PARKINSONISM AND RELATED FACTORS AMONG ELDERLY FARMERS LIVING IN A CHILLI FARM AREA IN HUA RUA SUB-DISTRICT, MUANG DISTRICT, UBONRATCHATHANI, THAILAND

Sunit Kukreja[1], Wattasit Siriwong[1, *], Somrat Lertmaharit[1, 2], Saowanee Norkaew[1], Mark Robson[3]

[1] College of Public Health Sciences, Chulalongkorn University, Bangkok 10330, Thailand
[2] Department of Preventive and Social Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand
[3] School of Environmental and Biological Sciences, Rutgers University, New Brunswick, NJ, USA

ABSTRACT:

Previous studies had reported that pesticide exposure and various types of pesticides used may cause the symptoms of parkinsonism. To explore the association of parkinsonism in farmers, the risks factors such the demographics and pesticide exposure and pesticide prevention must be studied. 271 participants that consisted of elderly farmers with average of 50 and above, both current and former, were selected for this study. The risk factors involved were analyzed using chi square to determine the association with the risk of parkinsonism. Age, pesticide combination and use of organochlorine and herbicides were the strongest risk factors parkinsonism ($p<0.01$). Other risk factors included medical history, years living in the area, farm size, farming experience and activities with pesticides and pesticide preparation at home. Use of medication to treat hypertension and diabetes as well as the correct use of personal protective equipment was found to reduce the risk of parkinsonism ($p<0.05$). Long-term exposure to pesticides, particularly organochlorine and all groups of herbicides, appear to have begun to cause the symptoms of parkinsonism among the farmers. Future studies will be required for understanding the mechanisms of PD in order to establish the causal relationship specific to a factor or specific pesticide such as those of organochlorine, paraquat or glyphosate.

Keywords: Parkinson's disease, Parkinsonism, Elderly, Farmers, Exposure, Pesticides

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INTRODUCTION

Thailand is an agricultural country with high usage and import of pesticides. It ranks 3rd among Asian countries in terms of pesticide import as well as consumption [1]. Some of these pesticides include herbicides, insecticides, growth stimulators, etc. Pesticide could be useful in terms of crop protection but the residue from the exposure could cause harmful side effects to the human body.

Pesticides usage was increased by four fold from years 2000-2010 with more than 100,000 tons of active ingredients exported to Thailand. Herbicides (glyphosate, paraquat, dichloride, 2, 4-D, ametryn and atrazine) make up the most pesticide imports, followed by insecticides (chlorpyrifos, fenocarb, cartap, hydrochloride, cypermethin, and methomyl) and fungicides [2]. Using pesticides would require proper and correct use of PPE or personal protective equipment. The frequent use of pesticide and the overdose of application have put the farmers in great risk of developing Parkinson's disease (PD) or the symptoms of parkinsonism. The four cardinal symptoms of PD are bradykinesia, rigidity, tremor at rest, and loss of postural reflexes [3]. Age is the strongest risk factor for PD and researches have pointed out that men are more likely than women to have PD [4].

According to Pezzoli and Cereda [5], people who work with pesticides, herbicides, and

* *Correspondence to: Wattasit Siriwong*
E-mail: wattasit.s@chula.ac.th

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chemical solvents or are exposed to them elsewhere, develop PD at higher rates than people who do not. PD risk is doubled with exposure to herbicide paraquat or fungicides maneb, and mancozeb and risks increases with longer exposures and higher doses [5]. Pesticide causes disruption in the function of mitochondrial complex I which eventually leads to apoptosis of the cells and the malfunction of the central nervous system as well as oxidative injury. They also cause protein aggregation and altered dopamine levels by inhibiting or inducing other metabolizing enzymes causing damage to neurotoxins [6]. As of March 2011, 40,049 cases had been reported by PD registry. High prevalence is found in residents of the central plain valley of Thailand, an area with a large amount of pesticide use [7]. This indicated that pesticides can play role in triggering the symptoms of PD and induces the mechanism of the underlying genetic factors responsible for causing PD.

The objective of this study is to find the prevalence of parkinsonism among the elderly farmers residing near chilli farm area in Hua Rua sub-district and to explore the association between socio-demographic characteristics, pesticide exposure and the risk of parkinsonism.

MATERIALS AND METHODS

This was a cross sectional study and chi square was used to analyze the risk factors of Parkinson's disease. The study population was farmers or former farmers of Hua Rua sub-district, Nai Muang District, Ubonratchathani Province. There were total of 16 villages with 2,247 households. The estimated population of elderly farmers in that district was approximately 2,293 people. Purposive sampling and quota sampling was used to select the elderly farmers aged 50 years or more. To be included in this study, participants must be at least 50 years of age and must have lived in Hua Rua sub-district for 30 years or more. Farmers were excluded if they had history of cardiac, renal or hepatic insufficiency, were using neurological related medication or had injuries or head trauma. Sample size was calculated by estimation population proportion with missing and drop out considered and the sample size that would represent this population was 271.

Data was collected by questionnaire and face to face interview. Prior to conducting the research, there would be coordination with the leader of the community and personnel at the sub-district health promotion hospital and the interview would be conducted at the sub-district health promotion hospital. Flyer would also be used so that participants are aware about the research. This research would require assistance and all assistants would be trained by the researcher. The questionnaire consisted of 3 parts: socio-demographic characteristics, Parkinson screening, and pesticide exposure and prevention. Socio-demographic characteristics part asked about the general information such as age, gender, education levels, duration of work as farmers, number of working days per week, smoking status, alcohol consumption and family history. Parkinson screening part asked about the symptoms after the long term exposure. Some symptoms included difficulty in movement, poor body balance, loss of muscle control, trembling or shakiness and the stiffness of the body. Lastly, pesticide exposure and prevention part contained questions concerning frequency of use, storage site, hygiene, use of PPE, history of pesticide use and the duration exposure. These three parts provided risk factors of parkinsonism for farmers who had exposure with pesticides both directly and indirectly.

The SPSS software for windows version 17.0 (University's license) was used for analyzing quantitative data. For descriptive statistics, nominal variables were calculated as frequency and percent. For inferential statistic, chi-square test was used to find association between parkinsonism and related factors. Crude odd ratio (OR) was also computed to determine the level of risk.

The study protocol was approved by the Ethical Committee of Chulalongkorn University COA No.030.1/57. All participants signed a consent form prior to participating in the study. In case of any severe cases found, the farmers were advised to visit physicians immediately.

RESULTS

As the risk factors of parkinsonism were studied among the farmers of Hua Rua Sub-district, associations were found between socio demographics, farming characteristics, pesticide prevention, pesticide exposure and risk of parkinsonism. Age, medical history and medication were found to be statistically significant in Table 1. Years living in the area, farming size in Rai (1 Rai is approximately 1,600 sqm^2), farming experience and years of using pesticides were found to be statistically significant in increasing the risk of parkinsonism (Table 2). Use of correct PPE was found to be significant and effective in reducing the risk of parkinsonism (Table 3). Pesticide preparation at home was also statistically significant. Lastly, in terms of pesticide usage and duration, organochlorine insecticide and all three groups of herbicide was significant in determining the risk of

Table 1 Association between socio demographics characteristics and risk of parkinsonism

Characteristics	Risk of parkinsonism			
	χ^2	*P-value*	Crude OR	95% CI
Gender	0.446	0.504	1.277	0.622-2.624
Age	13.144	<0.01*	8.429	2.259-31.449
BMI	0.301	0.583	0.654	0.142-3.008
Education	0.279	0.597	0.544	0.055-5.5381
Smoking	3.168	0.075	0.285	0.066-1.235
Drinking	0.096	0.757	0.885	0.407-1.922
Medical history	6.486	0.011*	2.637	1.225-5.674
Medication	6.581	0.038*	0.473	0.231-0.970
1st degree relative with PD	1.172	0.279	0.856	0.815-0.899

* (chi square, p<0.05)

Table 2 Association between farming characteristics and risk of parkinsonism

Characteristics	Risk of parkinsonism			
	χ^2	*P-value*	Crude OR	95% CI
Years living in this area	11.509	0.001*	5.818	1.945-17.406
Farming Status	3.032	0.082	1.847	0.919-3.711
Farm size (RAI)	4.912	0.027*	3.379	1.087-10.502
Farming experience	12.098	0.001*	4.292	1.812-10.171
No. of working hours per week	3.568	0.059	2.889	0.927-9.004
Years of using pesticides	5.935	0.015*	3.508	1.228-10.023
Last use of pesticide	0.134	0.714	0.675	0.081-5.596
Proximity (home & farm)	1.807	0.179	0.270	0.035-2.079

* (chi square, p<0.05)

parkinsonism. No. of types used was also significant as displayed in Table 4.

Table 1, there were a total of 271 farmers who participated in the study. There were 106 males (39.1%) and 165 females (60.9%). There were 38 participants who were at high risk of developing parkinsonian symptoms. Age range was from 50-89 with most participants between ages 50-59 (n= 128) and 60-69 (n= 80). The average age of participants was 68 years old. Most participants (71.2%) did not smoke and approximately (14%) were former smokers. Half of the participants (56.5%) did not drink and approximately 28% of participants drank, most of which were males. Medical history was divided into half with only 10 participants (3.7%) who do not know. Majority of the farmers had hypertension and diabetes and approximately 50.2% of them were on medication. These prescribed medications were to treat hypertension and diabetes. Most participants reported that they did not have a first degree relative with parkinson's disease (n= 222) while only 7 participants claimed that they do have first degree relative with parkinson's disease.

Table 2, most of the farmers had lived in Hua Rua sub-district for more than 50 years. 56.8% (ages 50-69) and 17.7% (ages 70-89) had lived in there for their entire life. 67.5% of the participants (n= 183) are currently doing farming while 32.5% (n = 88) were former farmers who were either too old to work or had decided to retire. Majority (94.5%) of the participants owned 1-20 Rais of farming area (1 Rai is approximately 1,600 sqm^2). These Rais include both their own and rented. Most farmers have had the working experience of 1-20 years (n=101, 37.3%) and 21-40 years (n=111, 41%). 25.8% of the participants claimed that they had never used pesticides while the rest had used for 1-19 years (30.6%), 20-39 years (34.3%) and more than 40 years (9.2%). 70 farmers claimed that they had never used pesticide. Majority of the farmers (70.8%) had used pesticides for 1-20 years with only 3.3% who used for more than 20 years. Lastly, most farmers lived nearby farming areas. Amount 211 participants lived within 0-199 meters of the farming area (some participants lived right next to farms) suggesting that they could be receiving high amount of pesticide exposure.

Table 3, 201 participants (74.2%) used pesticide by themselves with 70 participants (25.8%) hired other people to do it for them. 20.7% of the participants who used pesticide by themselves reported that they used only one type of pesticide in their farming activities. 32.8% used two pesticide combinations while 20.7% used more than two types

Table 3 Association between pesticide prevention and risk of parkinsonism

Pesticides prevention	Risk of parkinsonism			
	χ^2	*P-value*	Crude OR	95% CI
PPE use	7.193	0.007*	0.394	0.197-0.791
Eating or drinking at farm	2.046	0.153	1.648	0.827-3.281
Pesticide Preparation at home	3.970	0.046*	2.543	0.989-6.543
Pesticide storage at home	2.756	0.097	2.166	0.854-5.491
Source of drinking water	2.174	0.140	0.598	0.300-1.190
Water Treatment	0.352	0.553	0.785	0.353-1.748

* (chi square, p<0.05)

Table 4 Association between pesticide exposure and risk of parkinsonism

Activities with pesticide	Risk of parkinsonism			
	χ^2	*P-value*	Crude OR	95% CI
Pesticide application	1.266	0.260	1.641	0.688-3.916
No. of types of pesticides used	8.359	0.004*	6.750	1.554-29.323
No. of application times per year	0.621	0.431	0.600	0.166-2.163
Insecticides				
Organochlorine (a)				
Usage	25.594	0.000*	5.865	2.796-12.298
Duration	9.396	0.002*	5.732	1.656-19.843
Organophosphate (b)				
Usage	2.374	0.123	1.750	0.854-3.587
Duration	0.317	0.573	1.218	0.612-2.423
Carbamate (b)				
Usage	0.171	0.679	1.222	0.472-3.160
Duration	0.710	0.399	0.846	0.718-0.997
Other (b)				
Usage	0.291	0.589	0.786	0.327-1.888
Duration	0.049	0.825	0.773	0.078-7.664
Herbicides				
Dipyridyl (b)				
Usage	18.873	0.000*	4.571	2.210-9.455
Duration	18.886	0.000*	4.450	2.185-9.064
Glyphosate (b)				
Usage	8.933	0.003*	3.425	1.471-7.975
Duration	14.357	0.000*	5.252	2.064-13.364
Chlorophenoxy (b)				
Usage	22.788	0.000*	8.728	3.123-24.397
Duration	22.769	0.000*	10.089	3.276-31.073

* (chi square, p<0.05)
a – analyzed based on duration of use more than 15 years
b – analyzed based on duration of use 5 years or more

of pesticides in their activities.

Most farmers (60.5%) did not eat or drink in the farming area. 14.4% ate or drank sometimes. Approximately 25.1% always had food or drinks in the farm. Majority of the farmers never prepare pesticides at home neither do they store pesticides at home. Approximately half of the participants (58.3%) drink from tap water. 35.8% drank from underground water. Only 5.9% drank from well water. There were four options that participants used to drink water. 27.7% boiled their water, 33.6% filtered their water, and 11.4% used the method of precipitation. Lastly, 27.3% used other methods or drank their water right away.

Table 4, insecticides and herbicides were the two main types of pesticide used by the farmers. Insecticides used could be categorized into four main groups: organochlorine, organophosphate, carbamate and other groups such as abamectin and pyrethroids. There were three herbicide groups used by the participants: dipyridyl (paraquat), glyphosate, and chlorophenoxy (2-4D). 49 participants (18.1%) stated that they used organochlorine, 147 (54.92%) reported using organophosphate, 37 (13.7%) used carbamate and 59 (21.8%) used other groups. 34.7% of the participants used dipyridyl, 11.8% used

glyphosate and 6.3% used chlorophenoxy. Duration of usage for both insecticide and herbicide were grouped into less than 5 years, 5-15 years and more than 15 years. Organochlorine was analyzed based on 15 years because some types of organochlorine had been banned for more than 15 years. Few types had been banned for less than 15 years but there were continued used till present.

DISCUSSION

The objective of this study was to investigate the risk factors of parkinsonism among the farmers who were exposed to pesticides. PD is a disorder that is age related; therefore age was significant factor in determining the risk of PD [8]. The association of age towards parkinsonism becomes stronger as the age increases similar to the results from this study. Mean onset of PD is at 50 years old [5, 9]. The average age of participants in this study was approximately 68 years old and most participants were female. The prevalence of parkinsonism among the farmers in Hua Rua sub-district is 0.14. In this study, no specific gender was found to be associated with risk of parkinsonism. Previous studies [5] had suggested that man had higher risk of PD. This difference was due to the fact that most female participants had the average age of 60. At this age, women would be in post-menopausal and the estrogen that delayed the onset was reduced resulting in both groups at equal risk for developing PD [10].

Researches had suggested that smoking could be a protective factor for PD [8]. Those who had ever smoked had lower risk of PD compared to those who had never smoked. The effectiveness of nicotine would depend on the number of packets, duration of smoking [5]. In this study, smoking had no significance upon the risks level of parkinsonism. This was likely due to the fact that 61% of the participants were women and did not smoke. About 60% of the males did not smoke and 10% of those were former smokers. Those who used to smoke had quit smoking for more than 10 years meaning that they had lower protection from PD. There were no significant association between alcohol and risk of parkinsonism similar to previous studies [11, 12].

Most participants had a medical history of hypertension and diabetes. Both hypertension and Diabetes were found to be associated with the increasing risk of PD ($p<0.05$). According to Hu et al. [13], diabetes had positive association with the increasing risk of PD. Their studies also observed that diabetes was associated with rigidity and gait which is somewhat similar to the findings of this study [13]. Hypertension was also found to have positive association with PD especially in women. Study by Qiu et al. [14] had suggested that women with high normal blood pressure and hypertension had 60% higher chance of developing PD than men. From the cardiovascular perspective, as age increases, systolic pressure also increases [14]. Systolic hypertension in women could also be linked with the estrogen levels when women are at the post-menopausal period [15]. Medications used by participants were also found to be significant in reducing the risk of parkinsonism (OR=0.5). Mechanisms of this remains unclear although there had been proposed researches that drugs used to treat diabetes had some effects in treating parkinson's disease [16-18]. Moreover, calcium channel blockers used to treat hypertension also had the mechanisms to reduce the risk of PD although, like DM, more researches are required for further analysis [19].

According to this study, most of the participants had live in Hua Rua sub district for 50 years or more. Most farmers had 1-20 Rais which they use for various crops depending on the seasons. Most farmers have had at least 10 years of farming experience. All these factors indicated that the frequency of pesticide use and exposure was strongly associated with the risk of parkinsonism [20, 21] Majority of the participants had used pesticides during their lifetime as farmers. Years of exposure was also significant in this study ($p<0.015$) and in study from Simoniello et al. [22] ($p<0.05$).

The use of pesticide combination was the strong risk factors for developing PD. Freire and Koifman [23] found that insecticides particularly chlorpyrifos and organochlorines and herbicides such as paraquat when used in combination increase the odds of developing PD [23, 24] as obtained in this study (OR = 6.7). Even though some organochlorine pesticides such as DDT had been banned for a while, there were still some reports of usage [2]. No association was found in terms of gender but Dieldrin and DDT was associated with PD since some residues could be found in the brain [5]. The mechanism of how organochlorine caused neurotoxicity was through damaging the dopamine system and causing oxidative stress [25, 26].

Among the herbicides, dipyridyl (paraquat) and glyphosate was the most commonly used pesticides followed by chlorophenoxy. Those exposed to paraquat had the OR of 4.6 times. OR for participants to glyphosate was 3.4 times and chlorophenoxy was 8.7 times. Paraquat had strong association among the herbicide group due to its similarity in structure with MPTP [23]. A meta-analysis [27] reported the OR of paraquat ranging

from 1.8 to 4.4 while very few studies have found the association of parkinsonism with glyphosate. Proposed mechanism of how glyphosate increased the risk of PD was that it impairs the cytochrome P450 (CYP) pathway. Dysfunction of this pathway affects the neurotransmitter signaling resulting in neurological disorders [28]. Tanner et al. [29] also found association with 2-4 D where the OR was 2.9. Chlorophenoxy is known to cause dopamine depletion and protein aggregation. Disruptions in the anti-oxidant capability cause oxidative stress and cell apoptosis [5].

In this study the correct use of PPE could reduce the risk of parkinsonism (OR=0.4). Correct use of PPE was categorized based using 3 or more water proof equipment [30]. Rubber gloves and boots were used the water proof equipment used by majority of the participants. Other water proof equipment included goggles and respirators. Frequency of pesticide use, pesticide preparation and storage at home, eating or drinking at the farm during pesticide application and inappropriate protective clothing were all the risky behavior that could induce parkinsonism [20]. In this study, preparing pesticides at home could increase the risk of PD by 2.5 times. Well water drinking and underground water was not significant in this study because most participants drank tap water and had some water treatment [21].

CONCLUSION

The use of pesticides and pesticide exposure certainly had impact upon the risk of parkinsonism. Whether exposed via direct contact or not, participants were receiving some risks even though they were not categorized as having high risk. Some were exposed and influenced less than the others; nevertheless, they still have the potential risk of developing PD in the future. Future studies should focus towards the risk assessment and reducing the recall bias. This could lead to the better understanding of the association and causation of PD linking to specific pesticides or other influencing factors.

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