

Comparison of prostate specific antigen levels in serum between herbicides/dioxin-hot spot and non-sprayed areas in Vietnam

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Introduction

Between 1961 and 1971, the US military used over 80 million liters of chemical herbicides in Vietnam for general defoliation and crop destruction in a program code named Operation Ranch Hand¹. Vietnam War veterans exposed to Agent Orange (AO) have greatly increased risks of prostate cancer and even greater risks of getting the most aggressive form of the disease as compared to those who were not exposed². In 1998, the USA National Academy of Science concluded 'limited/suggestive evidence' of an association between AO and prostate cancer. Studies of the relation of AO with prostate cancer in recent years have focused on American veterans who had undergone the Vietnam War, but there are few studies about the relation of AO with prostate specific antigen (PSA) in Vietnam. The aim of this study was to compare the PSA levels between hotspot area and non-sprayed area.

Materials and methods

The study was conducted in Phu Cat district (Binh Dinh province) and Kim Bang district (Ha Nam province). Phu Cat airbase is one of three main dioxin hotspots in southern Vietnam. Subjects are known to have been living in and around the airbase prior to the war. Kim Bang district is located in northern Vietnam and did not experience herbicide operations during the war, which is why it was selected as the control site. Subjects consist of 101 men in hotspot area and 48 men in non-sprayed area aged over 50 years old. About 5 ml of whole blood and health status questionnaire were collected from each subject in August of 2009 and 2010. On 6 persons who showed high PSA levels (> 3 ng/ml) in 2009, follow-up study was conducted by urologist using PSA and digital examination in 2010.

Results and discussion:

Mean age of subjects in hotspot (68.0 years old) was significantly older than that (65.0 years old) in non-sprayed area (Table 1). No significant difference was shown to PSA values between hotspot (0.93 ng/ml) and non-sprayed area (0.76 ng/ml). Prevalence of high PSA levels (> 3 ng/ml) was not significantly different between hotspot (14 men; 13.9 %) and non-sprayed area (3 men; 6.4 %) (Table 2). After adjusting age, PSA values in hotspot was significantly higher than those in non-sprayed area ($p=0.04$) (Fig. 1). After follow-up to 6 persons, PSA levels in 2010 increased except for one (Table 3). In the control group, no significant difference was shown to PSA values between soldiers (0.72 ng/ml) and non- soldiers (0.83 ng/ml) (Table 4). No significant difference was shown to PSA values between subjects exposed to herbicide (0.76 ng/ml) and non- exposed subjects (0.76 ng/ml), either (Table 5). Depending on occupation (farmer and others), no significant difference was found between hotspot and non-sprayed area (Table 6,7). Recent cohort study to Vietnam War USA Veterans clarified that twice as many men exposed to Agent Orange were identified with incidence of prostate cancer; developed the disease at a younger age, and had a more aggressive variant than their unexposed counterparts². This study was first conducted on dioxin and PSA in Vietnam. It was not determined whether PSA levels were different between hotspot and non-sprayed area even though significant difference was shown after age-adjust and prevalence of high PSA levels was higher tendency in hot spot than in non-sprayed area. The sample size is not enough to evaluate PSA. Further study will be needed.

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References:

1. Stellman JM, Stellman SD, Christian R, Weber T, Tomasallo C. (2003); *Nature*. 422: 681-7
2. Chamie K, White RW deVere, Lee D, Ok JH, Ellison LM. (2008); *Cancer*. 113(9): 2464-70

Table 1 Characteristics of the subjects in hotspot and non-sprayed areas

		Hot spot area			Non-sprayed area			P-value
		N	Mean±SD number	%	N	Mean±SD number	%	
Age	(years)	101	68.0±6.1(54-81)		47	65.0±4.8(56-77)		0.004 ¹⁾
Height	(cm)	101	156.9±5.5		47	159.7±5.1		0.003 ¹⁾
Weight	(kg)	101	49.2±7.6		47	52.0±7.6		0.006 ¹⁾
BMI		101	19.9±2.5		47	20.7±2.6		0.08 ¹⁾
Family income	(VND)	94	(1.3±1.4)×10 ⁶		46	(1.2±1.1)×10 ⁶		0.9 ¹⁾
PYesent Job	(Yes)	101	69	68.3	47	22	46.8	0.01 ²⁾
Kind of pYesent job								
Multiple-choice	(Yes)	69	2	2.9	22	0	0	
Farmer	(Yes)	67	52	77.6	22	10	45.5	
Worker	(Yes)	67	0	0	22	1	4.5	
Fisher	(Yes)	67	0	0	22	1	4.5	
Teacher	(Yes)	67	0	0	22	0	0	
Other job	(Yes)	67	15	22.4	22	10	45.5	
Past Job	(Yes)	101	36	35.6	47	37	78.7	0.0001 ²⁾
Kind of post job								
Multiple-choice	(Yes)	36	1	2.8	37	1	2.7	
Farmer	(Yes)	35	15	42.9	37	10	27.0	
worker	(Yes)	35	1	2.9	37	8	21.6	
Fisher	(Yes)	35	0	0	37	0	0	
Teacher	(Yes)	35	2	5.7	37	3	8.1	
Other job	(Yes)	35	17	48.6	37	15	40.5	
Level of education								
Elementary school	(Yes)	101	50	49.5	47	11	23.4	
Junior high school	(Yes)	101	32	31.7	47	27	57.4	
High school	(Yes)	101	16	15.8	47	6	12.8	
University	(Yes)	101	1	1.0	47	3	6.4	
Unknown		101	2	2.0	47	0	0	
Alcohol habit	(Yes)	101	46	45.5	47	23	48.9	0.7 ²⁾
Kind of Alcohol								
Multiple-choice	(Yes)	46	8	17.4	23	9	39.1	
Beer	(Yes)	38	16	42.1	14	2	14.3	
Wine	(Yes)	38	22	57.9	14	8	57.1	
Other alcohol	(Yes)	38	0	0	14	1	7.1	
Unknown		38	0	0	14	3	21.4	
smoke habit	(Yes)	101	62	61.4	47	36	77	0.07 ²⁾
Join the army	(Yes)	101	34	33.7	47	32	68.1	0.0001 ²⁾
Exposure to Herbicides during the Vietnam War								
Yes		101	26	25.7	47	22	46.8	0.02 ²⁾
No		101	64	63.4	47	24	51.1	
Unknown		101	11	10.9	47	1	2.1	
Herbicides were sprayed directly on body								
Yes		101	10	9.9	47	8	17.0	0.13 ²⁾
No		101	85	84.2	47	39	83.0	
Unknown		101	6	5.9	47	0	0	
Level of exposure with herbicides								
Heavy	(Yes)	101	35	34.7	47	14	29.8	
Average	(Yes)	101	3	3	47	3	6.4	
Slight	(Yes)	101	0	0	47	3	6.4	
Never	(Yes)	101	0	0	47	0	0	
Had trees fallen leafs in you Resident place	(Yes)	101	25	24.8	47	19	40.4	
Your wife were exposed by Herbicides								
Yes		101	16	15.8	47	1	2.1	0.002 ²⁾
No		101	75	74.3	47	46	97.9	
Unknown		101	10	9.9	47	0	0	
Level of exposure with herbicides								
Heavy	(Yes)	16	13	81.3				
Average	(Yes)	16	1	6.3				
Slight	(Yes)	16	0	0				
Never	(Yes)	16	0	0		2		
Exposure to pesticides	(Yes)	101	61	60.4	47	25	53.2	0.41 ²⁾
Exposure to other chemicals	(Yes)	101	9	8.9	47	6	12.8	0.47 ²⁾
Your wife had reproductive failure	(Yes)	101	32	31.7	47	22	46.8	0.08 ²⁾
Kind of reproductive failure								
Abortion	(Yes)	32	24	75	22	16	72.7	
Still birth	(Yes)	32	6	18.8	22	5	22.7	
Preterm delivery	(Yes)	32	5	15.6	22	3	13.6	
Other	(Yes)	32	1	3.1	22	1	4.5	
Your children have birth defects	(Yes)	101	11	10.9	47	7	14.9	0.49 ²⁾

Data are Means±SD or number(%), BMI(body mass index)

¹⁾ t-test, ²⁾ Chi-square-test

Table 2 PSA levels in hotspot and non-sprayed areas

		Hot spot area			Non-sprayed area			P-value
		N	number	%	N	number	%	
PSA(Mean±SD)	(ng/ml)	101	1.38±1.43		47	1.02±0.99		0.11 ¹⁾
PSA(GM GSD)	(ng/ml)	101	0.926 2.45		47	0.759 2.09		0.18 ¹⁾
PSA>3ng/ml	(ng/ml)	101	14	13.9	47	3	6.4	0.27 ²⁾

¹⁾ t-test, ²⁾ Fisher's exact test

Table 3 Follow-up studies of PSA levels in serum in 2010 and their variance rate those PSA levels were over 3 ng/ml in 2009 at a hotspot area

Age	Serum PSA (ng/mL)		Variance rate (%)
	2009	2010	
73	7.48	8.65	15.7
64	3.84	7.88	105.4
80	3.15	3.0	-4.8
75	3.37	5.09	51.0
74	6.06	8.02	32.5
60	4.49	6.42	43.1

Table 4 Comparison of PSA between soldiers and non-soldiers in control area

Kim Bang	Soldier	Non-soldier	P-value*
N	32	15	
Age(Mean±SD) (years)	64.9±4.6	65.3±5.3	0.83
PSA(GM GSD) (ng/ml)	0.72 2.0	0.83 2.40	0.6

*t-test(PSA were shown values of logarithmic transformation)

Table 5 Comparison of PSA between exposed and non-exposed persons in control area

Kim Bang	Exposed	Non-exposed	P-value*
N	22	24	
Age(Mean±SD) (years)	65.6±4.1	64.9±5.1	0.58
PSA(GM GSD) (ng/ml)	0.76 2.0	0.76 2.24	0.96

*t-test(PSA were shown values of logarithmic transformation)

One person answered "unknown" was excluded

Table 6 Comparison of farmer's PSA between hotspot and non-sprayed areas

Farmer	Hot spot area	Non-exposed area	P-value*
N	52	10	
Age(Mean±SD) (years)	69±5.4	62±3.7	0.0002
PSA(GM GSD) (ng/ml)	0.95 2.63	0.91 2.14	0.92

*t-test(PSA were shown values of logarithmic transformation)

Two persons of multiple-choice were excluded

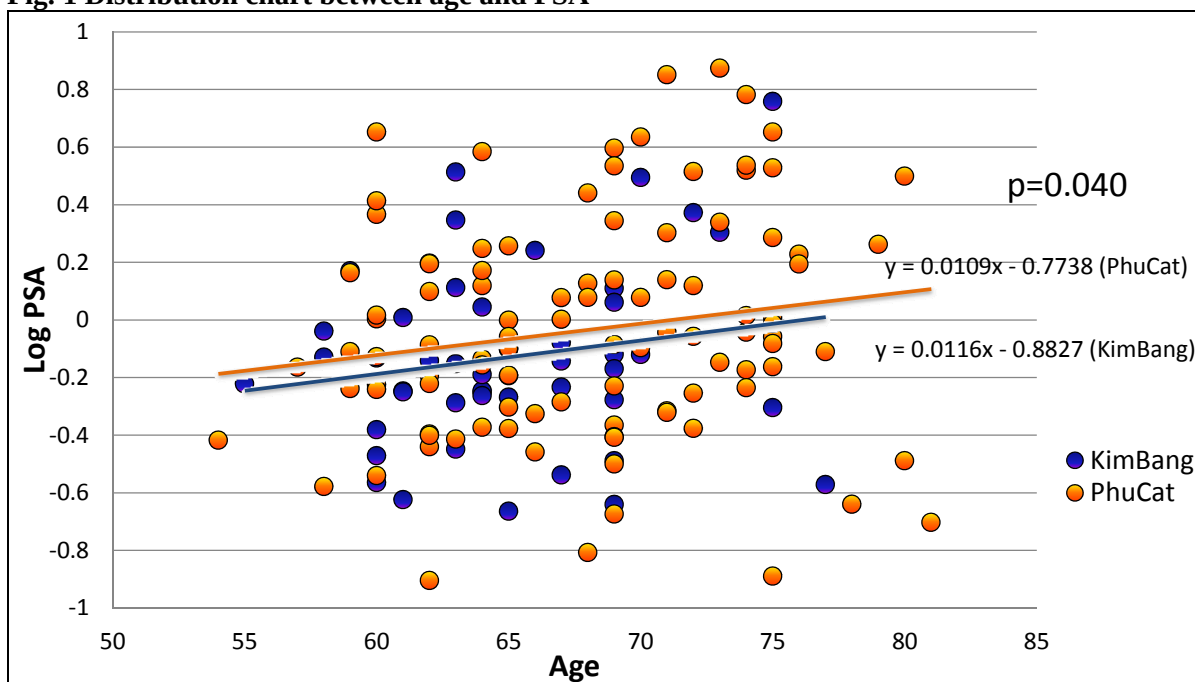
Table 7 Comparison of other occupational PSA between hotspot and non-sprayed areas

Other job	Hot spot area	Non-exposed area	P-value*
N	15	10	
Age(Mean±SD) (years)	64.5±4.5	65±5.7	0.82
PSA(GM GSD) (ng/ml)	0.93 2.04	0.71 2.0	0.34

*t-test(PSA were shown values of logarithmic transformation)

Two persons of multiple-choice were excluded

Fig. 1 Distribution chart between age and PSA



*PSA were expressed by logarithm

Analysis of covariance (ANCOVA) was used.