ORIGINAL ARTICLE

Exposure to PCDD/Fs From Peatland Fires Induces Oxidative Stress Among Fire-fighters in Peninsular Malaysia

Ahmad Shalihin Mohd Samin[1,2], Yin-Hui Leong[1], Mohamed Isa Abd Majid[1,2], *Tengku Sifzizul Tengku Muhammad[2]

[1] Malaysia National Poison Centre, Universiti Sains Malaysia, 11800 Minden, Penang, Malaysia
[2] Institute of Climate Adaptation and Marine Biotechnology, Universiti Malaysia Terengganu, 21030 Kuala Nerus, Terengganu, Malaysia

ABSTRACT

Introduction: Annually, the Malaysian Fire & Rescue Department receive at least 1,500 calls relating to open-burning particularly during the El Niño season. Combatting peatland fire is a lengthy process involving a large participation of the fire squad. Consequently, exposure to cancerous chemicals, specifically dioxins, to the fire-fighters is very high. This study examines the level of 17 congeners of dioxin/furan and its correlation with the level of oxidative stress biomarkers, 8-OHdG in the blood serum of the fire-fighters. **Methods:** Forty-two fire-fighters from five states in Malaysia identified as having involved with peatland fire extinguishing consented to donate 10 mL of their whole blood taken from cubital fossa. The blood samples were spun at 2,500G for 15 minutes and the separated serum were extracted using Accelerated Solvent Extraction method for analysis of 17 dioxin/furan congeners. A 20µL serum from each sample was drawn for oxidative stress biomarker analysis using enzyme-linked immunosorbent assay (ELISA) and its association with dioxins level. **Results:** The concentrations of dioxin/furan range between 0.0452 pg/g serum lipid to 1147.41 pg/g serum lipid. The geometric mean concentration of the most toxic congeners, 2,3,7,8-TCDD is 0.065 pg TEQ g-1 serum lipid whereas the mean±SD Control and Expose group are 7.41±5.62 and 15.14±37.06 pg TEQ g-1 serum lipid, respectively. Significantly important, the median (iqr) of the 8-OHdG concentration level detected is 13.00 (20.62) ng/mL ranging between 3.83 ng/mL to 101.00 ng/mL. **Conclusion:** The study establishes that fire-fighters extinguishing peatland fires are potentially exposed to dioxin/furan that induced the 8-OHdG level.

Keywords: Peatland fire; Fire-fighters; PCDD/Fs; 8-OHdG; Occupational exposure

Corresponding Author:
Tengku Sifzizul Tengku Muhammad, PhD
Email: sifzizul@umt.edu.my
Tel: +60124218501

INTRODUCTION

Fire-fighters are the first responders for all fire calls including open burning such as peatland forest fires. The nature of their job exposes them to many risks, among others developing non-communicable diseases (NCDs) both acute and chronic, due to high exposure to various chemicals during firefighting. Metals or heavy metals including lead, antimony, cadmium, uranium; aromatic hydrocarbons such as polyaromatic hydrocarbons, benzene, formaldehyde, toluene, methyl chloride; and minerals such as silica, asbestos, crystalline as well as different gases are harmful when exposed to fire-fighters. However, the biggest concern during fires is the formation of vast amounts of toxic by-products such as polyhalogenated aromatic hydrocarbons (PHAHs) such as chlorinated and brominated dibenzo-p-dioxins and dibenzofurans that remain persistent in the environment (1–3). According to the Fire and Rescue Department of Malaysia (FRDM), from the total exigency calls received in 2018, 38, 500 calls were fire-related and of this number 15, 629 fires involved open-burning, scrubs, forest and peat (4,5). Fires in peatland burning usually require days or even weeks to extinguish due to the massive area involved. The smouldering type of fires released smoke which have been found contains not just inorganic compounds but also volatile and semi-volatile organics (VOCs and SVOCs) including dioxin-like compound (dl-c) (6). The fire-fighters who involved in the peatland fires which need longer period of time in extinguishing process are at risk of developing diseases associated with dioxins exposure.

Dioxins, a persistence organic pollutant (POPs) emitted naturally through anthropogenic sources e.g., emissions from incinerator, landfill activities, chlorine-based factories and peatland forest burning. Dioxins

are common names for polychlorinated dibenzo-para-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) are groups of contaminants of almost planar tricyclic aromatic substances with very similar chemical properties (7). PCDDs and PCDFs can be divided into groups on their degree of chlorination which is known as homologues (8). Of the 210 congeners, seven PCDDs and ten PCDFs have been classified as the "dirtiest" congeners to the environment and humans. This is because of their similar structure to the most toxic congener, which is 2,3,7,8-tetrachlorodibenzo-para-dioxin, (2,3,7,8-TCDD or TCDD) (9). PCDD/Fs are categorised as by-products under the three types of chemicals recognised as causing adverse effects to humans and the environment in the Stockholm Convention. PCDD/Fs are listed by the Stockholm Convention as unintentional by products. Relevant parties have been urged to curb the emission of these chemicals(10). According to Leong et. al (11), human exposure to PCDD/Fs are mainly through dermal contact, inhalation and dietary intake wherein 90% of the exposure among the general population are from consumption of animal products and fish. As PCDD/Fs are highly lipophilic and tend to bioaccumulate and biomagnifies through the food chain, the half-life of the congeners in human is estimated to be 7-11 years depending on factors of age, dosage, length of exposure, diet and overall health condition (12–14).

Animal studies have demonstrated that TCDD cause oxidative stress in various tissues (15–17). The oxidative stress is mediated by the Aryl hydrocarbon receptor (AhR) following TCDD administration resulting in multiple tissues and species(18). Studies have also shown that a wide variety of antioxidants protect against TCDD-induced reactive oxygen species (ROS) generation and the harmful effects of dioxin-like compounds. These findings suggest that TCDD congeners may cause harm by changing the redox state in various organs, leading to oxidative stress and related tissue damage (19).

8-hydroxy-2'-deoxyguanosine (8-oxodGuo or 8-OHdG) is one of the most common free radicals that causes DNA lesions. The existence of 8-OHdG has been shown to retard replication dependability while increasing the likelihood of adenine combination into the complementary strand resulting in G–T transversions. Agents that raise 8-OHdG levels will therefore increase the risk of cancer. Hence, 8-OHdG appears to be a viable technique for detecting mutagenic and carcinogenic chemicals in human biomonitoring (20–22). Numerous studies relating to chemical exposure, physical stress, diabetes and tobacco smoking that induce oxidative stress have applied 8-OHdG levels as a biomarker (23–25).

The aim of this study is to evaluate the level of PCDD/Fs in the blood serum of fire-fighters from five selected states in Peninsular Malaysia whose duties involved combating peatland fires and correlate the PCDD/Fs level with their oxidative stress 8-OHdG biomarker level. This study finding will provides valuable information to the FRDM concerning the level of exposure of hazardous chemicals emitted from peatland wildfires which are potentially cancer-causing to their fire-fighters. Not only FRDM, but this study will also serve as a reference for other related department such as Forestry Department and Department of Environment (DOE) for appropriate actions on annual fire incidents. Furthermore, the findings of this study could potentially assist the FRDM towards developing better policies and strengthen exiting guidelines in protecting their fire-fighters.

MATERIALS AND METHODS

This study has received Ethical Approval from the Human Research Ethical Committee of USM (JEPeM), ethical number 17010015. Prior to blood sampling, 371 fire-fighters from five states in Malaysia were surveyed for their demographics and background. Based on analysis from self-answered questionnaire, 30 of the subjects were grouped as Expose and 12 as Control based on the main criteria of whether they had responded to peat burning operations in the past five years. Prior to the blood taking, the selected fire-fighters' weight and height were measured for bodyfat percentage. They were also instructed to fast overnight prior to the blood taking process. 10-15 mL of blood from each subject was drawn from cubital fossa. The collected blood was transferred into two 9 ml sterile Vacutest® clot activator, red cap, (Vacutest® kima, Padua, Italy) and allowed to coagulate before it was spun at 2500g for 15 minutes to obtain the serum samples. Serum samples were labelled and kept frozen at -20℃ for analysis within a week.

PCDD/Fs Analytical procedure

The analytical procedure of PCDDs and PCDFs in serum samples were measured as described in the USEPA Method 1613b (26) and Zhang et. al (27) using gas chromatography with high-resolution mass spectrometry (GC-HRMS). All solvents used for the procedure were pesticide grade residue. In brief, 1-2 mL serum was extracted with Dionex ASE 350 Accelerated Solvent Extractor (Thermo Fisher Scientific, CA USA), n-hexane/dichloromethane/acetone mixture (45:45:10 v/v) were used as solvent extraction. The extracted sample was concentrated to near 1 mL and purified using tandem columns of acid silica gel column and carbon mini-column (CAPE Technologies,

South Portland, ME USA). The system was pressurised to create a flow rate of 1 mL/min. The interested congeners were collected from the carbon mini-column using 40mL toluene twice that eluted 17 PCDD and PCDF congeners. The fraction containing PCDD/Fs was concentrated almost to dryness and then dissolved to approximately 50 µL nonane. For the Quality Control (QC) and Quality Assurance (QA), 13C-labelled surrogate standards and injection standards were spiked prior to extraction and before instrumentation analysis. The percentage recovery of the labelled compound was acceptable between 40% to 140% for all 17 congeners of 2,3,7,8-substituted extraction standards which is within the acceptable range by the USEPA 1613b. The World Health Organization Toxic Equivalency Factors (WHO2005-TEF) were used to report PCDD/Fs Toxic Equivalent Quotients (TEQs) (28).

Measurements of serum 8-OHdG level

Serum 8-OHdG level was measured using competitive Enzyme Linked Immunosorbent Assay (ELISA) principle. The commercial ELISA kit, catalogue number E-EL-0028, 96T (Elabscience, Texas, USA) was employed in this study in accordance with the original manufacturer user manual. The prepared samples were measured spectrophotometrically at a wavelength of 450 ± 2 nm. The concentration of 8-OHdG in the samples was determined by comparing the optical density (OD) of the samples to the standard curve.

Statistical Analysis

For comparison of two independent groups with normal distribution, the student t-test was used; in the case of non-normal distribution, the Mann-Whitney U test was applied. The Chi-squared test was used for the comparison of the categorical data. The correlation between PCDD/Fs TEQ and the 8-OHdG level was assessed with Spearman correlation analysis. Statistical data calculations were performed using IBM SPSS Statistics, version 26 (IBM Corp., Armonk, N.Y., USA) predictive analytics software.

RESULTS

Forty-two fire-fighters were recruited (voluntarily) from five selected states in Peninsular Malaysia (Pahang, Terengganu, Kelantan, Johor and Selangor). Socio-demographic characteristics of those subjects are reported in Table I. Fire-fighters were assigned into two groups, Control (n = 12) and Expose (n = 30) with median age 38 and 40.50 years old respectively. The median Body Mass Index (BMI) for the Control group is 24.59 kgm-2 and 26.84 kgm-2 among the Expose group, comparatively higher. However, the median for Percentage Body Fat (%BF) for both groups are at good level with 17.90% and 21.85% for Control and Expose respectively. Fire-fighters in this study had job experience ranging from 5.5 to 22.50 years, with the median being 13 years for the Control group and 17.50 years for the Expose group. There was no significant statistical difference in the socio-demographic traits of the fire-fighters ($p > 0.05$). Questionnaire responses on hours and number of times involved in environmental fires extinguishing included garden, bushes/scrubs, forest, and peatland fires. Peatland fires extinguishing recorded the highest Mean± SD in number of calls (173.23±171.32) and hours of involvement (1861.67±1043.18). Only the Expose group reported that they have been involved in environmental fires, especially peatland fires.

The Toxic Equivalent Quotient (TEQ) value were based on toxic equivalent factors (TEFs) reported by the WHO(28). The serum PCDD and PCDFs, seven and ten congeners concentration respectively are expressed in pg/g lipid and the total TEQ are presented in Table II. The concentrations of the 17 congener PCDD/Fs of all analysed samples varied from 0.4524 to 1147.4075 pg/g serum lipid. Geometric mean concentration of total PCDDs (7 congeners), total PCDFs (10 congeners) and total PCDDs+PCDFs (17 congeners) are 158.85, 167.26 and 326.10 pg/g serum lipid respectively. Both congeners, PCDDs and PCDFs contributed to the total concentration

Table I : General characteristics of the fire-fighters volunteered donating blood samples

	Control n = 12 Median ($Q_1 – Q_3$)	Expose n = 30 Median ($Q_1 – Q_3$)	P-value[a]
Age, years	38.00 (30.50 – 46.00)	40.50 (33.25 – 45.25)	0.451
BMI, kg/m^2	24.59 (22.74 – 28.83)	26.84 (25.19 – 29.82)	0.113
Body Fat, %	17.90(14.38 – 24.99)	21.85 (18.99 – 26.58)	0.113
Operational experience as fire-fighters, year	13.00 (5.50 – 22.50)	17.50 (10.00 – 22.00)	0.309

[a] Significance level (p) in group comparison: Mann-Whitney U test

Table II : PCDD/Fs concentrations (pg/g lipid) in blood serum sample (N=42)

Congeners or TEQ	Minimum	Maximum	AM[a]	SD[b]	GM[c]	WHO_{2005}TEF	GM[c] WHO_{2005}-TEQ
PCDDs							
2,3,7,8-TCDD	0.0452	93.3354	4.0767	18.3469	0.0648	1	0.0648
1,2,3,7,8-PeCDD	0.0452	86.6256	4.4742	17.5387	0.1080	1	0.1080
1,2,3,4,7,8-HxCDD	0.4524	50.9456	5.7709	11.6562	1.0505	0.1	0.1050
1,2,3,6,7,8-HxCDD	0.4524	97.4572	5.3066	18.2535	0.6931	0.1	0.0693
1,2,3,7,8,9-HxCDD	0.4524	56.6465	5.3561	12.6608	0.9394	0.1	0.0939
1,2,3,4,6,7,8-HpCDD	4.5245	47.9595	6.4528	7.7205	5.1736	0.01	0.0517
OCDD	150.8159	150.8159	150.8159	0.0000	150.8159	0.0003	0.0452
PCDFs							
2,3,7,8-TCDF	0.0452	19.8579	0.6792	3.1898	0.0631	1	0.0631
1,2,3,7,8-PeCDF	1.5082	17.6455	1.8924	2.4900	1.5991	0.03	0.0480
2,3,4,7,8-PeCDF	0.1508	47.8991	3.0691	10.8008	0.2390	0.3	0.0717
1,2,3,4,7,8-HxCDF	0.4524	32.7572	2.1319	6.6850	0.5957	0.1	0.0596
1,2,3,6,7,8-HxCDF	0.4524	45.3805	3.5797	8.9572	0.7748	0.1	0.0775
1,2,3,7,8,9-HxCDF	0.4524	165.9578	6.4301	26.7253	0.6917	0.1	0.0692
2,3,4,6,7,8-HxCDF	0.4524	33.3454	1.4597	5.2450	0.5394	0.1	0.0539
1,2,3,4,6,7,8-HpCDF	4.5245	45.2448	6.2589	6.9678	5.1848	0.01	0.0518
1,2,3,4,7,8,9-HpCDF	4.5245	1147.4075	36.2497	176.1275	6.7552	0.01	0.0676
OCDF	150.8159	150.8159	150.8159	0.0000	150.8159	0.0003	0.0452
Total PCDDs	156.7882	583.7858	182.2531	86.1766	158.8453		0.5381
Total PCDFs	163.3789	1706.3116	212.5666	247.1885	167.2588		0.6076
Total (PCDDs+PCDFs)	320.1671	2290.0974	394.8197	333.3650	326.1041		1.1457

[a]Arithmetic Mean [b]Standard deviation [c]Geometric Mean

Table III : 8-OHdG Biomarker Concentration Level in Blood Serum of Fire-fighters

	Range (Min-Max) ng/mL	Median (Iqr) ng/mL	Z-statistic[a]	*P*
Overall Samples (N=42)	3.83 – 101.00	13.00 (20.62)		
Control (n=12)	5.01 – 17.83	11.76 (6.89)	-1.643	0.1
Expose (n=30)	3.83 – 101.00	15.13 (37.99)		

[a]Mann-Whitney test, significant at p<0.05

Table IV : Spearman's correlation coefficients between 8-OHdG and serum dioxins level and various independent variables

Variables	Dioxin levels[a]	8-OHdG	Age	BMI	%BF	Working period
Dioxin level[a]	1	-0.272	0.078	0.006	0.006	0.061
8-OHdG	-0.272	1	0.110	-0.089	-0.089	0.100
Age	0.078	0.110	1			
BMI	0.006	-0.089		1		
%BF	0.006	-0.089			1	
Working period	0.061	0.100				1

[a]Total TEQ value PCDD/Fs

of the dioxins equally. On the individual congeners contribution of PCDD and PCDF towards the concentration of Dioxins, the highest geometric mean concentration were contributed by OctaCDD and OctaCDF with 150.8159 pg/g lipid serum respectively followed by 1,2,3,4,7,8,9-HeptaCDF (6.7552 pg/g serum lipid), 1,2,3,4,6,7,8-HeptaCDF (5.1848 pg/g serum lipid) and 1,2,3,4,6,7,8-HeptaCDD (5.1736 pg/g serum lipid). OctaCDD and OctaCDF contributed 46% each for the total concentration of PCDDs and PCDFs. 1,2,3,4,7,8,9-HeptaCDF and 1,2,3,4,6,7,8-HeptaCDF contributed nearly 4% to the overall concentration of Dioxins congeners. Congeners of PCDDs and PCDFs in pg WHO2005-TEQ g-1 serum lipid level ranged between 0.0452 to 0.1080 (Table II). The geometric mean of total PCDDs and PCDFs WHO2005-TEQ concentrations in samples are 0.5381 and 0.6076, respectively. The geometric mean of the overall congeners WHO2005-TEQ concentration is 1.15 pg WHO2005-TEQ g-1 serum lipid WHO2005-TEQ g-1 serum lipid. The pre-dominant congeners contributed to the total PCDDs and PCDFs TEQ level were derived from the 1,2,3,7,8-PentaCDD and 1,2,3,4,7,8-HexaCDD. The range of WHO2005-TEQ for each subject was between 0.554 and 150.905 pg WHO2005-TEQ g-1 serum lipid with a geometric mean of 3.62 pg WHO2005-TEQ g-1 serum lipid. Comparatively, the Control group showed higher geomean of TEQ (5.52 pg WHO2005-TEQ g-1 serum lipid) than the Expose group (3.05 pg WHO2005-TEQ g-1 serum lipid).

In Table III, the median (Iqr) level of the biological marker for oxidative stress, 8-OHdG in blood serum in overall sample was 13.00(20.62) ng/mL, ranged between 3.83 to 101.00 ng/mL. Fire-fighters in the Expose group (15.13, Iqr 37.99) had higher concentration of 8-OHdG level compared to the Control group (11.76, Iqr 6.89); however, both were not significantly different statistically. Table IV shows two-tailed Spearman's correlation coefficients between serum 8-OHdG levels and dioxins TEQ was not significant and negatively correlated (r=-0.272, p=0.081). Also, 8-OHdG concentration negatively correlated with BMI and %BF but not significantly different statistically.

DISCUSSION

To our best knowledge, this is the first study of its kind quantifying the levels of 8-OHdG and dioxins serum lipid in fire-fighters involved with putting out tropical peatland fires. In this study, we sought to determine whether PCDDs and PCDFs, a carcinogenic, induces oxidative stress that damages DNA and mutagen formation. Fire-fighters who are expose to peatland fire suppression were anticipated to have higher level of dioxins and 8-OHdG concentrations compared to those who were not actively involved in similar activities. According to Chernyak et. al (29), such exposure to fire-fighters varies depending on the number of fires, types of fire-fighting performed, job responsibilities and personal habits. Activities during and after fire combating and self-cleaning after fire suppression are also factors that exposes fire-fighters via inhalation and dermal contact (30,31).

The results indicates that fire-fighters who were exposed to peatland fire suppression have fairly higher mean concentration of total PCDDs (182.25±86.18) and PCDFs (212.57±247.19) compared with Taiwanese fire-fighters involved with multiple types of fires (30) and New Zealand fire-fighters who were stationed near a herbicide plant and frequently visited(32). Both studies involved almost similar number of subjects as with this study. However, in this study, the geometric mean (GM) of TEQ was presented due to the non-normal distribution of the TEQ concentration also used by Leong et. al (33) and Edelman et. al(34). The overall GM WHO2005-TEQ of the 17 congeners is 1.15 pg TEQ g-1 serum lipid, lower compared to the Taiwanese (12 pg TEQ g-1 lipid), New Zealand (8.7 pg TEQ g-1 lipid) or Russia (12.4 pg TEQ g-1 lipid) fire-fighters studies (29,30,32). This is because the TEQ is described in GM while other studies reported in arithmetic mean (AM). However, the AM of the overall samples TEQ was 12.93 pg TEQ g-1 serum lipid comparable to Hsu et. al(30), with 15.14 pg TEQ g-1 serum lipid and 7.41 pg TEQ g-1 serum lipid in the Expose and Control group respectively. Subjects in the Control group in this study show higher TEQ compared to the general population sample, either individual or pooled (35). The higher level of dioxins TEQ in serum lipid of the Control subjects could be due to other factors such as involvement in other types of fires that also contribute to PCDD/Fs emission e.g., structure fires, life style and daily food intake that contribute >90% of dioxins to human body burden (31). In this study, the predominant PCDDs and PCDFs congeners that contribute to the total dioxins' concentration are OCDD and OCDF. This is similar to several studies involving fire-fighters. (29,30,32,36). This study observes no statistical difference between the Control and Expose group when PCDD/Fs TEQ in the groups were compared. This could be due to the relatively small sample size in the Control group.

Many studies have reported the concentration of serum 8-OHdG using a kit in application with competitive ELISA method acknowledged to produce reliable and valid data in discovering the oxidative DNA damage (37–39). In this work, 8-OHdG concentration was utilised to correlate with dioxins congeners concentration to test the hypothesis that 8-OHdG concentration is positively correlated with dioxins concentration and increases as dioxins concentration rises. The results shows that the

8-OHdG concentration level among the Expose subjects are higher compared to those assigned as Control who were less exposed to the peatland fires. The negative correlation between the biological marker, 8-OHdG and TEQ serum dioxins level in this study aligns with Yoshida et. al (40). According to Yoshida et. al (40), negative correlation may be caused by oxidative damage activating the DNA repair system or upregulating the main defences.

CONCLUSION

This study offers crucial baseline information on the background of PCDD, PCDF and 8-OHdG concentrations in Malaysian fire-fighters who are regularly involved with fighting annual peatland fires. The fire-fighters in this study who dealt more frequently with peatland fires and spent longer duration at the burning site showed higher level of PCDD/Fs compared to other fire-fighters whose exposure to peatland fires were less. This study also detected the exposed fire-fighters having higher 8-OHdG level in their blood serum. However, this study shows negative association between the dioxins' concentration and oxidative stress biomarker. Medical surveillance is suggested because of the high level of dioxins and 8-OHdG biomarkers. It is also recommended that fire-fighters involved in peatland fires must adhere strictly to existing Standard Operating Procedures provided by the Malaysia Fire and Rescue Department. This study has a limitation number of participant due to not many of the fire-fighter volunteered to participate in donating their blood for chemical analysis.

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