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Prevalence of pesticide related occupational diseases among Indonesian vegetable farmers – A collaborative work

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A R T I C L E I N F O

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A B S T R A C T

Objective: This study was done to understand the prevalence of various occupational diseases including dry eyes, nail dystrophy, and neuropathy related to pesticide exposure in Indonesian local vegetable farmers.
Methods: The data were collected through questionnaires and physical examination involving dermatology, neurology, and ophthalmology domains at Ngablak District, Magelang, Central Java directed to local vegetable farmers. Ocular Surface Disease Index (OSDI) questionnaire and the Schirmer test were used. Analysis was done using descriptive statistics using the Statistical Package for the Social Sciences (SPSS 21.0) and presented in tables.
Results: Inadequate spraying equipment and improper storage of pesticides were found. Out of 105 farmers, 41.9 % experienced occupational skin diseases (OSD). Definite cognitive impairments were found in 3.4 % of subjects but probable in 28.3 % of subjects. Neuropathies were found in 61.7 % of subjects, and dry-eyes syndrome were found in 28.78 % of subjects.
Conclusion: There was a high prevalence of peripheral neuropathy and tremor, dry eyes syndrome in one-third of the population, and the most common skin problem was nail discoloration, with a low incidence of contact dermatitis.

1. Introduction

Indonesia is a multipotential agricultural country that has 39 million laborers working in agriculture, forestry, and fishery domains [7]. Farmers contribute significantly to the number of laborers [8], which makes pesticides as one of the most commonly used substance as it has the ability to repel, kill, and control pests that may damage crops yield [1,56]. The use of pesticides among Indonesian farmers has increased from 11,587.2 to 17,977.2 tons during 1998–2000. In 2012, 813 brand names were registered in Indonesia, and 3207 brand names were listed in Pesticide Commission 2016 [5,3]. Despite their benefits, pesticides are also known to have carcinogenic effects and cause some negative health effects, including dermatological, neurological, respiratory, and reproductive diseases [56,6]. WHO estimated 20,000 fatality cases annually due to the use of pesticides among farmers. Recently, this incident has the tendency to increase, reaching 2 million of pesticide poisoning with 40,000 fatalities annually [56,28].

Pesticides enter the human body through contact with the skin, inhalation, or ingestion, with skin as the most common route of exposure. The absorption process will continue as long as the chemical remains in contact with the skin, which can cause some skin problems. The risk is much higher if Personal Protective Equipment (PPE) is not used properly [37].

Ngablak is a district in Magelang with total agricultural area of 3525 Ha, consisting of 73 farmer groups that spreads across 16 villages. Most of them are vegetable farmers [53]. Previous studies have reported a

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high number of pesticide poisoning in Ngablak [39]. Another study reported that 94.9 % of 78 farmers did not use PPE properly, 75 % had poor pesticide handling, and 78.2 % had mild, 16.7 % moderate, and 1.3 % severe pesticide poisoning [42].

This study was done to know and understand about the prevalence of occupational diseases related to pesticide exposure in Indonesian local vegetable farmers.

2. Materials and methods

This cross-sectional study was done in a sample of 105 farmers for both dermatology and ophthalmology examination and 120 farmers for neurology examination. Participants were recruited from 3 out of 94 hamlets. These hamlets were selected based on the high number of farmers. No previous study had been done on pesticide exposure in this population. These locations are cultivated villages of the Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada. The subjects were farmers who use pesticides in their routine and had sufficient literacy skills.

The data were collected through farmers' workplace observation, guided interviews by specific questionnaires, dermatology, neurology, and ophthalmology physical examination. The routines of farmers using pesticides were observed, starting from preparation to cleaning. They were then invited for an interview-based questionnaire and physical examinations. The questionnaires were translated into Bahasa Indonesia, then adapted for the particular circumstances of these Javanese farmers.

The modified Nordic Occupational Skin Questionnaire (NOSQ-2002 LONG) was used to gather information related to occupational skin problems. The diagnosis of occupational skin diseases was established through dermatology examination, confirmed by workplace observation and interviews based on standardized, reliable questionnaires by a dermatologist.

Another examination was conducted to determine the neurological impact of pesticide exposure. Cognitive impairment was assessed by Mini-Mental State Examination (MMSE) and interpreted based on Damping & Siste scoring system. The results of MMSE are divided into three groups: normal, probable, and definite cognitive impairment. Attention function of cognition was assessed by the Stroop test, and the result was divided into delayed and normal groups. Delayed results were determined by interference score of > 13 s [44]. Neuropathy was assessed by Diabetic Neuropathy Symptom (DNS) and Diabetic Neuropathy Examination (DNE) questionnaires. Diagnosis was made if there is > 1 symptom reported from DNS and > 3 from DNE questionnaires.

In order to investigate the prevalence of dry eye syndrome, Ocular Surface Disease Index (OSDI) questionnaire and Schirmer test were used. Analysis was done to observe the variables associated with dry eyes syndrome, including length and duration of work, hypercholesterolemia, diabetes mellitus, hypertension, heart disease, and smoking history.

All subjects were given the informed consent form that has been reviewed and approved by the Medical and Health Research Ethics Committee of Faculty of Medicine, Public Health, and Nursing Universitas Gadjah Mada-Dr. Sardjito General Hospital, Indonesia to sign. A copy was given to the participant.

The data were analyzed using the Statistical Package for the Social Sciences (SPSS 21.0).

3. Results

3.1. Subject characteristics

The majority of the subjects were male (75.2 %), aged between 20 and 49 years (61 %), with elementary school education (64 %), and had been working for ≥ 20 years (60 %) with a working duration of ≥ 6 h daily (65.7 %). As many as 57 (54.3 %) farmers reported that they never used PPE during work, while twenty (19.1 %) farmers always used PPE. The detailed information of subject characteristics is shown in Table 1. Most farmers routinely wear a hat, long-sleeve cotton T-shirts, long pants, and shoes without rubber gloves and safety boots. However, some farmers do wear cotton gloves, and others were barehanded and barefooted. The summary of potential hazard exposure and PPE recommendation are given in Table 2.

3.2. Pesticides characteristics

The farmers reported seventeen brands with their corresponding active ingredients. The active ingredients of pesticides were identified based on Material Safety Data Sheet (MSDS), National Institute for Occupational Safety and Health Institute (NIOSH), PubChem, and the pesticide label. According to those references, the ingredients were categorized into irritant or sensitizer towards the skin. Moreover, the pesticides were classified based on the hazard level according to the WHO Recommended Classification of Pesticides by Hazard. The chemicals used and their characteristics are listed in Table 3.

3.3. Prevalence of occupational skin disease (OSD) related to pesticide

Table 4 shows that 44 (41.9 %) out of 105 farmers had OSD. The most common diseases were nail discoloration (28.6 %), onycholysis (21.9 %), contact dermatitis (11.4 %), nail deformity (8.6 %), and hypopigmentation (3.8 %). OSD occurred more frequently in subjects who worked as a farmer for ≥ 20 years (25.7 %), worked ≥ 6 h daily (28.6 %), and did not use appropriate PPE (23.8 %). Table 5 presents OSD prevalence based on the NOSQ interview and skin examination.

Nail dystrophy cases which consist of nail discoloration (66.7 %), nail deformity (17.15 %), and onycholysis (42.9 %), were mostly located on the toenails (Fig. 1).

A total of twenty-three (21.9 %) cases of dermatitis were seen predominantly on the dorsal surface and nine (8.6 %) cases of hypopigmentation were located on the lower limb. The diagnosis of OSDs and their predilection are shown in Table 5.

3.4. Prevalence of neurological problems related to pesticide

The neurological examinations were done on 120 farmers with long-term pesticide exposure. Definite cognitive impairment was found in four (3.4 %) subjects, and probable cognitive impairment was found in thirty-four (28.3 %) subjects. Delayed attention was found in eighty-two (68.3 %) subjects, twice more than the normal group (29.2 %). Seventy-four subjects (61.7 %) had neuropathy based on symptoms or clinical examination (Table 6).

3.5. Prevalence of ophthalmological problem due to pesticide

From a total of 105 farmers with long-term pesticide exposure, sixty-six workers agreed to be examined by an ophthalmologist. The incidence of dry-eyes syndrome was found in nineteen (28.9 %) farmers. However, dry-eyes syndrome was not associated with their length of work ($p = 0.561$) and work duration each day ($p = 0.634$). Smoking was closely associated with dry-eyes syndrome ($p = 0.011$). There were no differences in subjective symptoms and OSDI scores between dry eyes group and normal group ($p > 0.05$). However, Schirmer test on both eyes showed significantly lower results in dry eyes group ($p < 0.001$ on both eyes) compared to normal group (Table 7).

4. Discussion

4.1. Known toxicokinetic and toxicodynamic properties of chemical pesticides, fungicides, and herbicides

Organophosphates are the most commonly used type of pesticide due

Table 1
Demographic characteristics and prevalence of occupational skin disease (OSD) related to pesticides.

Categories	Frequency N (%)	OSD (individual) N (%)	OCD N (%)	Non-contact OSD N (%)			
				Nail discoloration	Onycholysis	Nail deformity	Hypopigmentation
Gender							
Male	79 (75.2)	39 (37.1)	10 (9.5)	27 (25.7)	20 (19.1)	9 (8.6)	4 (3.8)
Female	26 (24.8)	5 (4.8)	1 (1.0)	3 (2.9)	3 (2.9)	0	0
Age range (years)							
20–49	64 (61.0)	26 (24.8)	6 (5.7)	16 (15.2)	13 (12.4)	4 (3.8)	3 (2.9)
50–79	37 (35.2)	16 (15.2)	4 (3.8)	12 (11.4)	10 (9.5)	5 (4.8)	0
≥ 80	4 (3.8)	2 (1.9)	1 (1.0)	2 (1.9)	0	0	1 (1.0)
Educational level							
Illiterate	12 (11.4)	4 (3.8)	0	4 (3.8)	3 (2.9)	2 (1.9)	0
Elementary	64 (61.0)	32 (30.5)	9 (8.6)	26 (24.8)	19 (18.1)	9 (8.6)	3 (2.9)
JHS	22 (21.0)	5 (4.8)	1 (1.0)	2 (1.9)	2 (1.9)	0	1 (1.0)
SHS	7 (6.7)	3 (2.9)	1 (1.0)	2 (1.9)	2 (1.9)	0	0
Working duration per day (h)							
< 6	35 (33.3)	14 (13.3)	3 (2.9)	13 (12.4)	11 (10.5)	3 (2.9)	0
≥ 6	69 (65.7)	30 (28.6)	8 (7.6)	18 (17.1)	12 (11.4)	6 (5.7)	4 (3.8)
Length of working as a farmer							
< 20	45 (42.9)	17 (16.2)	4 (3.8)	10 (9.5)	6 (5.7)	3 (2.9)	2 (1.9)
≥ 20	60 (57.1)	27 (25.7)	7 (6.7)	21 (20.0)	17 (16.2)	6 (5.7)	2 (1.9)
The use of PPE							
Never	57 (54.3)	25 (23.8)	4 (3.8)	18 (17.1)	12 (11.4)	8 (7.6)	3 (2.9)
Not always	28 (26.7)	15 (14.3)	7 (6.7)	10 (9.5)	8 (7.6)	0	1 (1.0)
Always	20 (19.1)	4 (3.8)	0	3 (2.9)	3 (2.9)	1 (1.0)	0

to their chemical structures that make them chemically inert, therefore, resistant to thermal hydrolysis, photolytic degradation, and chemical decomposition [46]. Organophosphates rapidly degrade under the sun and are mostly water-soluble, making them easier to use with lower costs, but they also pose a risk of increased environmental contamination. Acute and chronic exposures to organophosphates show toxicity in plants, aquatic life, and human. The lethal mode of action lies in their stimulation to acetylcholine receptors by binding to acetylcholinesterase, therefore aggregating the amount of acetylcholine neurotransmitter. Extensive and chronic exposures may lead to symptoms such as diaphoresis, excessive urination, miosis, lacrimation, salivation, and bronchospasm [20]. Carbamates also display toxicokinetic and toxicodynamics similar to organophosphates [27]. Although rare in mammals and humans, neonicotinoids show other different mechanisms of action with similar effects. Neonicotinoids act as acetylcholine receptor agonists [24], showing features similar to the toxicity of organophosphates.

Pyrethroid compounds are more commonly used as commercial insecticides. Due to poor dermal absorption, they rarely cause toxicity. However, accidental chronic exposure and deliberate ingestions can still happen. Pyrethroids act mainly on sodium and chloride channels by modifying the voltage-sensitive gating characteristics of sodium channels, delaying their closure. Depending on the duration of extended closure, it will create a repetitive firing phenomenon and leads to clinical features such as paresthesia. GABA channels might also be affected at a higher concentration, resulting in seizures [40]. GABA-related mechanism of action is also seen in macrocyclic lactones. Though still unclear, a higher concentration may pass through the blood-brain barrier (BBB), manifesting as sleepiness and low energy level during the day [54].

Studies on the effect of fungicides on human health are still limited. Propineb, one subtype of fungicides, is found to influence and interfere with the cholinergic transmission in model human neuroblastoma cells, although there is no evidence of its toxicity [35]. Another subtype of fungicide, mancozeb, is associated with neural tube defects, but the mechanism behind its possible mode of action is still unknown [38]. Another study linked mancozeb with the development of Parkinson's disease. The study showed a toxicological pathway by intracellular acidification and oxidative stress leading to massive protein S-thiolation [17]. Chlorothalonil has no known study of its toxicity in humans. However, it has been identified that the metabolites of chlorothalonil have embryotic toxicity and endocrine effects on several aquatic ecosystems, such as zebrafish, through a mechanism called molecular docking. It blocks the enzyme substrates necessary for cellular respiration in the gills of zebrafish [55]. Famoxadone and cymoxanil have also been studied with zebrafish larvae. Both substances can induce oxidative stress, resulting in an increase in cell apoptosis in embryos. Acetylcholinesterase activity is significantly higher in embryos with substance exposure [16].

A common herbicide, paraquat dichloride, has been causing many fatalities due to accidental or voluntary ingestion. The substance mainly accumulates in the lung with redox cycling and intracellular oxidative stress generation as its main molecular mechanism. It is expressed abundantly in the membrane of alveolar cells type I, II, and Clara cells. Therefore, it has increased morbidity and mortality due to pulmonary symptoms and ineffective treatment [18]. There are many active chemical compounds with unclear mechanisms of toxicity, especially in humans. However, it is highly possible that manifested toxicity is not purely caused by one chemical compound but more of a complex and chronic interaction between living organisms and pesticides active ingredients.

4.2. Working process and pesticides handling

The flowchart of pesticide handling is shown in Fig. 2 which involves three main stages: preparation, application, and cleaning. Although most farmers commonly use inorganic pesticides, which contain chemical compounds, some prefer semi-organic pesticides for health and safety reasons. Generally, both semi-organic and chemical serve the same purpose, the difference lies in the preparation process, where semi-organic pesticides require some biological matter and takes a longer time than the chemical ones.

During ingredients mixing, pesticide may spill or splash to an exposed skin. Fungicide, one of the ingredients which contains Propineb, is a skin sensitizer and may cause an allergic skin reaction. Skin irritation can also be caused by insecticides containing chlorpyrifos. Prolonged exposure to chlorpyrifos may cause slight skin irritation. Repeated exposure may cause skin burns.

Things to consider when applying pesticides are the selection and correct use of the sprayer. Often times the farmers do not consider the

Table 2
Potential hazard exposure and requirement of Personal Protective Equipment in workplace observation.

Area of operation	Potential hazards present	PPE required	PPE commonly used	Observation in workers practices
Preparation	– Direct exposure through splashing and spilling from pesticide when mixing process – inhalation of pesticide powder	Hat Goggles Respiratory mask Overall outfit Apron Rubber gloves Safety boots	Hat Oral-nasal mask Cotton gloves Long-sleeve T-shirt Long pants Shoes	Almost all farmers using PPE wear hat, long sleeves shirt, and long pants. Some farmers add oral-nasal masks, cotton gloves, and footwear. Footwear could be safety boots or flip-flops.
Application	– Direct skin contact through – Wind direction and wind speed – Droplets of pesticides' aerosol – Direct contact from treated crops – Inhaled or ingested airborne droplets	Hat Goggles Respiratory mask Overall outfit Apron Rubber gloves Safety boots	Hat Oral-nasal mask Cotton gloves Long-sleeve T-shirt Long pants Shoes	Almost all farmers using PPE wear hat, long sleeves shirt, and long pants. Some farmers add oral-nasal masks, cotton gloves, and footwear. Footwear could be safety boots or flip-flops.
Cleaning	– Direct contact to the leftover's pesticide in the equipment when cleaning and disposing	Hat Goggles Respiratory mask Overall outfit Apron Rubber gloves Safety boots	Hat Oral-nasal mask Cotton gloves Long-sleeve T-shirt Long pants Shoes	Almost all farmers using PPE wear hat, long sleeves shirt, and long pants. Some farmers add oral-nasal masks, cotton gloves, and footwear. Footwear could be safety boots or flip-flops.

wind direction, adding to the increased danger of exposure. The leftover pesticides are usually dumped on the ground and may harm non-target areas.

The cleaning process involves two steps: equipment cleaning and personal clean up. First, the farmers repeatedly washed their equipment using clean water and disposed of the used water to the ground. During this activity, chemical substance leftovers from the equipment may splash onto the farmer's body. Once the equipment cleaning is finished, it is stored on a high shelf in their house. If worn, the farmers remove PPE and perform personal cleanup by washing hands, feet, and taking a shower with water. The used work clothing is usually washed separately from daily laundry to avoid contamination.

4.3. *Work safety standards and the use of Personal Protective Equipment (PPE)*

Based on MSDS and WHO recommendations, the sprayer operators should use PPE properly while handling pesticides. This includes hats, goggles, respiratory masks, overall outfit, apron, rubber gloves, and safety boots. Based on the interview, the majority of the farmers wore hats, long sleeves shirts, long pants, and boots. A few also wore masks, aprons, and goggles. However, none of them used PPE thoroughly.

Table 3
List of the chemicals used, hazard classification and characteristic based on interview confirmed by observation.

Chemical substance	Active ingredients	N (%)	Classification of hazard	Characteristic
Insecticide	*Organophosphate*			
	Chlorpyrifos	10 (9.5)	II	Irritant
	Profenofos	23 (21.9)	II	Sensitizer and irritant
	Acephate	1 (1.0)	II	Irritant
	Pyrethroids			
	Lambda cyhalothrin	26 (24.8)	II	Irritant
	Cypermethrin	12 (11.4)	II	Sensitizer
	Deltamethrin	2 (1.9)	II	Not Irritant or sensitizer
	Macrocyclic Lactone			
	Abamectin	6 (5.7)	Ib	Irritant
	Emamectin benzoate	3 (2.9)	II	Irritant
	Insect Growth Regulators			
	Lufenuron	3 (2.9)	II	Sensitizer
	Neonicotinoids			
	Imidacloprid	5 (4.8)	Not listed	Not Irritant or sensitizer
	Anthranilic Diamides			
	Chlorantraniliprole	2 (1.9)	IV	Not irritant or sensitizer
	Carbamate			
	Methomyl	1 (1.0)	Ib	Not irritant or sensitizer
	Nereistoxin analogue			
	Cartap hydrochloride	1 (1.0)	II	Not irritant or sensitizer
	Dimehypo	1 (1.0)	Not listed	Irritant
Fungicide	Propineb	16 (15.2)	IV	Sensitizer
	Mefenoxam	3 (2.9)	Not listed	Irritant
	Cymoxanil	2 (1.9)	II	Irritant
	Famoxadone	2 (1.9)	IV	Irritant
	Chlorothalonil	1 (1.0)	IV	Sensitizer
	Mancozeb	NA	IV	Sensitizer and irritant
Herbicide	Paraquat dichloride	1 (1.0)	II	Irritant
Others	ATONIK	3 (2.9)	Not listed	Not irritant or sensitizer
	Goat urine	1 (1.0)	Not listed	Irritant
	Effective Microorganism (EM^{R})	NA	Not listed	Not sensitizer or irritant
	Water (diluent)	NA	Not listed	Irritant
	Alkyl Dimethiconal	NA	Not listed	
	Unknown	23 (21.9)	-	

In every stage of pesticide handling, proper PPE is required by the farmers to protect them from hazardous chemical exposure through skin absorption, eye contact, inhalation, and ingestion.

4.4. *Working process and PPE usage*

Our observation showed that farmers handled the pesticides by performing three main processes i.e. preparation, application, and

Table 4
OSD prevalence data obtained from the NOSQ questionnaire and skin examination.

	Total n (%)
Farmers without skin problem related to pesticide	71 (67.6)
Farmers currently reported skin problem related to pesticide	5 (4.8)
Farmers with history of skin disease related to pesticide	29 (27.6)
Farmers with current skin disease related to pesticide (according dermatological examination)	44 (41.9)

cleaning. However, some essential parts in each of those processes were still ignored. In practice, the farmers did not read the instructions on the pesticide label before handling; sixty (57.1%) farmers, however, claimed otherwise. A former study on 136 Ethiopian farmers showed that the reasons for ignoring labels were illiteracy, inability to understand the content, and reluctance [36]. These behaviors were also presented in a study in Egypt, with most farmers having lower education [21]. The Environmental Protection Agency (EPA) suggests that operators read, understand, and follow the label before applying pesticides for safe and effective product use [1,2].

The preparation and application process are the activities with the highest potential for exposure to hazardous chemicals where accidental poisoning can occur so that using PPE properly can reduce the risks of exposure [2]. The pesticide mixture could splash or spill over unprotected skin during mixing and loading the tank. In our observation, the farmers combined two types of pesticides into one container even though some pesticides could not work well together, hence, some undesirable effects might appear because of this process. Other than that, the farmers stood on an unstable surface when mixing and loading the pesticide into the knapsack sprayer tank. This could increase the risk of slipping and spilling of pesticides. Furthermore, they did this process around the river, potentially contaminating the water.

The pesticide was sprayed onto the targeted crop in the application process. Based on our observation, the farmers sprayed the pesticides without any specific methods. Indeed, there are many things to consider in this process, such as checking the equipment to prevent leakage of the pesticide mixture, considering the weather condition, i.e., wind speed, wind direction, and temperature, and also checking the delivery rate to apply a pesticide in the correct dose [2,4]. In the same way, a study conducted in India also found that 34 % of pesticide applicators did not follow the right wind direction [47].

After spraying, the farmers cleaned the equipment using river water and disposed of the pesticide residues into the same river, resulting in a contaminated river. In addition, almost all farmers stored the equipment inside their house, which is not safe as any residues could contaminate their house environment. In comparison, Singh and Gupta found that 50 % of Indian farmers stored the equipment in the field, and the remaining farmers stored it in their houses [47].

4.5. Inventory of the hazardous chemicals in pesticide handling

The chemicals used were mainly from class II pesticides which means moderately hazardous. The majority of farmers used lambda cyhalothrin as insecticide from a group of chemicals called pyrethroid. A report retrieved from the Philippine General Hospital in 2000–2001, reviewed by Lu, concluded that the most commonly used pesticides were mixed (39 %) containing three groups of pesticide: organophosphates, carbamates, and pyrethroids, followed by rodenticides (15 %). Pyrethroid

Fig. 1. Nail dystrophy due to pesticide exposure.

Table 6
The result of neurological problems based on MMSE, stroop test, and neuropathy examinations in 120 farmers.

Examination	Interpretation	Total n (%)
MMSE	Definite cognitive impairment	4 (3.4)
	Probable cognitive impairment	34 (28.3)
	Normal	82 (68.3)
Stroop Test	Delayed	82 (68.3)
	Normal	35 (29.2)
Neuropathy	Based on Symptoms Reported	71 (59.2)
	Based on Neurological Examination	8 (6.7)

Table 5
Predilection of OSD related to pesticides.

	OCD	Nail discoloration	Nail deformity	Onycholysis	Hypopigmentation
Right dorsal arm	0	0	0	0	1 (1.0)
Right dorsal hand	4 (3.8)	0	0	0	0
Right dorsal finger	6 (5.7)	5 (4.8)	0	0	0
Left volar arm	0	0	0	0	1 (1.0)
Left dorsal arm	0	0	0	0	1 (1.0)
Left dorsal hand	2 (1.9)	0	0	0	0
Left dorsal finger	3 (2.9)	6 (5.7)	0	0	0
Right lower limb	0	0	0	0	3 (2.9)
Right dorsal foot	3 (2.9)	0	0	0	0
Right toes	0	30 (28.6)	9 (8.6)	23 (21.9)	0
Left lower limb	0	0	0	0	3 (2.9)
Left dorsal foot	3 (2.9)	0	0	0	0
Left toes	1 (1.0)	29 (27.6)	9 (8.6)	22 (21.0)	0
Face	1 (1.0)	0	0	0	0

Table 7
Prevalence, risk factors, and clinical sign and symptoms of dry eye syndrome in farmers.

Variables	Dry eye syndrome	Normal	p-value
Baseline Characteristics			
Amount	19 Subjects	47 Subjects	
Age, years	53.1 ± 15.6	47.3 ± 11.9	0.109
Length of Work, years	23.5 ± 16.6	24.9 ± 14.2	0.561
Work Durations, hours/day	6.1 ± 2.6	6.4 ± 2.4	0.634
Height, cm	150.8 ± 30.9	158.4 ± 7.8	0.279
Weight, kg	53.7 ± 13.4	57.7 ± 9.4	0.381
BMI, kg/m^2	21.9 ± 5.2	22.9 ± 3.3	0.662
Systolic Blood Pressure, mmHg	135.4 ± 35.8	136.5 ± 24.4	0.637
Diastolic Blood Pressure, mmHg	77.8 ± 19.3	82.2 ± 15.1	0.911
Risk Factors			
Hyper-cholesterol, %	11.1	5.3	0.383
Diabetes Mellitus, %	0	5.3	0.226
Hypertension, %	14.8	15.8	0.915
Heart Disease, %	0	2.6	0.396
Smoking, %	66.7	48.7	0.011*
Clinical Sign & Symptoms (OSDI Scores)			
Subjective Symptoms			
Itchy Eyes, %	77.8	84.6	0.443
Watery Eyes, %	81.5	87.2	0.526
Red Eyes, %	77.8	92.3	0.091
Ocular Symptoms			
Sensitive to Light	0 (0–4)	0 (0–4)	0.490
Feel Gritty	0 (0–4)	0 (0–4)	0.410
Painful or Sore Eyes	0 (0–3)	0 (0–3)	0.756
Blurred Vision	0 (0–4)	0 (0–4)	0.773
Poor Vision	0 (0–3)	0 (0–4)	0.444
Vision Related Function			
Reading	0 (0–4)	1 (0–4)	0.257
Driving at Night	0 (0–2)	0 (0–2)	1.000
Working with Computer/ATM	0 (0–2)	0 (0–2)	0.705
Watching Television	0 (0–3)	0 (0–3)	0.648
Environmental Triggers			
Windy Conditions	1 (0–4)	0 (0–4)	0.158
Places with Low Humidity	0 (0–4)	0 (0–4)	0.259
Places with Air Conditioning	0 (0–0)	0 (0–2)	0.405
Schirmer Test			
Right Eyes, mm	9.7 ± 4.7	19.9 ± 5.8	< 0.001*
Left Eyes, mm	8.7 ± 4.8	19.2 ± 6.4	< 0.001*

ATM: Automated Teller Machine; BMI: Body Mass Index; OSDI: Ocular Surface Disease Index; p-value < 0.05 was considered statistically significant.

was reported to have the highest incidence of poisoning during this period. Based on an epidemiologic study in the same review, pyrethroid was the most frequently used pesticide which amounted to 27.2 %, followed by organophosphates (18.0 %), carbamates (9.5 %), mixed pesticides (7.9 %), and chlorophenoxy compounds (4.0 %) [22,33]. However, not all pesticides could be identified due to the lack of labels on the packaging, or even farmers did not know the name of the pesticide they used precisely.

The incidence of occupational disease related to the pesticide in Indonesia is expected to be high because of the following reasons: (1) the extensive use of pesticides; (2) unawareness of the farmers about the adverse effect of pesticides on human health; (3) noncompliance of the farmers to apply pesticide according to safety instruction; and (4) inappropriate use of PPE during work.

4.6. Occupational skin disease related to pesticide

A total of twenty-nine (27.6 %) farmers had OSD obtained from the NOSQ interview, whereas more farmers (n = 44, 41.9 %) were diagnosed had OSD from the dermatological examination. This higher tendency of examination results also occurred in the study conducted by Bregnhoj et al. [15]. They found that 37 of the 764 hairdressing apprentices had hand eczema based on examination, while only 27 admitted they had eczema. This difference might be due to the feeling of shame, fear of being avoided by people, and also a language barrier that probably occurs during the interview.

The most common disease among subjects was nail discoloration (28.6%), with the majority of cases were localized on the toes. Other nail dystrophies such as onycholysis (21.9 %) and nail deformity (8.6 %) were also found. A study carried out in Trinidad on paraquat spray operators found that fifty-five out of 296 had nail damage, with the most common lesion being nail discoloration [25]. Exposure to paraquat concentrates, a highly toxic herbicide, may cause blackening of the nails, loss of nail surface, and abnormal nail growth. Its mechanism, however, in damaging the nails is poorly understood. The author hypothesizes the paraquat concentrates enter the nail-fold and reach the nail matrix which can interfere with the formation of the nail [43,45]. The majority of this research subjects, however, used lambda cyhalothrin, and paraquat was rarely used.

This study discovered vegetable farmers in Ngablak were at medium prevalence (10.5 %) of contact dermatitis. A study conducted in eastern North Carolina showed similar percentage, in which 12.2 % of farmers had contact dermatitis [26]. A lower prevalence of contact dermatitis among farmers was found by Gamsky et al. [22] in California. Out of 759 California farmers, 2 % had dermatitis and 13 % had a lichenified hand dermatitis.

Macular hypopigmentation was seen in four (3.8 %) farmers mainly on the limb region. Ghosh and Mukhopadhyay [23] concluded that insecticide was one of the causative agents (contribute 1.7 %) of hypopigmentation in a study involving 864 chemical leukoderma cases. Similarly, another study [49] agreed that hypopigmentation has occurred following the contact dermatitis reaction to the carbamate herbicides.

4.7. Ophthalmological problem due to pesticide

One-third of the farmers was found having dry eyes syndrome although no association was found between their habit and pesticide exposure. The authors' finding on association between smoking and dry eyes syndromes was similar with a study in India, with smokers had lower Schirmer Test and abnormalities in corneal sensation and tear meniscus height [51]. The association between dry eyes syndrome and smoking might be due to the decreasing tear stability and sensitivity of cornea and conjunctiva in patients with smoking behavior [44]. Meta-analysis study showed significant association between hypertension, hyperglycemia, and hyperlipidemia on risk of developing dry eye syndrome [50]. Our study didn't show significant association, which may be caused by low prevalence of metabolic disorder in farmer population compared to the general population. We assumed that dry eye is associated with multi-risk factors such as environment (i.e. chronic pesticide exposure), lifestyle, age, sex, systemic drug history, and systemic diseases.

We found no differences in subjective symptoms or based on OSDI scoring to determine clinical symptoms differences between dry eye groups and normal groups. However, there were significantly lower Schirmer test results on dry eye groups compared with normal. Similar results were found in Ghanaian and Indian populations, where no significant correlation was found between Schirmer test and dry eye symptoms [29,52]. Dry eye syndrome is a complex disease and Schirmer test without other findings was neither considered as gold standard examination nor superior than other objective examinations and clinical symptoms. In contrast, Schirmer test was easy to use and cheaper than other examinations. Considering other aspects, this study showed Schirmer test could be used for screening tools to prevent and educate the population at risk (farmers) on developing dry eye symptoms.

4.8. Neurological problem due to pesticide

In this study, 31.7 % of subjects were found with probable and definite cognitive impairment. Cognitive decline and impairment were not only found in this study [30]. PHYTONER study, a four-year prospective

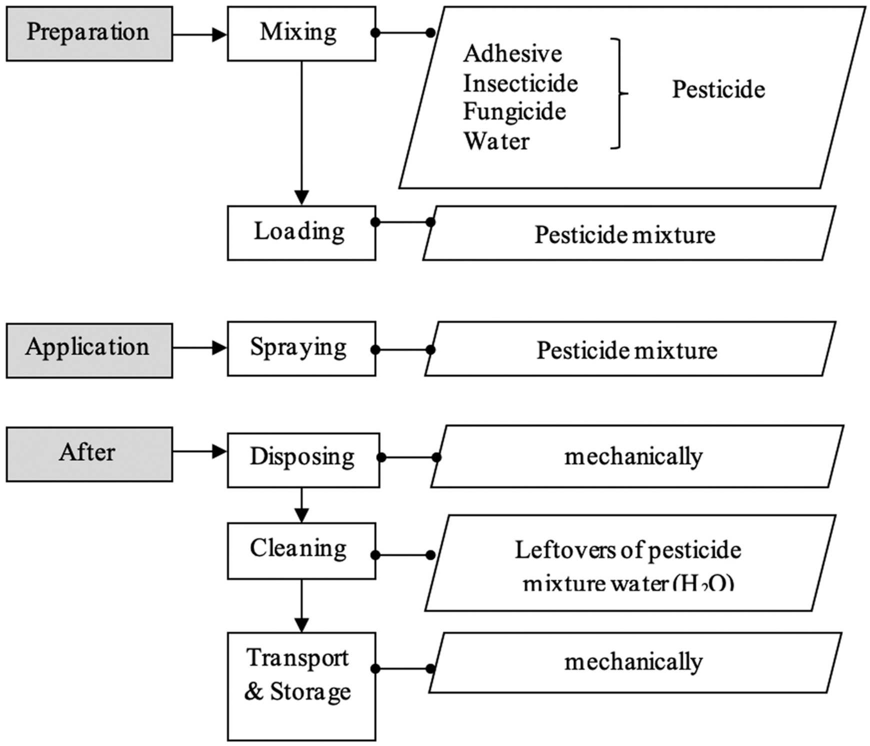

Fig. 2. Flowchart of the working process in inorganic pesticide management.

study in France, found a significant two-point lower score in MMSE in the exposed group [9]. In another study, pesticide exposure was associated with mild cognitive dysfunction in the aging population [14]. Cognitive impairment mechanism in the chronically exposed pesticide group was still unclear, but some evidence showed that pesticide exposure, especially organophosphate, could lead to higher oxidative stress marker [11]. This high oxidative stress could lead to lower MMSE score and cognitive decline [41].

Attention function is one of the cognitive domains and the Stroop test is a neurobehavioral tool to access the attention domain. We found a quite large prevalence of delayed Stroop test results, with 68.3 % from 120 subjects. PHYTONER study also found organophosphate exposed group had a significantly higher risk to perform poorly in the Stroop Test examination, with odds ratios ranging from 1.40 to 2.26 [12]. The mechanism of how chronic pesticide exposure induced lower attention function in adults was still unclear but may follow the same pathway as cognition disturbance induction from pesticide.

Peripheral neuropathy symptoms were found in 71 subjects (59.2 %) and abnormal neurological findings were found in eight subjects (6.7 %). Pesticide exposure, acute or chronic, could lead to neuropathy. One of the most studied pesticide-induced neuropathies is organophosphate induced delayed neuropathy (OPIDN) [19]. OPIDN is caused by acute intoxication of organophosphate and usually occurs one to four weeks after exposure. Exposure to high dose organophosphate led to distal axon degeneration of peripheral and central nervous system. This caused paresthesia, distal numbness, progressive weakness, and depression of deep tendon reflexes [32]. Neuropathy caused by chronic exposure to low organophosphate was still a debatable field. One study in Iran found 40 % of farm sprayers had abnormal neurological findings and significant difference in electrodiagnostic assessment except for peroneal compound muscle action potential (CMAP) distal latency, sural sensory nerve action potential (SNAP) amplitude, and sural nerve conduction velocity (NCV). The problem was, both mean values of subjects with neuropathy and the normal group were in the normal range value [13]. This raised a question on how to determine chronic pesticide exposure neuropathy. Even in chronic exposure, the pesticide's dose must be high too, the reason being is there was still no evidence of peripheral neuropathy caused by low-level chronic exposure [31].

This study found eighty-four subjects (71.7 %) had at least one type of tremor from the Tremor Rating Scale examination. Tremor and pesticide had been studied extensively, and both rest and action tremors could be found in humans [34]. Tremors could be induced in acute intoxication or chronic exposure to pesticides. The mechanism of tremors induction in chronic exposure relates to the effect of pesticide in central dopamine, causing Parkinsonism tremor [10]. For pyrethroid intoxication, there were two types of syndrome. Type I – fine tremor which progresses to whole-body tremor (called Tremor Syndrome), and Type II – coarse tremor, profuse salivation, and clonic seizure (choreoathetosis syndrome). This syndrome is caused by neurotoxicity mechanism of pyrethroid in slower activation of voltage-gated sodium channels (type I and II), decreased opening probability of voltage-gated chloride channels (type II), and inhibition of GABA-gated chloride channels (type II) [48]. This could explain the high prevalence of tremors in this study.

5. Conclusion

Pesticides are widely used by Indonesian farmers, with the majority uses inorganic pesticides which all contain chemical compounds, and the rest prefers semi-organic pesticides for health and safety reasons.

This study found high prevalence of peripheral neuropathy and tremor, dry eyes syndrome in one-third of the population, and the most common skin problem was nail discoloration, with a low incidence of contact dermatitis.

CRediT authorship contribution statement

Sri Awalia Febriana: Conceptualization, Investigation, Writing – original draft. **Miya Khalidah:** Investigation, Project administration. **Fariz Nurul Huda:** Software, Investigation. **Sri Sutarni:** Writing – review & editing, Conceptualization. **Indra Mahayana:** Resources, Formal analysis, Methodology. **Niken Indrastuti:** Data curation, Validation. **Ismail Setyopranoto:** Writing – review & editing, Data curation. **Fajar Waskito:** Visualization, Investigation. **Suhardjo Prawiroranu:** Conceptualization, Writing – review & editing. **Ery Kus Dwianingsih:** Methodology, Formal analysis, Resources. **Rusdy Ghazali Malueka:** Supervision, Funding acquisition, Conceptualization, Writing – review & editing.

Ethics approval and consent to participate

The study was reviewed and approved by the Medical and Health Research Ethics Committee of Faculty of Medicine, Public Health, and Nursing Universitas Gadjah Mada - Dr. Sardjito General Hospital, Indonesia with approval number KE/FK/0571/EC/2019.

Statements and Declarations

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

The data that has been used is confidential.

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