EVALUATION OF DIABETES PREVALENCE OF MILITARY PERSONNEL WORKING IN DIOXIN-CONTAMINATED AIRBASES IN VIETNAM

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SUMMARY

Objectives: *To evaluate the risk of diabetes of military personnels in three dioxin-contaminated airbases in Vietnam, including Bien Hoa, Da Nang and Phu Cat.* ***Subjects and methods:*** *A total of 699 military personnels (666 men and 33 women) from three dioxin-contaminated airbases (Bien Hoa, Da Nang, and Phu Cat) were recruited for the study from August to December of 2017. Plasma glucose and HbA1c concentrations were measured and prevelance of prediabetes and diabetes based on these indexes were estimated.* ***Results:*** *The prevalence of males with glucose levels > 7.0 mmol/L and HbA1c > 6.4% was 2.1% and 1.5%, respectively and overall rate of diabetes was 2.9%. Only one female showed HbA1c > 6.4% (3.0%), and no women showed glucose levels > 7.0 mmol/L. The prevalence of pre-diabetes was 21.2% for glucose index and 20.1% for HbA1c index and the overall rate of pre-diabetes was 35.3% in males. In women, these prevalence were 33.3%, 30.3% and 45.5%, respectively. In men, there were positive and significant correlations between age, the length of service and plasma glucose as well as HbA1c.* ***Conclusions:*** *The prevalence of diabetes was low whereas that of pre-diabetes was high in military personnels. Plasma glucose levels increased with the length of service, suggesting that a long history of dioxin exposure in the airbases may increase the risk of diabetes.*

* Keywords: Dioxins; Agent orange; Type 2 diabetes mellitus; Military personnels.

INTRODUCTION

Dioxin is a group of chemical compounds that are persistent organic pollutants in the environment and accumulate in organisms and the human body. From 1962 to 1971, the US military carried out a campaign of herbicide spraying in Vietnam (coding Ranch Hand) in order to effectively target defoliation and crop destruction of opposite forces. Unfortunately, the herbicides (approximately 2/3 of which was agent orange, were contaminated with the most toxic congener of dioxins-2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-tetraCDD). Several former U.S military airbases in Vietnam that used for storage of herbicides during the campaign,

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such as Bien Hoa, Da Nang and Phu Cat were reported as hot spots of dioxin contamination [7]. Military personnels and the populations working and living inside and around these airbases have been at higher risks of dioxin exposure. Several recent epidemiology studies showed that dioxin concentration in breast milk of mothers living near Bien Hoa and Da Nang airbases were 3 - 4 times higher than in the North of Vietnam [3]. Similarly, dioxin concentrations in blood of men living near Phu Cat and Bien Hoa airbase were significantly higher than those in the North [4]. It raised public concern of dioxin effects on human health in these populations.

Since 1994, scientists from National Academies of Sciences, Engineering, and Medicine (U.S) comprehensively evaluated scientific and medical information regarding the health effects of exposure to dioxins. According to the classifications of dioxin-related diseases by biennial reports, it was not clear whether the evidence regarding exposure to the dioxins and type 2 diabetes mellitus should be classified as "limited or suggestive" or "sufficient" due to controversial results among studies [1]. However, in 2008, diabetes was classified as one of 17 dioxin-related diseases by the Ministry of Health in Vietnam. Type 2 diabetes accounts for 90 - 95% of all diagnosed diabetes cases, however, its causes are not completely understood. There is a strong link with age, obesity, physical inactivity and poor diet and nutrition [8]. Therefore, it needs furthers studies to clarify the associations of dioxins and diabetes.

The purpose of the present study was: *To evaluate the risk of diabetes of military personnels in three dioxin-contaminated airbases in Vietnam, including Bien Hoa, Da Nang, Phu Cat through analyzing plasma glucose and HbA1c concentrations.*

SUBJECTS AND METHODS

1. Subjects and locations

From August to December of 2017, a total of 699 military personnels in three dioxin-contaminated airbases of Bien Hoa, Da Nang and Phu Cat were recruited for the study.

* Criteria for selection:

Military personnels have worked in target airbases for at least 1 year; age ranges from 20 - 55.

As the most contaminated airbase, number of subjects was the highest in Bien Hoa (n = 305), followed by Da Nang (n = 221) and Phu Cat (n = 173). Written informed consent was obtained from all of the subjects according to a process reviewed and approved by the local medical units in the each airbase and Vietnam Military Medical University. The biomedical ethics committee at Vietnam Military Medical University approved the study design (No.2061/QD-HVQY).

2. Methods

This is a cross-sectional study.

* Procedures:

- Information collection: Each subject was interviewed and examined in local health stations in each airbase by a medical doctor. Basic information such as age,

gender, smoking habits, drinking, education, marriage, and residence were collected by questionnaires. Medical information of each subject was recorded in a consistent study form.

- Local nurses measured the height, weight of each subject.

- Determination of plasma glucose and HbA1c concentrations: Venous blood samples (5 mL) were collected from each subject between 7:30 and 11:00 a.m after an overnight fast and were stored in heparin tubes for measurement of plasma glucose and EDTA tubes for measurement of HbA1c concentrations.

* Diagnostic criteria of pre-diabetes, diabetes:

Reference ranges for plasma glucose and HbA1c were made on the guidelines of diagnosis and treatment by Health Ministry (2017) based on diagnostic criteria of the American Diabetes Association (ADA).

- Diagnostic criteria of diabetes: Glucose > 7.0 mmol/L, and/or HbA1c > 6.4%.

- Diagnostic criteria of prediabetes: Glucose: 5.6 - 7.0 mmol/L, and/or HbA1c: 5.7 - 6.4%.

* Statistical analysis:

SPSS (version 21.0) was used for statistical analysis. A total of 699 subjects (666 men and 33 women) completing the questionnaires and blood collections were analyzed. Subjects were divided into male and female groups. General information, plasma glucose and HbA1c concentrations as well as the prevalence of normality, pre-diabetes, and diabetes were described as means ($\overline{X} \pm$ SD) or percentage (%).

Associations of plasma glucose and HbA1c concentration with age (years), the length of service, and BMI were illustrated by correlation coefficients of Spearman's rho tests. Statistical significance was set at $p < 0.05$.

RESULTS

Table 1: Characteristics of subjects.

Characteristics	Males	Females
	$\overline{X} \pm$ SD	$\overline{X} \pm$ SD
Age (years)	41.6 ± 6.9	47.8 ± 5.1
Height (cm)	167.3 ± 4.7	156.2 ± 4.5
Weight (kg)	65.5 ± 7.9	54.1 ± 7.1
BMI (kg/m^2)	23.4 ± 2.4	22.1 ± 2.3
Length of service (years)	17.4 ± 7.7	21.4 ± 9.1
Smoking (%)	63.7	0.0
Alcohol consumption (%)	94.0	8.8
Activities of daily living in airbase (%)	34.2	89.3

(SD: standard deviation; BMI: body mass index)

Both males and females had a long length of service in these dioxin-contaminated airbases (17.4 years and 21.4 years, respectively). The average BMI of subjects were within normal limits (< 25). The prevalence of smoking and alcohol consumption was high in men (63.7% and 93.4%, respectively) but quite low in women (0.0% and 8.8%, respectively).

Table 2: Mean values of plasma glucose and HbA1c.

	Males			Females			p
	Min	**Max**	**$\overline{X}$ ± SD**	**Min**	**Max**	**$\overline{X}$ ± SD**	
Glucose (mmol/L)	2.8	14.0	5.1 ± 0.98	4.5	6.6	5.3 ± 0.66	0.25
HbA1c (%)	1.9	10.4	5.2 ± 0.57	4.2	7.0	5.3 ± 0.57	0.23

(Min: minimum; Max: maximum; HbA1c: hemoglobin A1c)

Mean values of plasma glucose (< 5.6 mmol/L) and HbA1c (< 5.7%) in men and women were within the normal range, with no statistically significant difference between two groups (p = 0.23).

Table 3: Blood glucose level and HbA1c in the healthy subjects and military personnels with pre-diabetes and diabetes.

Group			HbA1c (n, %)			Total (n, %)
			< 5.7%	**5.7 - 6.4%**	**> 6.4%**	
Males	Glucose (mmol/L)	< 5.6	419 (62.9)	91 (13.7)	1 (0.2)	511 (76.7)
		5.6 - 7.0	97 (14.6)	40 (6.0)	4(0.6)	141 (21.2)
		> 7.0	6 (0.9)	3 (0.4)	5 (0.7)	14 (14.6)
	Total (n, %)		522 (78.4)	134 (20.1)	10 (1.5)	666 (100.0)
Females	Glucose (mmol/L)	< 5.6	18 (54.5)	4 (12.1)	0 (0.0)	22 (72.6)
		5.6 - 7.0	4 (6.2)	6 (18.2)	1 (3.0)	11 (27.4)
		> 7.0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Total (n, %)		22 (60.7)	10 (30.3)	1 (3.0)	33 (100.0)

There were 19 male military personnels (2.9%) with diabetes, only one female showing HbA1c > 6.4% (3.0%), and no women showing glucose levels > 7.0 mmol/L. Meanwhile, the prevalence of prediabetes was high, approximately 1/5 (21.2% for glucose index and 20.2% for HbA1c index) in men, and approximately 1/3 (33.3% for glucose index and 30.3% for HbA1c index) in women. According to standard guideline of pre-diabetes with glucose levels of 5.6 - 7.0 mmol/L and/or HbA1c of 5.7 - 6.4%, the prevalence of pre-diabetes was 35.3% in men and 45.5% in women.

Table 4: Relationship between age, length of service and BMI with plasma glucose and HbA1c.

	Males				Females			
	Glucose		HbA1c		Glucose		HbA1c	
	r	p	r	p	r	p	r	p
Age	0.11	0.004	0.13	0.001	-0.11	0.55	-0.20	0.27
Length of service	0.09	0.027	0.06	0.13	0.03	0.87	-0.04	0.83
BMI	0.05	0.23	0.06	0.11	0.06	0.77	-0.06	0.77

(r: correlation coefficient; p value by Spearman's rho)

In men, there were positive and significant correlations between age and plasma glucose (r = 0.11; p = 0.004) as well as HbA1c (r = 0.13; p = 0.001). Length of service was positively and significantly correlated with plasma glucose (r = 0.09; p = 0.027), but not with HbA1c. However, there was no significant correlation between BMI and plasma glucose as well as HbA1c. In women, there were no significant correlations between ages, length of service in dioxin-contaminated airbases and BMI with either plasma glucose or HbA1c concentrations.

DISCUSSIONS

In this study, the prevalence of subjects showing plasma glucose levels > 7.0 mmol/L and/or HbA1c > 6.4% was 2.9%, which was higher than our previous reports being 1.6% [5]. In another study conducted on 90 men and 305 women living around Da Nang and Bien Hoa airbases (mean age: 38.8 for men and 39.9 for women), the prevalence of diabetes was only 1.1% in men and 1.6% in women [2], which was lower than that in general population in Vietnam (5.7%) [9]. However, the incidence of diabetes increased with age, 3 - 4 times higher in over-50-year age group as compared with group under age 40 years. In this study, we found significant and positive correlations between glucose and HbA1c with age in men. Even though the diabetes prevalence was low, the prevalence of prediabetes was quite high in this population, approximately 35% for men and 45% for women, and higher than that in general population in Vietnam (13.7%) [6]. The subjects in these studies were relatively young (approximately 40 years old), therefore, they may be at a high risk of diabetes in later years.

Regarding associations between dioxin exposure and diabetes, several worldwide epidemiological studies on US veterans participating in Ranch Hand campaign have been carried out. Michalek et al revealed a strong association between 2,3,7,8-TCDD and diabetes in Ranch Hand veterans after adjustment for calendar

period of service, days of spraying [10]. Longnecker et al evaluated the association of plasma dioxin level with prevalence of diabetes and with levels of plasma insulin and glucose among 1,197 veterans and showed associations between dioxin exposure and diabetes [11]. An exceptionally large epidemiological study on diabetes and mortality rate on more than 111,000 Korean Vietnam veterans alive in 2000 showed a higher risk of developing type 2 diabetes in those with high exposure to herbicide after an adjustment for age, military rank, smoking, drinking, domestic herbicide exposure, physical activity, education, income, and BMI [12]. However, in a statistics on diabetes - related mortality rate on 180,639 Korean Vietnam veterans with herbicide exposure, there was no difference in levels of exposure among the groups. Another longitudinal 20-year study on Vietnamese veterans also reported abnormalities on glucose, diabetes prevalence and use of oral medications to control an increased diabetes, and time of diabetes onset decreased with dioxin exposure in men. Meanwhile, there was no significant association in women [6]. In the present study, we found a positive association with weak level between length of service and fasting plasma glucose in men, indicating that a long history of dioxin exposure in the airbases increases the risk of diabetes.

The causes of type 2 diabetes are not completely understood but there is a strong link with overweight, obesity, increasing age as well as ethnicity and family history. Some important disease modifying risk factors include: excessive adiposity (obesity), poor diet and nutrition, physical inactivity and smoking [9]. Increasing BMI is a major risk factor for diabetes mellitus. Both men and women in the overweight category ($25 \leq BMI \leq 30$) were at an increased risk of developing diabetes, with the increasing rate of 30% and 10%, respectively. At $30 \leq BMI \leq 40$, both genders were at a 100% of greater risk of diabetes than those with a normal BMI. $BMI \geq 40$ increased the odds of getting diabetes as much as 150% for women and 180% for men [9]. In our study, the average BMI of subjects were within normal limits, and we did not find the significant association between BMI with plasma glucose and HbA1c.

There are some limitations in the present study. Without an age-matching control group, it is difficult to speculate whether the dioxin exposure increases the prevalence of prediabetes and diabetes in these military personnels. Furthermore, due to a small number of female workers in the military airbases, the limited sample size of female group might lead to bias in estimation of the prevalence as well as risk factors.

CONCLUSION

Based on the plasma glucose and HbA1c concentrations, the diabetes prevalence of military personnels in dioxin-contaminated airbases was low (2.9 - 3.0%). However, the prevalence of pre-diabetes was quite high, approximately 35% in men, and 45% in women. Plasma glucose levels increased with length of service, indicating that a long history of dioxin exposure in the airbases may increase the risk of diabetes.

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