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TYPES AND TOXICITY LEVELS OF PESTICIDES: A STUDY OF AN AGRICULTURAL AREA IN BREBES REGENCY

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Abstract

Introduction: *Previous studies found that young children, children, pregnant women, and farmers are at risk of pesticide exposure. Organophosphate pesticides are detected in children's urine, but other types of pesticides, their toxicity classification, and their toxicity level have not been identified. Hence, this study aims to identify types and toxicity levels of pesticides that are possible causes of health problems in an agricultural area.* ***Methods:*** *The population of the study were 1,017 households in two villages of an agricultural area of Brebes Regency, Indonesia. The data were collected from 166 participants using a cross-sectional design involving questionnaires to identify the characteristics of the respondents and observations to identify the pesticide, pesticide packaging, and pesticide residue in their houses. The toxicity levels of the pesticides were identified based on the pesticide toxicity classification recommended by the World Health Organization (WHO). Potential health problems due to pesticides were subsequently identified based on literature reviews.* ***Results and Discussion:*** *According to the results, organophosphate, carbamate, and pyrethroid pesticides were found in 30.7% of the respondents' houses. The toxicity levels of the pesticides ranged from highly hazardous (Ib) to unlikely presenting acute hazard (U). The potential health problems due to pesticides varied from poisoning symptoms to genetic disorders and polymorphisms.* ***Conclusion:*** *There were three types of pesticides with toxicity levels ranging from highly hazardous to unlikely presenting acute hazard in the agricultural area in Brebes Regency.*

INTRODUCTION

The use of pesticides for agricultural purposes contributes to an increased risk of pesticide exposure in rural areas (1). A previous study of an agricultural land in Brebes Regency revealed that organophosphate pesticide metabolites were found in 28.9% of the children's urine. The concentrations of the organophosphate pesticide metabolites were between 0 Parts Per Million (ppm) and 0.223 ppm (2). Pesticides may interfere with endocrine functions (3). Exposure to organophosphate pesticides is associated with Thyroid Hormone Disorders (TSH, FT4) with a p-value of 0.005 and a Prevalence Ratio (PR) of 2.4 (4). Farmers and pregnant women also are at risk of pesticide exposure. Shallot farmers may be exposed to pesticides when they apply pesticides in the soil. A previous study revealed that shallot farmers who frequently sprayed pesticides had a chance of infertility, with a p-value of 0.024, an Odds Ratio (OR) of 2.66, and 95%CI of 1.1–6 (5). Meanwhile, pregnant women living in agricultural areas who were exposed to pesticides gave birth to babies with low birth weight (OR = 6.8; 95%CI = 2.0–22.9) (6). Furthermore, parental involvement in agricultural activities is a risk factor of Attention Deficit Hyperactive Disorder (ADHD) in early childhood (OR = 1.58; 95%CI = 1.231–2.028) (7).

Children, pregnant women, and shallot farmers can be exposed to pesticides in various ways, such as consuming food and drinks contaminated with pesticides, being involved in agricultural activities, residing in a farming area, applying pesticides, and the like (8).

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Children and pregnant women living in agricultural areas may be exposed to pesticides through pesticide drift or evaporation of pesticides from the agricultural area. Shallot farmers may also bring pesticide contaminants into their homes after they come into contact with pesticides through spraying (9). Another study found that most school children exposed to pesticides lived in agricultural areas since birth, and 23% of them got the exposure from shallot farming activities (4).

Agricultural lands, properties, and neighborhoods are suspected as pesticide sources. However, the previous study only revealed one type of pesticide in the urine, that is, organophosphate pesticides, while farmers use many types of pesticides to protect their crops, especially shallots (2). In addition, the toxicity of pesticides needs to be identified. Therefore, this study is important to identify the types and toxicity level of pesticides used by the community in agricultural area of Brebes Regency.

METHODS

Observations were carried out to people who lived in the agricultural area located in two villages in Brebes Regency. The agricultural area in question was shallot farming which uses a lot of pesticides. The population were parents of elementary school students identified in the previous study (2). The sample size was determined by the diagnoses of the Thyroid Stimulating Hormone (TSH) of the school children. If the level of TSH was ≥4.5 mIU/L, they were categorized as hypothyroid (54 school children); whereas, if the level of TSH was between >0.5 and <4.5 mIU/L, they were categorized as euthyroid (112 school children). Subsequently, interviews were carried out to their parents to identify the pesticides at their houses. The data were collected through questionnaires and observations inside and outside the respondents' houses. The questionnaires were distributed to identify the characteristics of the respondents. Meanwhile, the observations were aimed at identifying pesticides from leftover pesticides, pesticide packages or containers, and equipment used to spray or apply pesticides. The pesticide brands, types, groups, active ingredients, and formulations were identified from the pesticide packages or containers. If the containers were not legible, the respondents told the trademark and the active ingredients traced by researcher from the manufacturers through their websites. Furthermore, to identify the toxicity level of the pesticides, the active ingredients were compared with those in the classification of pesticide toxicity recommended by the World Health Organization (WHO) (10). Potential health effects due to pesticides were identified based on literature reviews.

This study received ethical approval from the Committee of Health Research Ethics of the Faculty of Public Health, Diponegoro University, with the number of 91/EC/FKM/2016.

RESULTS

Brebes Regency is located 1 to 500 meters above sea level. The total area of Brebes Regency is 166,296 km² with a population of 1,781,379 people. About 70% of the population work in the agricultural sector, 40% of whom are farmers and farm workers. The harvested area of shallots constitutes 30,954 ha, producing 3,759,742 quintals with an average production of 121.46 quintals per ha. As a result, shallot farming contributes to the gross income of Brebes Regency by 58%. The largest shallot farms in Brebes Regency are spread across 11 subdistricts, namely Larangan, Wanasari, Bulakamba, Brebes, Tonjong, Losari, Kersana, Ketanggungan, Songgom, Jatibarang, and Banjarharjo. Bulakamba subdistrict is in third place after Larangan and Wanasari Subdistricts. Shallot farming in Brebes Regency contributes to the demands for shallot production in Central Java (72.39%) and Indonesia (30.62).

The average age of the respondents was 42.1 years, which is considered productive (see Table 1).

Table 1. Characteristics of Respondents and Identification of Pesticides

Characteristics of Respondents	Total	Percentage (%)
Age (year)		
26–35	39	23.5
36–45	78	47
46–55	39	23.5
56–65	8	4.8
>65	2	1.2
Level of Education		
Never attended school	1	0.6
Did not finish elementary school	23	13.9
Finished elementary school	112	67.5
Finished junior high school	18	10.8
Finished high school	9	5.4
Completed higher education	3	1.8
Type of Occupation		
Unemployed	1	0.6
Farmer and farm worker	62	37.3
Pesticide trader	1	0.6
Small trader	83	50
Others (construction worker, private worker, civil servant)	19	11.4
Identification of Pesticides in the House		
Presence	51	30.7
Absence	115	69.3

Based on the age category, most of the population were 36–45 years old. Most of them were elementary school graduates and worked as small traders.

This study also found pesticides in 30.7% of the respondents' houses. Table 2 shows the types, groups, and active ingredients of the pesticides.

Table 2. Types, Groups, Active Ingredients, and Toxicity Levels of Pesticides in the Respondents' Houses

Brand	Type (Based on the Target Organism)	Group	Active Ingredient	Classification of Pesticide Toxicity	LD_{50} (mg/kg body weight)
Starban 585EC	Insecticide	Organophosphates	Chlorpyrifos 530 g/l	II	135
Dursban 200 EC	Insecticide	Organophosphates	Chlorpyrifos 200 g/l	II	135
Sidajos 430 EC	Insecticide	Organophosphates	Dimethoate 430 g/l	II	c150
Destan 400 EC	Insecticide	Organophosphates	Dimethoate 400 g/l	II	c150
Roundup 486 SL	Herbicide	Organophosphates	Glyphosate 486 g/l	III	4,230
Indocron 500 EC	Insecticide	Organophosphates	Profenofos 500 g/l	II	352
Vondozeb 80 WP	Fungicide	Carbamate	Mancozeb 80%	U	>8,000
Dithane M-45	Fungicide	Carbamate	Mancozeb 80 %	U	>8,000
Colanta 70 WP	Fungicide	Carbamate	Propineb 70%	U	8,500
Antracol 70 WP	Fungicide	Carbamate	Propineb 70%	U	8,500
Emcindo 500 EC	Insecticide	Carbamate	BPMC/butylphenyl methylcarbamate 500 g/l	II	620
Baycarb 500 EC	Insecticide	Carbamate	Fenobucarb; BPMC 500 g/l	II	620
Benhur 500 EC	Insecticide	Carbamate	BPMC 500 g/l	II	620
Naga 50 EC	Insecticide	Carbamate	BPMC 50 g/l	II	620
Marshall 200 EC	Insecticide	Carbamate	Carbosulfan 200.11 g/l	II	250
Buldok 25 EC	Insecticide	Pyrethroid	Beta cyfluthrin 25 g/l	Ib	c11
Prado 25EC	Insecticide	Pyrethroid	Beta cyfluthrin	Ib	c11
BM Cyperkil 50 EC	Insecticide	Pyrethroid	Cypermethrin 50 g/l	II	c250
Pounce 20 EC	Insecticide	Pyrethroid	Permethrin 20 g/l	II	c220
Decis 25 EC	Insecticide	Pyrethroid	Deltamethrin 25 g/l	II	c135
Anta 50 EC	Insecticide	Pyrethroid	Emamectin benzoate 50 g/l	III	53-237
Prothol 10 EC	Insecticide	Pyrethroid	Emamectin benzoate 10 g/l	III	53-237
Abenz 22 EC	Insecticide	Pyrethroid	Emamectin benzoate 22g/l	III	53-237
Bosmex 25 EC	Insecticide	Pyrethroid	Abamectin 25 g/l	Ib	8.7
Confidor 5 WP	Insecticide	Neonicotinoid	Imidacloprid 5 g/l	II	450
Besvidor 25 WP	Insecticide	Neonicotinoid	Imidacloprid 25 g/l	II	450
Tumagon 100 EC	Insecticide	Pyrol	Chlorfenapyr 100g/l	II	441
Arjuna 200 EC	Insecticide	Pyrol	Chlorfenapyr 200g/l	II	441
Prowl 330 EC	Herbicide	Dinitroaniline	Pendimethalin 336 g/l	II	1,050
Amistar top 325 SC	Fungicide	Azoxystrobin	Azoxystrobin 200 g/l and Difenoconazole 125 g/l	U	>5,000 1,453
Rovral 50 WP	Fungicide	Iprodione	Iprodione 50%	III	3,500
Rapid 20 WG	Herbicide	Metsulfuron methyl	Metsulfuron methyl 20 %	U	>5,000
Prevathon 50 SC	Insecticide	Chlorantraniliprole	Chlorantraniliprole 50 g/l	U	>5,000

Classification of pesticides toxicity based on pesticide active ingredients: Ia = extremely hazardous (oral < 5, dermal < 50); Ib = highly hazardous (oral 5-50, dermal 50-200); II = moderately hazardous (oral 50-2000, dermal 200-2000); III = slightly hazardous (oral > 2000, dermal > 2000); U = unlikely presenting acute hazard in normal use (5000 or higher). The unit is in mg/kg body weight.

Insecticides and fungicides were most commonly used by the farmers. Insecticides kill insects, while fungicides remove fungi from shallots and onion bulbs. Based on the groups, organophosphates, carbamates, and pyrethroids are most commonly used by the farmers. Organophosphate pesticides contain common active ingredients such as chlorpyrifos, dimethoate, glyphosate, and profenofos. Carbamate pesticides mostly contain mancozeb, propineb, BPMC, and carbosulfan. The active ingredients contained in pyrethroid pesticides are cypermethrin, permethrin, emamectin, deltamethrin, and beta-cyfluthrin. Most pesticides are usually in liquid form, which in part helps emulsify the pesticide formulations, while the rest is suspended and dispersed.

DISCUSSION

Transportation and Fate of Pesticides from the Shallot Farm

The farmers applied pesticides on shallot farms during the planting sessions in wet and dry seasons. They used pesticides more frequently in the wet season due to fungal attack. Pesticides that are sprayed to control shallot pests spread to the soil, air, and water, and the pesticide residue affected the farmers. Pesticides could spread in the environment in a number of ways, including runoff, leaching, volatilization, pesticide drift, and biological magnification (11–12). When pesticides are applied to soil, runoff can flow into nearby water bodies, contaminating surface water and potentially affecting aquatic life. Leached pesticides can penetrate the soil and contaminate groundwater if they are not bound to the soil particles. Some pesticides can evaporate and spread into the air, leading to airborne contamination and potential exposure to humans and animals living near the shallot farm. Moreover, during the application, pesticide particles from shallot farming can be transported by air and carried by the wind, potentially affecting non-targeted areas and organisms. In biological magnification, pesticides can move up the food chain when they are ingested by small organisms that are consumed by larger organisms. In other words, pesticides in soil, air, and water would undergo a process of degradation in a short or long time, depending on the physical, chemical, and biological conditions of the medium (13).

Sometimes the farmers brought home a few packages of pesticides and leftover pesticides seen in shallot farming areas. In addition, pesticides that stuck to their clothes or body would be carried into their houses. Based on the observations in the respondents' houses, it was found that there were various types of pesticides with different active ingredients. More than three types of pesticides were found in one house. The pesticides were stored in the kitchen along with the pesticide spraying equipment. Insecticides and fungicides were the most common pesticides found in the respondents' houses since the farmers chose pesticides that could kill the most attacking pests, such as insects and fungi. These findings are consistent with other research findings that found the same types and groups of pesticides (14–15).

Insecticides and Fungicides at the Respondents' Houses

Insecticides and fungicides found in the respondents' houses were used to control the number of pests that may lead to crop failure, especially when fungal attack increased significantly in the wet season. Based on previous research, the most common types of fungi found in the shallot farming areas of Brebes Regency were *Alternaria porri*, *Colletotrichum gloeosporioides*, *Porenospora destructor*, and *Fusarium oxysporum*. In addition to Brebes Regency, *Fusarium oxysporum* and *Colletotrichum sp.* were also found in other areas of shallot farming such as Kalimantan (16). Meanwhile, insecticides were used to control shallot pests such as *Spodoptera exigua*, *Spodoptera litura*, and *Thrips tabaci* (15). The aforementioned insects and fungi grow well in the tropics. The respondents who worked as shallot farmers, both male and female, handled the shallots from the beginning (planting) to the end (postharvest) to ensure the success of the shallot farming. The farmers planted shallots with bare hands and only wore long sleeves, trousers, and hats. They did not were the complete Personal Protective Equipment (PPE) to handle the shallots, such as boots, gloves, face or respiratory protection, and eye protection. As a result, pesticides could stick to their clothes and parts of their body that were not protected by the clothes or PPE. Subsequently, when they went home, they brought the pesticides into their houses along with them.

Pesticide Packaging Labels

The pesticide packaging or container labels found in the respondents' houses showed the instructions for using the pesticides, including the dosage, volume of the solution, and first aid instructions. Moreover, the pesticide packaging included the pesticide formulation, namely Emulsifiable Concentrate (EC), Suspension Concentrate (SC), and Wettable Powder (WP). The 80 WP label means that the pesticide was formulated in powder form with microscopic particles dissolved in a liquid (water) with more than 80% active ingredients. The average volume of the insecticide solution applied ranged from 13.29 to 15.17 liters per ha (17). The farmers sprayed the pesticides regularly every 3–4 days per week and 15–20 times in the growing season. The volume of the insecticide used on the agricultural area of 30,954 ha was around 13.29–15.17 liters per ha and was estimated to be around 411,378.66–469,572.18 liters per ha in the growing season. The use of pesticides in Brebes Regency was usually to prevent shallot pests. Pesticides were also used to preserve shallot bulbs stored in the house. Pesticides were applied by spraying the shallots and spreading pesticide powders on the shallot bulbs. Spraying pesticides on the shallots was usually done at 6 to 9 AM and 3 to 5 PM. Each farmer applied more than three, even up to seven, types of pesticides. The dosage of pesticides usually exceeded the recommended dosage on the packaging labels. Therefore, it may be necessary to educate the farmers to comply with the recommendations for pesticide application, including wearing Personal Protection Equipment (PPE).

The use of pesticides to control shallot plant pests; usually, there were leftover pesticides. Some of them were brought home by the farmers, whereas some others were left in the farm. Leftover pesticides and pesticide packages and containers were found in 51 houses. The leftover pesticides that were left in the farm and brought home were either in solid form such as powder or in liquid form. There were various types of materials for making pesticide containers, including plastic, cardboard, cans, and glass bottles. These containers were stored in the kitchen and outside the house. The respondents usually stored the pesticides and leftover pesticides in the kitchen, by hanging them on the wall, on the corner of the siding, on the terrace, or in certain places outside the house.

Mechanisms and Pathways of Pesticide Exposure

Household members can be exposed to pesticides stored at home through several mechanisms. White pesticide powder as a preservative was found and used to protect shallot bulbs stored on wooden racks and placed in the kitchen. The floors of the respondents' houses were made of earth and cement or ceramics. Pesticide drift that fell on the floor would mix with or stick to the dust; thus, cleaning the floors would spread the pesticides that stuck to the dust throughout the house. In addition to pesticides, the respondents used equipment such as sprayers, buckets for pesticide formulations, and clothes specifically worn for pesticide spraying. Previous studies confirmed pesticide storage inside and outside the house. For example, 38.4% of farmers in Ethiopia (18) and 44.4–55.0% of farmers (19) stored pesticides in their kitchen or houses, while 59.5% of farmers in Pakistan stored them in separate rooms in their houses (20). Another example is that 44% of farmers in Ghana stored pesticides in their bedrooms (21) and in Ethiopia, 30.5% of farmers stored them under their beds (22). For outdoor storage, 96% of farmers in Vietnam stored pesticides in separate places outside their houses and 1% of farmers in Vietnam (23) and 9% of farmers (22) keep pesticides in their kitchens.

Pesticide exposure occurs directly and indirectly. Pesticides may contaminate people through the skin, inhalation, and ingestion of solids, liquids, or gases (24). Farming activities could expose the surrounding community to pesticide drift from the pesticide storage or the air, thereby allowing the pesticides to enter the respiratory tract or come into contact with the skin. Moreover, pesticide drift may contaminate the food or drink consumed by the farmers. Besides direct exposure to pesticides, pesticides stored in the house could also contaminate the food and drink at home, especially if pesticides, pesticide residues, or pesticide packages are stored near the food processing area, such as the kitchen. Pesticides are volatile in liquid and powder forms, so they spread quickly. If pesticides are stored in the kitchen, pesticide drift can spread in the kitchen and contaminate food, drink, and dining utensils. Previous studies revealed that pesticides were found around the houses in agricultural areas (25–26).

Storing pesticides inside and around the house poses a risk of exposure to people who live there. Pesticides are volatile and fly around in the house. Infants, toddlers, pregnant women, and older people usually spend much time at home. They are at higher risk of being exposed to pesticides compared to those who spend much time outside the house. A study confirmed that pesticide exposure in farming areas tends to be higher in children and is associated with indoor pesticide storage (27). Furthermore, older children and teenagers spend a lot of time playing outdoors, including on the terrace, in the yard, with the neighbors, and in the shallot farming area. Pesticides could be in the house of farmers who did not spray pesticides because pesticide drift could be transferred by dust, wind, and the like (28). In fact, some people stored shallot bulbs which may contain pesticide residues on the terrace and in the yard. Beside playing at outdoor, pesticide can expose to children due to involved in farming activities in the farming area (2).

There are activities that may cause people to be exposed to pesticides, such as formulating, spraying, and storing pesticides; living in the houses with pesticides or pesticide drift; and playing outside the house in agricultural areas. Figueiredo created a model for the journey of pesticides from the farm to the house by considering several aspects. These aspects include the application of pesticides in agriculture, drift models, volatilization models, dispersion models, ventilation models, and dust absorption models for indoor dust. Moreover, pesticides applied to an agricultural land can spread across the agricultural area, even the settlements due to weather conditions (29–30). Pesticide levels at home in agricultural areas vary depending on the distance from the farming area and the spraying season (31). Previous research found that the overall concentrations of pesticides in the dust were higher during the application period, and the concentrations were higher in the houses closer to than in the houses far from the agricultural land (29). The exposure to pesticides causes health problems, ranging from mild health problems to serious health problems. The exposure levels of the pesticides depend on the dosage, the duration, and the frequency of exposure (32).

Classification of Pesticides, LD_{50}, and Types of Toxicity

Our findings showed that organophosphate was classified into categories II and III. Carbamate was classified into categories II, III, and U, whereas pyrethroid was classified into categories Ib, II, and III. Moreover, neonicotinoid pesticides were classified into category II. Pyrol, dinitroaniline, iprodione, metsulfuron-methyl, and chlorantraniliprole were classified into categories II, III, and U. The most toxic active ingredients were beta-cyfluthrin and abamectin, which belong to category Ib of the pyrethroid group. The Lethal Dose 50 (LD_{50}) of beta-cyfluthrin and abamectin were 11 mg/kg body weight and 8.7 mg/kg body weight respectively. The WHO recommended a classification of pesticide toxicity based on hazard. The toxicity levels of pesticides vary widely, ranging from harmless to extremely hazardous. The classification of pesticide hazard is based on the chemical structure, the route of exposure, the active ingredient, and the type of target organism (11). Table 2 shows the toxicity levels of pesticides from very dangerous (Ib) to unlikely to cause acute hazard in normal use (U). Pesticide toxicity classified as oral and dermal toxicity was tested on rats following standard toxicology procedures. In determining toxicity levels of pesticides, most pesticides are at a Lethal Dose of 50 (LD_{50}) by acute oral exposure (mg/kg body weight). However, dermal toxicity should be considered the most because most of the exposures occur through the skin. Dermal exposure is considered high risk if the dermal LD_{50} value indicates a more significant hazard than the oral LD_{50} value (8). The effects of pesticide toxicity on human health range from mild to severe, with acute and chronic exposure. Some symptoms of pesticide poisoning include weakness, perspiration, lack of appetite and depression, irritation, and acetylcholinesterase level below the limit value (33). Moreover, pesticide toxicity found in humans includes genotoxicity (34), hepatotoxicity (35), hepatotoxicity (36), neurotoxicity (37), nephrotoxicity (38), and carcinogenicity (39–40). Several mechanisms of action of pesticides include an imbalance between free radicals and antioxidants, enzyme inhibition, DNA damage, gene expression, and mimicry (12).

Organophosphate and Its Potential Health Effects

The active ingredients of organophosphate pesticides are chlorpyrifos, dimethoate, glyphosate, and profenofos. Both acute and chronic exposure to various pesticide groups leads to health problems (24). Organophosphates (OPs) are pesticide groups with a double bond with a central phosphor atom. The double bond is either sulfur or oxygen, R1 and R2 groups, ethyl or methyl structure, and a leaving group specific for organophosphate, where R2 is an aromatic compound or aliphatic compound and R1 is a methyl (41). The clinical manifestations of contact with organophosphate compounds include muscarinic effects, nicotinic effects, and effects on the central nervous system. Muscarinic effects include sweating, excessive salivation, lacrimation, bronchospasm, dyspnea, miosis, gastrointestinal symptoms, and blurred vision. Nicotinic effects include hypertension, muscle fasciculations, and muscle cramps. Nicotinic effects also include motor weakness, tachycardia, and paralysis. The effects on the central nervous system include anxiety, dizziness, insomnia, and nightmares. More effects on the central nervous system include headaches, tremors, confusion, ataxia, and comma (42). Organophosphate pesticides tend to inhibit cholinesterase enzymes and disrupt endocrine (3, 43–44). Organophosphate exposure could cause arrhythmias, coronary artery disease, congestive heart failure, metabolomic disorders, insulin resistance, cancer, and changes in gene expression (40, 45–48). Organophosphate exposure also affects insulin resistance, neurobehavioral function, blood profile, oxidative stress, and metabolism of carbohydrates, fats, and proteins in the cytoplasm/ mitochondria/ peroxisomes (49–54). The toxic effects of OPs on nephrons through molecular mechanisms include binding of albumin to the OPs, the interaction of OPs complex and serum albumin and their metabolites with kidney tissues and cells, and the protection of albumin against OPs (55). Chronic organophosphate exposure results in higher pancreatic insulin secretion, causing pancreatic hypertrophy. Insulin is a hormone that has a vital role to activate glucose transporter 9, which mediates glucose into the cells. In addition, the regulation of insulin secretion is vital in controlling plasma glucose. Acetylcholinesterase is located in the pancreas, in either acinar cells or insulin-secreting beta cells. Acetylcholine binds to beta-cell muscarinic receptors. Then, the cytosolic calcium concentration increases, increasing the efficiency of calcium-mediated exocytosis, which activates insulin secretory activity. Acetylcholinesterase also occurs in the alpha cells of the pancreas, which stimulate insulin secretion in a paracrine fashion in the pancreas (56).

Carbamate and Its Potential Health Effects

The active ingredients of carbamate pesticides are mancozeb, propineb, fenobucarb, and BMPC. Carbamates are a group of pesticides with a double bond where the carbon atom is located at the center. The double bond is oxygen, R1, and R2 groups. There are three types of carbamate pesticides based on the target organism: insecticides with R1 being a methyl group, herbicides with R1 being aromatic compounds, and fungicides with R1 being a benzimidazole group (41). Carbamate could cause health problems such as unconsciousness, vomiting, convulsions, cyanosis (57), and cholinesterase inhibition. In addition, pesticides in this group disrupt endocrine function, impair child development and IQ (58), decrease lung function (59), and cause central nervous system tumor (60). Patients who tried to commit suicide using pesticides usually experienced sudden respiratory and cardiac arrest (61). This pesticide group also triggers oxidative stress (51) and damages the enzymatic pathways involved in the metabolism of carbohydrates, fats, and protein within the cytoplasm, mitochondria, and peroxisomes (52).

Pyrethroid and the Potential Health Effects

The active ingredients of pyrethroid pesticides are beta-cyfluthrin, cypermethrin, permethrin, deltamethrin, emamectin, and abamectin. Pyrethroids are a group of manufactured pesticides similar to natural pyrethrum produced by chrysanthemums. The pyrethroid group could cause several health problems, including paranesthesia and respiratory tract, eyes, and skin irritations. Increased risk of deaths in general and of deaths due to cardiovascular disease (54) affects the levels of anti-Mullerian hormone, follicle-stimulating hormone, and the number of antral follicles (62). Pyrethroid also causes nephrotoxic, hepatotoxic, cardiotoxic, immunotoxin, neurotoxic, and behavioral effects and generates oxidative stress that causes changes in DNA, RNA, protein, fat, and carbohydrate molecules (63). Pyrethroids also affect the HPG axis-related reproductive outcomes (64). In addition, pyrethroid pesticide toxicology tests showed a weak, if any, effect on tumor occurrence. There is evidence of increased tumors in the liver and lungs caused by permethrin, cypermethrin, and bifenthrin. However, at the highest dosage tested, only tumors were detected, which is much higher than any human exposure (65).

Neonicotinoid and Its Potential Health Effects

The active ingredient of neonicotinoid is imidacloprid. Neonicotinoid pesticides are used to coat the seeds to prevent pest infestation (66). A previous study found that Neonicotinoids (NEOs) were spread in the environment. NEOs are found in drinking water and food at concentrations below the acceptable daily intake. Moreover, neonicotinoid pesticides may cause health problems, including adverse developmental or neurological outcomes, autism spectrum disorder, memory loss, and finger tremors. NEOs could also cause acute respiratory, cardiovascular, and neurological symptoms. Oxidative genetic damage and congenital disabilities also resulted from exposure to NEOs (67). Thiacloprid and thiamethoxam at relatively low concentrations induce PII and I.3-mediated CYP19 aromatase gene expression and activity of aromatase (68). They also cause changes in the structure and stability of DNA (69). Acetamiprid induces DNA damage in all concentrations tested depending on the dosage (70). The potential health risks associated with exposure to NEOs were revealed in the current study. Some of the early health problems due to exposure to these pesticides include impaired insulin and glucose homeostasis among non-diabetic adults. In addition, there are a progressive decrease in sperm motility among healthy men, an increase in the levels of serum lipid molecules in the general population, and urinary steroid hormones in men of reproductive age. Furthermore, healthy individuals' urinary oxidative stress markers correlate with internal NEO levels (71).

Other Groups of Pesticides and the Potential Health Effects

The active ingredients of other pesticides are chlorfenapyr, pendimethalin, metsulfuron-methyl, and chlorantraniliprole. Chlorfenapyr, a pesticide from the pyrrole group, may trigger health problems. A previous case report mentions neurological complications, included body weakness, dizziness, delirium with visual hallucinations at 114 hours and 122 hours post-ingestion. After 156 hours of exposure, a brief tonic seizures was followed by an increased heart rate. The patient died 157 hours after ingesting the pesticide (72). Chlorfenapyr intoxication causing dermal manifestations may be harmful. For example, a 49-year-old patient died five days after exposure to this pesticide (73). Another study revealed the clinical feature of chlorfenapyr-induced toxic leukoencephalopathy in a 71-year-old male patient (74). The risk for pancreatic cancer is higher after exposure to the dinitroaniline group, such as pendimethalin (40). Another study revealed that chlorfenapyr induces cellular toxicity in Human Liver Cells (HepG2 cells). It also induces mitochondrial damage associated with accumulation of Reactive Oxygen Species (ROS) and excess mitochondrial calcium. This ultimately leads to apoptosis and autophagy in HepG2 cells (75).

Potential health problems due to exposure to various pesticides may occur, especially among household members. These effects are harmful, especially for vulnerable groups such as pregnant women and children, considering the high maternal and child mortality in this agricultural area.

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CONCLUSION

This study revealed three most common groups of pesticides in the agricultural community in Brebes Regency: organophosphates, carbamates, and pyrethroids. In addition, insecticides, fungicides, and herbicides were the most common types of pesticides used in the area. The pesticides were stored indoor (e.g., in the kitchen and on wooden racks) and outdoor (e.g., on the terrace and outside the house). Pesticides stored around the house may endanger the people who inhaled the pesticide drift, consumed contaminated food or drink, or came into contact with it on the skin. The toxicity levels of pesticides found in the respondents' houses ranged from very dangerous (Ib) to unlikely presenting acute hazard in normal use (U). The potential health problems due to pesticides varied from poisoning symptoms to genetic disorders and polymorphisms. Further research is needed to prove that the health problems are the results of exposure to pesticides in agricultural communities.

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