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The Relationship Between Paraquat Exposure, Cholinesterase Activity, and Hematological Results Among Sugar Cane Plantation Workers in South Sumatra, Indonesia: A Cross-Sectoral Mediation Analysis

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ABSTRACT

Paraquat is a significant health problem among plantation workers in developing countries. This study analyzed the relationship between pesticide exposure, cholinesterase activity, hemoglobin levels, and oxygen saturation (SpO_2) as well as the mediating role of cholinesterase activity in workers. An analytical observational study with a cross-sectional design was conducted on 90 respondents using random sampling techniques. 66.7% of respondents experienced cholinesterase activity inhibition, 64.4% had hemoglobin levels < 13 g/dL, and 38.9% showed SpO_2 values < 95%. Multivariate logistic regression results showed that the use of complete personal protective equipment (PPE) was strongly associated with normal cholinesterase activity (adjusted OR = 56.89; 95% CI: 2.58–1256.94). Other significant factors included spraying duration ≤ 4 hours/day (adjusted OR = 42.13; 95% CI: 2.04–871.99), spraying frequency ≤ 2 times/week (adjusted OR = 30.41; 95% CI: 1.14–814.96), and spraying time (adjusted OR = 62.77; 95% CI: 2.08–1891.12) ($p < 0.05$). Structural equation modeling (SEM) analysis showed that cholinesterase activity significantly mediated pesticide handling behavior and hemoglobin levels with an indirect effect of $\beta = 0.159$ ($p = 0.003$) and a good model fit index (RMSEA = 0.045). These results indicate that cholinesterase inhibition is a biological pathway of paraquat exposure with hematological disorders. Limitations include the cross-sectional design, which does not allow causal inference, sample size, and limitations in generalizing to the worker population.

1. INTRODUCTION

Paraquat is one of the herbicides that remains widely used in agricultural sectors of developing countries due to its high effectiveness and relatively low cost [1]. Although its use has been restricted or banned in many countries, paraquat continues to be applied extensively in tropical agricultural regions, including Indonesia [2]. This situation poses considerable occupational health risks, particularly for workers directly involved in pesticide mixing and spraying activities [3].

The primary toxic mechanism of paraquat involves redox cycling, which generates excessive reactive oxygen species (ROS) and induces systemic oxidative stress [4]. This process leads to cellular damage in multiple tissues, especially organs with high oxygen demand, such as the lungs and the hematopoietic system [5].

Unlike organophosphate and carbamate pesticides, paraquat is not a potent direct inhibitor of cholinesterase. Nevertheless, several occupational health studies have reported altered cholinesterase activity among workers exposed to paraquat [6-8]. In this context, cholinesterase may function as a non-specific biomarker reflecting cumulative toxic stress, mixed pesticide exposure, or secondary metabolic disturbances rather than direct enzymatic inhibition.

Long-term pesticide exposure has also been associated with hematological alterations, including reduced hemoglobin levels and impaired oxygen transport [9]. Oxidative damage to erythrocyte membranes and disruption of erythropoiesis are considered key mechanisms contributing to anemia among agricultural workers [10]. However, the biological pathway linking pesticide-handling behaviors to hematological outcomes has not been fully elucidated, as most previous studies examined behavioral factors, biochemical biomarkers, and hematological parameters separately [11].

This study aims to analyze the relationship between pesticide exposure, cholinesterase activity, hemoglobin concentration, and oxygen saturation (SpO_2), as well as to evaluate the mediating role of cholinesterase among sugarcane plantation workers exposed to paraquat. This study tested the following hypotheses: (1) unsafe pesticide handling behavior is associated with changes in cholinesterase activity; (2) changes in cholinesterase activity are associated with lower hemoglobin concentration and oxygen saturation; and (3) cholinesterase activity mediates the relationship between pesticide handling behavior and hematological outcomes.

2. MATERIALS AND METHODS

2.1 Study design and setting

This study employed an analytical observational design with a cross-sectional approach. The research was conducted in a sugarcane plantation located in Ogan Ilir Regency, South Sumatra Province, Indonesia. Data collection was carried out from October to December 2024.

2.2 Population and sample

The study population consisted of all workers directly involved in paraquat spraying activities at the study site. A total of 90 eligible workers were included using random sampling techniques.

2.3 Sample size considerations

The sample size of 90 workers represented all paraquat sprayers who met the inclusion criteria at the study site. Although no prior statistical power analysis was conducted, this sample size met the minimum requirements for exploratory mediation analysis using structural equation modeling (SEM) with a simple model and a limited number of parameters. A good model fit indicates adequate estimation stability, but the possible limitation in power to detect small effects still needs to be considered in future studies.

2.4 Data collection

Sociodemographic characteristics and pesticide-handling behaviors were collected through structured interviews. Laboratory examinations included measurements of cholinesterase activity, hemoglobin concentration, and oxygen saturation using standardized procedures.

2.5 Data analysis

Data was analyzed using Chi-square tests, multivariate logistic regression, and SEM. A p-value < 0.05 was considered statistically significant.

2.6 Ethical considerations

Ethical approval for this study was obtained from the Health Research Ethics Committee, Faculty of Public Health, Universitas Sriwijaya (Approval No. 405/UN9.FKM/TU.KKE/2024). All participants were informed about the study objectives, procedures, potential benefits, and risks, and provided written informed consent prior to participation in accordance with the Declaration of Helsinki.

3. RESULTS

This section presents the findings of the study on the relationship between paraquat pesticide exposure, cholinesterase levels, hemoglobin levels, and oxygen saturation among sugarcane plantation workers. The results are systematically organized, including the characteristics of respondents, univariate and bivariate analyses, as well as structural model analysis. All data are presented in tables and descriptive explanations to facilitate a comprehensive understanding of the research findings obtained from the field.

Table 1. Distribution of respondent characteristics (n = 90)

Characteristic	Category	n (%)
Age	Working-age population (15–64 years)	13 (14.4)
	Older adults (> 64 years)	77 (85.6)
Gender	Male	80 (88.9)
	Female	10 (11.1)
Work Duration	Short (≤ 5 years)	50 (55.6)
	Long (> 5 years)	40 (44.4)
Education	Elementary School	35 (38.9)
	Junior High School	35 (38.9)
	Senior High School	14 (15.6)
	No School	6 (6.7)

Note: Percentages are calculated based on the total sample (n = 90). Age categories follow WHO (2020) classification.

Table 1 presents the distribution of demographic characteristics among 90 sugarcane plantation workers. The majority of respondents were classified as older adults (> 64 years), accounting for 85.6% of the sample, while only 14.4% belonged to the working-age population (15–64 years). These findings indicate that most pesticide sprayers were older individuals, who may have increased physiological vulnerability to toxic exposures. In terms of sex, the respondents were predominantly male (88.9%), whereas females accounted for only 11.1% of the sample. This pattern reflects the gender-based division of labor commonly observed in agricultural settings, where pesticide spraying and other physically demanding tasks are typically performed by men. Regarding work duration, 55.6% of participants had a relatively short employment period (≤ 5 years), while 44.4% had worked for more than five years. Differences in employment duration may contribute to varying levels of cumulative pesticide exposure and associated health risks. Overall, the educational level of the respondents was low. Most participants had completed only primary education (38.9%) or junior secondary education (38.9%), while 15.6% had completed senior secondary education, and 6.7% had no formal education. This low educational attainment may influence workers' awareness, understanding, and compliance with safe pesticide handling practices.

Table 2 summarizes the distribution of pesticide (paraquat) usage behavior among 90 sugarcane plantation workers. The majority of respondents (66.7%) used incomplete personal protective equipment (PPE), while only 33.3% reported using complete protection consisting of at least five items (gloves, mask, boots, protective clothing, and eye protection). The limited use of complete PPE highlights a significant gap in occupational safety compliance among field workers. In terms of spraying duration, most workers (64.4%) reported poor practice, spraying for more than 4 hours per day, while only 35.6% had good spraying duration (≤ 4 hours per day). Extended exposure time increases the likelihood of paraquat absorption through inhalation or dermal contact. Regarding spraying frequency, two-thirds of the workers (66.7%) sprayed more than twice per week, indicating high exposure frequency.

Similarly, most respondents (74.4%) sprayed at inappropriate times of the day, often under conditions of high temperature and sunlight, which can enhance paraquat volatilization and absorption risk. For spraying dose, 53.3% of the respondents reported using inappropriate concentrations or quantities, while 46.7% used appropriate doses according to recommended guidelines. In addition, 57.8% of workers mixed more than four types of pesticides at once, a practice considered poor due to the potential for chemical interactions and increased toxicity.

Table 2. Pesticide (paraquat) usage behavior (n = 90)

Behavior	Category	n (%)
PPE	Complete	30 (33.3)
	Incomplete	60 (66.7)
Spraying Duration	Good (≤ 4 h/day)	32 (35.6)
	Poor (> 4 h/day)	58 (64.4)
Spraying Frequency	Good (≤ 2 times/week)	30 (33.3)
	Poor (> 2 times/week)	60 (66.7)
Spraying Time	Appropriate	23 (25.6)
	Not Appropriate	67 (74.4)
Spraying Dose	Appropriate	42 (46.7)
	Not Appropriate	48 (53.3)
Mixture Quantity	Good (≤ 4 types)	38 (42.2)
	Poor (> 4 types)	52 (57.8)

Note: Personal protective equipment (PPE) items include gloves, mask, boots, protective clothing, and eye protection. Good/poor classification [12].

Table 3. Biological parameters (n = 90)

Parameter	Category	n (%)
Cholinesterase (U/L)	Toxic (< 5,320 or > 12,920)	60 (66.7)
	Normal (5,320–12,920)	30 (33.3)
Hemoglobin (g/dL)	Abnormal (< 13)	58 (64.4)
	Normal (≥ 13)	32 (35.6)
Oxygen Saturation (%)	Abnormal (< 95%)	60 (66.7)
	Normal (≥ 95%)	30 (33.3)

Note: Biological thresholds follow standard occupational health references: Cholinesterase, hemoglobin, SpO_2 [6, 11, 13].

Table 3 presents the distribution of biological parameters, including cholinesterase, hemoglobin, and oxygen saturation levels, among 90 sugarcane plantation workers exposed to paraquat. The findings indicate that a substantial proportion of workers exhibited alterations in key biological indicators compared with established occupational health standards. A total of 66.7% of respondents had toxic cholinesterase levels (< 5,320 or > 12,920 U/L), whereas only 33.3% were within the normal range (5,320–12,920 U/L). This suggests a high level of pesticide exposure capable of inhibiting cholinesterase enzyme activity, which can affect both the peripheral and autonomic nervous system functions. The reference threshold for cholinesterase who identified as a sensitive biomarker for pesticide toxicity in agricultural workers [6]. Regarding hemoglobin, 64.4% of participants had abnormal levels (< 13 g/dL), while 35.6% were classified as normal (≥ 13 g/dL). This finding indicates a high prevalence of anemia among plantation workers, likely associated with impaired iron metabolism and oxidative damage to erythrocytes caused by chronic paraquat exposure. The reference values for hemoglobin follow World Health Organization standards [11]. Additionally, 66.7% of workers exhibited abnormal oxygen saturation ($SpO_2 < 95\%$), suggesting reduced oxygen-carrying capacity in the blood. This mild-to-moderate hypoxemia may result from oxidative stress and pulmonary tissue injury due to long-term inhalation of paraquat-containing aerosols. The oxygen saturation cutoff values were adopted, which are widely applied in occupational respiratory assessments [13].

Table 4. Bivariate analysis: Association between pesticide usage and cholinesterase levels

Factor	Cholinesterase	OR (95% CI)	P-Value
PPE Usage	Complete	53 (88.3%) Normal / 7 (11.7%) Toxic	68.14 (16.31–284.66)
	Incomplete	3 (10%) / 27 (90%)	Reference
Spraying Duration	Good	52 (89.7%) / 6 (10.3%)	129.78 (1.57–10,751.9)
	Poor	4 (12.5%) / 28 (87.5%)	Reference
Spraying Frequency	Good	52 (86.7%) / 8 (13.3%)	57.41 (1.49–2,207.01)
	Poor	4 (13.3%) / 26 (86.7%)	Reference
Spraying Time	Appropriate	54 (80.6%) / 13 (19.4%)	56.58 (1.51–2,119.86)
	Not Appropriate	2 (8.7%) / 21 (91.3%)	Reference

Note: PPE = Personal Protective Equipment; OR = Odds Ratio; CI = Confidence Interval. “Reference” indicates baseline category. Bivariate analysis conducted using Chi-square test.

Table 4 presents the bivariate association between pesticide usage behaviors and cholinesterase levels among sugarcane plantation workers. The analysis demonstrates that several behavioral factors related to pesticide handling were significantly associated with cholinesterase inhibition. Workers who used complete PPE had a significantly lower prevalence of toxic cholinesterase levels (11.7%) compared with those using incomplete PPE (90%). The use of complete PPE was 68 times more likely to protect workers (OR = 68.14; 95% CI = 16.31–284.66; $p < 0.001$). These findings highlight the strong protective role of PPE in minimizing dermal and inhalation exposure to paraquat [14]. Similarly, those with short spraying duration (≤ 4 hours/day) showed a markedly lower risk of cholinesterase toxicity (10.3%) compared with workers spraying for more than four hours per day (87.5%), with an odds ratio of 129.78 (95% CI = 1.57–10,751.9; $p < 0.05$). This result suggests that longer spraying times significantly increase the probability of pesticide absorption through prolonged contact and respiratory exposure. In terms of spraying frequency, respondents spraying ≤ 2 times per week had a substantially lower risk of cholinesterase inhibition (13.3%) than those spraying > 2 times per week (86.7%), yielding an OR = 57.41 (95% CI = 1.49–2,207.01; $p < 0.05$). This implies that repeated exposure without adequate recovery periods contributes to cumulative pesticide effects. Furthermore, spraying time was also significantly related to enzyme inhibition. Workers who sprayed at appropriate times (e.g., morning or late afternoon when temperatures are moderate) showed a lower prevalence of toxic cholinesterase levels (19.4%) compared with those who sprayed at inappropriate times (91.3%), with an OR = 56.58 (95% CI = 1.51–2,119.86; $p < 0.05$).

Table 5 presents the final multivariate logistic regression model assessing factors associated with cholinesterase levels among sugarcane sprayers. The results indicate that several behavioral variables significantly influence cholinesterase status. Workers who used complete PPE were 56.89 times more likely to maintain normal cholinesterase levels compared to those with incomplete PPE use (p = 0.011). Similarly, those with shorter spraying durations (≤ 4 hours/day) had a 42.13 times higher likelihood of normal cholinesterase levels (p = 0.016), while spraying frequency ≤ 2 times/week increased the odds by 30.41 times (p = 0.042). Additionally, spraying during appropriate times of the day showed a 62.77-fold increase in the likelihood of normal cholinesterase activity (p = 0.017).

Table 5. Multivariate logistic regression for cholinesterase levels (final model)

Variable	B	Sig.	Exp(B)	95% CI for Exp(B)
PPE Usage	4.041	0.011	56.89	2.575–1,256.94
Spraying Duration	3.741	0.016	42.13	2.036–871.99
Spraying Frequency	3.415	0.042	30.41	1.135–814.96
Spraying Time	4.139	0.017	62.77	2.083–1,891.12
Constant	-21.064	–	–	–

Note: PPE = Personal Protective Equipment; CI = Confidence Interval; Exp(B) represents adjusted Odds Ratios from logistic regression. Significance level p < 0.05.

Table 6. Mediation analysis: Effect of pesticide behavior on hemoglobin via cholinesterase

Path	Coefficient	T-Statistic	P-Value
PPE → Cholinesterase	0.335	3.434	0.001
Spraying Duration → Cholinesterase	0.333	3.149	0.002
Spraying Frequency → Cholinesterase	0.240	2.878	0.004
Spraying Time → Cholinesterase	0.282	3.094	0.002
Cholinesterase → Hemoglobin	0.475	4.923	0.000
PPE → Cholinesterase → Hemoglobin	0.159	3.016	0.003

Model Fit Indices: $\chi^2/df = 1.87$; RMSEA = 0.045; CFI = 0.962; GFI = 0.938; TLI = 0.949, indicating a good overall model fit [15]. Mediation analysis was performed using SEM.
Note: PPE = Personal Protective Equipment; Coefficients represent standardized effects. Mediation significance determined at p < 0.05 [16].

This study uses a variance-based SEM (Partial Least Squares–SEM) approach, which is more tolerant of small sample sizes, non-normal data distributions, and predictive and exploratory analysis objectives. Sample adequacy is also supported by model fit indices and path significance results, which indicate stable and statistically significant parameter estimates, including a significant cholinesterase mediation effect (β = 0.159; p = 0.003) with an RMSEA value of 0.045, indicating good model fit. In addition, the relatively large and consistent path coefficient values reinforce the reliability of the estimates despite the limited sample size.

Table 6 summarizes the mediation analysis evaluating the indirect effects of pesticide-handling behaviors on hemoglobin concentration through cholinesterase activity. The SEM results showed that all behavioral determinants of PPE usage, spraying duration, frequency, and time were significantly associated with cholinesterase activity, which in turn had a strong positive influence on hemoglobin levels. Model fit indices confirmed that the proposed SEM demonstrated an acceptable fit to the data ($\chi^2/df = 1.87$; RMSEA = 0.045; CFI = 0.962; GFI = 0.938; TLI = 0.949), indicating that the hypothesized pathways adequately represented the observed relationships. The use of complete PPE showed a significant positive association with cholinesterase activity (β = 0.335, p = 0.001), suggesting that consistent use of protective gear reduces pesticide absorption and helps maintain enzyme stability. Similarly, shorter spraying duration (≤ 4 hours/day) (β = 0.333, p = 0.002), lower spraying frequency (≤ 2 times/week) (β = 0.240, p = 0.004), and appropriate spraying time (β = 0.282, p = 0.002) were significantly related to higher cholinesterase activity. Furthermore, cholinesterase activity had a significant positive effect on hemoglobin concentration (β = 0.475, p < 0.001), indicating that lower enzyme levels reflecting higher pesticide exposure may contribute to anemia among workers. The indirect pathway from PPE to hemoglobin through cholinesterase was also significant (β = 0.159, p = 0.003), confirming the mediating role of cholinesterase in linking behavioral safety practices to hematological outcomes. Although SEM is typically applied to larger sample sizes, its application in this study is justified by the parsimonious model structure, strong theoretical foundation, and good model fit indices (RMSEA = 0.045; CFI = 0.962). These results indicate that the model estimates are sufficiently stable despite the relatively limited sample size.

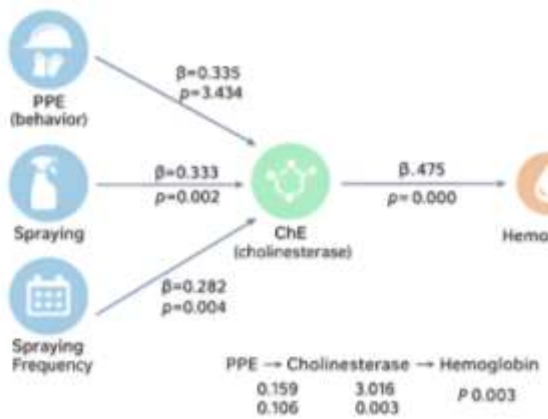

Figure 1. Conceptual risk reduction model for paraquat exposure among agricultural workers

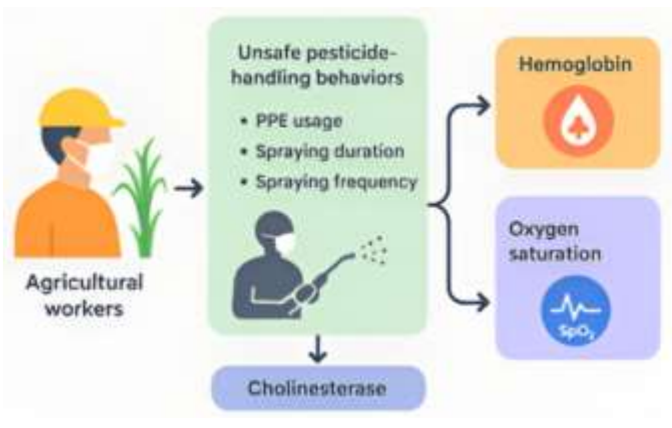

Figure 2. Conceptual framework of the relationship between paraquat handling behavior and cholinesterase activity, hemoglobin levels, and oxygen saturation (SpO_2) in plantation workers

Figures 1 and 2 illustrate the hypothesized pathways linking unsafe pesticide-handling behaviors to hematological and physiological outcomes among agricultural workers. Key behavioral factors, including PPE usage, spraying duration, and spraying frequency, affect cholinesterase activity, which functions as a central biochemical mediator. The improper use of pesticides is linked to a general lack of adequate training, indicating that many farmers do not have sufficient knowledge or skills to apply pesticides correctly [1, 17]. Changes in cholinesterase activity then influence hemoglobin levels and oxygen saturation (SpO_2), reflecting the systemic hematotoxic and hypoxic effects of paraquat exposure. This conceptual model provides a framework for designing integrated occupational risk reduction strategies in agricultural settings.

4. DISCUSSION

This study confirms the paradox of cholinesterase activity in paraquat exposure, given that paraquat does not directly inhibit cholinesterase as organophosphates and carbamates do. Therefore, cholinesterase cannot be considered a specific biomarker of paraquat exposure, and this limitation must be acknowledged. However, the significant relationship found indicates that chronic paraquat exposure can trigger systemic oxidative stress and possible mixed pesticide exposure in plantation environments, which indirectly affects cholinesterase enzymatic function. In this context, cholinesterase better reflects the cumulative biological response to occupational toxic load and acts as a mediator linking paraquat exposure to hematological disorders, particularly decreased hemoglobin levels. However, interpretation of the findings is limited by the cross-sectional design, limited sample size, and limitations of generalization, so further research with more specific biomarkers and a longitudinal design is still needed.

4.1 Interpretation of cholinesterase changes under paraquat exposure

The relationship between paraquat exposure and changes in cholinesterase activity should be interpreted with caution. Paraquat is not a direct cholinesterase inhibitor; therefore, the observed reduction in enzyme activity likely reflects indirect mechanisms rather than a specific inhibitory effect. These mechanisms may include oxidative stress, impaired hepatic function, exposure to mixed pesticide formulations, or cumulative metabolic toxic burden resulting from chronic occupational exposure. In this context, cholinesterase should be considered a marker of systemic toxic stress rather than a paraquat-specific biomarker.

Consistent with this interpretation, approximately two-thirds of participants (66.7%) exhibited reduced cholinesterase activity (Table 3), suggesting chronic exposure to multiple toxic stressors commonly encountered during pesticide handling. Previous studies have similarly reported that repeated pesticide exposure without adequate protection leads to decreased cholinesterase activity through indirect biochemical pathways [18, 19]. Dermal absorption and inhalation during pesticide mixing, spraying, and equipment cleaning are likely to contribute to this effect. Correlation analysis further demonstrated a significant negative association between unsafe handling practices and cholinesterase levels ($r = -0.443$, $p < 0.001$), supporting the role of occupational behavior in exacerbating enzyme dysfunction.

4.2 Hemoglobin levels and occupational exposure

A substantial proportion of workers (64.4%) presented with hemoglobin concentrations below 13 g/dL, indicating potential oxidative stress–induced hemolysis and impaired erythropoiesis. Chronic paraquat exposure has been shown to damage erythrocyte membranes and interfere with heme synthesis via oxidative mechanisms [19]. Mediation analysis (Table 6) revealed that cholinesterase activity significantly influenced hemoglobin levels ($\beta = 0.475$, $p < 0.001$), suggesting that enzyme dysfunction serves as an intermediary link between toxic exposure and reduced oxygen-carrying capacity. This effect is likely mediated by increased ROS production and lipid peroxidation, which disrupt erythroid cell integrity and maturation. This study has limitations in terms of confounding variables or other factors that could potentially affect workers' hemoglobin levels, such as smoking behavior, alcohol consumption, and nutritional status.

4.3 Oxygen saturation and respiratory effects

Reduced oxygen saturation (SpO_2) was observed in 66.7% of participants (Table 3), consistent with the high prevalence of anemia in this population. Paraquat is known to accumulate in pulmonary tissue, where it induces alveolar epithelial damage and compromises gas exchange [20, 21]. The significant positive correlation between cholinesterase activity and SpO_2 ($r = 0.406$, $p = 0.001$) suggests that systemic toxic stress and oxidative injury jointly impair respiratory efficiency, reinforcing the interconnected nature of hematological and respiratory outcomes in paraquat-exposed workers. This study has limitations in terms of confounding variables or other factors that could potentially affect workers' hemoglobin levels, such as smoking behavior, alcohol consumption, and nutritional status.

4.4 Behavioral factors and personal protective equipment use

Work-related behavioral factors, including spraying duration, frequency, and timing, were significantly associated with cholinesterase activity. Workers engaged in prolonged or frequent spraying exhibited greater enzyme suppression. Conversely, consistent use of PPE was strongly associated with higher cholinesterase activity ($\beta = 0.335$, $p = 0.001$), indicating reduced internal exposure. These findings align with previous evidence demonstrating that proper PPE use can reduce pesticide absorption by up to 50% [22, 23]. Nevertheless, the low prevalence of complete PPE use among workers highlights persistent gaps in occupational safety compliance.

4.5 Mediating role of cholinesterase

SEM confirmed that cholinesterase activity mediates the relationship between pesticide-handling behavior and hemoglobin levels (indirect effect $\beta = 0.159$, $p = 0.003$). This finding suggests that behavioral exposure patterns influence hematological outcomes primarily through indirect biochemical pathways rather than through direct effects alone. Importantly, given the nonspecific nature of cholinesterase suppression in paraquat exposure, the enzyme appears to function as an integrative indicator of systemic toxic burden. Consequently, interventions aimed at reducing exposure and restoring biochemical homeostasis, such as antioxidant supplementation, hepatic function monitoring, and exposure minimization, may help mitigate hematotoxic effects [6, 24].

Recent studies further support the role of cholinesterase as a biochemical mediator between pesticide exposure and hematological alterations. Studies reported that chronic pesticide exposure significantly suppresses acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) activity, which correlates with reductions in hemoglobin concentration and red blood cell counts among agricultural workers [3, 25]. Additionally, cholinesterase inhibition was identified as an early biomarker of subclinical hematotoxicity in populations chronically exposed to organophosphate and bipyridyl herbicides, including paraquat [18]. Behavioral factors such as inconsistent PPE use and improper pesticide handling were shown to amplify this mediating effect.

Furthermore, studies demonstrated that oxidative stress and inflammatory responses triggered by cholinesterase dysfunction disrupt erythropoiesis and heme biosynthesis through indirect biochemical mechanisms. These findings reinforce the notion that improving pesticide safety behavior alone may be insufficient unless accompanied by strategies that address underlying enzyme dysfunction and systemic oxidative stress [3, 26].

Collectively, these results underscore cholinesterase as a central mediator in the pathway linking pesticide exposure behaviors to adverse hematological and physiological outcomes. Therefore, preventive strategies should integrate behavioral modification with biochemical restoration approaches, including antioxidant therapy, periodic enzyme monitoring, and reduction of cumulative toxic exposure [3, 27].

4.6 Implications and recommendations

The findings highlight the urgent need to strengthen occupational health policies and implement routine biomonitoring programs in plantation settings. Recommended measures include periodic cholinesterase assessment, mandatory and consistent PPE use, and targeted occupational health education. When designing educational strategies or programs to reduce the unsustainable use of pesticides, it is important to focus on increasing individuals' knowledge about pesticides, fostering positive attitudes toward environmentally friendly alternatives, and strengthening perceived behavioral control [28]. Policy-level interventions should also consider stricter regulation of paraquat use, substitution with less toxic alternatives, and comprehensive worker training programs. Future research employing longitudinal designs and molecular biomarkers of oxidative damage is warranted to better elucidate causal pathways and enhance the mechanistic understanding of pesticide-related toxicity.

5. CONCLUSIONS

This study shows that exposure to paraquat is associated with changes in cholinesterase activity and hematological profiles among sugarcane plantation workers. Cholinesterase activity acts as a biological mediator linking occupational exposure patterns to decreased hemoglobin levels, possibly through mechanisms related to oxidative stress. However, interpretation of these findings is limited by the cross-sectional study design, self-reported exposure assessment, single study location, lack of direct quantitative measurements of paraquat exposure, and potential confounding factors such as smoking habits, nutritional status, and alcohol consumption. Future longitudinal studies combining environmental and biological biomonitoring are needed to strengthen causal conclusions and to support the development of more effective occupational health risk reduction strategies.

CONTRIBUTIONS

The first author was responsible for designing the research framework, analyzing the data, writing the manuscript, and refining its final content. The second and third authors contributed to developing the research protocol, supervising the data collection process, and reviewing the quality of the methodology and analytical results. All authors have read, reviewed, and approved the final version of this manuscript and take full responsibility for the accuracy and integrity of its content and data.

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