

## LITERATURE REVIEW: IMPACT OF ORGANOPHOSPHATE PESTICIDE EXPOSURE ON CHOLINESTERASE ENZYME ACTIVITY AND ASSOCIATED RISK FACTORS FOR POISONING, 2017-2020

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### Abstract

**Introduction:** Organophosphate pesticides, which are used to control pests of crops, affect the nervous system by inhibiting the activity of cholinesterase enzymes in the body. This can be achieved by inhaling, eating, or applying it to the skin. This study research aims to determine the level of pesticide exposure that can inhibit the activity of the Cholinesterase enzyme in the blood. This study employed a systematic literature review with library sources used through Google Scholar and Science Direct, resulting in 16 research articles discussing cholinesterase enzyme activity due to exposure to organophosphates discussed in 2017-2020. **Discussion:** The results of a previous study found that exposure to organophosphates significantly reduced cholinesterase enzyme activity by 50-80%. Testing for cholinesterase as a biomarker of exposure to Organophosphate (OP) through acetylcholinesterase activity in red blood cells (AChE). This study explored the relationship between gender, age, knowledge of farmers, personal protective equipment, farmers' smoking behavior, and duration of spraying. **Conclusion:** Poisoning alters the activity of cholinesterase enzymes in the blood of farmers, resulting in acute and chronic health problems. Several factors have been found to correlate with organophosphate poisoning, including age, level of knowledge among farmers, use of personal protective equipment, smoking behavior, and duration of spraying activities.

## INTRODUCTION

Agriculture makes a great contribution to the life of a living in terms of the economy to satisfy basic needs. The number of crop pests has increased over time. Reducing the number of pests on crops and farmers will start using pesticides. Commonly used pesticides include carbamates and organophosphates (1). Organophosphate molecules can be absorbed through the skin, inhaled, or via the digestive tract. Once absorbed, the molecule binds to an acetylcholinesterase molecule in the red blood cells, rendering the enzyme inactive. This causes excess acetylcholine at the synapses and neuromuscular junctions. Overstimulation of nicotinic receptors at the neuromuscular junction can cause fasciculations and myoclonic jerk. Causes paralysis

due to depolarization block. Nicotinic receptors are found in the adrenal glands and can cause hypertension, sweating, tachycardia, and leukocytosis with a leftward shift (2).

In 2014, the World Health Organization (WHO) confirmed that 4,444 workers in the agricultural industry annually experienced between one and five million cases of poisoning worldwide, with a mortality rate of 5.5%, or around 220,000 people, accounting for 80% of these poisoning cases. Age, sex, knowledge, experience, skills, education, use of personal protective equipment, nutritional status, and exposure to pesticides are risk factors for poisoning by organophosphorus pesticides (3). According to a recent study published in public health, acute pesticide poisoning affects

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385 million farmers annually (4). In addition to poisoning, agricultural workers and farmers reported experiencing symptoms such as fatigue, excessive weakness, skin burning sensation, excessive sweating, changing skin color, vision, weakening and shrinking bloating, nausea, vomiting, diarrhea, abdominal cramps, abdominal pain, difficulty breathing, and chest pain (5).

Including pesticide-related suicides, studies have revealed that acute agricultural poisoning causes 11,000 deaths annually. There are approximately 256 million cases in Asia, and glyphosate is categorized as "carcinogenic" by the International Agency for Research on Cancer (IARC) (6). According to a meta-scientific study conducted by the University of Washington in 2019, pesticides are also associated with asthma, allergies, obesity, endocrine disorders, and miscarriage (7).

This study found an increased risk of glyphosate-induced malignant lymphoma, also known as non-Hodgkin's lymphoma. Pesticides are also linked to miscarriage (8). Pesticides, such as organophosphates, are known to attack the nervous system. Exposure to pesticides affects both the central and peripheral nervous systems, leading to many chronic diseases, such as Parkinson's disease, Alzheimer's disease, and Amyotrophic Lateral Sclerosis (ALS). Workers exposed to pesticides have also been linked to diabetes, chronic respiratory diseases, chronic nephropathy, autoimmune diseases, hyperglycemia/diabetes, and many other diseases (9).

Fertile women are a vulnerable group due to pesticide exposure, because pesticide exposure is a substance that can affect embryo formation and growth (10). Chronic and acute pesticide exposure is assessed by the levels of biomarkers, such as cholinesterase enzyme, acetylcholinesterase (AChE) activity in red blood cells, and butyrylcholinesterase (BChE) activity in plasma (11). Acetylcholinesterase (AChE) is a more accurate biomarker of chronic and low-intensity exposure for identifying farmers exposed to toxins (12). If the farmer's cholinesterase enzyme levels, normal cholinesterase levels in men are 4620-11500 U/L, while in women they are 3930-10800 U/L. Cholinesterase levels are interpreted as intoxication if cholinesterase activity in the blood decreases by more than 50% of normal or 3500 U/L (13).

Therefore, this study aimed to discuss the characteristics of farmers in this literature review by including farmers' knowledge, personal protective equipment, cholinesterase levels, sex, and frequency of spraying from articles with the population in this literature study were vegetable and rice farmers whose cholinesterase activity was inhibited due to exposure

to organophosphate pesticides from articles published between 2017 and 2020.

## DISCUSSION

Pesticides are generally defined as toxic chemicals that are used to control pests that harm humans. Pesticides have been widely used for the treatment of agricultural production, plantations, and the eradication of disease vectors (3). The types of pesticides often used include carbamates and organophosphates (1). Organophosphates are pesticides owing to their anticholinesterase inhibitory properties and cholinesterase activity in nerves. Cholinesterase is an enzyme (in the form of a biological catalyst) found in tissues. The body's job is to maintain muscles, glands, and nerve cells in an orderly and harmonious manner. When cholinesterase activity in body tissues quickly reaches low levels, it affects the voluntary movement of muscle fibers during fine or gross movements (3).

To strengthen their research on cholinesterase activity in farmers exposed to organophosphates, we gathered 16 references from 2017 to 2020. The inclusion criteria for literature selection were carefully established: articles must discuss cholinesterase activity in connection with exposure to organophosphates from 2017 to 2020. The selection process followed a systematic approach, starting with keyword identification. Given the research's aim to uncover cholinesterase activity in farmers facing organophosphate toxicity, the specified search terms included cholinesterase, farmers, organophosphates, and danger.

The primary focus of this research revolved around locating and accumulating evidence on cholinesterase levels in farmers exposed to organophosphates. After conducting a thorough review of the various reference groups, the research team meticulously examined the bibliographies of the downloaded journals to identify the most relevant sources. The authors employed online searches on esteemed data-driven platforms, such as ScienceDirect, Springer, PubMed, Elsevier, Wiley, Emerald, IG Library, and Gale, alongside general search engines, such as Google Scholar, using predetermined keywords. The final step involved categorizing the literature based on two key aspects: the year of publication (2017-2020) and the relevance of the articles. Specifically, articles published between 2017 and 2020 were given greater consideration.

This literature study primarily focused on the population of vegetable and rice farmers whose cholinesterase activity was inhibited by exposure to

organophosphate pesticides. The characteristics of these farmers, as examined in the literature, encompassed factors such as their knowledge, smoking habits, use of Personal Protective Equipment (PPE), cholinesterase levels, gender, and frequency of pesticide spraying. The analysis of the available data revealed that while

the prevention program appeared to safeguard farm workers who used the most toxic pesticides, it was not uniformly effective, as some individuals failed to take the necessary precautions. Furthermore, the program faced several challenges, including the complexity of electronic reporting.

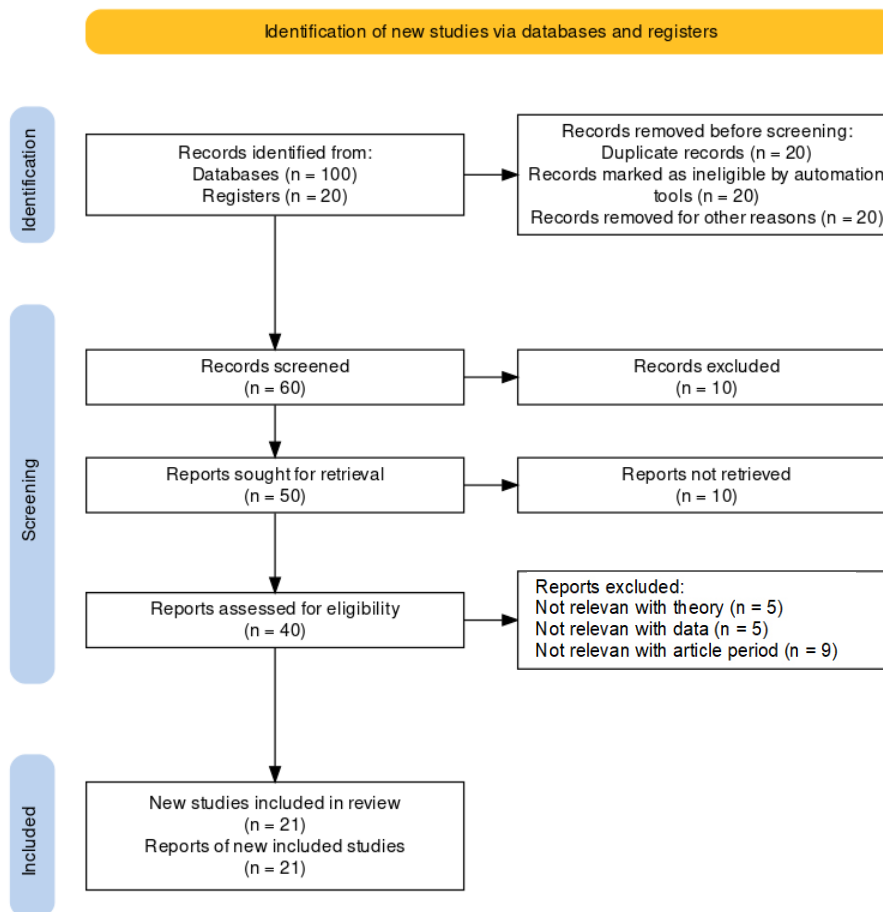


Figure 1. Prisma Flow Diagram

Table 1. List of Literature Review Articles on Cholinesterase Levels and Organophosphate

Authors	Title	Research Methods	Sample Amount	Results	Conclusion
Marisa M, Pratuna ND (5)	Analysis of Blood Cholinesterase Levels and Health Complaints in Kilometer Potato Farmers in Xi Sungai Penuh City	Cholinesterase test	30 samples.	The study results showed that: 1. Normal cholinesterase level in potato growers is 70%, moderate poisoning 6.7% and mild poisoning 23.3%. 2. The statistical results show that the significance value of the (p = 0.000)	Studies found that there is a relationship between cholinesterase levels and health complaints among potato farmers in Kilometer XI in Sungai Penuh.
Marcherya A (14)	Acetylcholinesterase And Butyrylcholinesterase As Markers Of Pesticide Poisoning	Study of literature	-	The study results showed that: 1. Organophosphates Pesticides work by inhibiting enzymes esterases, especially acetylcholinesterase to synapses and to the membrane of red blood. 2. Erythrocyte AChE activity can be determined biomarkers as a surrogate for AChE cholinergic substances are present in the nervous system.	Inhibition of cholinergic AChE can be measured by blood levels of AChE and BchE. Although AChE is the enzyme associated with acute exposure symptoms, BuChE is more commonly used as a biologic marker to test low levels of organophosphate exposure.

Authors	Title	Research Methods	Sample Amount	Results	Conclusion
Afata TN, Mekonen S, Tucho GT (17)	Evaluating the Level of Pesticides in the Blood of Small-Scale Farmers and Its Associated Risk Factors in Western Ethiopia	Cross sectional study	-	The study results showed that: 1. Farmers under 40 years of age was 21% less likely to be exposed to permethrin. 2. Male SSFs were 17 times more likely to be exposed to heptachlor than females. 3. Farmers with no formal education were 18 times more likely to be exposed to deltamethrin than those with more than primary education. 4. Farmers who used PPE inappropriately were 3.6 times and 6.21 times more likely to be exposed to cypermethrin, respectively.	This study found high levels of p,p'-DDE, p,p'-DDT, heptachlor, cypermethrin, permethrin, and deltamethrin in the blood of small scale farmers. Farmers who are older, less educated, and improperly use personal protective equipment are more likely to be exposed to pesticides.
Parasitekta A, Purwati P, Harningsi T (26)	The Effect of Spraying Time on Cholinesterase Enzyme Levels in Farmers Using Organophosphate Pesticide	Study of literature	-	The study results showed that: 1. Cholinesterase enzyme levels are affected not only by the duration of application, but also by the frequency of application and the use of personal protective equipment. 2. High frequency spraying without the use of personal protective equipment will affect the farmer's cholinesterase activity, even if the spraying time is <5 hours per day.	Application duration affects cholinesterase enzyme levels in farmers using organophosphate insecticides. The longer a farmer applies organophosphate pesticides, the lower the farmer's cholinesterase enzyme levels.
Marisa M and Arrasyid AS (18)	Examination of Pesticide Levels in the Blood of Shallot Farmers in Nagari Alahan Panjang	Cholinesterase test	50 samples.	Onion farmer Arahan Panjan's test results revealed that one of the farmers (aged 65 years old, 42 years of farming experience) had a lower than normal blood cholinesterase level.	Factors causing high exposure pesticides for farmers in Arakhan Panjang in other words, there is a lack of knowledge, not wearing PPE, spraying in the same direction as the wind and personal hygiene of farmers.
Siahaan S (19)	Factors Associated with the Incidence of Pesticide Poisoning in Vegetable and Palawija Farmers in Selat Village, Pemayung District, Batang Hari Regency 2018	Cross sectional study	60 samples.	Statistical test result: 1. There is a relationship between level of knowledge and pesticide poisoning with a value of (p = 0.019). 2. There is a correlation between the use of personal protective equipment and pesticide poisoning with a value of (p = 0.024). 3. There is a value (p = 0.000) association between downwind spraying and pesticide poisoning.	Farmers in Selat Yang village experienced 80.0% poisoning. To avoid pesticide poisoning, farmers are advised to further increase their productivity knowledge of pesticides, complete and appropriate personal protective equipment must be worn when spraying and pay attention to the direction of the wind when spraying.
Istianah, Yuniastuti A (30)	Relationship between Working Period, Spraying Time, Types of Pesticides, Use of PPE and Management of Pesticides with Poisoning Incidents in Farmers in Brebes Regency	Cross sectional study	86 samples	Statistical test result found a connection between: 1. Working time with value of (p = 0.049) in poisoned farmers. 2. Long working hours with value of (p = 0.044) in poisoned farmers. 3. Number of pesticide with value of (p = 0.000) in poisoned Use of personal protective equipment with value of (p = 0.000) in poisoned farmers. 4. Control of pesticides with value of (p = 0.000) in poisoned farmers.	Farmers who are suffering from poisoning there were 55 people (63.96%) and they does not suffer from poisoning is 31 people (36.04%). The causes of poisoning cases are the working hours of farmers, the amount of pesticides used, the adherence of the farmer to personal protective equipment and the way in which farmers handle pesticides.
Halisa SN, Ningrum PT, Moelyaningrum AD (20)	Analysis of Organophosphate Exposure to Cholinesterase Levels in Cabbage Vegetable Farmers in Tanjung Rejo Village, Jember Regency	Cross sectional study	90 samples	Statistical test result: 1. Individual factors value of (p = 0.003) shown in level of knowledge. 2. Environment shown humidity value of (p = 0.045), temperature (p = 0.006) and wind direction value of (p = 0.032). Have relationship with cholinesterase level.	There are two respondents with abnormal cholinesterase levels. There is a relationship between data level, humidity, temperature and wind direction reduced levels of cholinesterase.
Sandra PSM, Sofiana KD, Sutejo IR (13)	The Relationship between Cholinesterase Levels and Lung Function in Farmers Exposed to Organophosphate Pesticide in Sukorambi Village, Jember Regency	Cross sectional study	30 samples	Research results showed that 4 out of 30 samples (14.33%) abnormal levels of cholinesterase. A pulmonary function test shows 20% samples have obstructive disorders, 43.33% are limited by lung disorders and 36.67% (11/30) normal. Statistical test results showed a significant relationship with value of (p = 0.049).	There is a significant association between cholinesterase levels and lung function decline in farmers exposed to organophosphate pesticides in Sukorambi village, Jember Regency.

Authors	Title	Research Methods	Sample Amount	Results	Conclusion
Santaweesuk S< Boonyakawee P, Siriwong W (22)	Knowledge, attitude and practice of using pesticides and serum Cholinesterase levels among rice farmers in Nakhon Nayok Province, Thailand	Cross sectional study	188 samples	The study result showed that: 1. 47.9% the respondents had an average knowledge score. 2. 56.9% respondents had a neutral attitude toward pesticide use. 3. 46.6% respondents had a fairly proper practice of pesticide use. 4. The prevalence of abnormal SChE levels was 68.1% (38.3% unsafe and 29.8% risky) and the remainder was normal (3.7% normal and 28.2% safe).	The results showed that rice farmers had fairly good knowledge and a neutral attitude. However, the serum cholinesterase levels of the farmers were dangerous and risky. Farmers had a health hazard due to the use of pesticides. Prevalence of abnormal SChE levels among rice farmers.
Ulva F, Rizyana NP, Rahmi A (21)	Correlation between Knowledge Level and Symptoms of Pesticide Poisoning in Farmers Spraying Horticultural Plant Pesticide in Lembah Gumanti District, Solok Regency	Cross sectional study	128 samples	The study result showed that 41.1% from of 128 farmers showed symptoms of pesticide poisoning in the risk category and 46.4% of 128 farmers had Low knowledge.	There was a significant relationship between knowledge level and symptoms of pesticide poisoning among farmers who sprayed pesticides on horticultural crops in Lembah Gumanti district of Solok Regency in 2018.
Hidayatullah T, Berliana MI, Pangaribuan B, Wijaya A, Sumiwi SA, Goenawan H (27)	Relationship of Occupational Factors to Acetylcholinesterase Erythrocyte Activity and Cognitive Function in Farmers Using Organophosphate Pesticide	Analytic observation	69 samples	Statistical text result showed that there is significant difference between: 1. The frequency of spraying with value of (p = 0.035). 2. The duration of spraying with value of (p = 0.016). 3. The use of PPE with value of (p = 0.011). Had cognitive impairment in farmers using organophosphate pesticides.	There is a significant relationship between occupational factors on erythrocyte acetylcholinesterase activity and cognitive function in farmers using organophosphate pesticides.
Ramdan IM, Candra KP, Purwanto H (16)	Factors Associated with Cholinesterase Levels in Sprayers Using Paraquat Herbicide in Oil Palm Plantations in East Kalimantan	Cross Sectional study	326 samples	Most sprayers were aged between 26 and 34 years or older (31.9%), had at least 5 years of work experience (76.1%), and sprayed up to 4 hectares per day (84%). Mild toxicity occurred in 29 sprayers. (8.9%). Paraquat herbicide prevalence was significantly correlated age with value of (p = 0.000) and area sprayed per day with value of (p = 0.014).	The prevalence of paraquat among herbicide sprayers on oil palm plantations was relatively low. Reducing the amount of herbicide applied and reducing the sprayed area are necessary factors. Consideration must also be given to preventing herbicide poisoning from worsening.
Sari N, Mastra N, Habibah N (36)	Description of Cholinesterase Enzyme Levels in Blood in the Mekar Nadi Farmer Group, Batunya Village, Baturiti District	Descriptive study	30 samples	The results showed that 22 people (73.3%) had abnormal cholinesterase levels. On the other hand, eight farmers (26.7%) had normal cholinesterase levels.	Based on farmer characteristics, farmers with middle and high school education are often found to have abnormal cholinesterase levels. 70% of farmers have been working for more than 5 years and 73.3% of low cholinesterase farmers have been spraying for more than 3 years. hours and 53.3 hours. Farmers with low levels of cholinesterase didn't use PPE properly.
Venugopal D, Ravichandran B (31)	Occupational health risk of farmers exposed to pesticides in agricultural activities	Study of literature	309 articles	Based on literature review, health effect of farmers causes of exposure to pesticides: 1. 41% neurological disorders. 2. 13% cancer. 3. 8% poisoning. 4. 6% reproductive disruption. 5. 6% genotoxicity. 6. 7% respiratory problems. 7. 5% chronic kidney disease. 8. 14% other health effects.	Based on available targeted health risk factors according to occupational health research, unsafe use of pesticides can have a variety of health effects on humans. Farmers should have more knowledge about alternatives pesticides, color code classification of pesticides, negative side effects of exposure to pesticides.
Pawitra AS, Diyanah KC, Latif MT, Susanto BH, Lusno MFD (35)	Increased Thyroid Hormone Levels in Pesticide Sprayer at Agricultural Area	Cross sectional study	150 samples	The sprayer showed higher thyroid stimulating hormone (TSH) (4.776 ± 1.1166), lower triiodothyronine (T <sub>3</sub> ) (108.822 ± 18.810) and lower thyroxine (T <sub>4</sub> ) levels (7.808 ± 1.166) than other respondent that never been exposed to pesticides	Determinants that strongly influence pesticide TSH, T <sub>3</sub> and T <sub>4</sub> are sprayer use, duration of work, personal protective equipment, body position of the sprayer and type of pesticide.

### Organophosphate Exposure Routes

Farmers are at a high risk of pesticide poisoning and can be exposed to these chemicals through skin contact, inhalation, or ingestion (14). Exposure to organophosphates and carbamates induces acetylcholinesterase (AChE) activity. Cholinesterase is an enzyme found in cell fluid whose function is to stop the action of acetylcholine by hydrolyzing it into choline and acetic acid. Acetylcholine is a neurotoxin in the Central Nervous System (CNS), autonomic nervous system (sympathetic and parasympathetic), and the somatic nervous system (5). A cholinesterase activity below 4500 U/L is indicative of chronic intoxication (15). Organophosphates function by inhibiting acetylcholinesterase (AChE), an enzyme important for nervous system function, as it hydrolyzes the neurotransmitter acetylcholine within neural synapses (14).

### Cholinesteration Levels

Cholinesterase levels are used as a marker of pesticide exposure (13). Normal values of cholinesterase for women were 3999-10800 U/L and for men 4620-11500 U/L. The activity of cholinesterase in a person's blood is expressed as a percentage of cholinesterase activity in the blood. Poisoning diagnoses range from 76 to 100% including "normal," 51 to 75% including mild poisoning, 26 to 50% including moderate poisoning, and 0 to 25% including severe poisoning (5).

### Age of Farmers

Farmer age is related to blood cholinesterase activity, and older farmers have lower blood cholinesterase activity than average blood cholinesterase activity. This result makes sense because the age of a worker indicates the accumulation of exposure time and the ability of various body organs to respond to pesticide exposure (16). A study conducted in Western, Ethiopia showed a significant relationship between worker age and cholinesterase activity levels. Small-scale farmers (SSF) younger than 40 years were 21% less likely to be exposed to permethrin than small-scale farmers (SSF) older than 40 years with the value of Adjusted Odds Ratio (AOR) = 0.21; 95% CI:0.1 0.44 (17). The study found that one of the farmers had a cholinesterase level that was below normal. The farmer was 65 years old and had been farming for 42 years, but his cholinesterase level was below normal, or 2,835.6 UL (18).

### Knowledge of Farmers

Pesticide poisoning is a result of farmers not being informed about the dangers of pesticides, the

fact that many highly dangerous pesticides are still in circulation and readily available, and the lack of safe and affordable Personal Protective Equipment (PPE) available to farmers this occurs due to unavailability (19). Additionally, farmers trained in pesticide use were more aware of Personal Protective Equipment (PPE) use, understood side effects, and observed weather conditions before spraying. Educated farmers are more knowledgeable about pesticide safety so they can better understand and follow label instructions and gain insight into the side effects of improper pesticide chemicals (17).

The chi-square value obtained based on the statistical test conducted among vegetable farmers and back crop farmers in Serat Village, Pemayun District, Batang Hari Regency was ( $p = 0.019$ ) with ( $p < 0.05$ ), It shows that there is a correlation between knowledge and cholinesterase levels (19). This study is supported by a study conducted in Tanjung Rejo village in the Jember Regency. Based on the performed chi-square test, the knowledge level was shown to be ( $p = 0.003$ ) with ( $p < 0.05$ ), indicating a correlation between knowledge level and cholinesterase levels (20).

According to the results of a survey of farmers who sprayed pesticides on garden crops, the percentage of respondents who reported symptoms of pesticide poisoning was higher among respondents with low knowledge (76.9%) than among those with high knowledge (43.3%) (21). These health effects may be due to a lack of knowledge about the risks of pesticide exposure and negative attitudes towards safety, especially regarding the use of pesticides, leading to inappropriate use (22).

Farmers believe that some pesticides, such as paraquat, are safe for users. Therefore, there was no need to wear a gas mask during pesticide application. Additionally, the study found that some farmers still misunderstood that pesticides can only enter the body through inhalation. This was similar to previous research, which revealed that farmers continue to lack knowledge and understanding of the different ways pesticides can enter the human body. Consequently, protection may be inadequate when using pesticides (23). It can be concluded that cholinesterase levels in informed farmers are normal. Lack of knowledge prevented respondents from understanding pesticide information. Since the level of knowledge can be used as a basis for action, knowledge about pesticides influences the judicious use of pesticides according to the dose and influences cholinesterase levels (24).

### Personal Protective Equipment (PPE)

Pesticides are usually contact poisons; therefore,

the use of personal protective equipment by farmers if inhalation and skin contact are major routes of exposure to pesticides. Farmers who do not fully use PPE are at a greater risk of pesticide poisoning than farmers using personal protective equipment (25). Frequent spraying without Personal Protective Equipment (PPE) affects cholinesterase in farmers, even if the spraying time is 5 h/day (26). Based on a study conducted among 69 farmers in Lembang and Pungarengan, Bandung regions, three occupational factors ( $p < 0.05$ ) had a significant association with acetylcholinesterase (AChE) activities: education level ( $p = 0.044$ ), spraying frequency ( $p = 0.035$ ), and Personal Protective Equipment (PPE) use ( $p = 0.011$ ). Based on these statistical results, respondents with low levels of education and cognitive impairment or farm workers are 3.3 times more likely to experience decreased acetylcholinesterase (AChE) activity, compared to respondents who did not use Personal Protective Equipment (PPE) or plantation workers. In this case, the risk of decreased activity was 7.3 times greater Acetylcholinesterase (AChE) (27).

A farmer's behavior and attitude of not wearing Personal Protective Equipment (PPE) during spraying and not changing clothes after spraying could reduce acetylcholinesterase (AChE) activity by 939,049 U/L if spraying was carried out for one hour. The nebulization time should not exceed 1 h per week, as it is reduced by more than 25% compared to the normal acetylcholinesterase (AChE) level of approximately 3,500 U/L (18,28). Farmers must be equipped with personal protective equipment that they must wear to minimize penetration of pesticides through the respiratory, inhalation, and digestive tracts. Therefore, the use of masks, hats, gloves, long-sleeved shirts, and pants is strongly recommended to reduce the risk of pesticides entering the body that can affect cholinesterase levels (18).

### Gender of The Farmers

Acetylcholine acts as a bridge to the flow of nerve vibrations. Normal values for women were 3999-10800 U/L and for men were 4620-11500 U/L (5). Women are more resistant to pesticide poisoning than men because women have more fat and toxic substances can bind to fat (29). The results of a statistical test for sex using Spearman's test showed that her Sig value (two-tailed) was 0.481, indicating no association. However, a study on factors associated with blood AChE levels in farmers showed statistical significance between gender and Serum Cholinesterase (SchE) levels (20). This may be because women are physically weaker than men. Therefore, women in jobs that pose a risk of chemical

exposure have higher levels of pesticide residues in their bodies than men (22).

### Farmers Smoking Behavior

A survey of 69 farmers in Lembang and Pangalengan in Bandung found that almost all of them smoked. A total of 62 respondents were admitted to smoking, 8 (12%) had smoked for less than 10 years, 54 (78%) had smoked for more than 10 years, and the average age was 17 years. There were 7 non-smokers (10%) (27). Smoking while spraying may also contribute to pesticide ingestion by farm applicators if the hands are contaminated (18). Cigarettes contain nicotine compounds that inactivate cholinesterase, reduce cholinesterase activity, and potentially cause addiction (30). Subjects exposed to pesticides and those who smoked cigarettes showed significant effects on absolute telomere length compared to the unexposed groups, and telomere length represented a biomarker of occupational exposure (31). Therefore, telomere length acts as an internal clock that determines the lifespan of both cells and organisms (32).

### Duration of Spraying Pesticide

75% of pesticides were sprayed. The length of time workers are exposed to pesticides is an indicator of the likelihood of pesticide poisoning. According to the Regulation of the Minister of Manpower of the Republic of Indonesia No.3 of 1986, workers employed to handle pesticides must not be exposed for more than 5 hours per day and 20 hours per week (26). Statistical calculations using bivariate analysis using the Spearman test showed that his four risk factors, age ( $p = 0.016$ ), education level ( $p = 0.001$ ), and weight, were significantly associated with cognitive function with value of ( $p < 0.05$ ). It has been shown that there is a sex, the index is ( $p = 0.033$ ) and spraying time during work ( $p = 0.031$ ) (27).

Based on the results of statistical tests conducted on 69 farmers in Lembang and Pangalengan, Bandung, the value of the occupational factor of the spraying period was  $p = 0.016$ , and the OR value (CI 95%) 4.9 (1.3-18.1). Statistical analysis showed that farm workers who sprayed for more than 4 hours per day were 4.9 times more likely to have impaired cognitive function than those who sprayed for less than 4 hours per day (27). This may be because the longer the spray time, the greater is the cumulative effect of the resulting exposure, thereby impairing cognitive function (33).

### Impact of Poisoning Organophosphate

The greater the toxicity of pesticide use, the

greater the signs of poisoning. According to the collected data, approximately 500,000-1,000,000 pesticide poisonings occur worldwide each year, and approximately 500-1,000 people per year suffer from extremely fatal consequences such as cancer, disability, infertility, and liver failure (34). The results of a chi-square test based on a survey conducted among kilometer-sized potato farmers show that the significance of the p-value is 0.000. There is a relationship between cholinesterase levels and health complaints of potato farmers in Kilometer XI of Sungai Penuh as the significance value is ( $P < 0.05$ ) (5).

26 samples (86.67%) had normal cholinesterase levels, while 4 samples (13.33%) had abnormal cholinesterase levels. Pulmonary function test results showed that four patients had restrictive lung disease associated with decreased cholinesterase levels. This is because organophosphates affect the parasympathetic cholinesterase levels (13). A study conducted in an agricultural area found that farmers had lower levels of thyroid-stimulating hormone (TSH), triiodothyronine ( $T_3$ ), and thyroxine ( $T_4$ ) than those who had never been exposed to pesticides (35).

Decreased cholinesterase activity can also occur in various diseases, especially those that attack the liver. Acute and chronic viral infections of the liver, called hepatitis, can reduce cholinesterase enzyme activity by 30% to 50%, but advanced hepatitis, liver tumors, or other tumors that ferment within the liver reduce the activity of the cholinesterase enzyme. Cholinesterase can increase the enzyme cholinesterase by 50-70% (5). Based on available targeted health risk factors according to occupational health research, unsafe use of pesticides can have a variety of health effects on humans. Based on literature review showed that health effect of farmers due to exposure of pesticides: 41% neurological disorders; 13% cancer; 8% poisoning; 6% reproductive disruption; 6% genotoxicity; 7% respiratory problems; 5% chronic kidney disease; 14% other health effects (31).

## CONCLUSION

Organophosphates exert toxic effects by inhibiting acetylcholinesterase (AChE), a critical enzyme in the nervous system responsible for the breakdown of the neurotransmitter acetylcholine within neural synapses. The diagnosis of organophosphate poisoning varies across the spectrum, with percentages ranging from 76% to 100% for normal cases, 51% to 75% for mild poisoning, 26% to 50% for moderate poisoning, and 0% to 25% for severe poisoning. Several factors have been found to correlate with organophosphate poisoning,

including age, level of knowledge among farmers, use of personal protective equipment, smoking behavior, and duration of spraying activities. However, sex does not appear to be a concrete factor that influences the incidence of organophosphate poisoning. It is crucial to recognize that organophosphate poisoning can lead to both acute and chronic health problems, underscoring the importance of preventive measures and proper handling when dealing with these toxic substances.

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