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Exposure to Organophophate Pesticides and Neurobehavioral Performance among Paddy Farmers in Tanjung Karang, Selangor

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ABSTRACT

Objective: Pesticides are widely used throughout the world especially in the agriculture and pest control as well as for community health purposed. Agriculture workers are exposed to pesticide primarily throughout mixing, spraying, loading and cleaning up pesticide containers. The study aim was to determine whether pesticide exposure biomarker, blood cholinesterase level would affect the neurobehavioral performance of the paddy farmers. **Method**: To fulfill this objective, a total of 94 of paddy farmers as exposed group and 30 farmers as control group participated in this study by completing a set of questionnaire, capillaries blood were collected from finger prick technique and neurobehavioral score determined using WHO Neurobehavioral Core Test Battery (NCTB) . **Result:** Results showed that mean of blood cholinesterase level for exposed group (34.84) was significantly lower than the control group (88.33). The mean NCTB score for exposed group was 357.87 while for the control group was 369.67. There was a significant difference ($p< 0.05$) between both groups for Trial Making Test and Pursuit Aiming Test. The duration of employment (year) was the most significant variables related to the cholinesterase level ($p \leq 0.001$), in which, it significantly influenced the Benton Visual Retention Test ($p = 0.025$). The education level was significantly related to the Digit Symbol Test ($p = 0.023$), and the duration of employment (year) significantly related to Santa Ana Manual Dexterity Test ($p = 0.017$). **Conclusion**: In conclusion, duration of employment (year) significantly influenced the blood cholinesterase level which was related the Benton Visual Retention Test score, while the education level significantly influenced the Digit Symbol Test. The duration of employment (year) significantly related to the Santa Ana Manual Dexterity Test

Keyword: *Pesticide, Neurobehavioral test, Cholinesterase enzyme*

1. Introduction

Pesticides are toxic chemicals that are widely used throughout the world. It used extensively throughout the world in agriculture and in pest control as well as for community health purposes (Farahat et al., 2003 ; Rastogi et al., 2010). Agriculture workers are exposed to pesticides primarily through mixing of chemicals, loading into dispensers, application clean up, and disposal of empty chemical containers Pesticides are widely used in agriculture sector to kill a pest. Pesticides are any substance or mixture of substance intended for, preventing, destroying, repelling or mitigating any pest. Approximately 16 000 pesticide products are registered with the EPA. These products are based on approximately 600 active ingredients. Most pesticide products (approximately 80 percent by volume) are used by the agricultural industry (Donaldson et al., 2002). There are many types of pesticides used in the agriculture such as insecticides, algaecides, bactericides, fungicides, rodenticides, mollucicide, nematicides, miticides, virucides, and avicides.

Pesticides can cause a wide range of health problems, ranging from acute and persistent injury to the nervous system, injury to reproductive systems, birth defects, cancer and skin damage (AFHH, 2011), but primarily it damages the nervous system. The World Health Organization (WHO) estimate that each year, 3 million workers in agriculture in developing world experience severe poisoning from pesticides. Poisoning from pesticides affects 68 000 farmers and workers every day. Annually, as many as 25 million workers suffer from pesticide poisoning through the world. Some evidence for the presence of an undiagnosed reservoir of chronic neurotoxic disease related to pesticide exposure was found in a pilot study in the apple farming industry in Western Cape in 1992 (London et al., 1998). Acute effect for pesticides poisoning include nausea, vomiting, diarrhea, abdominal cramps, general weakness, headache, tremors and excessive sweating. In serious cases, respiratory failure and death can occur (Tapia et al., 2005). For chronic effect it is frequently involves a neurotoxin effect. Another effect include birth defects, toxicity to fetus, production of benign or malignant tumors, genetic changes, blood disorders, nerve disorder, endocrine disruption and reproduction effects (Diane et al., 2006).

Organophosphate pesticide is the inhibitor for cholinesterase enzyme. Cholinesterase is one of many important enzymes needed for the proper function of the nervous system of human, other vertebrates and insects. Their toxicity is primarily due to the inhibitory effect on acetyl cholinesterase (AChE), an enzyme whose function is to inactivate the neurotransmitter acetylcholine (ACh) at the junction of various nerve endings. Enzyme inhibition results in an abnormal accumulation of Ach at the cholinergic receptor sites, leading to “over-stimulation”. Ach can then build up, causing a “jam” in the nervous system. Thus when a person receives to great an exposure to cholinesterase inhibiting chemicals, the body is unable to break down the Ach. So the stimulation signal cannot stimulate (Smith et al., 1983).

Safety measures were not generally practised and workers have poor knowledge and training in the safe handling of these pesticides. These produced populations with higher exposures as described in the other studies reported to date (Farahat et al., 2002). This study examined the AChE enzyme levels due to the exposure to organophosphate (OP) pesticide and to determine the association between AChE enzyme with neurobehavioral performance of the paddy field farmers.

2. Materials and Method

2.1 Participants

This study was conducted during the pesticide application period at Sawah Sempadan, Tanjung Karang, Selangor with approximately 2, 300 hectares of paddy field area. Currently, the farmers used organophosphate (OP) insecticide, mollucicide, and herbicide to control pest infestation of the paddy plants. The participating farmers were selected based on these inclusion criteria, namely male, age below 60 years, not color blind and non-alcoholic. About 94 farmers were randomly selected from the name lists that fulfilled the inclusion criteria and have volunteered to participate in this study. Another group of 30 farmers who have the similar socio-demographic background and have not handled pesticide in their work activities, were randomly selected as the control group.

2.2 Equipments

2.2.1 Questionnaire

A set of questionnaires was used to gather information on socio-demographic, socio-lifestyle, work background, pesticide use, personal protective equipment (PPE) use and general health status.

2.2.2 Blood Cholinesterase Analysis.

The individual blood cholinesterase collected were analyzed using Cholinesterase Test Kit (LOVIBOND 412670 AF267). This is the rapid method for testing the cholinesterase level in whole blood. The test kit requires only 0.01 ml blood from each respondent, which may easily be obtained from finger pricks. There were two types of reagents used, namely the indicator and substrate solution. The indicator solution which consists of bromothymol blue dissolved in 250ml of deionized water (CO_2 free) while the substrate solution consists of 0.25g of acetylcholine perchlorate dissolved in 50ml of deionized water (CO_2 free). The entire test took about 4 minutes. The cholinesterase activity in the blood is expressed as a percentage (%) of the activity in normal blood. Table 1 indicates the percentage of cholinesterase activity in the respondents’ blood.

Table 1: Blood cholinesterase level in percentage.

Percentage (%)	Indicator
100.0 – 75.0	Normal
74.9 – 50.0	Over exposure
49.9 – 25.0	Serious over exposure
24.9 – 0.0	Very serious and dangerous over exposure

2.2.3 Neurobehavioral Test

The Neurobehavioral Core Test Battery (NCTB) consists of tasks that measure performance of neurologic function, such as the ability to learn, reaction time, memory, and coordination. It used widely to detect the dysfunction of nervous system caused by neurotoxin agents. The NCTB consists of seven tests, namely, the Benton Visual Retention Test, Digit Symbol Test, Digit Span Test, Pursuit Aiming Test, Time Reaction/Movement Test, Santa Ana Manual Dexterity Test and Trial Making Test (WHO, 1994). The raw score (raw data) from NCTB test should be modified to make it comparable to scores collected from other studies. The standard score for NCTB requires computation of mean and standard deviation from all subjects from each test and the standard score. Below is the standard score formula:

Standard Score = [(raw score – mean) / SD] x 10 + 50

2.3 Quality Control

Pre-test of questionnaire was conducted among 10 percent of the total respondent which aims to ensure the validity and reliability of the questions set. Standard Operating Procedure (SOP) of blood finger prick method was referred to in order to get the 0.01 ml of blood from the respondents. The World Health Organization (WHO) SOP for NCTB test also was referred and training was conducted before the test. This is to make sure the results are accurate and comparable to other results.

2.4 Study Ethic

An ethic application for research study was approved by Ethic Committee from Faculty of Medicine and Health Sciences (FMHS), UPM. Respondents were given details explanation on the potential risks and possible effects from participating this study by researcher. Only respondents who fulfilled the inclusion criteria and gave written consent were recruited.

3. Results

3.1 Socio-demography

This study was conducted on 94 paddy field farmers exposed to pesticide during mixing, loading and spraying activities. While for the control group made up of 30 farmers who were not exposed to the pesticide. The mean and different of socio-demography for both group are shown below (Table 2).

3.2 Socio-lifestyle, Types of Pesticide Used and Work Activities

About 63 of the exposed group (67%) and 20 of the control group (70%) were smokers, while 76 of the (81%) exposed group and 28 (81%) of the control group took bath after their work time. Daily clothes change was reported among all exposed and control group. In this study, result showed 88 persons (93.6%) apply insecticides in their paddy field, followed by 83 persons (88.3%) apply herbicides in their paddy field and 82 persons (87.2%) use mollucicide. From the result, it showed the exposed group carried out three types of work activities which were mixing, spraying, and fertilizing. There were 94 respondents (100%) who did mixing and spraying activities while 89 respondents (94.70%) did fertilizing activity.

Table 2: Respondents' socio-demography different between exposed and control group.

Variables	Mean (SD)		t	p
	Exposed (N = 94)	Control (N = 30)		
Age (Year)	40.65 (12.69)	47.63 (8.54)	-3.43	0.01*
Monthly Income (RM)	1299.36 (473.20)	1874.33 (267.11)	-8.33	$\leq$ 0.01*
Work Period (Year)	16.15 (13.18)	13.97 (6.66)	1.20	0.23
Number of children	2.38 (2.10)	4.33 (1.79)	4.581	$\leq$ 0.01*

N = 124; SD = Standard Deviation; **Significant* at p $\leq$ 0.05

3.3 Personal Protective Equipment (PPE) Use

The results showed that most of the exposed group used safety boot, mask and head cover. There were 89.4% who used mask, followed by 83.0% used head cover and 71.3% used safety boot when they do their work in the field.

3.4 Signs of Acute Exposure

From the result, health symptoms reported by the exposed group were diarrhea, excessive sweating, shivering, and difficulties in breathing, eye redness and muscle weakness (Table 3).

Table 3: Symptoms reported by the exposed group.

	Yes	No
Variables	**Freq (%)**	**Freq (%)**
Nausea	4 (4.3)	90 (95.7)
Vomiting	3 (3.2)	91 (96.8)
Diarrhea	24 (25.5)	70 (74.5)
Headache	8 (8.5)	86 (91.5)
Shiver	15 (16.0)	79 (84.0)
Excessive sweating	15 (16.0)	79 (84.0)
Blurred vision	9 (9.6)	85 (90.4)
Difficulty in breathing	10 (10.6)	84 (89.4)
Eye redness	11 (11.7)	83 (88.3)
Convulsion	2 (2.1)	92 (97.9)
Mouth foaming	0 (0.0)	94 (100.0)
Mental confusion	3 (3.2)	91 (96.8)
Muscle weakness	11 (11.7)	83 (88.3)
Coma	0 (0.0)	94 (100.0)
	0 (0.0)	94 (100.0)

N = 94

3.5 Blood Cholinesterase Level

The mean for the exposed group was lower than control group ($p < 0.001$). Statistics showed there was a significant difference in the cholinesterase level between the exposed and control group ($Z = -8.151$, $p \leq 0.001$) (Table 4)

Table 4: Blood cholinesterase level

Variable	Mean (SD)		Z	p
	Exposed N = 94	**Control N = 30**		
Cholinesterase Level in blood (%)	34.841 (23.324)	88.333 (8.644)	-8.151	≤ 0.001

N = 124
SD = Standard Deviation

3.6 Neurobehavioral Performance Score

The result showed that there were significant different between both group in the 2 of neurobehavioral test which is Trial Making test ($Z = -2.464$, $p = 0.014$) and Pursuit Aiming test ($Z = -4.468$, $p \leq 0.001$) (Table 5).

Table 5: Comparison of neurobehavioral performance scores for both groups

Variable	Mean (SD)		Z	p
	Exposed N = 94	**Control N = 30**		
Benton Visual Retention Test	50.96 (9.954)	53.33 (11.842)	-0.910	0.363
Digit Span Test	51.06 (10.418)	52.33 (8.584)	-1.042	0.297
Digit Symbol Test	56.91 (13.522)	58.67 (12.243)	-0.648	0.517
Santa Ana Manual Dexterity Test	49.68 (10.519)	53.33 (9.589)	-1.523	0.128
Time Reaction/Movement Test	49.47 (10.612)	47.00 (9.154)	-1.163	0.245
Trail Making Test	50.21 (10.972)	44.67 (7.761)	-2.464	0.014*
Pursuit Aiming Test	49.57 (10.966)	60.33 (11.885)	-4.468	≤0.001*
Total NCTB Score	357.87 (32.125)	369.67 (36.623)	-1.692	0.093

N = 124
SD = Standard Deviation
**Significant* at p ≤ 0.05

3.7 Relationship between Blood Cholinesterase Level with Neurobehavioral Performance Score

The result showed that there was significant inverse correlations between Benton Visual Retention Test with blood cholinesterase level ($p = 0.020$) (Table 6).

3.8 Selected Variables Which Influences Blood Cholinesterase Levels.

In this test, the dependent variable was cholinesterase level while independent variable was age, monthly income, duration of employment (year), duration of work daily (hour), PPE, smoking habit and smoking frequency (year). It showed that the duration of employment (year) was the only variables which significantly influenced the cholinesterase levels among the respondents (Table 7).

3.9 Selected Variables Which Influences Total Neurobehavioral Performance Score

Multiple Regression analysis was carried out to identify independent variable which significantly influenced the total NCTB scores. Coefficient of multiple determinations (R) is 0.027 that means about 3% of the selected predictors fit the model. Nonetheless, at the 5% significant level, none of the selected factors did not significantly influence the total NCTB scores among the exposed group.

3.10 Selected Variables Which Influenced Each Neurobehavioral Performance Score

Multiple Regression analysis was carried out to identify independent variable which significantly influenced the Benton Visual Retention Test score among the exposed group. In this test, the dependent variable was Benton Visual Retention Test score while independent variable was age, education years, duration of employment (year), duration of work daily (hour), cholinesterase level, PPE, smoking habit and smoking frequency (year).

Coefficient of multiple determinations (R) is 0.107 that means about 11% of the selected predictor factors fit the model. Nevertheless, at the 5% significant level, it showed that cholinesterase level is the only variables which significantly influenced the Benton Visual Retention Test scores ($p = 0.025$) (Table 8).

Multiple Regression analysis was used to identify the independent variable which significantly influenced Digit Symbol Test score showed that the education year is the only variables which significantly influenced the Digit Symbol Test score ($p = 0.023$) (Table 9). Results from the same statistical test also showed that duration of employment (year) was the only variables which significantly influenced the Santa Ana Manual Dexterity Test scores ($p = 0.017$) (Table 10).

Table 6: Correlations between cholinesterase levels with neurobehavioral score

Variable	Cholinesterase Level (%)	
	r	P
Benton Visual Retention Test	-0.240	0.020*
Digit Span Test	-0.025	0.812
Digit Symbol Test	-0.015	0.889
Santa Ana Manual Dexterity Test	-0.041	0.696
Time Reaction/Movement Test	-0.037	0.727
Trail Making Test	0.058	0.581
Pursuit Aiming Test	0.146	0.160
Total NCTB Score	0.096	0.290

N = 94; **Significant* at $p \leq 0.05$

Table 7: Selected variables which influence cholinesterase levels among the exposed group

Dependent Variable	Regression Coefficient (β)	t	P
(Constant)	-	2.913	0.005
Age	0.222	1.260	0.211
Monthly Income	-0.028	-0.281	0.780
Duration of Employment (Year)	-0.511	-3.711	$\leq$ 0.001*
Duration of Work Daily (Hour)	-0.079	-0.788	0.433
PPE	0.013	0.126	0.900
Smoking Habit	-0.067	-0.357	0.722
Smoking Frequency (Year)	-0.051	0.266	0.791

N = 94; Regression Method = Enter; F value = 2.613; r = 0.419; $R^2 = 0.175$

Table 8: Selected variables which influence Benton Visual Retention Test score among exposed group.

Dependent Variable	Regression Coefficient (β)	t	P
(Constant)	-	6.545	≤ 0.001
Age	0.021	0.111	0.912
Education (Year)	0.164	1.484	0.142
Duration of Employment (Year)	0.022	0.140	0.889
Duration of Work Daily (Hour)	-0.011	-0.103	0.919
Cholinesterase Level	-0.260	-2.274	0.025*
Smoking Habit	0.007	0.034	0.973
Smoking Frequency (Year)	-0.068	-0.336	0.738
PPE	-0.135	-1.254	0.213

N = 94; Regression Method = Enter; F value = 1.275; r = 0.327, R^2 = 0.107

Table 9: Selected variables which influence Digit Symbol Test score among exposed group.

Dependent Variable	Regression Coefficient (β)	t	P
(Constant)	-	3.755	≤ 0.001
Age	0.032	0.172	0.864
Education (Year)	0.255	2.308	0.023*
Duration of Employment (Year)	0.189	1.191	0.237
Duration of Work Daily (Hour)	0.037	0.358	0.722
Cholinesterase Level	0.016	0.140	0.889
Smoking Habit	0.074	0.375	0.709
Smoking Frequency (Year)	-0.033	-0.165	0.869
PPE	-0.108	-1.005	0.318

N = 94; Regression Method = Enter; F value = 1.321; r = 0.333, R^2 = 0.111

Table 10: Selected variables which influence Santa Ana Manual Dexterity Test score among exposed group.

Dependent Variable	Regression Coefficient (β)	t	P
(Constant)	-	6.310	≤ 0.001
Age	0.311	1.649	0.103
Education (Year)	-0.040	-0.359	0.720
Duration of Employment (Year)	-0.392	-2.437	0.017*
Duration of Work Daily (Hour)	-0.047	-0.447	0.656
Cholinesterase Level	-0.156	-1.348	0.181
Smoking Habit	-0.131	-0.656	0.514
Smoking Frequency (Year)	-0.153	-0.747	0.457
PPE	0.006	0.058	0.954

N = 94; Regression Method = Enter; F value = 0.978; r = 0.290 , R^2 = 0.084

4. Discussion

4.1 Socio-demography

This study involved 124 farmers which made up of 94 paddy farmers as exposed group while 30 small scaled farmers from other areas as control group. The paddy farmers were selected as exposed group because their widely usage of pesticide especially organophosphate pesticides. While the small-scale farmers was selected as control group because they never use of pesticide in their work task. The workers were selected by following the inclusive criteria such as age of 18 to 60, not alcoholic, literate, and not color blind. According to WHO (1986), matching process is very important when comparing between two study groups. This is because the confounding factors might influence the study group. For this study, these were the major confounding factors because they might influence the neurobehavioral performance.

4.2 Blood Cholinesterase Level

Blood usually was used as the biomarkers to determine the pesticide contamination in the body. In this study, capillary blood was drawn through the finger prick technique in order to determine the blood cholinesterase levels by using a rapid test kit. Previous study showed that organophosphate pesticide is the inhibitor for cholinesterase enzyme (Smith et al., 1983). Cholinesterase is one of many important enzymes needed for the proper function of the nervous system of human, other vertebrates and insects. The presence of pesticide in blood prevents the breakdown of acetyl cholinesterase and then causing a "jam" in the nervous system.

As shown in Table 1, blood cholinesterase level was determined based on the percentage the normal level. The analytical results showed that the cholinesterase enzyme levels in the blood of the exposed group was 34.84% (indicate as serious over exposure of 25 - 50%). While for control group showed the mean was 88.33% (indicate as normal exposure from 100 - 75%). The principle of test kit is based on the colorimetric concept which changes of color depending on the pH variation when blood cholinesterase liberates acetic acid. When the solution contain respondent blood were acidic, the color of solution changes from blue to yellow.

4.3 Neurobehavioral Performance Score and Comparison Between Exposed and Control Group

These results were similar to the WHO, in which the Time Reaction/Movement Test and Trial Making Test should have higher score for exposed group and lower score for control group. It is because Time Reaction is the test to show how fast the respondents react. Therefore, lower time for reaction, the better they perform in the test. The Trail Making Test also needs the faster time to settle the task, which indicates better neurobehavioral performance.

4.4 Relationship between Cholinesterase Levels with Neurobehavioral Performance Score

Cholinesterase levels can vary considerably between individuals, so a baseline must be established for each person prior to handling such pesticides or at least 30 days from the most recent exposure to organophosphates. Establishing an accurate baseline value often requires that two tests be performed at least 72 hours apart, but not more than 14 days apart. Handlers of organophosphates should have their cholinesterase levels monitored periodically, so they can compare results with the previously established baseline level (Fishel, 2012). In this study, capillaries blood was collected about two to three hour after the farmer perform their daily work task which were mixing, loading, and spraying the pesticide and the data collection for neurobehavioral test was conducted after the blood taken. In other words, this explained the reason of no significant relationship between cholinesterase levels with neurobehavioral performance. A more proper approach is recommended as accordance to previous (Fishel, 2012) where a baselines value and after pesticide exposure value of cholinesterase level shall be recorded when analyzing for the chronic neurobehavioral performance.

4.5 Selected Variables Which Influences Blood Cholinesterase Level

The duration of work showed the most significant variables which influenced the blood cholinesterase level. This result was supported by Mekonnen, (2005) which showed that an abnormal reduction in cholinesterase activity of workers exposed to chemical pesticides is almost always a result of absorption of an anti-cholinesterase compound. As a result, exposure of workers to organophosphate or carbamate pesticides is the main cause for significant depression of cholinesterase activity.

4.6 Selected Variables Which Influences Neurobehavioral Performance Score

The regression analysis showed that cholinesterase level was the variables which influences the most on the Benton Visual Retention Test. According to previous study (Wesseling, 2002), cholinesterase inhibitors bind to acetyl-cholinesterase, the enzyme that controls the transmission of the nerve impulses at the cholinergic synapses throughout the nervous system. This results in the accumulation of acetylcholine at the neuro-junctions and the appearance of a cholinergic syndrome. The same study also stated that workers previously poisoned with cholinesterase inhibiting pesticides tended to perform less well on psychomotor and visual motor tests as compared with a non-poisoned control group. Duration of work tend to be the most significant variables which influences the Santa Ana Manual Dexterity Test. This result showed that the longer duration of exposure to pesticide, the lower the level of cholinesterase level in blood of respondents.

5. Conclusion

In conclusion, no relationship was showed between blood cholinesterase levels with the total NCTB scores in both groups, however, there were significant relationship between cholinesterase with a test items namely Benton Visual Retention Test scores. There was a significant difference in the blood cholinesterase levels of both groups. The duration of employment was significantly related to the cholinesterase levels as well as the Santa Ana Manual Dexterity Test scores among exposed group which signified exposures to pesticides. The low cholinesterase levels impaired the NCTB tests which required motor and memory ability. Organophosphates, thus, are neurotoxin chemicals which should be controlled in the use and require adequate protection for long-term use in agricultural activities.

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