International Journal of Chemical and Biochemical Sciences
(ISSN 2226-9614)
Journal Home page: www.iscientific.org/Journal.html

Blood cholinesterase enzyme activity profile of fogging officers at the Makassar health quarantine centre

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Abstract

The use of pyrethroid chemicals as insecticidal compounds, which are indicated to be relatively safe for humans, has been shown to contribute to physiological system disruptions upon exposure. Therefore, it is crucial to continue exploring predictors that can affect cholinesterase enzyme activity as a preventive measure against health risks. This study aims to identify the relationship between factors influencing blood cholinesterase enzyme activity in fogging officers at the Makassar Health Quarantine Center. This research is an analytical observational study with a cross-sectional laboratory-based approach involving 31 fogging officers from the Makassar Health Quarantine Center, using correlation tests for statistical analysis. The results indicate that the statistical correlation values are low, showing a weak relationship between pesticide exposure characteristics (such as respondent age, work duration, body mass index, knowledge level, fogging actions, PPE use, insecticide dosage, fogging frequency, exposure duration, and health complaints) and the blood cholinesterase enzyme activity of the officers. However, laboratory reference values revealed abnormal cholinesterase levels in 6.45% of respondents, particularly among males. Additionally, 89.7% of respondents reported health complaints following fogging activities. Although the results do not show a strong or statistically significant correlation between pesticide exposure characteristics and blood cholinesterase enzyme activity in fogging officers, the finding of cholinesterase levels above laboratory reference values is important for further assessing the health conditions of exposed workers and targeting the best preventive evaluations according to occupational health and safety standards.

Keywords: Enzyme, Cholinesterase, Fogging, Pesticide, Pyrethroid

Full length article **Corresponding Author*, e-mail: wyudihidayat.kkpmks1@gmail.com Doi # https://doi.org/10.62877/53-IJCBS-24-25-19-53

1. Introduction

Cholinesterase level assessment in humans is a well-established practice in clinical pathology. However, the ongoing discovery of inhibitors that disrupt physiological functions necessitates further exploration [1], it becomes essential to conduct continuous monitoring of cholinesterase activity, especially for worker groups at risk of pesticide chemical exposure, such as exposure to pyrethroids [1-4]. Although World Health Organization states that pyrethroid pesticides are relatively safe for humans [5] ongoing studies are necessary as previous research has found that pyrethroid derivatives have adverse effects on various test animals, such as male Sprague-Dawley rats [6] and Channa striatus fish, causing detrimental health effects. In humans, low toxicity can occur [7-8] with common symptoms upon skin contact being paresthesia [5, 9], especially with intensive and long-term exposure [8, 10].

Pyrethroid pesticides are synthetic organic derivatives of pyrethrins [7, 9, 11] commonly used for controlling adult Ae. aegypti vectors worldwide, including in Indonesia [7, 12-15]. The mechanism of action and toxicity of pyrethroids exhibit neurotoxic effects by modulating the balance of sodium channels in the body, ultimately disrupting muscle cell function [9, 14, 16-18]. The use of pyrethroids in Indonesia is quite widespread, especially during fogging [15] as vector-borne disease cases (mosquitoes) in Indonesia are quite high due to the geographical condition of the country being located on the equator with a tropical climate [19-21], resulting in several regions experiencing malaria endemics and even outbreaks in more than 70% of the areas [22-24].

Despite the seemingly counterproductive efforts of mosquito control through fogging, exposure to certain insecticide chemicals for fogging officers has proven hazardous to health, affecting the digestive system, central nervous system, cardiopulmonary system, causing liver damage, kidney failure, skin cancer, biological cell function disruption, and even death [7, 25-27]. The use of pyrethroids in recent research findings, particularly among fogging officers, is quite limited, but some findings prove that these insecticides can cause poisoning [28-31]. Therefore, it is essential to remain aware of the dangers of pyrethroid exposure, given that fogging officers are involved in the work process from the pesticide mixing and loading stage to its application in the field.

One fogging implementation body with slightly different conditions from other health institutions is the Makassar Health Quarantine Center, which is responsible for preventing disease and health problems at entry points such as airports and seaports. Risk control at airports, seaports, and border crossing points is crucial, as entry points for people, vehicles, and goods must be free from disease-carrying vectors like the Aedes aegypti mosquito, which is a vector for diseases such as dengue fever, Zika, chikungunya, and yellow fever, which are quarantine diseases. The insecticides used in fogging activities at the Makassar Health Quarantine Center belong to the pyrethroid class (lambda-cyhalothrin and cypermethrin). Based on the background, this research aims to review the relationship between pesticide exposure characteristics and cholinesterase enzyme activity in the blood of fogging officers at the Makassar Health Quarantine Center.

2. Materials and methods

2.1. *Study Design*

This study is an analytical observational study with a laboratory-based cross-sectional approach, aiming to identify the relationship between factors influencing blood cholinesterase enzyme activity in fogging officers as the dependent variable against independent variables at a single point in time. Due to the practical reasons for using blood samples compared to urine, according to Simaremare [32] once the insecticide is absorbed by body organs, it appears in the circulatory system, thus blood specimens taken from the body are considered representative of the exposure. The study was conducted in the work area of the Makassar Health Quarantine Center from January to February 2024.

2.2. *Sample*

Based on the sample size calculation using the Slovin formula, 29 respondents were obtained, but due to the relatively small sample size, the researchers included the entire population of 31 health entomologists actively engaged in vector and disease carrier control through fogging at the Vector and Disease Carrier Control Sub-Section of the Environmental Risk Control Sub-Section, Makassar Health Quarantine Center. Blood samples were taken at the research location through a centrifuge process and then sent and examined at the Health Laboratory Center for Makassar.

2.3. *Procedure*

This research has received ethical approval from the Ethics Commission of the Faculty of Public Health, Hasanuddin University with protocol number 2124062003, every stage of administrative preparation including location research permits has been completed. Next, the researcher conducted outreach to the main agency to respondents regarding the aims and objectives of conducting the research. After the respondent understands the researcher's explanation, including agreeing to special conditions such as not consuming fruit and vegetables and not using mosquito coils/spray/electrical medication the day before carrying out fogging activities and taking blood samples, then they fill out a form of willingness to be a respondent (informed consent).

The researcher will follow the monitoring stage of field activities, including recording the results of observations of the implementation of fogging using an observation sheet and documenting the implementation of activities starting from the mixing and loading stage of pesticides, as well as the application of pesticides in the field. Primary data in this research was obtained from interviews using a questionnaire instrument containing a list of questions as a guide in conducting interviews including: respondents consisting of date of data collection, name, gender, and education. The research variables are the respondent's age, weight, height, cholinesterase levels, work period, length of exposure, dose/rate of pesticides used in fogging, frequency of carrying out fogging actions in a year, knowledge, actions, use of personal protective equipment, and health complaints experienced.

BMI is measured using a weight measuring instrument (detecto scale) and a microtoise height measuring instrument. The blood collection procedure with the cholinesterase enzyme examination parameters will be taken directly by the researcher, then the Medical Laboratory Scientist officer will separate the blood serum and then the blood sample will be taken to the Public Health Laboratory Center Makassar for examination. accredited SNI ISO 15189:2012 as a Medical Laboratory-Quality and Competency Services by the National Accreditation Committee (KAN) with number LM-093-IDN. The equipment and procedures used include:

1. Equipment and materials required for venous blood sample collection: tourniquet, medical gloves, alcohol swabs, adhesive bandage, vacutainer needle, holder, purple vacuum tubes containing Ethylene Diamine Tetraacetic Acid (EDTA) anticoagulant
2. Sample Identification : Blood sample tubes are labeled with a sequential number code and the respondent's identity, including full name and date of birth. Complete sample data is entered into the sample registration, which includes the sample number/code, respondent's full name, date of birth, date and time of sample collection, age, gender, and examination parameters.
3. Venipuncture Procedure :
   a. Greet and identify the respondent by asking them to verbally state their full name, address, and date of birth. Explain the purpose and goal of the blood collection and provide an overview of the phlebotomy procedure.
   b. Disinfect hands using antiseptic gel if hands are not very dirty, or wash with antimicrobial soap if hands are very dirty.

c. Wear gloves that fit the phlebotomist's hands properly.
d. Verify the examination requirements with the phlebotomist, such as fasting, specific physical activities, medication intake, etc. Ensure the respondent has no allergies to the phlebotomy equipment.
e. Prepare the equipment and materials, especially by attaching the needle to the holder.
f. Position the respondent comfortably for the phlebotomy and provide motivation or guidance to reduce fear.
g. Apply the tourniquet 3 to 4 inches above the elbow crease and locate the venipuncture site by palpating the vein. Ask the respondent to make a fist to facilitate finding the venipuncture site. The tourniquet should not be left on for more than one minute.
h. Disinfect the venipuncture site using an alcohol swab in a circular motion from the center outward, counterclockwise. Allow the alcohol to air dry.
i. Position the needle at a 15 to 30-degree angle to the skin surface with the bevel facing up. Insert the needle using the index finger and thumb of the right hand. The left hand holds the respondent’s arm to immobilize the arm and vein.
j. Insert the vacuum tube into the holder and press the tube until it locks.
k. Release the tourniquet as soon as blood begins to flow into the tube or before the tourniquet has been in place for one minute.
l. Allow the vacuum tube to fill completely until the blood flow stops naturally.
m. Remove the filled vacuum tube from the holder using the thumb and middle finger, with the index finger supporting the holder. Immediately invert the tube.
n. If collecting more than one tube of blood, follow the correct order of draw based on the type of vacuum tube.
o. After removing the last tube from the holder, gently withdraw the needle and immediately press the puncture site with dry gauze or cotton for approximately one minute.
p. Once the bleeding has stopped, remove the gauze and cover the wound with an adhesive bandage.
q. Label the tube with the respondent’s identity, including full name, time, and date of blood collection.

Equipment, Storage Procedures, and Blood Sample Transport using the Internal Sample Transportation System [33] :

a. Equipment needed includes: plastic containers, cooled transport boxes (cool boxes), gel ice packs, specimen labels, and shipping forms.
b. Prosedur sample shipment procedure must consider the sample shipping requirements, such as: shipment time must not exceed the stability period of the analyte being tested, samples must not be exposed to direct sunlight, packaging must meet recommended packaging standards, shipping temperature must comply with the requirements based on the analyte being measured.

2.4. *Statistical analysis*

The data was collected using structured questionnaires and blood sample tests for cholinesterase enzyme levels conducted by the Health Laboratory Center for Makassar. The data was then inputted into Microsoft Excel 2016 and IBM SPSS Version 26 for further analysis. The normal reference values for cholinesterase enzyme levels provided by the laboratory are 4620-11500 U/l for males and 3930-10800 U/l for females. After the data cleaning stage, descriptive analysis and correlation tests were performed.

3. Results

An analysis of fogging officers at the Makassar Health Quarantine Center revealed a higher proportion of male respondents (58.1%, n=18) compared to females (41.9%, n=13). The most prevalent age group was 30-39 years old (48.4%, n=15). Educational backgrounds varied, with the highest proportion holding a Diploma IV / Bachelor's degree (48.4%, n=15).

Blood cholinesterase examination results (Figure 2) indicated that male respondents had levels exceeding the normal laboratory reference ranges (Male: 4620-11500 U/l; Female: 3930-10800 U/l). The median cholinesterase value for males was 8,554 U/l (range: 6,122 - 15,034 U/l), with one outlier. Females had a median value of 7,413 U/l (range: 5,527 - 9,790 U/l).

Table 2 summarizes blood cholinesterase enzyme levels, revealing two respondents with abnormal values exceeding the reference range (further illustrated in Figure 2). Notably, no significant correlation was observed between pesticide exposure characteristics (age, work duration, body mass index, knowledge level, fogging actions, PPE usage, insecticide dosage, fogging frequency, and exposure duration) and blood cholinesterase activity among fogging officers.

Interestingly, Table 2 also highlights a statistically significant relationship (correlation coefficient: 0.599) between health complaints and blood cholinesterase activity among fogging officers using pyrethroid insecticides (lambda-cyhalothrin and cypermethrin). Table 3 details post-fogging health complaints, with dizziness being the most frequently reported condition (10 respondents), followed by headaches (7 respondents) and nausea.

4. Discussions

Statistical testing revealed a weak relationship between the investigated pesticide exposure characteristics (age, work experience, body mass index, knowledge level, fogging actions, PPE usage, insecticide dosage, fogging frequency, and exposure duration) and blood cholinesterase enzyme activity in fogging officers. This low correlation suggests that changes in the independent variables are only slightly associated with changes in the dependent variable, or blood cholinesterase activity. However, the health complaints reported by the respondents showed a statistically significant relationship with blood cholinesterase enzyme activity in fogging officers at the Makassar Health Quarantine Center.

More complex, the findings of two respondents with abnormal levels of cholinesterase in their blood must still be a concern for the employer to provide support such as recovery time (leave), including guidance for health examinations by a specialist doctor, even though there were no specific health complaints reported during this research. Previous studies have stated that systemic effects of pyrethroids can appear 4-48 hours after exposure [9] whereas this study only observed within a limited timeframe which may have missed undocumented health complaints. Furthermore, reports indicate that patients with pyrethroid poisoning require about 6 days to recover [9] and experimental tests by Ahmed [34] have shown a sudden increase in AChE activity due to cypermethrin exposure, highlighting the importance of continuous health condition evaluations for workers exposed to chemicals in preventing undesired conditions.

According to the International Labour Organization [35] The health hazards are not limited to substances labeled as hazardous; some hazardous substances can be produced during the work process, so all elements of control measures must be periodically inspected and reviewed to ensure their effectiveness remains intact. Additionally, the toxicity of pyrethroids varies greatly, depending on the route of entry into the body (ingestion, inhalation, and dermal exposure) and the dosage amount, directly affecting the nervous system in humans, leading to subjective symptoms of poisoning [9, 36-37]. High concentrations of exposure can inhibit conduction and cause paralysis; Type II pyrethroids also decrease chloride flux and affect γ-aminobutyric acid receptors, leading to cataleptic seizures [9]. Elevated levels of cholinesterase in blood due to exposure to cypermethrin pyrethroids were also found in Simaremare's study [32] compared to other types of pyrethroids, though observations were made using pregnant women exposed to pesticides.

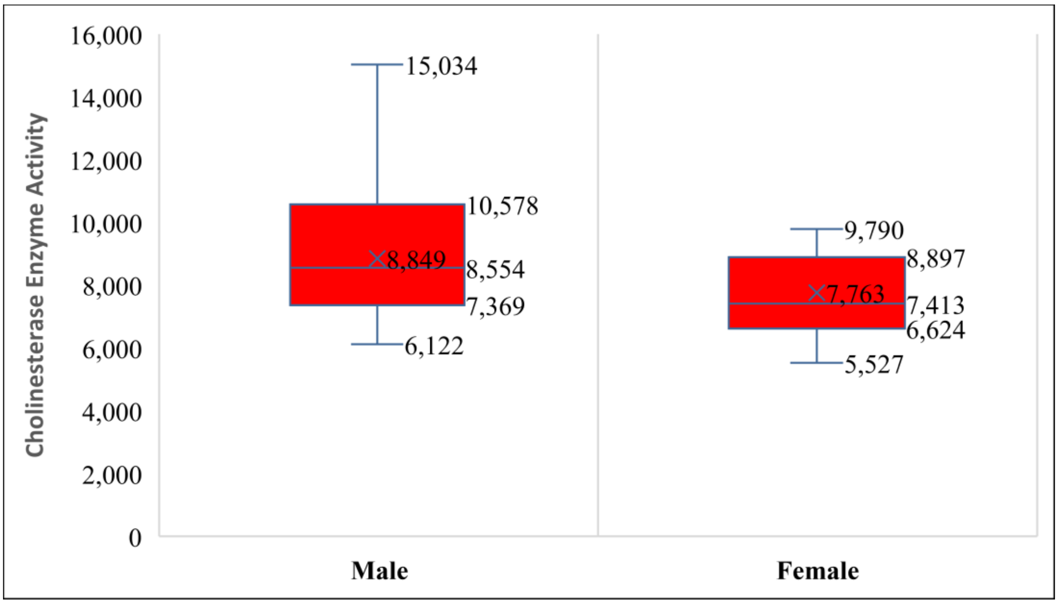
An increase in cholinesterase levels above normal limits among workers was also identified by Shentema [38] in flower plantation areas in Ethiopia, indicating a high incidence of pesticide poisoning, yet further identification was deemed necessary. A literature review study by Aulia [39] on farmers using organophosphate pesticides found higher AChE levels among farmers who did not adhere to proper pesticide usage procedures. Regarding the accuracy of pesticide dosage use among respondents in this study, it was assumed that all used the correct dosage, suggesting other predictors may have led to abnormal values.

Furthermore, according to WHO [5] symptoms frequently reported in pesticide poisoning include skin sensations of burning, heat, or irritation, allergic reactions, and dizziness, though only paresthesia can clearly be linked to pyrethroid exposure, even at low concentrations, and these complaints are temporary, particularly in sensitive individuals. There were reports of paresthesia in two respondents in this research, with one also reporting eye irritation and throat pain, despite normal cholinesterase levels in the examination. However, further medical studies are needed to prove poisoning resulting from a combination of health complaints. Nausea, headache, and dizziness are associated with the presence of organic solvents [5, 37] while coma and seizures are life-threatening signs [10].

The researchers acknowledge limitations in this study, including the identification of health complaints only after fogging without follow-up to review possible additional clinical symptoms, the small sample size, and the absence of a comparator to justify the core issues. Therefore, future research is expected to review studies by expanding the sample size or considering other objects with similar tasks and work functions (fogging). Additionally, expanding variables could support the justification of abnormal findings.

Table 1. Distribution of respondent characteristics

	Frequency (n=31)	Percent (%)
Gender		
Male	18	58.1
Female	13	41.9
Age		
20-29 Years	5	16.1
30-39 Years	15	48.4
40-49 Years	8	25.8
50-59 Years	3	9.7
Education		
Senior High School	9	29.0
Diploma III	7	22.6
Diploma IV/ S1 Degree	15	48.4



** Normal reference values (M : 4620-11500; F: 3930-10800)*

Figure 2. Comparison of Blood Cholinesterase Enzyme Levels Based on Gender

Table 2. Bivariate Analysis Results

Variable	Cholinesterase Enzyme Levels		*Correlation Coefficient[a]*
	Normal	Abnormal	
	Frequency (%)	Frequency (%)	
Age			0.174
≥ 36 years	14 (48.3%)	2 (100%)	
< 36 years	15 (51.7%)	0 (0.0%)	
Years of Service			0.172
>5 years	23 (79.3%)	1 (50.0%)	
≤5 years	6 (20.7%)	1 (50.0%)	
Body Mass Index			0.251
Overweight	14 (48.3%)	0 (0.0%)	
Thin	1 (3.4%)	0 (0.0%)	
Normal	14 (48.3%)	2 (100%)	
Level of Knowledge			0.115
Low	5 (17.2%)	0 (0.0%)	
High	24 (82.8%)	2 (100%)	
Fogging Action			0.086
Inadequate	3 (10.3%)	0 (0.0%)	
Good	26 (89.7%)	2 (100%)	
Use of Personal Protective Equipment			0.048
Incomplete/ Insufficient	1 (3.4%)	0 (0.0%)	
Complete	28 (96.6%)	2 (100%)	
Insecticide Dosage			-[b]
Incorrect dosage	0 (0.0%)	0 (0.0%)	
Correct dosage	28 (100%)	2 (100%)	
Fogging Frequency			-[b]
Repeated (≥24 jam)	0 (0.0%)	0 (0.0%)	
Once (<24 jam)	28 (100%)	2 (100%)	
Exposure Duration			-[b]
> 4 hours	0 (0.0%)	0 (0.0%)	
≤ 4 hours	28 (100%)	2 (100%)	
Health Complaints			0.599
Have complaints	26 (89.7%)	0 (0.0%)	
Without complaints	3 (10.3%)	2 (100%)	

a. The correlation coefficient obtained from the linear relationship between two variables ranges from -1 to +1.
b. No statistics are computed because the category variable is a constant.

Tables 3. Details of Health Complaints reported by respondents

ID Respondent	Paresthesia	Hypersensitivity	Conjunctivitis	Cephalalgia	Dizziness	Nausea	Vomiting	Fasciculation	Convulsion	Pharyngitis	Dyspepsia	Dysphagia	Tremor	Aphthous stomatitis	Syncope	Total Health Complaints	Cholinesterase Enzyme Level Examination Result
CANL	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	1	Normal
CCLP	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	2	Normal
CDBP	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	1	Normal
CDEP	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	1	Normal
CDIL	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	1	Normal
CEML	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	2	Normal
CHEL	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	1	Normal
CHPP	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	1	Normal
CHRP	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	1	Normal
CILL	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	1	Normal
CJNL	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	1	Normal
CJUL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	Abnormal
CJYL	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	1	Normal
CKAL	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	2	Normal
CMML	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	1	Normal
CMRP	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	Normal
CMSL	-	+	-	-	-	+	-	-	-	-	-	-	-	-	-	2	Normal
CMUP	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	1	Normal
CNHP	-	-	-	+	+	+	-	-	-	-	-	-	+	-	-	4	Normal
CRAL	-	-	-	-	-	-	-	+	-	-	-	-	+	-	-	2	Normal
CRVP	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	Normal
CSAL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	Normal
CSKL	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	1	Normal
CSML	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	Normal
CSRL	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	2	Normal
CSVP	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	1	Normal
CSYL	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	Abnormal
CTWP	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	1	Normal
CUGP	+	-	+	-	-	-	-	-	-	+	-	-	-	-	-	3	Normal
CWAL	-	-	+	+	+	+	-	-	-	-	-	-	-	-	-	4	Normal
CYRP	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	1	Normal
TOTAL	**2**	**3**	**4**	**7**	**10**	**7**	**0**	**1**	**0**	**1**	**0**	**0**	**5**	**0**	**0**		

5. Conclusions

The research data indicates that at least one out of fifteen respondents was found to have abnormal cholinesterase enzyme levels, following exposure to pyrethroid insecticides during fogging activities. However, the analysis of variables such as age, length of service, body mass index, level of knowledge, fogging practices, use of personal protective equipment (PPE), insecticide dosage, fogging frequency, and exposure duration showed a statistically weak correlation with the activity of cholinesterase enzyme in the blood of fogging personnel at the Balai Besar Kekarantinaan Kesehatan Makassar. Conversely, the health complaints reported by respondents statistically demonstrated a significant correlation with cholinesterase enzyme levels.

Acknowledgments

The author would like to express gratitude to the Directorate General of Health Workers for financial support for study and research costs, the Health Quarantine Centre for providing the research site, and the Health Laboratory Center for Makassar for conducting the lab tests.

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