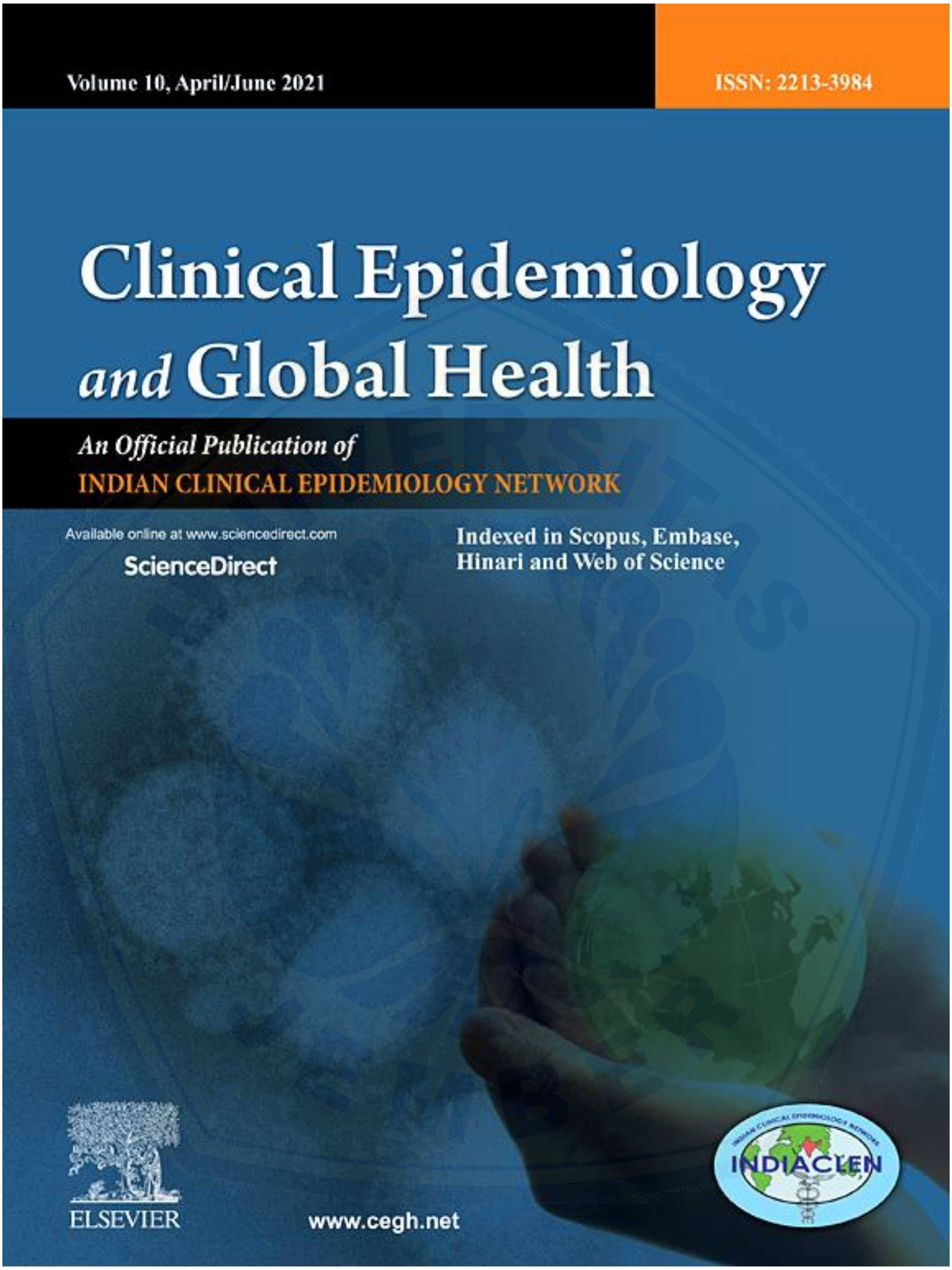

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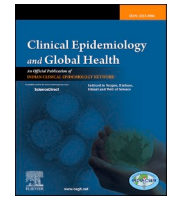

Neurobehavioral performance of Indonesian farmers and its association with pesticide exposure: A cross-sectional study

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ABSTRACT

Background: Acute and chronic pesticide exposure affect human health. The study aimed to assess the neurobehavioral performance and its association with pesticide exposure factors among Indonesian farmers.
Methods: A cross-sectional study was conducted among farmers living in Jember, Indonesia. Basic individual characteristics and pesticide exposure factors were documented using questionnaire-based interviews. The neurobehavioral performance was assessed by the German Q18 questionnaire and the WHO Neurobehavioral Core Test Battery (NCTB) consists of the Digit Span, Digit Symbol, Pursuit Aiming, and Trail making instruments. Data were presented descriptively and analyzed statistically using the chi-square test.
Results: As many as 90 farmers were recruited. Most farmers were 45–55 years old and had a normal nutritional status and moderate smokers. The neurobehavioral performance of the farmers was 62.22% normal and 37.78% abnormal. The most common neurobehavioral deficits were short memory, concentration difficulties, excessive fatigue, frequent headache, and tremor. The chi-square test showed that the spraying frequency ($p = 0.006$), the spraying duration ($p = 0.002$), the working years ($p = 0.013$), and the PPE usage ($p = 0.022$) associated with neurobehavioral performance, but the pesticide types ($p = 0.289$) and spraying time ($p = 0.627$) did not associated with neurobehavioral performance.
Conclusion: Although most farmers showed a normal neurobehavioral performance, some pesticide exposure factors demonstrated an association with neurobehavioral performance among Indonesian farmers. Multiple approaches including implementation of the regulation, choosing alternative biopesticides, and regular counseling on all aspects of pesticides, their impact on health are recommended to minimize pesticides' negative effects.

1. Introduction

Pesticides are chemical substances used in various agricultural practices to protect plants from pests and increase crop production. There are various pesticides, including insecticides, fungicides, herbicides, bactericides, rodenticides, nematicides, etc. The global use of pesticides reaches 3.5 million tons per year. Three major countries contributing to pesticide usage are China, the USA, and Argentina.[1] Indonesia is at the 74th rank worldwide with 1.597 tons of pesticides used in 2018.[2,3] As an agricultural country, Indonesia has a large portion of its population living in the agricultural sector. The Indonesian farmers rely heavily on pesticides as plants protection from pests. The Ministry of Agriculture data shows an increase in pesticides number by year and is marked by the increasing sales volume of pesticides globally.[4]

Many pesticides have been associated with health and environmental problems.[5] Several factors, such as contacts with pesticide residues in the environment, including crops, water, and soil, pose the farmers as a population at risk of experiencing various health problems due to exposure to pesticides.[6] Pesticide exposure to human occurs through several routes, including dermal, oral, and inhalation. The type of pesticides, duration and route of exposure, and individual health status, including nutritional and skin conditions, determine possible health outcomes. Pesticides are metabolized, excreted, and bioaccumulated in body fat. Several negative health effects that have been linked with pesticides include dermatological, gastrointestinal, respiratory, reproductive, endocrine, carcinogenic, and neurological effects.[5,7]

The disorder of neurobehavioral performance due to pesticide exposure includes adverse changes in both the central and peripheral nervous system, resulting in changes in memory, mood, attention, thinking irregularities, and disorientation.[8] The other symptoms are

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difficulty concentrating, dizziness, persistent headaches, excessive fatigue, and insomnia.[9] Disorders of the nervous system depend on the dose, frequency of exposure, type of pesticides, toxicity, and pesticide exposure duration. The incidence of neurobehavioral disorder on farmers can decrease cognitive function, leading to decreased performance, especially in long-term exposure.[9] In this study, we analyzed the association of pesticide exposure factors with farmers' neurobehavioral performance in Sukogidri Village, a small village in Jember, Indonesia. Jember is a regency that supports national agricultural commodities, and Sukogidri is a village where the majority work as a farmer and contribute a large percentage of a farmer in Jember whose tobacco as the main commodity. Therefore there is a high use of pesticides.[10]

2. Methods

2.1. Population and sampling

This cross-sectional study was conducted in Sukogidri Village, Jember, East Java Province, Indonesia, from December 2018 to January 2019. The study population was all farmers in the study area, as many as 846 people. The minimum required sample size determined by the Slovin formula was 90 respondents with a confidence level of 95% and a margin of error of 10% ($e = 0.1$). The respondents who met the inclusion and exclusion criteria were recruited based on the stratified random sampling technique. The inclusion criteria were farmers who were registered in a farmer group in the study area, do not have either mental disorders or experiencing mental retardation, be able to read, write, speak and respond well. The exclusion criteria were individuals with a history of stroke, goiter, and had suffered from head injuries, consuming drugs such as benzodiazepines, opiates, anticonvulsants, barbiturates, and antipsychotics.

2.2. Data collection

The data were collected using questionnaire-based interviews by trained-health professionals. Basic individual characteristics include age, nutritional status, smoking habit, alcohol consumption, and pesticide exposure factors, including the pesticide type, spraying frequency, spraying time, spraying duration, working years, and the PPE usage. Respondents obtained an explanation about the study and signed informed consent before the study. The neurobehavioral performance was screened using the German Q18 questionnaire. It consists of 18 questions to measure the neurobehavioral symptoms with the cut-off point 5 for men and 6 for women.[11] Since all respondents were men, the study used cut-off point 5 to determine an abnormal neurobehavioral symptom. Further, the WHO Neurobehavioral Core Test Battery (NCTB) consists of the Digit Span, Digit Symbol, Pursuit Aiming, and Trail Making instruments were performed by the clinician to assess the neurobehavioral performance. The test is common as an instrument for research and population screening and is reliable and sensitive to neurotoxic disorders. The NCTB test should be conducted by a health professional or trained test administrator based on an operational guide for the NCTB.[12,13] The test was done by respondents step by step in 600 s (10 min), started with the Digit Span test, followed by the Digit Symbol Test, then the Pursuit Aiming Test and the last was the Trail Making Test. The neurobehavioral performance was classified as normal if all score tests >40 and abnormal if one of the score tests was ≤ 40.[11,12] The neurobehavioral performance was examined in a comfortable room to maximize the respondent's concentration.

2.3. Data analysis

Data were entered, cleaned, and analyzed using SPSS software version 25. The data was first presented descriptively by frequencies and percentages to display respondents' characteristics such as age, nutritional status, smoking habit, alcohol consumption, and factors of pesticide exposure, including the pesticides type, the spraying frequency, the spraying time, the spraying duration, the working years, and the PPE usage, as well as the neurobehavioral symptoms and neurobehavioral performance. The chi-square test was used to determine the association of each factor of pesticide exposure and the neurobehavioral performance with a degree of significance $p < 0.05$.

3. Results

The respondents' basic characteristics and factors of pesticide exposure were shown in Table 1. Most respondents (35.56%) were 45–55 years old, 61.11% had a normal nutritional status, 39 respondents (43.34%) were moderate smokers, and 100% did not consume alcohol. Table 2 displayed the neurobehavioral symptoms screened by the German Q18 questionnaire. Using the cut-off point 5, 56 respondents (62.22%) were normal, and the rest suffered from an abnormal neurobehavioral performance. The most common neurobehavioral deficits were short memory (57.78%), concentration difficulties (57.78%), excessive fatigue (53.33%), frequent headache (60.00%), and tremor (54.44%).

Table 3 presented the farmer's neurobehavioral performance assessed using the WHO-NCTB consists of the Digit Span Test, the Digit Symbol, the Pursuit Aiming, and the Trail Making Tests. The neurobehavioral performance test's interpretation was classified as normal if each score test >40. Consistent with the German Q18 questionnaire, the WHO-NCTB revealed 56 respondents (62.22%) had a normal and 34 respondents (37.78%) suffered from an abnormal neurobehavioral performance. Analysis using a chi-square test showed that the Digit Span Test, the Digit Symbol Test, and the Pursuit Aiming Test significantly associated the neurobehavioral performance with the p-values of 0.000 for each test, while the Trail Making Test revealed no significant association (p-value $= 0.197$). The distribution of 34 abnormal neurobehavioral performances was as follows: 58.82% had an abnormality on a single test, 32.35% showed an abnormality in a combination of two tests, and 8.83% had an abnormality on three tests types. The majority had an abnormality in the Digit Span Test (38.23%).

The chi-square test was performed to determine the association between the pesticide exposure factors and farmers' neurobehavioral performance, as shown in Table 4. There was no significant association between the pesticides types, the pesticides spraying times, and the smoking habit with neurobehavioral performance (p-value $= 0.289$, 0.627, and 0.481, respectively). However, there was a significant association between pesticide spraying frequency ($p = 0.006$), pesticide spraying duration ($p = 0.002$), working years ($p = 0.013$), and the PPE usage ($p = 0.022$) with neurobehavioral performance.

Table 1
Basic characteristics of farmers.

Characteristics	Number (N)	Percentage (%)
Age		
15–24 years	13	14.44%
25–34 years	15	16.67%
35–44 years	30	33.33%
45–55 years	32	35.56%
Nutritional Status		
Underweight	17	18.89%
Overweight	9	10.00%
Obesity	9	10.00%
Normal	55	61.11%
Smoking Habit		
Mild smokers	29	32.22%
Moderate Smoker	39	43.34%
Heavy smokers	3	3.33%
Do not smoke	19	21.11%
Alcohol consumption		
Yes	–	0.00%
No	90	100.00%

Table 2
Distribution of the farmer's neurobehavioral symptoms screened by the German Q18 Questionnaire.

No	Questions	Responses	
		Yes (N/%)	No (N/%)
1	Do you have a short memory?	52 (57.78%)	38 (42.22%)
2	Have your relatives told you that you have a short memory?	34 (37.78%)	56 (62.22%)
3	Do you often have to make notes about what you must remember?	19 (21.11%)	71 (78.89%)
4	Do you generally find it hard to get the meaning from reading newspapers and books?	20 (22.22%)	70 (77.78%)
5	Do you often have problems with concentrating?	52 (57.78%)	38 (42.22%)
6	Do you often feel irritated without any particular reason?	31 (34.44%)	59 (65.56%)
7	Do you often feel depressed without any particular reason?	14 (15.56%)	76 (84.44%)
8	Are you abnormally tired?	48 (53.33%)	42 (46.67%)
9	Do you have palpitation of the heart even when you don't exert yourself?	30 (33.33%)	60 (66.67%)
10	Do you sometimes feel an oppression in your chest?	7 (7.78%)	83 (92.22%)
11	Do you often perspire without any particular reason?	35 (38.89%)	55 (61.11%)
12	Do you have a headache at least once a week?	54 (60.00%)	36 (40.00%)
13	Are you less interested in sex than what you think is normal?	0 (0.00%)	90 (100.00%)
14	Do you often feel sick?	25 (27.78%)	65 (72.22%)
15	Do you have numb feelings in your hands or feet?	31 (34.44%)	59 (65.56%)
16	Is there a weak feeling in your arms or legs?	25 (27.78%)	65 (72.22%)
17	Do your hands tremble?	49 (54.44%)	41 (45.56%)
18	Does alcohol not agree with you?	90 (100.00%)	0 (0.00%)

Table 3
Distribution of neurobehavioral performance of farmers based on neurobehavioral tests and its statistical analysis.

Neurobehavioral Test	Neurobehavioral Performance				p-value
	Normal		Abnormal		
	N	%	N	%	
Digit Span	67	74.4%	23	25.56%	0.000
Digit Symbol	76	84.44%	14	15.56%	0.000
Pursuit Aiming	76	84.44%	14	15.56%	0.000
Trail making	89	98.89%	1	1.11%	0.197
Neurobehavioral Performance	**56**	**62.22%**	**34**	**37.78%**	

Table 4
Distribution of pesticide exposure factors and its correlation with neurobehavioral performance.

Factors of Pesticide Exposure	Neurobehavioral Performance			
	Normal (N/%)	Abnormal (N/%)	Total (N/%)	p-value
Pesticides type				
Insecticide	48 (65.75%)	25 (34.24%)	73 (100%)	
Fungicide	5 (50.00%)	5 (50.00%)	10 (100%)	0.289
Herbicide	2 (33.33%)	4 (66.67%)	6 (100%)	
Bactericide	1 (100.00%)	0 (0.00%)	1 (100%)	
Spraying Time				
Morning	39 (63.93%)	22 (36.07%)	61 (100%)	
Afternoon	0 (0.00%)	0 (0.00%)	0 (0.00%)	0.627
Evening	17 (58.62%)	12 (41.38%)	29 (100%)	
Spraying Frequency				
1–2 x/month	19 (73.08%)	7 (26.92%)	26 (100%)	
3–4 x/month	25 (75.76%)	8 (24.24%)	33 (100%)	0.006
5–6 x/month	12 (41.38%)	17 (58.62%)	29 (100%)	
>6 x/month	0 (0.00%)	2 (100%)	2 (100%)	
Spraying Duration				
≤1 h	19 (70.37%)	8 (29.63%)	27 (100%)	
1–2 h	23 (82.14%)	5 (17.86%)	28 (100%)	0.002
≥2 h	14 (40.00%)	21 (60.00%)	35 (100%)	
Working Years				
>10 years	16 (44.44%)	20 (55.56%)	36 (100%)	
6–10 years	23 (69.70%)	10 (30.30%)	33 (100%)	0.013
0–5 years	17 (80.95%)	4 (19.05%)	21 (100%)	
Personal Protective Equipment (PPE) Usage				
Less	26 (50.98%)	25 (49.02%)	51 (100%)	
Enough	25 (73.53%)	9 (26.47%)	34 (100%)	0.022
Well	5 (100%)	0 (0.00%)	5 (100%)	
Smoking Habit				
Mild smokers	17 (58.62%)	12 (41.28%)	29 (100%)	
Moderate Smoker	23 (58.97)	16 (41.03%)	39 (100%)	0.481
Heavy smokers	3 (100%)	0 (0%)	3 (100%)	
Do not smoke	13 (68.42%)	6 (31.58%)	19 (100%)	
Total	**56 (62.22%)**	**34 (37.78%)**	**90 (100%)**	

4. Discussion

As many as 12.37% Indonesian live as a farmer who potentially had intensive exposure to pesticides. Acute and chronic exposure to pesticides affects the many systems of human health, including the nervous system. This study found that some pesticide exposure factors such as spraying frequency, spraying duration, working years, and PPE usage correlate with neurobehavioral performance, except pesticide types and spraying time. The study was conducted in Sukogidri Village, a small area in Jember, Indonesia, where most residents live as farmers with tobacco commodities.[10] Basic characteristic data revealed that most farmers were 45–55 years old, making them have a higher risk of pesticide poisoning due to decreased nerve function. Based on a previous study, a decrease in nerve function occurs every five years of age after 28 years,[14] where the reduction of the nervous system's function by age could happen due to residual toxic substances that enter the brain and accumulate in brain tissue causing nerve cell damage.[15] This causing abnormality of neurotransmitters synthesis in nerve cells, which further resulted in neurobehavioral performance disorders.

We also examined the nutritional status of farmers. The majority of respondents had a normal nutritional status measured by body mass index (BMI). The study observed that respondents with abnormal nutritional status tended to have lower neurobehavioral performance than the normal. However, some studies on the association of pesticide exposure with nutritional status showed inconsistent results. The previous longitudinal study reported the association between pesticide exposure and weight gain, possibly due to endocrine disruption.[16] But, some studies showed the adverse effects of pesticide exposure, including weight loss, as observed in 18.8% of respondents in this study.

The smoking habit is considered as one of the confounding factors related to pesticide exposure to human health, including neurobehavioral performance. Cigarettes may negatively affect human health due to their nicotine substances that significantly affect brain function, especially in the large dose by produce endorphins, which further causing nerve disorders.[17] However, our study indicated no significant association between the smoking habit and neurobehavioral performance. The majority of respondents were moderate smokers with an average consumption of 12 cigarettes per day, but most of them and all heavy smoker respondents showed a normal behavioral performance. Our study was similar to the previous study which reported the prevalence of mental health problems among tobacco growers suggested due to pesticides and other chemicals used in farming activities and the heavily exposed nicotine via dermal absorption during tobacco farming.[18] It is known that tobacco exposure may cause toxicity to workers during harvesting which can occur by dermal contact, even with intact skin. Tobacco farmers can have nicotine levels as high as regular smokers.[19] And the nicotine absorption from tobacco may increase in wet tobacco leaves.[18] Another study also reported the indication of intense nicotine exposure as a risk factor for tobacco farmer's mental health, although the effect of these exposures on farmer's mental health remains unclear.[20] Studies found that nicotine increases cholinergic neurotransmission by binding to the acetylcholine receptor,[21] while the basal forebrain cholinergic systems innervate the cerebral cortex and subcortical nuclei. Therefore, changes in cholinergic neurotransmission could affect various parts of the brain which play a crucial role in cognitive processes and complex behavior.[22] Our findings indicated that nicotine exposure among farmers occurs due to farming activities especially from tobacco plants rather than smoking habits.

The spraying frequency is one of the pesticide exposure factors associated with neurobehavioral performance. In this study, most farmers applied pesticides 5–6 x/month. The frequency of spraying depends on the crop types, pesticides types, and pests. On average, insecticide and fungicide application on the crops was 10–20 times a year.[23] The spraying frequency also depends on the number of pests. The more the pest number, the more often the spraying frequency, meaning more exposure to pesticides, leading to an increased risk of neurobehavioral effects.

Another important pesticide exposure factor associated with neurobehavioral symptoms is the spraying duration. Indonesian regulation recommends the pesticide usage maximum duration of 4 h per day in a week to avoid unwanted effects.[24] While WHO recommends a maximum of 5–6 h per day of long pesticides spraying and must carry out health tests, including blood cholinesterase levels every week. The spraying duration correlated with pesticide exposure and absorption by the body results in accumulation and further increases neurobehavioral effects.[25] Study reported a significant relationship between the last contact with the decrease of cholinesterase activity. The last contact for less than two weeks was 5.8 times the risk of experiencing poisoning than more than two weeks.[26] Another study showed that neurobehavioral effects are correlated with exposure intensity and duration of pesticide usage.[27]

The working years are also associated with neurological symptoms. Most respondents worked as a farmer for more than ten years. A prolonged and repeated pesticide exposure for more than ten years could persist in brain nerve disorders. It was high risk and proven to decrease neurobehavioral performance.[28,29] The longer the farmer becomes a sprayer, the higher the possibility of pesticide exposure, which further increases the risk of pesticide poisoning and other health problems. Farmers who have more than ten years working period tend to have worse neurobehavioral performance than farmers whose working period was under ten years.[29] Cumulative exposure to low levels of pesticides for many years in agricultural work is associated with neurological impairment, as measured by the selective attention, symbol digit, reaction time tests.[30] However, stopping pesticide usage for a long time results in free poisoning because of pesticide release from the blood.[9] The study is similar to previous research that the longer and the more frequent pesticides spray results in pest resistance, which may force farmers to choose higher toxic pesticides and may cause neurobehavioral impairment.[31]

The study showed a significant relationship between PPE usage and neurobehavioral performance. The majority of respondents applied the PPE poorly. It is known that the proper use of PPE is the right step to reduce pesticide exposure, which further avoids the health effects of pesticide use. Several factors correlated with the poorly use of PPE were the lack of PPE availability, negative attitudes, and practice of PPE usage due to uncomfortably.[32] The PPE usage is associated with cholinesterase levels in spraying farmers. The complete use of PPE when spraying is essential to avoid pesticide exposure and is expected to reduce farmers' risk of pesticide poisoning.[25] Studies conducted in Indonesia reported poor and non-standard PPE usage in farmers due to the lack of knowledge, attitude, and practice, and lack of PPE availability.[25]

The two pesticide exposure factors that did not associate with neurobehavioral performance were pesticide types and spraying time. Although this contradicted previous studies.[17,33] Our study observed that most farmers used insecticides compared to other pesticides types. They also used organophosphate chlorpyrifos, which is known to cause human poisoning and nerve functional effects, including motoric skills. However, it is known that the neurobehavioral symptoms usually arise after chronic low dose exposure than acute pesticide exposure due to temporary acetylcholinesterase activity disorder.[33] Concerning the spraying time, most farmers sprayed pesticides in the morning and evening. Spraying was usually carried out at 7:00 to 9:00 a.m. and continued in the afternoon from 3:00 to 5:00 p.m. if needed. Studies showed that the best time for pesticide application/spraying is during the cooler part of the day, such as the early morning and early evening, and when conditions allow plants to dry quickly. In the early morning, foliage allows drying before temperature 85-90 °F.[34] Pesticide application should be avoided on sweltering days with temperatures above 90 °F because the active substances in pesticides can vaporize and be break down by UV light and drift onto non-target surfaces.[35]

The study implied that the most associated factor of pesticide exposure on the neurobehavioral performance was the spraying duration, followed by the spraying frequency, the working years, and PPE usage. The factors indicated the chronic low dose of pesticide exposure on farmers which the most affected neurological function has been reported is behavior. Behavior is the result of various sensory, motor, and associated function of the nervous system and the neurotoxic pesticides can adversely affect one or more of these functions, disrupt learning and memory process, as the finding of the study that the most common neurobehavioral deficits were short memory, concentration difficulties, excessive fatigue, frequent headache, and tremor. Our result was consistent with the previous study that there were long-term cognitive effects of chronic exposure to pesticides.[36,37] Although the mechanism involved in this neurological symptom due to chronic exposure of pesticides is not well established and need to be explored further to identify the best means to protect human against a pandemic of neurotoxicity.

The present study's major limitation is that it was a cross-sectional study, using structured-questionnaire and self-reporting data, making it difficult to infer causal relationships between variables. Future research should focus on the direct observation of the farmer's activity when applying pesticides.

5. Conclusion

There is an association between pesticide exposure and neurobehavioral performance in Indonesian farmers. The pesticide exposure factor includes the spraying duration, frequency of spraying, working length, and PPE use. The best practice of farmers in this study to choose an appropriate time for pesticide spraying was good to continue. However, some approaches are recommended to minimize the negative effect of pesticides on human health, especially in the neurological system, including choosing alternative biological pesticides or using low toxicity pesticides. The government's regulation on controlling all aspects of pesticides from circulation, distribution, storage, and pesticide usage needs to be implemented in the field setting. Further, it needs to provide regular counseling about pesticides and their impact on health, choose appropriate pesticides, correct application, and socialize with farmers about the importance of using PPE.

Ethical approval

The study has received ethical approval from the Ethical Committee for Health Research of the Medical Faculty of the University of Jember, Indonesia (No. 1272/H25.1.11/KE/2018).

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Author's contributions

ES conceptualized and designed the study. INP collected the data. All authors contributed to the data interpretation, drafting of the article, and approval of the final version.

Declaration of competing interest

The authors declare no competing interest.

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