

## ASSOCIATION BETWEEN PESTICIDE EXPOSURE AND TYPE 2 DIABETES MELLITUS AMONG FEMALE FARMERS: A CROSS-SECTIONAL STUDY

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### Abstract

**Introduction:** The widespread use of pesticides in agriculture has been linked to an increased risk of diabetes mellitus. Long-term exposure to pesticides can disrupt glucose metabolism, trigger insulin resistance, and raise susceptibility to diabetes mellitus. This study investigates the association between pesticide exposure and the incidence of type 2 diabetes mellitus. **Methods:** This analytical observational study with a cross-sectional design involved 162 female farmers selected by purposive sampling from a population of 2,187, using the Lemeshow formula. Independent variables included work duration, types and frequency of pesticide use, spraying duration and direction, PPE usage, and cholinesterase levels. The dependent variable was type 2 diabetes mellitus. Data were collected through questionnaires, observation, and clinical tests for blood glucose and cholinesterase levels. Logistic regression was performed at 95% CI and  $\alpha = 0.05$ . **Result and Discussion:** The results showed that 69.1% of female farmers exposed to pesticides had diabetes with lower cholinesterase levels as a significant indicator ( $p < 0.001$ ; OR=3.897; 95% CI=2.087-7.277). Factors such as working duration  $\geq 10$  years ( $p = 0.010$ ; OR=3.564; 95% CI=1.359-9.346), number of pesticides types ( $p = 0.023$ ; OR=3.370; 95% CI=1.187-9.570), spraying duration ( $p = 0.020$ ; OR=3.083; 95% CI=1.197-7.940), and PPE usage ( $p = 0.007$ ; OR=3.601; 95% CI=1.416-9.159) were associated with type 2 diabetes mellitus. **Conclusion:** Pesticides, particularly organophosphates and carbamates, act as endocrine-disrupting chemicals that impair pancreatic function and increase oxidative stress, contributing to insulin resistance. Female farmers more vulnerable to these effects due to hormonal sensitivity, making gender specific approaches essential. Strict regulations and farmer education are crucial to reduce long-term health risks.

## INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic condition characterized by high blood glucose levels due to insulin resistance and impaired pancreatic  $\beta$ -cell function (1,2). Based on the data from the International Diabetes Federation (IDF), diabetes causes more than 4 million deaths each year, with the global prevalence in 2021 reaching 10.5% of the adult population, and almost half of them are unaware of their condition. By 2024, an estimated 537 million people worldwide will be living with diabetes. This number is even projected to jump to 783 million by 2045 (3).

According to a WHO report in 2022, about 14% of adults have diabetes, and by 2021 the disease will be the direct cause of 1.6 million deaths. In addition, diabetes is also recognized as one of the leading causes of kidney failure and accounts for about 11% of total deaths from cardiovascular disease (4).

Diabetes mellitus occupies the second largest proportion after hypertension of all non-communicable diseases (NCDs) reported in Central Java, at 10.7%. The number of people with diabetes mellitus in Central Java Province in 2022 was 623,973 people (5). Based on Semarang Regency Health Profile in 2023, there were

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8,849 cases of diabetes mellitus (6). Non-communicable diseases (NCDs) type 2 diabetes mellitus is the second highest in the Sumowono Health Center, which has an increase in the graph of new cases every year.

Based on data from Sumowono Health Center in 2021 the incidence of type 2 diabetes mellitus was 658 cases consisting of 359 women and 309 men. In 2022 there were 500 cases consisting of 371 women and 129 men. While in 2023 there were 602 cases consisting of 421 women and 181 men. The data shows that there is an increase in cases of type 2 diabetes mellitus every year in women at the Sumowono Health Center. The findings report from the health center shows that the majority of women affected by diabetes have livelihoods as farmers. There were 42 female farmers who had a history of type 2 diabetes mellitus in 2024 (January-October 2024).

Diabetes mellitus is often dubbed the “silent killer” because it develops slowly with no obvious symptoms, so many people don’t realize they have it (7). Without proper management, the disease can lead to a variety of serious non-communicable complications, such as heart problems, stroke, and kidney failure (8). One of the main causes of type 2 diabetes mellitus is an unhealthy lifestyle, including a diet high in calories, low in fiber, and rich in sugar and saturated fat, often accompanied by a lack of physical activity (9). Not only that, exposure to environmental pollutants such as persistent organic pollutants (POPs) including dioxins, PCBs, and organochlorine pesticides also contributes as a risk factor due to their lipophilic nature that allows accumulation in body tissues (10). A number of studies have shown a positive association between exposure to organophosphate pesticides and the incidence of type 2 diabetes, especially in women, who are biologically more susceptible to the disease than men (OR: 1.20; 95% CI: 0.83-1.75). This is particularly important in relation to this study, as the majority of horticultural farmers in the study area are female dominated, which increases their health risk due to exposure to pesticides (11). This risk is associated with suppression of the enzyme acetylcholinesterase, which leads to reduced pancreatic beta cell function and insulin production (12).

This vulnerability can also be seen from a biological standpoint with changes in lower estrogen levels during perimenopause and menopause. These changes are known to reduce insulin sensitivity, increase visceral fat and initiate systemic inflammation. When these factors occur together with exposure to endocrine-disrupting pesticides, the likelihood of women farmers developing type 2 diabetes increases considerably (13).

Data from the Food and Agriculture Organization

(FAO) shows that in the last three decades, pesticide use worldwide has increased by almost 50% compared to the 1990s. This increase can be observed in the total amount consumed and the consumption rate from about 1.2 kg to 1.8 kg per hectare of agricultural land (14). Until 2020, global pesticide use was expected to remain constant at 2.7 million tons of active ingredients, with an average use rate of 1.8 kg/ha. This indicates that pesticides remain an important element in the global food production system (15). Global pesticide use currently averages 0.37 kg per individual. Asia is the region with the highest usage rate, reaching 3.7 million tons per year. Among countries in Southeast Asia, Indonesia ranks at the top of pesticide use in agriculture, illustrating the heavy reliance on pesticides in supporting agricultural output (16).

Based on information from the Ministry of Agriculture of the Republic of Indonesia in 2022, the application of pesticide use in Indonesia is still relatively high and continues to grow, from 5,002 types registered in 2019 to 5,509 types in 2021 (17). This increase reflects the increased use of pesticides in agricultural activities, raising concerns about their effects on public health and the environment. Most of these pesticides have a variety of active chemical compounds, increasing the likelihood of public exposure to hazardous substances. Prolonged continuous exposure, especially to combinations of multiple pesticides, has been linked to an increased risk of metabolic disorders such as diabetes (18).

Exposure to pesticides can damage the body’s hormones and increase the chances of developing type 2 diabetes. Some studies indicate that the more often individuals are exposed to pesticides, the more likely they are to face metabolic problems such as diabetes (19). These substances function as endocrine-disrupting compounds (EDCs), which can damage pancreatic function and reduce insulin secretion, thereby disrupting the glucose regulation process in the body (20).

Several factors such as length of work, frequency of pesticide spraying, and use of personal protective equipment (PPE) also contribute to the increased risk of diabetes. High spraying frequency was found to correlate with an increased risk of diabetes, with an Odds Ratio (OR) of 7.4 (95% CI: 7.0-8.8) (21). In addition, inconsistent use of personal protective equipment (PPE) was also shown to be associated with diabetes risk, with more than double the odds of those who used PPE completely (OR: 2.45; 95% CI: 0.17-11.10) (22). This study aims to determine the association between pesticide exposure and the incidence of type 2 diabetes in the community in Sumowono District, Indonesia.

## METHODS

This study used an analytical observational design with a cross-sectional approach, which aims to see the relationship between variables without intervening in the research subjects. Data were collected from people who live in the agricultural area of Sumowono Subdistrict and work with pesticides. The independent variables in this study include working duration, number of types of pesticide, spraying duration, frequency duration, PPE usage, spraying direction, spraying time, and cholinesterase levels while the dependent variable is the incidence of type 2 diabetes mellitus.

The population in this study was female farmers, totaling 2,187 farmers. The sample consisted of 162 farmers, determined using the Lemeshow formula and selected through a random sampling technique. The inclusion criteria for the sample were farmers who were involved in spraying pesticides and were less than 60 years old. The target population specifically focused on female farmers, thus only women meeting these criteria were included in the study. Data collection involved the use of structured questionnaires and direct observations conducted both within and around the respondents' residences. The questionnaires gathered information regarding respondent demographics and their pesticide spraying practices. Meanwhile, observations were made to detect the presence of pesticides through pesticide residues, packaging or storage containers, and tools used in the process of spraying or applying pesticides. In addition, the participants also underwent fasting plasma glucose (FPG) tests and capillary blood sampling for cholinesterase testing.

Data analysis used logistic regression at a 95% confidence interval and 5% alpha. Ethical clearance was granted by The Health Ethics Commission of the Faculty of Public Health, Diponegoro University with registration number: 113/EA/KEPK-FKM/2025. Informed consent from each respondent was obtained before the interview, and data were identified.

## RESULT

Sumowono Sub-district lies at an elevation ranging from 500 to 1,000 meters above sea level and covers an area of 49.98 km<sup>2</sup>. The region is inhabited by around 45,000 people, where most of the population depends on the agricultural sector, especially in horticulture. The leading horticultural commodities cultivated in Sumowono Sub-district include curly red chili, cabbage, carrots, tomatoes, beans, leeks, *petsai* (mustard greens), eggplant, squash, and avocado. The horticultural sector in Sumowono Sub-district contributes significantly to the regional economy, not only to meet the needs of the local market, but also as a commodity

marketed to other regions. The existence of productive horticultural agriculture in this sub-district plays a role in sustaining the welfare of the local community and encouraging agricultural-based economic growth. Agricultural activities commonly carried out by women farmers in this horticultural farming system have the potential to be exposed to pesticides. This is not only during spraying activities, but also through activities such as mixing and preparing pesticides, weeding, harvesting, and packaging the harvest.

**Table 1. Characteristics of Respondents and Pesticide Identification**

Characteristics of Respondents	Total	Percentage (%)
<b>Ages</b>		
25-35	49	30.2
36-45	42	25.9
46-55	41	25.3
>55	30	18.5
<b>Education Level</b>		
Did not finish elementary school	13	8
Graduated elementary school	125	77.2
Graduated junior high school	20	12.3
Graduated high school	4	2.5
<b>Working Duration</b>		
≥ 10 years	119	73.5
< 10 years	43	26.5
<b>The Number of Types of Pesticides</b>		
≥ 2 types	128	79.0
< 2 types	34	21.0
<b>Spraying Time</b>		
≥ 5 hours per day	110	67.9
< 5 hours per day	52	32.1
<b>Spraying Frequency</b>		
≥ 4 days per week	65	40.1
< 4 days per week	97	59.9
<b>Spraying Time</b>		
at risk	18	11.1
not at risk	144	88.9
<b>Spraying Direction</b>		
Unidirectional	90	55.6
Opposite direction	72	44.4
<b>PPE Usage Practice</b>		
Score ≤ 5	96	59.3
Score >5	66	40.7
<b>Body Mass Index</b>		
≥ 25 kg/m <sup>2</sup>	98	60.5
< 25 kg/m <sup>2</sup>	64	39.5
<b>Family History of Diabetes</b>		
Yes	129	79.6
No	33	20.4
<b>Cholinesterase Levels</b>		
Severe Poisoning	47	29.0
Moderate Poisoning	42	25.9
Mild Poisoning	62	38.3
Normal	11	6.8
<b>Blood Sugar Levels</b>		
Diabetes	112	69.1
Normal	50	30.9

Table 1 shows the characteristics of the respondents in this study, which showed that the majority were aged 25-35 years with the last education level of elementary school. Most of the respondents had worked as farmers for  $\geq 10$  years (73.5%). In terms of pesticide spraying, 79.0% used  $\geq 2$  types of pesticide mixtures, 67.9% sprayed for  $\geq 5$  hours per day, and 40.1% sprayed  $\geq 4$  days per week. Most farmers (88.9%) sprayed in the morning, which was considered to have a lower risk.

However, 55.6% of respondents did not pay attention to the direction of the wind when spraying, and 59.3% did not use complete Personal Protective Equipment (PPE). In addition, 60.5% of respondents were obese with a BMI  $\geq 25$  kg/m<sup>2</sup>. Examination of cholinesterase levels showed that most farmers experienced poisoning, with mild poisoning being the most dominant category (38.3%) and severe poisoning (29%). The prevalence of diabetes among respondents reached 69.1%, with 79.6% of them having a family history of diabetes.

**Table 2. Characteristics of Respondents and Pesticide Identification**

Brand	Type	Group	Active Ingridient	Classification of pesticide toxicity	LD50 (mg/kg body weight)
Abacel 18 EC	Insecticide	Avermectin	Abamectin 18 g/l	II	8.7
Ace-One 75 SP	Insecticide	Orghanophosphate	Acephate 75%	III	866
Antracol 70 WP	Fungicide	Carbamate	Propineb 70%	U	8,500
Anvil 50 SC	Fungicide	Triazole	Hexaconazole	III	>5,000
Amistartop 325 SC	Fungicide	Azoxystrobin	Azoxystrobin 200 g/l	U	>5,000
Acrobat 50 WP	Fungicide	Morfolin	Difenoconazole 125 g/l	V	1,453
Agrimec 18 EC	Insecticide	Avermectin	Dimethomorph 50%	II	3,980
Absina 36 EC	Insecticide	Avermectin	Abamectin 18 g/l	II	8.7
Antila 80 WP	Fungicide	Ditio-Carbamate	Abamectin 36 g/l	II	8.7
Avidor 25 WP	Insecticide	Neonicotinoid	Mancozeb 80%	U	8,000
Basta 150 SL	Herbicide	Glufosinate	Imidacloprid 25%	II	450
Buzzer 500 EC	Insecticide	Organophosphates	Glufosinate ammonium 150 g/L	III	2,000
Bion M 1/48 WP	Fungicide	Ditio-Carbamate	Profenofos 500 g/l	II	352
Curacron 500 EC	Insecticide	Organophosphates	Acibenzolar-S-methyl 1%	U	8,000
Callicron 500 EC	Insecticide	Organophosphates	Mancozeb 48%	II	352
Copicide 77 WP	Fungicide	Anilida	Profenofos 500 gr/l	II	352
Dithane M-45	Fungicide	Carbamate	Profenofos 500 g/l	II	352
Demolish 18 EC	Insecticide	Avermectin	Copper Hydroxide 77%	U	>8,000
Decis 25 EC	Insecticide	Pyrethroid	Mancozeb 80%	U	>8,000
Dursban 200 EC	Insecticide	Organophosphates	Abamectin 18 gr/l	II	8.7
Dangke 40 WP	Insecticide	Carbamate	Deltamethrin 25 g/l	II	c135
Dafat 75 WG	Insecticide	Organophosphates	Chlorpyrifos 200 g/l	II	135
Emacel 30 EC	Insecticide	Avermectin	Methomyl 40%	Ib	17
Fostin 610 EC	Insecticide	Pyrethroid	Acephate 75%	II	850
Gracia 103 EC	Insecticide	Avermectin	Emamectin Benzoate 30 g/l	II	53
Gramoxone 276 SL	Herbicide	Bipyridyl	Chlorpyrifos 550 g/L	II	135
Hoky 30 EC	Insecticide	Pyrethroid	Cypermethrin 60 g/L	II	250
Kardan 50 SP	Insecticide	Carbamate	fluxametamide 103 g/l	Ib	11
Kenlon 480 EC	Herbicide	Pyridine Acid	Paraquat dichloride 276 g/L	II	150
Ken-Pronil	Insecticide	Phenylpyrazole	Cypermethrin 30 g/l	II	250
Manzate 82 WP	Fungicide	Dithiocarbamate	Cartap Hydrochloride 50%	II	100
Nativo 75 WG	Fungicide	Pirimidin dan Triazol	Triclopyr butoxyethyl ester 480 g/L	II	630
Prevathon 50 SC	Insecticide	Chlorantraniliprole	Fipronil 50 g/L	II	97
Rumba 500 EC	Insecticide	Organophosphates	Mancozeb 83%	U	>5,000
Rizotin 100 EC	Insecticide	Pyrethroid	Trifloksistrobin 25%	III	3125
Roundup 486 SL	Herbicide	Organophosphates	Tebukonazol 50%	U	>5,000
Smart 486 SL	Herbicide	Organophosphates	Chlorantraniliprole 50 g/l	II	352
Spontan 400 SL	Insecticide	Nereistoxin	Profenofos 500 g/l	II	352
Supremo 480 SL	Herbicide	Glycine	Chypermethrin 40%	II	250
Starane 290 EC	Herbicide	Pyridine Acid	Glyphosate 486 g/l	III	4,230
Starbud Plus 575 EC	Insecticide	organophosphate and pyrethroid	Glyphosate isopropylamine 486 g/l	III	>5,000
Taekwondo 25 EC	Insecticide	Pyrethroid	Dimethoate 400g/l	II	50
Turex WP	Insecticide	Pyrethroid	Isopropylamine Glyphosate 480 g/L	II	4800
Tenano 360 SC	Insecticide	Diamide	Fluroxypyr-methylheptyl ester 290 g/L	II	1,000
Victory 80 WP	Fungicide	dithiocarbamate	Chlorpyrifos 540 g/L	II	135
Winder 25 WP	Insecticide	Neonicotinoid	Deltamethrin 35 gr/L	II	50-500
			Lambda-cyhalothrin 25 g/L	II	56
			Delta-endotoxin	II	2000
			Spinetoram 60 g/l	III	60
			Methoxyfenozide 300 g/l.	III	300
			Mancozeb 80%	IV	450
			Imidacloprid 100 g/l.	II	450



**Table 3. Bivariate Analysis of the Association Between Pesticide Spraying Practices and Diabetes Among Horticultural Farmers**

Pesticide Use Practices	Incidence of Diabetes				Total		P – Value
	Diabetes (people)	Percentage (%)	Non-Diabetes (people)	Percentage (%)	Total (people)	Percentage (%)	
<b>Working Duration</b>							<0.001
≥ 10 years	95	79.8	24	20.2	119	100	
< 10 years	17	39.5	26	60.5	43	100	
<b>The Number of Types of Pesticides</b>							0.001
≥ 2 types of pesticide	97	75.8	31	24.2	128	100	
< 2 types of pesticide	15	44.1	19	55.9	34	100	
<b>Spraying Duration</b>							0.007
≥ 5 hours/day	84	76.4	26	23.6	110	100	
< 5 hours/day	28	53.8	24	46.2	52	100	
<b>Spraying Frequency</b>							0.001
≥ 4 days of the week	55	84.6	10	15.4	65	100	
< 4 days of the week	57	58.8	40	41.2	97	100	
<b>Practical Use of PPE</b>							<0.001
Incomplete	79	82.3	17	17.7	96	100	
Complete	33	50	33	50	66	100	
<b>Spraying Time</b>							0.568
At risk	14	77.8	4	22.2	18	100	
Not at risk	98	68.1	46	31.9	144	100	
<b>Spraying Direction</b>							0.071
Opposite direction	68	75.6	22	24.4	90	100	
Unidirectional	44	61.1	28	38.9	72	100	
<b>Body Mass Index</b>							0.001
Obesity	78	79.6	20	20.4	98	100	
Normal	34	53.1	30	46.9	64	100	
<b>Family History of Diabetes</b>							1.000
Yes	89	69	40	31	129	100	
No	23	22.8	10	30.3	33	100	
<b>Cholinesterase Levels</b>							<0.001
Severe poisoning	44	93.6	3	6.4	47	100	
Moderate poisoning	37	88.1	5	11.9	42	100	
Mild poisoning	29	46.8	33	53.2	62	100	
Normal	2	18.2	9	81.8	11	100	
<b>Total</b>	<b>112</b>	<b>60.9</b>	<b>50</b>	<b>30.1</b>	<b>162</b>	<b>100</b>	

From the results of the analysis in Tables 3 and 4, the most significant independent contributors to the incidence of type 2 diabetes mellitus in female farmers in Sumowono Sub-district were working duration, number of pesticide types, spraying duration, incomplete use of PPE, and cholinesterase levels.

**Table 4. Multivariate Logistic Regression Analysis of Pesticide Spraying Practices and Type 2 Diabetes Mellitus Among Horticultural Farmers**

Variable	B	p-value	OR	95% CI
Working Duration	1.271	0.010	3.564	1.359 – 9.346
Number of Pesticide Types	1.215	0.023	3.370	1.187 – 9.570
Spraying Duration	1.126	0.020	3.083	1.197 – 7.940
Incomplete PPE Use	1.281	0.007	3.601	1.416 – 9.159
Cholinesterase Levels	1.360	<0.001	3.897	2.087 – 7.277
Constant	-12.249	<0.001	<0.001	
Mcfadden R <sup>2</sup>	0.410	<0.001		

Table 5 shows the results of a logistic regression analysis on blood cholinesterase levels and the incidence of type 2 diabetes mellitus, with severe poisoning as the reference category. The B coefficient values were all negative. This means that the chance of diabetes occurrence decreases from the reference category (severe poisoning). The lighter the level of intoxication (or the closer to normal cholinesterase levels are), the smaller the chance of a person having diabetes.

**Table 5. Logistic Regression Multivariate Analysis of Cholinesterase Level Category with Type 2 Diabetes Mellitus Incidence**

Cholinesterase Levels	Coef (B)	p-value	OR	95% CI
Moderate Poisoning	-3.906	<0.001	0.020	0.002-0.173
Mild Poisoning	-3.758	0.001	0.023	0.003-0.195
Normal	-1.826	0.061	0.161	0.024-1.086

## DISCUSSION

This study identified that 69.1% of female farmers in Sumowono Sub-district were affected by type 2 diabetes mellitus. This percentage is considered high relative to the global prevalence reported by the International Diabetes Federation in 2025, which stands at 11.1%, suggesting the presence of specific risk factors that contribute to the increase in cases (23). Diabetes prevalence had a positive association with most of the pesticide exposure indices. All variables, including tenure, number and type of pesticides, duration of spraying, PPE usage, and cholinesterase levels, were found to have a significant association with the incidence of type 2 diabetes mellitus.

The results of the analysis showed that the most dominant independent contributors associated with the incidence of type 2 diabetes mellitus in female farmers in Sumowono Sub-district, Semarang Regency, Indonesia. These factors were working duration, number of types of pesticide, spraying duration, incomplete use of PPE, and cholinesterase levels. These factors simultaneously contributed to the incidence of type 2 diabetes mellitus in female farmers by 41% (McFadden  $R^2=0.410$ ).

The study found a statistically significant relationship ( $p=0.006$ ) between farming tenure exceeding 10 years and the risk of developing type 2 diabetes mellitus among female agricultural workers in Sumowono Sub-district. Farmers with a tenure of more than 10 years were at more than 3 times at risk of developing type 2 diabetes mellitus ( $OR=3.824$ ). This finding is in line with a previous study where pesticide tenure was associated with type 2 diabetes mellitus (24). Another study also confirmed that the risk of pesticide exposure increases along with the working duration of farmers, which increases the risk of diabetes (25). The study revealed that the majority of respondents had worked for over 10 years, having started farming from elementary school age due to economic pressures and local cultural norms. Long-term accumulation of pesticides can lead to diabetes because it disrupts mitochondrial function, triggers oxidative stress and inflammation, and damages the hormonal balance that disrupts glucose metabolism and causes insulin resistance. In addition, pesticides can also accumulate in body fat, potentially leading to metabolic disorders such as obesity, which in turn increases the risk of diabetes (26-27).

A significant association ( $p=0.023$ ) was also observed between the number and types of pesticides used and the incidence of type 2 diabetes among female farmers. Those who applied mixtures containing two or more pesticide types had over three times the likelihood of

developing the disease ( $OR=3.370$ ). Researchers found that farmers mixed more than two types of pesticides, some even up to 10 types, to save time and money. In addition, farmers believe that the more pesticides they mix, the more effective the spraying will be in controlling various types of pests at once. A study using 2003-2018 NHANES data shows that exposure to a mixture of multiple pesticides is more likely to cause diabetes than exposure to one pesticide alone (28).

Another study also revealed that a mixture of pesticides is more likely to cause metabolic disorders, especially type 2 diabetes rather than exposure to a single type of pesticide alone (29). The use of pesticide mixtures in large quantities not only increases exposure to various chemical compounds, but also increases the potential for synergistic toxic effects. When several types of pesticides are used simultaneously, their combined impact on the body can be significantly greater than that of individual compounds. This combined effect can disrupt the body's metabolic balance, especially in terms of glucose regulation, thus disrupting the performance of the hormone insulin (30-31).

The analysis showed that spraying duration was significantly associated with the incidence of type 2 diabetes ( $p=0.020$ ). Farmers who engaged in spraying for more than five hours daily had twice the risk of developing the disease ( $OR=3.083$ ). This study has similarities with previous studies where the duration of pesticide spraying that deviates from established standards is associated with a decrease in blood cholinesterase levels, which increases the risk of diabetes (32). A separate study also demonstrated a significant association between the length of spraying activity and diabetes occurrence among farmers (33).

Observations in the field found that most farmers manage a large area of land independently without the help of additional labor. In addition, farmers also consider that working on their own land helps reduce operational costs, which contributes to the long duration of spraying activities carried out by farmers. The duration of pesticide spraying has been regulated by the Government of Indonesia in Regulation of the Minister of Manpower Number PER-03/MEN/1986 of 1986 Concerning Requirements for Occupational Safety and Health in Places that Manage Pesticides. The regulation explains that the duration of pesticide spraying should not exceed 5 hours of exposure per day (34). Pesticides may impair glucose homeostasis by triggering mechanisms including lipid toxicity, oxidative imbalance, chronic inflammatory responses, buildup of acetylcholine, and alterations in gut microbial composition. Studies show that the longer a person is exposed to pesticides, the

greater the likelihood of metabolic disturbances leading to type 2 diabetes.

This length of exposure is also linked to the buildup of chemicals in the body's tissues, which can amplify the effects of toxins and accelerate disruptions in the hormonal and metabolic systems (35). The results of the analysis also showed that the habit of using Personal Protective Equipment (PPE) had a significant association with the incidence of type 2 diabetes ( $p=0.007$ ). Incomplete use of PPE in farmers increases the risk of developing type 2 diabetes mellitus more than 4 times ( $OR=3.601$ ). This study is in line with previous studies where incomplete PPE use is associated with pesticide poisoning characterized by low blood cholinesterase levels, which increase the risk of diabetes (36). Another study also confirmed that incomplete PPE use is associated with cholinesterase levels in oil palm plantation workers, which increases the risk of diabetes (37).

Studies have indicated that limited awareness among farmers regarding the use of PPE serves as a contributing factor to increased pesticide exposure, which may play a role in the development of type 2 diabetes mellitus. Some of the reasons cited include the limited availability of PPE, discomfort from wearing masks that make breathing difficult, and the habit of wearing flip-flops rather than boots when spraying pesticides. PPE that farmers should use includes boots, canvas shoes, long-sleeved overalls and long pants (coveralls), hat, gloves, apron, and face shield or mask (38).

Boots and canvas shoes serve to protect the feet from exposure to pesticides spilled or splashed on the ground and prevent contact through the skin of the feet. Coveralls and aprons cover the whole body and the front of the body to avoid direct contact with the skin. Hats serve to protect the head from exposure to pesticides and sunlight. Gloves protect the skin of the hands when spraying, mixing, and cleaning pesticide equipment. Face shields or masks protect the respiratory tract from pesticide particles or vapors that can be inhaled (39). In addition, the practice of incomplete use of PPE causes direct exposure to the body without adequate protection, so the risk of pesticide entry through the skin or respiratory tract becomes higher (40-41).

Findings from the cholinesterase level assessment indicated that a majority of the farmers exhibited signs of poisoning, with 47% falling into the severe category. The analysis revealed a statistically significant association between blood cholinesterase concentrations and the incidence of type 2 diabetes mellitus ( $p<0.001$ ). In this study, the group with severe poisoning served as a comparison. The analysis showed that compared to

people with severe poisoning, farmers with moderate, mild, or normal cholinesterase levels had a lower risk of developing diabetes. The lighter the level of poisoning (or the closer the cholinesterase levels are to normal), the lower the chance of developing diabetes. Farmers with moderate poisoning had a 2% risk of developing diabetes compared to farmers with severe poisoning ( $p<0.001$ ,  $OR=0.020$ ). Farmers with mild poisoning had a 2.3% risk of developing diabetes compared to farmers with severe poisoning ( $p=0.001$ ,  $OR=0.023$ ). Meanwhile, farmers with normal cholinesterase levels had no association with the incidence of diabetes ( $p=0.061$ ).

Cholinesterase levels are one of the main biomarkers used to assess the level of exposure to pesticides, especially from the organophosphate and carbamate groups. Pesticides in this group work by inhibiting the activity of acetylcholinesterase (AChE) and butylcholinesterase (BChE) enzymes, which can disrupt the nervous system and metabolism. Decreased levels of cholinesterase enzymes due to pesticide exposure have been linked to metabolic disorders that increase the risk of insulin resistance and type 2 diabetes (42). Several previous studies have shown that individuals with lower cholinesterase levels have a higher risk of developing type 2 diabetes than those with normal enzyme levels (43). Another study also found that farmers exposed to pesticides had significantly reduced cholinesterase levels, especially due to exposure to organophosphate pesticides (44).

This study has several limitations. The study was only conducted on female farmers in Sumowono sub-district, so the results cannot be generalized to other populations. In addition, this study has not fully considered confounding factors that can affect the incidence of diabetes, such as diet, history of chronic diseases, living habits, and genetic factors. The measurement of cholinesterase levels also used a modified Michel method with a bromthymol blue indicator and a tintometer, which has low accuracy and sensitivity, which could affect the accuracy of the results.

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## CONCLUSION

The results of this study indicate that length of work, type and amount of pesticides used, duration of spraying, inadequate use of PPE, and cholinesterase levels have a significant association with the incidence

of type 2 diabetes in horticultural farmers. Proper use of personal protective equipment and efforts to reduce long-term exposure to pesticides are essential to prevent more serious health impacts in the future. Future research with broader sample sizes and more advanced analytical models is necessary to validate these outcomes and to explore deeper interrelations among these contributing factors.

### AUTHORS' CONTRIBUTION

All authors contributed to the conceptualization and design of the study. WM: conducted the literature review, analyzed the data, and drafted the initial manuscript. OS and YHD: provided research supervision and guidance throughout the study. MR: reviewed and provided substantial critical input on the manuscript. NZ: contributed to data interpretation and offered advisory support during the research process. All authors reviewed and approved the final version of the manuscript.

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