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Risk Assessment Of Inhalation Exposure To Formaldehyde Among Workers In Medical Laboratories

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Abstract

Formaldehyde (FA) is widely used in medical laboratories and has been classified by International Agency for Research on Cancer (IARC) as a group 1 carcinogen. The aim of this study was to assess the health risk of inhalation exposure to formaldehyde among staff in medical laboratories such as those in pathology, anatomy, forensics, and parasitology. A total of 33 staff members were included in the study. Data on FA exposure were collected by air monitoring in the laboratory areas by using Gasmet DX-4030, and the human health risk was assessed by the guidelines of the US. Environmental Protection Agency (2009). The study showed that 21.21% of the personnel exposed to FA had health risks with non-carcinogenic effects (hazard quotient range = 0.02 to 11.4), and with regard to cancer risk, the highest risk was found to be in pathology technicians ($6.51x10^{-4}$), followed by investigative mortuary personnel, residents, embalming mortuary personnel, and instructors or those working in forensic laboratories ($3.25x10^{-4}$, $6.07x10^{-5}$, $3.39x10^{-5}$, and $1.27x\ 10^{-5}$, respectively). Those staff had a higher than acceptable risk of cancer ($>10^{-6}$). It is recommended that workers' FA exposure should be reduced by working with formalin in a fume hood, reducing exposure h and using respiratory cartridges.

Keywords: *Formaldehyde, Inhalation, Occupational exposure, Cancer risk, Health risk.*

1. Introduction

Formalin is one of a number of chemicals in the working environment that can cause cancer. Carcinogenesis of this substance occurs when it is changed from a solution to formaldehyde vapour (FA). It has been found that wh[1]en humans inhale FA, the most serious health effect is cancer, i.e. nasal cavity cancer [1-2]. This chemical is widely used as a food preservative to increase the shelf life of fruit and fish in tropical countries [3] and in the manufacturing of shoes, poly (vinyl chloride) (PVC), glue, paint [4], and the construction industry [5]. In addition, FA can be found in the general atmosphere from new buildings because FA is an important ingredient found in many building materials, e.g., paint [6] and it also has benefits in investigative medical procedures.

Formalin is used in medical laboratories, e.g. the anatomy lab, and is used intravenously to preserve a body. Pathology and parasitology laboratories use formalin in fixing specimens and

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biopsies for detection during pathological examination. Those workers in the laboratories exposed to FA are mortuary personnel, investigative mortuary personnel, pathology technicians, residents and instructors, who are at risk of being harmed by the toxic FA, resulting in both acute and chronic effects on health from inhalation of FA.

Previous studies, have shown health effects or symptoms of FA exposure, when exposed to even a small amount, which begin with smell recognition. Irritation of the respiratory system, dry skin disorders, eczema, eye irritation, excessive lacrimation, allergic dermatitis, bronchial asthma were observed. It is also affected on blood cell abnormality, i.e. abnormalities in white blood cells (WBCs), red blood cells (RBCs), and platelets [7]. In addition, technicians who carried out embalming showed health effects ranging from effects on smell to burning eyes and a stinging nose [8]. If high doses are received for a long time, it will eventually cause nasal cancer, especially among the occupational groups that are exposed to FA frequently, e.g. those who work in hospitals in high-risk occupations. It has been shown in medical students who took a course in practical anatomy that they had a risk of developing cancer from FA exposure through inhalation approximately five or 10 years later [9].

Thus, it is important to assess the health risks of the exposure to FA in the working environment. This study aimed to investigate the potential cancer risk of FA inhalation of the medical laboratory workers in a hospital.

2. Materials and methods

2.1 Study and collection relevant data

This study was conducted in a hospital in Makkah, Saudi Arabia and the data were collected in four laboratories of the university hospital, namely the pathology, anatomy, parasitology, and forensic laboratories. There were 33 medical laboratory workers enrolled in the study, consisting of embalming personnel, investigative mortuary personnel, pathology technicians, residents, and instructors. Data on the working conditions (working time, FA exposure frequency, working period, personal protective equipment use, occupational health training) were collected by questionnaire. The inclusion criteria were that participants had to 1) be over 20 years old, 2) have working experience in laboratories involving FA exposure of at least one year, and 3) be a volunteer. The volunteers were grouped according to their exposure to FA, in similar exposure groups (SEG). The representative workers of all medical laboratories in this setting were considered to consist of mortuary personnel (n=11), pathology technicians (n=11), investigative mortuary personnel (n=3), residents (n=6) and two instructors. Altogether, there were 23 males and 10 females.

2.2 Air sampling and analysis for formaldehyde concentration

FA concentration was measured in four laboratories. Sampling equipment was located in the centre of each lab or close to the working location at a height of 1.5 meters. Air samplings for FA concentration were performed following the recommended standard method (NIOSH 3800), by using a portable direct reading instrument (Gasmet DX-4030) at a sampling flow rate of 0.3 l/min. Extractive Fourier transform infrared (FTIR) spectroscopy was used as a measurement technique to quantify samples collected every four-hour (h) period at one location (site) in the laboratory according to the data quality objective and quality control requirements [10].

There were two sampling sites in the anatomy laboratory, three sampling sites in pathology, two sampling sites in forensics, and two sampling sites in parasitology. FA concentrations were compared with the REL-NIOSH recommended standard value of 0.016 mg/kg (19.65 µg/m^3) and a maximum of exposure (Ceiling) of 0.1 mg/kg (12.2 µg/m^3) [10].

2.3 Risk assessment

FA exposure and risk assessment was calculated by following the US.EPA [11] guidelines. Exposure concentration (EC), and exposure time (ET) values were calculated according to working conditions, and the inhalation uptake was considered as inhalation at 55% of the calculated exposure concentration (EC) [12]. The exposure intake, or EC, was calculated as follows.

$$EC = (CA \times ET \times EF \times ED) / AT \quad (1)$$

EC = Exposure concentration in air ($\mu g/m^3$)

CA = The FA concentration in ambient air, based on the air monitoring in each area of work ($\mu g/m^3$) ET = Exposure time, based on the time working with FA in each working position (h/d)

EF = Exposure frequency; 219 (days/year (d/y)) (the reference value of the working day of health care workers in the hospital according to US.EPA [11]

ED = Exposure duration; 25 years (y) [11]

AT = 25 y x 365 d/y x 24 hr/d = 219,000 (h) for the adverse health effect or AT = 70 y x 365 d/y x 24 h/d = 631,200 (hr) for the lifetime cancer risk

2.3.1 The non-carcinogenic risk characterization

An adverse health effects assessment was carried out by considering the hazard quotient (HQ), calculated as follows….

HQ = Hazard Quotient

EC = Exposure concentration ($\mu g/m^3$) at 55% inhalation uptake

where RfC= 9.8 $\mu g/m^3$ [13]; if HQ >1, there is a potential health risk from exposure, and if HQ $\leq$ 1, there is likely to be an acceptable risk of a non-carcinogenic health effect.

2.3.2 The lifetime cancer risk characterization

The cancer risk was calculated as follows.

$$Risk = IUR \times EC \quad (3)$$

IUR = Inhalation Unit Risk; 1.3×10^{-5} ($\mu g/m^3$) [14]

EC = Exposure concentration ($\mu g/m^3$) at 55% inhalation uptake.

If the lifetime cancer risk is more than 1.00×10^{-6}, exposure is likely to cause cancer in the long term, so it should be managed to reduce risk. If the lifetime cancer risk is less than or equal to 1.00×10^{-6}, it is an acceptable risk of cancer from environmental exposure.

3. Results and discussion

3.1 Characteristics of workers

The study population consisted of 33 laboratory workers, i.e. there were 11 embalming mortuary personnel, three investigative mortuary personnel, 11 pathology technicians, six residents and two anatomy instructors. The average age was 39 years old and most of the workers were 31-40 years old, education was mainly at the bachelor's degree level (39.39%), and the working time at the hospital ranged from eight h to more than 10 h (h/d). However, the workers had an exposure time of between 15 min and maximum eight h at each laboratory work location and condition where there was formaldehyde exposure. This exposure period reported by workers was further used for health risk assessment.

3.2 Formaldehyde concentration in ambient air (µg/m^3)

FA concentrations were measured in four laboratories and the average concentration in eight h of working time (time weight average: TWA) was higher than the standard 0.016 mg/kg or 19.65 µg/m^3 [10]. The average concentration in the pathology laboratory was 0.48 mg/kg, or 593.85 µg/m^3 in the anatomy laboratory, it was
0.05 mg/kg, or 66.32 µg/m^3 in the parasitology laboratory, it was 0.02 mg/kg, or 20.88 µg/m^3 and in the forensic laboratory, it was 0.03 mg/kg, or 34.39 µg/m^3. The highest concentrations (ceiling concentrations) of each area, namely the pathology and anatomy laboratory, and the forensic mortuary, were higher than the limit value set by The National Institute for Occupational Safety and Health (NIOSH) [10] at 0.1 mg/kg or 122 µg/m^3 (see

Table 1).

	TWA (min-max)		Ceiling	
	min-max; mg/kg	min-max; µg/m^3	mg/kg	µg/m^3
Pathology (n=3)	0.137-0.83	168.27-1,019.42	49.99	61,398.76
Anatomy (n=2)	0.032-0.064	39.90-78.61	0.19	233.36
Parasitology (n=2)	0.011-0.025	13.51-30.71	0.10	122.82
Forensic (n=2)	0.027-0.036	33.16-44.22	0.14	171.95

This study found that the average concentration of FA in the air of working environments was less than the TLV-TWA (0.75 mg/kg or 92.12 µg/m^3) of the eight-hour Thai Labour regulation [15], whereas it was higher than the standard set by NIOSH [10]. The results are consistent with another study in medical laboratories, where the average FA concentration was 600 µg/m^3 [8]. For mortuary personnel in forensic laboratories, the concentration found by personal air monitoring was 30 µg/m^3 while the concentration for residents in the anatomy laboratory was 380 µg/m^3, both of which were higher than the occupational setting standard set by NIOSH [9]. In addition, in a study in a gross anatomy laboratory at one medical school, the FA concentration range was similar to the one in our study (0.02-2 mg/kg or 24.57- 2,000.46 µg/m^3) [16]. The FA concentration in the medical laboratories of other countries has also been reported, e.g., in an Italian workplace, it was 0.04 mg/kg [17], and a gross anatomy laboratory of a hospital in Japan allowed the ceiling concentration to be 0.25 mg/kg [18]. The fact that our study had a concentration in the pathology laboratory (0.48 mg/kg) that was higher than those in other studies suggests that further health risk assessment on personal exposure to formaldehyde is required. In addition, the ceiling concentration of the pathology laboratory was 49.99 mg/kg, which was more than 20 times higher than the TLV-STEL set in the Thai regulation (2 mg/kg).

3.3 Formaldehyde inhalation exposure; EC (µg/m^3)

FA inhalation intake among workers ranged from 0.21 to 112.14 µg/m^3, as shown in Table 2.

Laboratories	FA exposure; EC55% (µg/m^3)				HQ	HQ>0.5	Laboratories
	Min	Max	95% CI	95th Percentile	Min	Max	n (%)
Pathology (n=11)	1.85	112.14	112.14	5.20-52.59	0.19	11.44	7 (63.64)

Anatomy (n=11)	0.91	7.30	7.30	2.19-5.79	0.09	0.74	4 (36.36)
Parasitology (n=6)	1.15	2.30	2.30	1.04-2.02	0.12	0.23	0
Forensic (n=5)	0.21	0.95	0.95	0.09-0.84	0.02	0.10	0

With regard to each position, the results showed that the workers that had the highest FA intake were the pathology technicians. Their range of FA exposure was 1.15-112.14 μg/m^3, which was followed by the investigative mortuary personnel (0.47-70.09), the residents (1.46 - 13.07 μg/m^3), the embalming mortuary personnel (0.21-7.30 μg/m^3), and the instructors (0.95-2.74 μg/m^3). With regard to the laboratories, the results showed that the pathology laboratory workers had the highest FA exposure range, which was 1.85 - 112.14 μg/m^3, followed by the workers in the anatomy laboratory, who had a range of 0.91-7.30 μg/m^3, the workers in the parasite laboratory, who had a range of 1.15-2.30 μg/m^3, and the workers in the forensic laboratory, who had an FA exposure range of 0.21-0.95 μg/m^3 (as shown in Table 2, 3).

The following is an example calculation for exposure concentration in air for the residents of the pathology laboratory.

EC = (CA × ET × EF × ED) / AT CA = 168.27 μg/m^3

ET = 4 h/day, EF = 219 day/year, ED = 5 or 10 years

This study considered AT as the lifetime period for carcinogenic risk and non-carcinogenic risk; therefore, AT = 613,200 h for lifetime cancer risk and AT = 219,000 h for non-carcinogenic risk. The calculated EC was

1.20 and 3.37 μg/m^3, respectively and the final EC at 55% inhalation uptake was 0.67 and 1.85 μg/m^3 for the resident of five years exposure in pathology laboratory. The estimation on ED of 5 or 10 years of the residents was according to the previous study [9].

	Min	Max	95th Percentile	Min	Max	n (%)
Embalming mortuary personnel (n=11)	0.21	7.30	7.30	0.02	0.74	3 (27.27)
Investigative mortuary personnel (n=3)	0.47	70.09	70.09	0.05	7.15	2 (66.67)
Pathology technicians (n=11)	1.15	112.14	112.14	0.12	11.44	4 (36.36)
Residents (n=6)	1.46	13.07	13.07	0.15	1.33	2 (33.33)
Instructors (n=2)	0.95	2.74	2.74	0.10	0.28	0

3.4 Non-carcinogenic risk assessment on adverse health effects

The assessment of the health risk from long-term FA exposure via inhalation was performed using the representative concentration of each area and a time period of exposure relative to each position when considering a 55% inhalation uptake of EC [12] and an RfC = 9.8 μg/m^3 [13]. The HQ range was 0.02 to 11.44, which indicated 21.21% of those workers had a health risk (HQ >1) and 63.64% of pathology laboratory workers had adverse effects on health. When considering a HQ >0.5 at the occupational health action level, the workers who had a risk of adverse health effects consisted of embalming mortuary personnel, investigative mortuary personnel, pathology technicians, and residents (as shown in Table 2, 3).

HQ = EC/RfC

EC$_{55\%}$ = 3.37x 55/100 = 1.85 μg/m^3

RfC = 9.8 µg/m^3

Therefore, HQ is 0.19, which shows that the health risk for the residents was acceptable (HQ <1) from this example.

Regarding assessment of non-carcinogenic risk as a long-term exposure health effect, 21.21% of the medical laboratory workers had a health risk, particularly those from the pathology laboratory. The previous study among workers exposed to FA in a medical laboratory showed that most of them had risk of HQ<1; however, there were also other workers that had a health risk of HQ>1 from higher exposure [19]. Since this study assessed the adverse health effects specific to the residents in the anatomy lab, the results of the previous study were similar to our study for the residents in the pathology laboratory, who had a risk of adverse health effects when considering the action level (HQ>0.5). This is in contrast to the risk of workers in the common workplace (office, shops, classrooms, etc.). It has been shown that most of those workers had acceptable risk [20]. With regard to the difference in working time period affecting the probability of risk, the industrial workers had a fixed period of eight h exposure, but in the laboratory, workers were mostly exposed to the chemicals for a shorter time during shift work, i.e. less than 8 h/day.

3.5 Cancer risk assessment

From the results of the cancer risk assessment, we found that all workers had an increased cancer risk (>1 $x10^{-6}$) from formaldehyde exposure in the working environment, and the workers in the pathology laboratory had the highest cancer risk. Their lifetime risk of cancer was 6.51 $x10^{-4}$, which was followed by the workers in the anatomy, parasitology, and forensic laboratories, whose risk was 3.39 $x10^{-5}$, 1.07 $x10^{-5}$, and 4.39 $x10^{-6}$, respectively. With regard to the position, the results showed that the pathology technicians had the highest risk of cancer (6.51 x 10^{-4}), followed by the investigative mortuary personnel, the residents, the embalming mortuary personnel, and the instructors, whose risk were 3.25 x 10^{-4}, 6.07 x 10^{-5}, 3.39 x 10^{-5}, and 1.27 x 10^{-5}, respectively
(as shown in Table 4, 5).

Laboratories	Cancer risk	
	Min	Max
Pathology (n=11)	$8.59x10^{-6}$	$6.51x10^{-4}$
Anatomy (n=11)	$4.23x10^{-6}$	$3.39x10^{-5}$
Parasitology (n=6)	$5.33x10^{-6}$	$1.07x10^{-5}$
Forensic (n=5)	$9.88x10^{-7}$	$4.39x10^{-6}$

Table 5:

Laboratories	Cancer risk	
	Min	Max
Mortuary personnel (n=11)	$9.88x10^{-7}$	$3.39x10^{-5}$
Investigative mortuary personnel (n=3)	$2.19x10^{-6}$	$3.25x10^{-4}$
Pathology technicians (n=11)	$5.33x10^{-6}$	$6.51x10^{-4}$
Residents (n=6)	$6.78x10^{-6}$	$6.07x10^{-5}$
Instructors (n=2)	$4.39x10^{-6}$	$1.27x10^{-5}$

The following is an example of the cancer risk assessment calculation of the residents [9]

Risk = IUR x EC,
IUR = 1.3 $x10^{-5}$ (µg/m^3) [11]

When EC = 0.67 µg/m^3, the above formula calculated that Risk = 8.59 $x10^{-6}$, which means the

residents had a lifetime risk of cancer (>1 $x10^{-6}$) equal to eight persons in a 1,000,000 population. As shown in Table 6, all residents had potential risk of developing cancer after two years of FA exposure (>1.0 $x10^{-6}$).

Years	FA intake; EC55% ($\mu g/m^3$)	Cancer risk
	Min - Max	Min - Max
1	0.08–0.47	$1.07x10^{-6}$ – $6.07x10^{-6}$
2	0.17–0.93	$2.15x10^{-6}$ – $1.21x10^{-5}$
5	0.41–2.33	$5.37x10^{-6}$ – $3.03x10^{-5}$
10	0.83–4.67	$1.07x10^{-5}$ – $6.07x10^{-5}$

In the cancer risk assessment, it was found that a longer exposure to FA resulted in an increased risk of cancer. When considering the working period of the residents with FA exposure over one, two, five or 10 years, those periods of exposure were different from medical laboratory workers in the hospital and had to be taken into account in the calculation of cancer risk. Since the residents were not routinely exposed to chemicals as much as other health workers that had 25 years' exposure, from the estimation of risk from 1 year to 10 years exposure, the results showed that residents had a higher risk of cancer when the exposure was extended to further years. That estimation is consistent with the previous study among medical students who were at risk of developing cancer after two years of FA exposure [9].

The cancer risk of the pathology and anatomy laboratory workers correlates with the genotoxic effect that has been reported from formaldehyde exposure [21]. There was a study of medical clinic workers in China who were exposed to FA in the therapy room [22] which found that the cancer risk range was slightly higher than that of the medical laboratory workers in our study. With regard to the pathology laboratory, there was a study in Malaysia concerning the FA exposure while putting specimens on slides for examination, and the cancer risk, which was calculated using the same predictive mathematical model, showed a potential cancer risk [19]. In the non-medical field, studies of FA assessment for cancer risk in gasoline station workers [23,24] found a cancer risk in the same range as the one found in our study. Although the results of those studies and our study were similar, the working conditions of the workers were different, especially the exposure time among laboratory workers, which varied among laboratory workers when compared to those doing routine work. It was shown that the medical laboratory workers' exposure to FA was less than eight h a day but the cancer risk was the same as that of other workers' risk. When the dose exposure was considered according to individual body weight (kg) and an inhalation rate of 20 m^3/day, following the United States. Environmental Protection Agency (EPA) standard [25] for chronic daily intake (CDI) assessment and cancer risk [26], it was found that all workers had a cancer risk which ranged from 2.31 $x10^{-6}$ to 9.96 $x10^{-4}$.

When comparing between the work positions in the laboratory, a higher cancer risk seemed to be found in the functions with longer working exposure to FA concentrations, particularly among the pathology technicians and the investigative mortuary personnel. On the other hand, there was a previous study, which used the CDI of FA exposure for assessment of the lifetime cancer risk among academic staff on the campus who were exposed to FA for 8-12 h per day [27], and they found that workers had a cancer risk similar to that found in our study ($1.12x10^{-4}$). In implementations to lower the risk of adverse health effects and cancer, a semi-quantitative health risk matrix should be applied in the individual exposure assessment of workers, as suggested from the previous findings in occupational settings [28], and the number of h involving FA exposure should be limited according to the position.

4. Conclusion

This study presents the results of a cancer risk assessment and long-term health risk assessment among workers in Thai medical laboratories exposed to formaldehyde. The workers had an increased cancer risk and some of them were at risk of adverse health effects from formaldehyde exposure. The pathology laboratory workers exposed to the highest concentration of formaldehyde in their working environment had the highest risk of cancer. The suggestion is that health surveillance should be provided for all workers by using a semi-quantitative occupational health risk assessment. FA concentrations were not personally monitored, which was a limitation of this study, so this should be done for the further investigation of quantitative risk assessment. In addition, personal exposure should be reduced by the using respiratory cartridges while working with formalin and working in a fume hood. Reducing the number of h exposed to FA and supporting the safer working conditions with good laboratory design and practice are recommended.

5. Ethical approval

This study was approved by Ethics Committee for Human Research

6. References

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