017). Regarding the structural differences of pathobiology laboratories in Iranian medical centers as well as differences in hours of presence of different workers in the laboratory environment and exposure pattern, it seems reasonable to achieve these results.

Examination of health problems due to respiratory exposure to formaldehyde showed that wheezing (24%), burning eyes (25%), and cough (21.7%) had the highest prevalence among health problems. Also, the mean concentration of formaldehyde in respiratory air of those with cough, wheezing, burning eyes, lachrymation, and nasal burning was higher than those without these symptoms, and the difference was statistically significant. Formaldehyde has a high solubility in water and, after exposure, rapidly absorbed into the mucus of upper respiratory tract and mainly into the nasal cavity, sinuses, and throat, 97% of which are water. The mucus blanket is the first line of defense against formaldehyde exposure (Dimenstein 2009). Human studies have also shown that chronic respiratory exposure to formaldehyde stimulates the nose, throat, and eyes (14). Rahimifard et al. found that healthcare workers exposed to formaldehyde had symptoms of cough, wheezing, and burning sensation in the nose and eyes (Viegas et al. 2010). Azeri et al. reported that pathobiology employees exposed to formaldehyde had complained of various symptoms such as cough, throat irritation, burning and itching of the nose, and irritating eyes (Azari et al. 2012).

In this study, for the first time, non-carcinogenic risk was determined based on two reference concentrations (RfC) including RfC provided by the US-EPA for the general population and OSHA-provided PEL for the occupational population, and their results were compared. The results of the mean non-carcinogenic risk in the surveyed workers showed that when the non-carcinogenic risk was calculated for the general population ($gRfC_{FA} = 3.6\ \mu g/m^3$), the mean HQ was 178.49. But when the non-carcinogenic risk was calculated for labor societies ($PEL = 922\ \mu g/m^3$), the mean HQ was determined 0.69. As a result, according to the HQ of the general population, the non-carcinogenic risk for all subjects was higher than the reference level (HQ > 1). But according to the HQ of labor societies, the non-carcinogenic risk, only in 33.3% of the employees was at an unacceptable level (HQ > 1). According to the results of the study of health problems caused by respiratory exposure to formaldehyde in the surveyed workers, such as the prevalence of wheezing (24%), burning eyes (25%), and cough (21.7%), it can be concluded that the use of OSHA's PELs for occupational population compared with the RfC provided by the US-EPA (OEHHA) for public population has higher accordance with the prevalence of health problems reported by employees. Because as the non-carcinogenic risk of exposure to formaldehyde with a $gRfC_{FA} = 3.6\ \mu g/m3$ was 178 times higher than the reference value, in fact, all workers must have reported health problems. But the results of evaluation of health problems caused by respiratory exposure to formaldehyde do not indicate this. It is therefore recommended when estimating the non-carcinogenic risk of exposure to chemical compounds for occupational population using the US-EPA (OEHHA) method, PEL, TLV, REL, etc. provided by various organizations for workers should be used rather than RfC. Of course, these results are specific to this study, and further investigations are needed in other studies. The results of non-carcinogenic risk determination using $RfC_{FA} = 3.6\ \mu g/m^3$ are consistent with the results of similar studies. In the study of Karami et al., non-carcinogenic risk of respiratory exposure to formaldehyde was 281.8 times higher than the reference value in pathobiology workers (Karami Mosafer et al. 2017). Also, in a study in Taiwanese office buildings, for assessing formaldehyde exposure, it was showed that the non-carcinogenic risk limit due to respiratory exposure was 38.984 to 330.693 (Wu et al. 2003).

The mean carcinogenic risk of respiratory exposure to formaldehyde in the study subjects was 3.45×10^{-4} or 3.45 per 10,000 people. The highest mean carcinogenic risk was found in lab workers (4.44×10^{-4}). The lowest mean carcinogenic risk was also seen in the servant's occupational group (6.16×10^{-5}). According to the US-EPA standards, the acceptable risk level for environmental exposures of public to chemicals is 1 in 1,000,000 and in occupational communities is 1 in 10,000 (Gratt 1996; Mohammadyan et al. 2019). The

mean carcinogenic risk of respiratory exposure to formaldehyde in the present study was 3.45 times higher than the reference value according to the reference value in labor societies (reference value: 10^{-4}), and 81.7% (*n*:49) of employees were at unacceptable risk level. In the study of Karami et al., on occupational exposure risk assessment to formaldehyde in the pathology lab employees of Hamadan Hospitals in Iran, the mean carcinogenic risk of respiratory exposure to formaldehyde was 25.4×10^{-5} (Karami Mosafer A et al. 2017). In a study aimed at determining carbonyl compounds and cancer risk in Brazilian hospitals, Cavalcante et al. reported the risk of respiratory exposure to formaldehyde in pathology lab workers in the range of 5.23×10^{-7} to 1.35×10^{-4} (Cavalcante et al. 2006). Sousa et al. determined the carcinogenic risk of respiratory exposure to formaldehyde in the range of 2.84×10^{-6} to 3.57×10^{-5} (Sousa et al. 2011). The mean carcinogenic risk of respiratory exposure to formaldehyde in the present study was slightly higher than the mean carcinogenic risk in the study performed by Karami et al. (25.4 per 100,000 in Karami et al.'s study and 34.5 in the 100,000 in the present study). In addition, the mean carcinogenic risk of respiratory exposure to formaldehyde in the present study was 2.55 times higher than the maximum carcinogenic risk in Cavalcante study (1.35 per 10,000 people) and 9.66 times higher than the maximum concentration of formaldehyde in the Sousa study (0.357 per 10,000 people). The most important reason for the difference between the results of this study and the studies of Cavalcante and Sousa is the difference in the calculation of carcinogenic risk. Because in their study the risk of carcinogenicity was calculated for 40 years, in the present study, it was determined for 30 years. While given the similarity of the calculation of carcinogenic risk in the present study with that of Karami et al., the difference in results was slight, which may be due to difference in formaldehyde concentration and differences in exposure status of the employees.

One of the limitations of the present study was the difference in the pattern of exposure of employees during weekdays and during different seasons of the year. In the present study, we did not consider the effect of control systems and the use of respiratory protective equipment on the exposure rate of workers to formaldehyde. Also, the use of questionnaire to determine the health problems of employees can be one of the limitations of the present study, because data collection using self-reporting methods can be influenced by respondents. Lack of control group use is another limitation of the present study.

Formaldehyde is widely used as a preservative and chemical fixative in tissue processing in pathological laboratories due to its high ability to penetrate to tissue (2.7 mm every 4 h) and low cost. Its use in floor and equipment disinfection is another application of this chemical in pathology laboratories. Therefore, it is somewhat difficult to remove it because of increased laboratory costs and the absence of other tissue stabilizing agents in Iran. As a result, given the high risk of carcinogenic and non-carcinogenic exposure to formaldehyde in pathology employees, especially lab worker, the use of management controls such as adherence to guidelines and safe working procedures and reduction of exposure time by increasing the number of personnel employed, as well as the use of engineering controls such as local ventilation systems and use of respiratory protection equipment when performing sample passing and tissue processing to reduce exposure levels of all employees to less than the permitted exposure level, seems necessary.

Conclusion

Due to the high respiratory exposure of pathology employees to formaldehyde and developed health problems in the upper respiratory tract and eyes as well as the high risk of carcinogenic and non-carcinogenic respiratory exposure to formaldehyde, the use of management controls such as adherence to guidelines and safe working procedures and reduced time of exposure by increased number of personnel employed and also the use of engineering controls such as local ventilation systems as well as the use of respiratory protection equipment to reduce the level of respiratory exposure of all employees to less than the permissible exposure limit seem necessary.

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Data availability All data generated or analyzed during this study are included in this published article.

Compliance with ethical standards

Competing interests The authors declare that they have no competing interests.

Ethical approval The present study was approved by the Ethics Committee of the Birjand University of Medical Sciences through ethical code: Ir.bums.REC.1395.129.

Consent to participate Not applicable.

Consent to publish Not applicable.

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