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Masters Program in Public Health, Universitas Sebelas Maret
Meta-Analysis

Pesticide Exposure and Its Correlation with Hemoglobin and Cholinesterase in Farmers Who Used Pesticide

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ABSTRACT

Background: Agriculture is the most important sector in basic human needs. Farmers must improve the quality of agricultural products by using synthetic chemicals, someone who experiences pesticide poisoning will have low cholinesterase levels. This study aims to analyze pesticide exposure to hemoglobin and cholinesterase levels in farmers who use pesticides.
Subjects and Method: This was a systematic review study and meta-analysis conducted with the PRISMA diagram guidelines. The search for articles was carried out taking into account the eligibility criteria defined in the PICO model. Population= farmers using pesticides, Intervention= exposed to pesticides, Comparison= not exposed to pesticides, Outcome= hemoglobin and cholinesterase levels. The article search process was carried out between 2002-2022 from the Pubmed, Science Direct, Google Scholar, Springer Link, Hindawi, and Plose one databases. The keywords used were “hemoglobin”, “exposed pesticide”, “cholinesterase level”, “farmers”, “hemoglobin AND exposed pesticide”, “cholinesterase level AND farmers”, “hemoglobin AND farmers”. The inclusion criteria in this study were the full text of a cross-sectional study, discussing pesticide exposure to hemoglobin and cholinesterase levels in farmers using pesticides, published in English. Final results are presented in the mean SD of the multivariate analysis. Data analysis was performed using RevMan 5.4 software.
Results: A meta-analysis was conducted on 13 articles originating from America, Asia, Africa, and Europe. The results of the meta-analysis showed that farmers exposed to pesticides experienced a decrease in hemoglobin, but it was not statistically significant (SMD= -0.28; 95% CI= -1.10 to 0.54; p=0.500). Pesticide exposure reduced cholinesterase levels in farmers using pesticides, the results were statistically significant (SMD= -2.48; 95% CI= -3.68 to -1.27; p<0.001).
Conclusion: The results of the meta-analysis showed that pesticide exposure decreased hemoglobin and cholinesterase levels in farmers using pesticides.

Keywords: hemoglobin, cholinesterase levels, farmers

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BACKGROUND

Agriculture is the most important sector in meeting basic human needs, so farmers must improve the quality of their agricultural products by using synthetic chemicals to get optimal agricultural results. As a result of the use of synthetic chemicals, farmers are very vulnerable to exposure to the chemicals used, including pesticides. One of the blood test parameters to measure poisoning due to the use of pesticides in farmers can use the parameter of cholinesterase levels in the blood. (Kwanhian et al., 2019).

Pesticides are chemicals that function to control pests and prevent damage to plants. The main active compounds of this material are organophosphates, chlorinated hydrocarbons, and carbamide derivatives (Cuenca et al., 2020). Organophosphate and carbamate pesticides are neurotoxic by inhibiting acetylcholinesterase (AChE), with AChE unable to bind to acetylcholine to stop synaptic transmission. Inhibition of AChE in humans can cause many acute symptoms including dizziness, nausea, difficulty breathing, and even death. In addition, the nonspecific effect produces reactive oxygen species that attack lipids, proteins, and deoxyribonucleic acid (DNA), causing oxidation and membrane damage, enzyme inactivation, DNA damage, and cell death. Several authors have investigated the adverse haematological effects of organophosphates on blood hemoglobin, hematocrit level, red blood cell count, platelet count, and white blood cell count (Araoud et al., 2012).

A person who experiences pesticide poisoning will have low levels of CHE. Some pesticides are anti-CHE which can reduce the activity of CHE enzymes in the body. Decreased enzyme activity can result in nervous system disturbances, poisoning, and even death. Pesticide contamination in humans that enters the body can cause signs and symptoms that can be felt by sufferers and can be observed by others (Talcott, 2017).

People generally think it's normal for the symptoms that arise in themselves after applying pesticides. They do not check with hospitals or health workers regarding the symptoms that arise which result in undetected cases of pesticide poisoning in the community so that chronic effects cannot be prevented. Symptoms and signs of poisoning vary, including headache, general weakness or fatigue, sweating, vomiting, blurred vision and seizures (BPPSDMK, 2018).

The use of PPE at the time of spraying can affect the number of pesticide particles entering the body of the sprayer. The more complete the PPE used when spraying, the smaller the possibility of abnormal CHE levels (Achmadi, 2016). Worldwide, an estimated three million cases of pesticide poisoning occur each year, resulting in more than 250,000 deaths. It is estimated by the World Health Organization (WHO) that about 18.2 per 100,000 agricultural workers experience work-related pesticide poisoning worldwide. In addition, more than 168,000 people die from pesticide poisoning every year, with most of them coming from developing countries (WHO, 2016 in Ssemugabo, 2017).

Indonesia itself, in 2016 there were 771 cases of pesticide poisoning based on data referenced from the National Poisoning Information Center (Sikernas). Pesticide poisoning in the period April-June 2017 was recorded as many as 180 cases (BPOM, 2017). This research was conducted because research on pesticide poisoning associated with hygene behavior has several references but research on pesticide poisoning associated with hematological parameters has not been widely studied. The purpose of this study was to analyze the relationship between hemoglobin and pesticide poisoning by measuring cholinesterase levels in farmers using pesticides.

SUBJECTS AND METHOD

1. Study Design

This study was conducted using a systematic review and meta-analysis. The articles used in this research came from the database, Google Scholar, PubMed, Science

Direct, Springer Link, Hindawi, and Plose One between 2002 and 2022. Articles were selected based on the PRISMA diagram. The keywords used to search for articles were “hemoglobin”, “exposed pesticide”, “cholinesterase level”, “farmers”, “Hemoglobin AND exposed pesticide”, “cholinesterase level AND farmers”, “hemoglobin AND farmers”.

2. Inclusion Criteria

The inclusion criteria in this study were: full text articles with cross-sectional study design, articles with appropriate titles and relating to the effect of pesticides on hemoglobin and cholinesterase levels in pesticide-using farmers, articles published in English and/or Indonesian, Include the results The research consisted of the number of respondents and the Mean SD, and the comparison of the results of hemoglobin and cholinesterase tests on farmers exposed to pesticides with controls.

3. Exclusion Criteria

The exclusion criteria for this study were: a cross-sectional study using hematological examination, cholinesterase levels, pesticide exposure in the research group, articles published before 2002, and non-farmer exposure to pesticides.

4. Operational Definition of Variables

The article search was conducted based on the eligibility criteria used using the PICO model. Population: farmers using pesticides, Intervention: exposure to pesticides, Comparison: not exposed to pesticides, Outcome: hemoglobin and cholinesterase levels.

Pesticide exposure: The entry of pesticides into the body through oral, inhalation, and skin. Hemoglobin: Metalloprotein in red blood cells that functions to transport oxygen from the lungs to the rest of the body.

Cholinesterase levels: Enzymes found in cellular fluids that function to stop the action of acetylcoline by hydrolyzing it into choline and acetic acid.

5. Study Instruments

This research was conducted using the PRISMA diagram and article quality was assessed using the Critical Appraisal for Cross-Sectional study from CEBMa.

6. Data Analysis

The data from this study were analyzed using the Review Manager application (RevMan 5.4). Forest plots and funnel plots were used to determine the size of the relationship and heterogeneity of the data. Fixed effect model is used to determine homogeneous data, while random effects model is used for heterogeneous data.

RESULTS

The article search process was carried out through several journal databases including Google Scholar, PubMed, Science Direct, Springer Link, Hindawi, and PLOS One. The process of searching for related articles can be seen in the PRIMSA diagram in Figure 1.

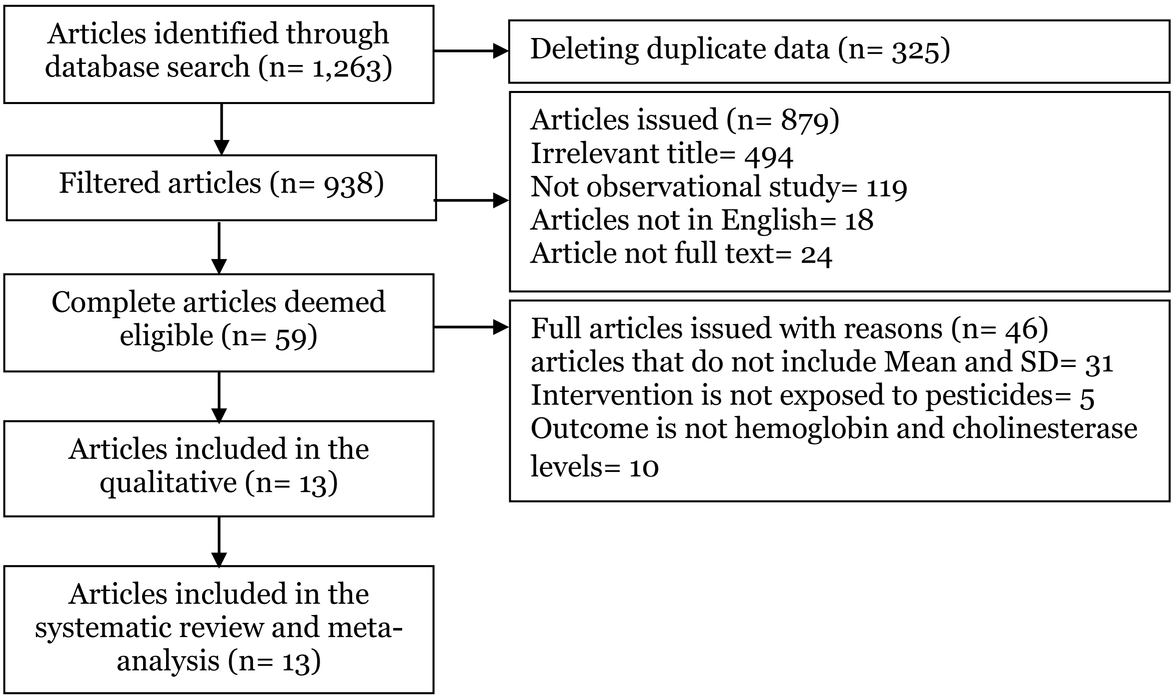


Figure 1. PRISMA Flowchart

Figure 2. Map of study area

1. Results of the quality assessment of the cross-sectional study of pesticide exposure to hemoglobin in farmers

Table 1. Assessment of study quality using a cross-sectional study check list published by CEBMa

No	Indicators	Publication (Author and Year)					
		Ahmadi et al. (2017)	Aroonvilariat et al. (2015)	Cestonaro et al. (2020)	Lermen et al. (2013)	Garcia et al. (2016)	Nambunmee et al. (2021)
1	Do these objectives clearly address the research focus/problem?	1	1	1	1	1	1
2	Are cross-sectional research methods suitable to answer the research question?	1	1	1	1	1	1
3	Is the research subject selection method clearly written?	1	1	1	1	1	1
4	Does the sampling method not introduce bias (selection)?	1	1	0	1	1	1
5	Does the research sample taken represent the designated population?	1	1	1	1	1	1
6	Was the sample size based on pre-study considerations?	1	1	1	1	1	1
7	Was a satisfactory response achieved?	1	1	1	1	1	1
8	Are the research instruments (exposure to pesticides, Hb levels and cholinesterase levels) valid and reliable?	1	1	1	1	1	1
9	Was statistical significance assessed?	1	1	1	1	1	1
10	Was a confidence interval given for the main outcome?	1	1	1	1	1	1
11	Have confounding factors been taken into account?	1	0	1	1	1	1
12	Are the results applicable to your research?	1	1	1	1	1	1
	Total	**12**	**11**	**11**	**12**	**12**	**12**

Note: 1: Yes; 0: No

Table 1. Cont.

No	Indicators	Publication (Author and Year)					
		Neupane et al. (2014)	Sine et al. (2021)	Hassanin et al. (2017)	Kori et al. (2019)	Kwanhian et al. (2019)	Sosan et al. (2010)
1	Do these objectives clearly address the research focus/problem?	1	1	1	1	1	1
2	Are cross-sectional research methods suitable to answer the research question?	1	1	1	1	1	1
3	Is the research subject selection method clearly written?	1	1	1	1	1	1
4	Does the sampling method not introduce bias (selection)?	1	0	1	1	1	1
5	Does the research sample taken represent the designated population?	1	1	1	1	1	1
6	Was the sample size based on pre-study considerations?	1	1	1	1	1	1
7	Was a satisfactory response achieved?	1	1	1	1	1	1
8	Are the research instruments (exposure to pesticides, Hb levels and cholinesterase levels) valid and reliable?	1	1	1	1	1	1
9	Was statistical significance assessed?	1	1	1	1	1	1
10	Was a confidence interval given for the main outcome?	1	1	1	1	1	1
11	Have confounding factors been taken into account?	1	1	1	1	1	1
12	Are the results applicable to your research?	1	1	1	1	1	1
	Total	**12**	**11**	**12**	**12**	**12**	**12**

Note: 1: Yes; 0: No

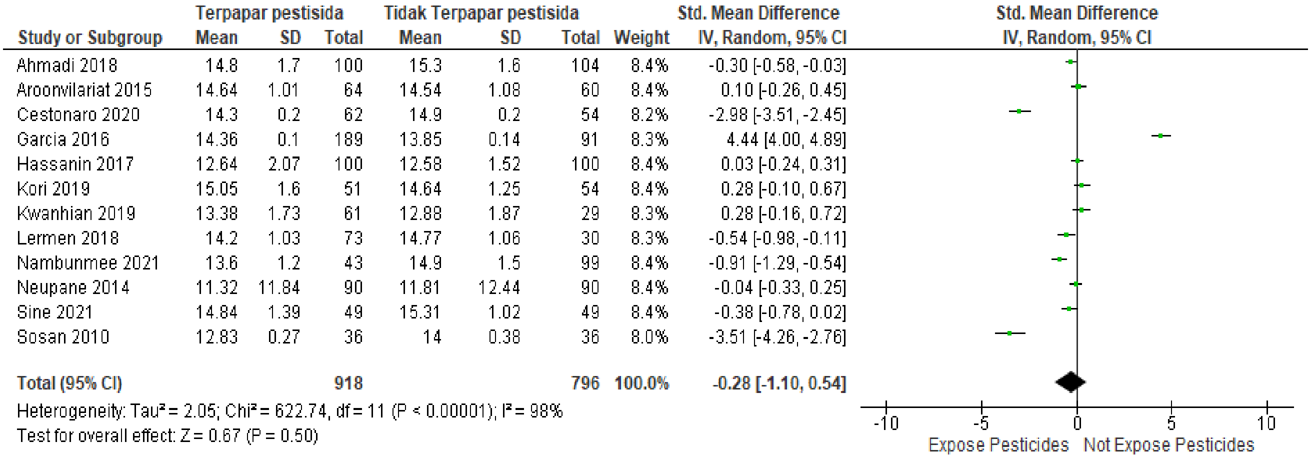
Table 2. Description of primary studies meta-analysis of pesticide exposure to hemoglobin in farmers

Author (Year)	Country	Study Design	Sample	Population	Intervention	Comparison	Outcome	Exposed to pesticides		Not exposed to pesticides	
								Mean	SD	Mean	SD
Ahmadi et al. (2018)	Iran	Cross-sectional	204	100 pesticide spraying farmers working in greenhouse	Exposure to pesticides	Not exposed to pesticides	Hemoglobin	14.80	1.70	15.30	1.60
Aroonvilari at et al. (2015)	Thailand	Cross-sectional	124	64 pesticide-using farmers aged 20 to 60	Exposure to pesticides	Not exposed to pesticides	Hemoglobin	14.64	1.01	14.54	1.08
Cestonaro et al. (2020)	Brazil	Cross-sectional	116	62 farmers exposed to pesticides aged 23 to 71 years	Exposure to pesticides	Not exposed to pesticides	Hemoglobin	14.30	0.20	14.90	0.20
Garcia et al. (2016)	Spain	Cross-sectional	280	189 farmers aged 18-66	Exposure to pesticides	Not exposed to pesticides	Hemoglobin	14.36	0.10	13.85	0.14
Lermen et al. (2018)	Brazil	Cross-sectional	93	73 workers in the citrus farming sector aged 13-69 years	Exposure to pesticides	Not exposed to pesticides	Hemoglobin	14.20	1.03	14.77	1.06
Nambunmee et al. (2021)	Thailand	Cross-sectional	142	43 farmers from lowland Thailand	Exposure to pesticides	Not exposed to pesticides	Hemoglobin	13.60	1.20	14.90	1.50
Neupane et al. (2014)	Nepal	Cross-sectional	180	90 vegetable farmers using pesticides	Exposure to pesticides	Not exposed to pesticides	Hemoglobin	11.32	11.84	11.81	12.44

Table 2. Cont.

Author (Year)	Country	Study Design	Sample	Population	Intervention	Comparison	Outcome	Exposed to pesticides		Not exposed to pesticides	
								Mean	SD	Mean	SD
Sine et al. (2021)	Morocco	Cross-sectional	98	49 farmers exposed to pesticides	Exposure to pesticides	Not exposed to pesticides	Hemoglobin	14.84	1.39	15.31	1.02
Sosan et al. (2010)	Nigeria	Cross-sectional	72	76 farmers from Osun and Ondo areas who use pesticides	Exposure to pesticides	Not exposed to pesticides	Hemoglobin	12.83	0.27	14.00	0.38
Hassanin et al. (2017)	Egypt	Cross-sectional	200	100 pesticide spraying workers	Exposure to pesticides	Not exposed to pesticides	Hemoglobin	12.64	1.01	12.58	1.52
Kori et al. (2019)	India	Cross-sectional	105	51 agricultural sector workers exposed to pesticides	Exposure to pesticides	Not exposed to pesticides	Hemoglobin	15.05	1.6	14.64	1.25
Kewanhian et al. (2019)	Thailand	Cross-sectional	100	37 rice farmers using pesticides	Exposure to pesticides	Not exposed to pesticides	Hemoglobin	13.38	1.73	12.88	1.87

1. Pesticide exposure to hemoglobin in pesticide-using farmers



Study or Subgroup	Terpapar pestisida Mean	SD	Total	Tidak Terpapar pestisida Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Ahmadi 2018	14.8	1.7	100	15.3	1.6	104	8.4%	-0.30 [-0.58, -0.03]
Aroonwilariat 2015	14.64	1.01	64	14.54	1.08	60	8.4%	0.10 [-0.26, 0.45]
Cestonaro 2020	14.3	0.2	62	14.9	0.2	54	8.2%	-2.98 [-3.51, -2.45]
Garcia 2016	14.36	0.1	189	13.85	0.14	91	8.3%	4.44 [4.00, 4.89]
Hassanin 2017	12.64	2.07	100	12.58	1.52	100	8.4%	0.03 [-0.24, 0.31]
Kori 2019	15.05	1.6	51	14.64	1.25	54	8.4%	0.28 [-0.10, 0.67]
Kwanhian 2019	13.38	1.73	61	12.88	1.87	29	8.3%	0.28 [-0.16, 0.72]
Lermen 2018	14.2	1.03	73	14.77	1.06	30	8.3%	-0.54 [-0.98, -0.11]
Nambunmee 2021	13.6	1.2	43	14.9	1.5	99	8.4%	-0.91 [-1.29, -0.54]
Neupane 2014	11.32	11.84	90	11.81	12.44	90	8.4%	-0.04 [-0.33, 0.25]
Sine 2021	14.84	1.39	49	15.31	1.02	49	8.4%	-0.38 [-0.78, 0.02]
Sosan 2010	12.83	0.27	36	14	0.38	36	8.0%	-3.51 [-4.26, -2.76]
Total (95% CI)			**918**			**796**	**100.0%**	**-0.28 [-1.10, 0.54]**

Heterogeneity: $Tau^2 = 2.05$; $Chi^2 = 622.74$, df = 11 ($P < 0.00001$); $I^2 = 98\%$
Test for overall effect: Z = 0.67 (P = 0.50)

Figure 3. Forest plot of pesticide exposure to hemoglobin in pesticide-using farmers

The forest plot showed that farmers exposed to pesticides experienced a decrease in hemoglobin of 0.28 units lower than farmers who were not exposed to pesticides and this result was not statistically significant (SMD= -0.28; 95% CI= -1.10 to 0.54; p=0.500). The heterogeneity in this study showed I^2= 98%, so that the distribution of the data was declared heterogeneous (random fixed effect).

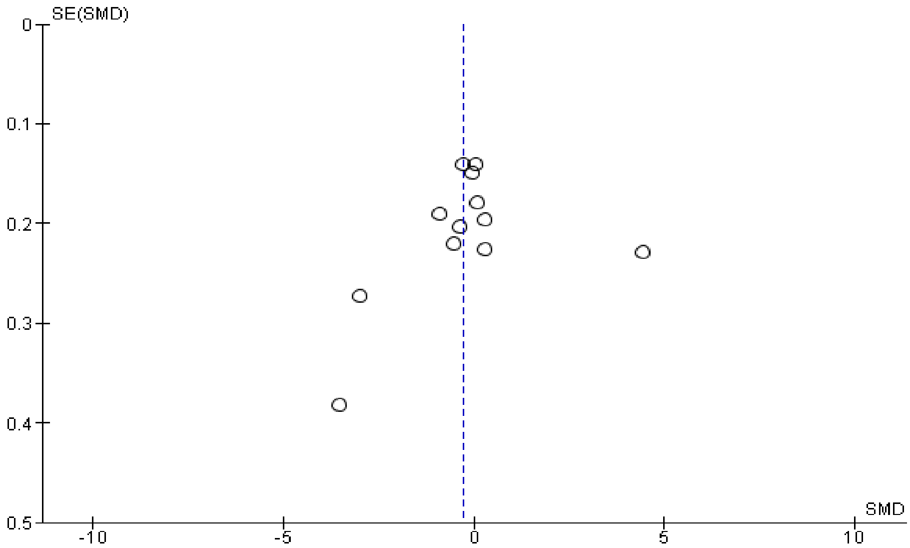


Figure 4. Funnel plot of pesticide exposure to hemoglobin levels in farmers using pesticides

The funnel plot in Figure 4 shows the same number of studies with estimates above and below the average estimate, in other words the shape of the funnel plot is more or less symmetrical so it does not indicate publication bias.

2. The results of the quality assessment of the cross-sectional study of pesticide exposure on cholinesterase levels in farmers

Table 3. Assessment of study quality using a cross-sectional study check list published by CEBMa

No	Indicators	Publication (Author and Year)							
		Ahmadi et al. (2017)	Aroonvi-lariat et al. (2015)	Cestonaro et al. (2020)	Fareed et al. (2013)	Garcia et al. (2016)	Nambunmee et al. (2013)	Neupane et al. (2014)	Sine et al. (2017)
1	Do these objectives clearly address the research focus/problem?	1	1	1	1	1	1	1	1
2	Are cross-sectional research methods suitable to answer the research question?	1	1	1	1	1	1	1	1
3	Is the research subject selection method clearly written?	1	1	1	1	1	1	1	1
4	Does the sampling method not introduce bias (selection)?	1	1	0	1	1	1	1	0
5	Does the research sample taken represent the designated population?	1	1	1	1	1	1	1	1
6	Was the sample size based on pre-study considerations?	1	1	1	1	1	1	1	1
7	Was a satisfactory response achieved?	1	1	1	1	1	1	1	1
8	Are the research instruments (Hb levels and cholinesterase levels) valid and reliable?	1	1	1	1	1	1	1	1
9	Was statistical significance assessed?	1	1	1	1	1	1	1	1
10	Was a confidence interval given for the main outcome?	1	1	1	1	1	1	1	1
11	Have confounding factors been taken into account?	1	0	1	1	1	1	1	1
12	Are the results applicable to your research?	1	1	1	1	1	1	1	1
	Total	12	11	11	12	12	12	12	11

Note: 1: Yes; 0: No

Table 4. Description of the primary study of pesticide exposure to cholinesterase levels in farmers

Author (year)	Country	Study Design	Sample	Population	Intervention	Comparison	Outcome	Exposed to pesticides		Not exposed to pesticides	
								Mean	SD	Mean	SD
Ahmadi et al. (2017)	Iran	Cross-sectional	204	100 farmers spraying pesticides working in greenhouse	Exposure to pesticides	Not exposed to pesticides	Cholinesterase levels	23.00	10.00	30.30	7.00
Aroonvilariat et al. (2019	Thailand	Cross-sectional	124	64 pesticide-using farmers aged 20 to 60	Exposure to pesticides	Not exposed to pesticides	Cholinesterase levels	41.11	11.53	52.91	11.92
Cestonaro et al. (2020)	Brazil	Cross-sectional	116	62 farmers exposed to pesticides aged 23 to 71 years	Exposure to pesticides	Not exposed to pesticides	Cholinesterase levels	11.35	4.07	17.04	8.28
Fareed et al. (2013)	India	Cross-sectional	243	166 pesticide sprayers on plantation	Exposure to pesticides	Not exposed to pesticides	Cholinesterase levels	42.03	23.10	57.02	30.70
Garcia et al. (2016)	Spanish	Cross-sectional	280	189 farmers aged 18-66	Exposure to pesticides	Not exposed to pesticides	Cholinesterase levels	19.24	0.49	29.63	0.59
Nambunmee et al. (2019)	Thailand	Cross-sectional	142	43 farmers from lowland Thailand	Exposure to pesticides	Not exposed to pesticides	Cholinesterase levels	13.83	6.00	10.73	0.83
Sine et al. (2013)	Morocco	Cross-sectional	98	49 farmers exposed to pesticides	Exposure to pesticides	Not exposed to pesticides	Cholinesterase levels	7.82	2.00	10.51	2.40
Neupane et al. (2014)	Nepal	Cross-sectional	180	90 vegetables farmers exposed pesticides	Exposed to pesticides	Not exposed to pesticides	Cholinesterase levels	32.40	34.50	35.30	37.50

2. Pesticide exposure to cholinesterase levels in farmers using pesticides

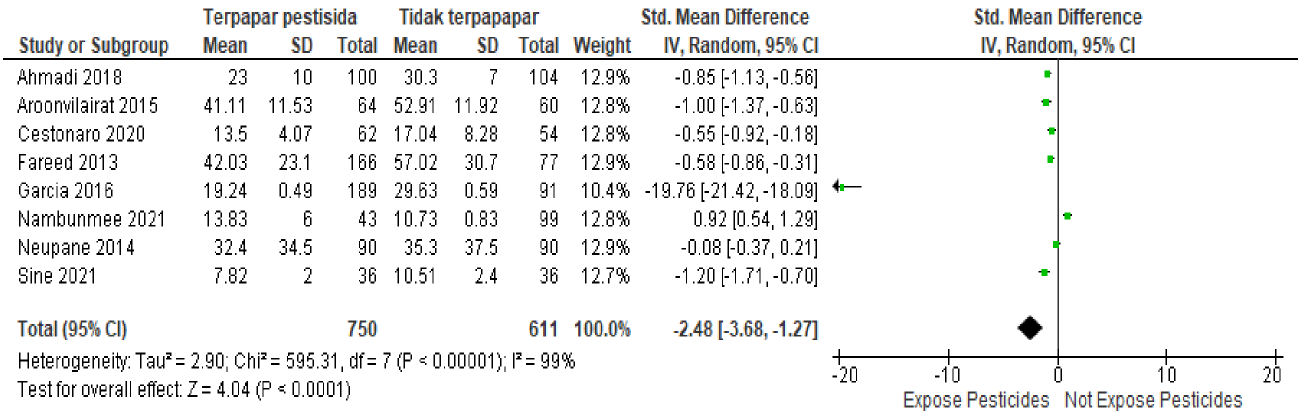


Figure 5. Forest plot of pesticide exposure to cholinesterase levels on pesticide-using farmers

The forest plot showed that farmers exposed to pesticides experienced a decrease in cholinesterase levels by 2.48 units lower than farmers who were not exposed to pesticides and this result was statistically significant (SMD= -2.48; 95% CI= -3.68 to -1.27; p<0.001). The heterogeneity in this study showed I^2= 99%, so that the distribution of the data was declared heterogeneous (random fixed effect).

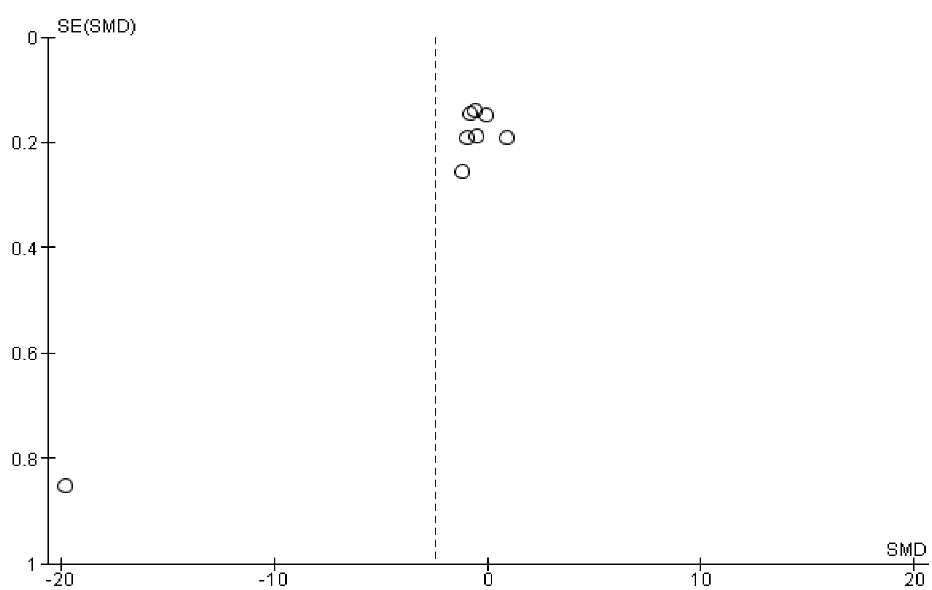


Figure 6. Funnel plot of pesticide exposure to cholinesetrase levels on pesticide-using farmers

The funnel plot in Figure 5, shows a tendency for more studies to have a larger estimate than the average estimate, which indicates an underestimate of publication bias.

DISCUSSION

Pesticides are an important source of hazards in agriculture that can cause morbidity and mortality worldwide, especially in developing countries. It is estimated that there are 3 million cases of acute pesticide poisoning that occur every year with 250,000 people dying (Gunnel et al, 2007).

High sulfate content in pesticides can form sulfhemoglobin bonds, which will cause hemoglobin to become abnormal and unable to carry out its function in delivering oxygen. Anemia can occur in patients with organophosphate and carbamate pesticide poisoning because the form of sulfhemoglobin and methemoglobin in red blood cells causes a decrease in hemoglobin levels, resulting in hemolytic anemia. The incidence of hemolytic anemia occurs due to contact with pesticides caused by enzymatic defects in red blood cells and the number of red blood cells and the amount of toxic substances that enter the body.

This meta-analysis investigated pesticide exposure to hemoglobin in pesticide-using farmers with a sample size of 1,714 individuals from 12 cross-sectional studies conducted in America, Africa, Europe, and Asia. The findings of this study explain that exposure to pesticides causes a decrease in hemoglobin. The forest plot results revealed that farmers exposed to pesticides experienced a decrease in hemoglobin compared to farmers who were not exposed to pesticides (SMD= -0.28; 95% CI= -1.10 to 0.54). Consequently, pesticide exposure may be a risk factor for reduced hemoglobin levels in pesticide-using farmers. Confounding factors were found such as length of exposure to pesticides, duration of spraying, age, gender, use of personal protective equipment, and correct hygiene habits.

Pesticide exposure to hemoglobin in farmers who use pesticides is not statistically significant, it can be caused by pesticide exposure which can be influenced by the duration of pesticide use so that it can cause chronic poisoning. Based on the entrance of pesticides into the human body through the skin, mouth (swallowing), and lungs (inhalation). Chronic poisoning can occur due to exposure to toxic substances in low doses over a long period of time. Some of the factors that can influence it include the use of appropriate PPE, the age of farmers who are still productive, proper nutritional status, and proper hygiene habits in pesticide waste management (Mohammed et al., 2013).

A study involving 200 respondents consisting of 100 farmers using pesticides and 100 healthy people as controls in Egypt, revealed that farmers used excessive amounts of pesticides (not as recommended on the packaging) without knowing the toxicological effects. In this study, it was found that pesticide spraying workers who were often exposed to pesticide mixtures showed abnormalities in several hematological parameters and kidney function (Hassanin et al., 2017).

The cholinesterase enzyme is an enzyme found in cellular fluids whose function is to stop the action of acetylcholine by hydrolyzing it into choline and acetic acid. The use of pesticides to control plant pests carries the risk of accidents to humans in the form of chronic or acute poisoning and death if the poisoning level is severe and is related to the level of cholinesterase inhibition in the blood (Ramsingh, 2010).

This meta-analysis investigated pesticide exposure to hemoglobin in pesticide-using farmers with a sample size of 1,387 individuals from 8 cross-sectional studies conducted in America, Africa, and Asia. The findings of this study explain that exposure to pesticides causes a decrease in cholinesterase levels. The results of the forest plot revealed that farmers exposed to pesticides experienced a decrease in cholinesterase levels compared to farmers who were not exposed to pesticides (SMD = -2.48; 95% CI = -3.68 to -1.27). Consequently, pesticide exposure may be a risk factor for reduced cholinesterase levels in pesticide-using farmers.

If a person is exposed to organophosphate pesticides, cholinesterase will bind to pesticides that are irreversible. Then a reaction will occur with acetylcholine, so that the examination will show a decrease in cholinesterase activity or an increase in acetylcholine levels. The decrease in cholinesterase activity in erythrocytes can last for 1 to 3 weeks, while the decrease in cholinesterase activity in platelets lasts up to 12 weeks or 3 months (Ramsigh, 2010).

The research of Nambunmee et al. (2021) with the results ($p<0.001$) showed that farmers who sprayed pesticides experienced a significant decrease in cholinesterase levels compared to the control group who were not exposed to pesticides. Low AChE indicates excessive pesticide exposure can cause health problems. Another finding from a cross-sectional study in the Northern Thailand region, Thailand which included 97 farmers consisting of 70 conventional farmers using pesticides and 27 as controls who had never been exposed to pesticides and were in good health. The results of this study indicate that conventional farmers who use pesticides have lower cholinesterase levels than modern farmers (Forte et al., 2021).

Limitations in this study may occur because the results of the meta-analysis of pesticide exposure to hemoglobin and cholinesterase levels in farmers using pesticides with a cross-sectional study design experienced publication bias, article search bias because it only used 6 databases, and language bias because it only used articles in English. Pesticide exposure can reduce hemoglobin and cholinesterase levels in farmers who use pesticides.

AUTHORS CONTRIBUTION

Arum Nuryati is the main researcher who selects the topic, searches for and collects research data. Setyo Sri Rahardjo and Bhisma Murti analyzed the data and review research documents.

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This study is self-funded.

CONFLICT OF INTEREST

There is no conflict of interest.

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