Renal and Hepatic Toxicity of Alpha-Cypermethrine Pesticide Used on Agricultural Farmers Living Closed to Tigris river, Iraq

Sarhan Rashid Sarhan [1*], Mohammed H.M. Merah [2]

Abstract

The study was conducted from October 15, 2021, to February 15, 2022, in Wasit Governorate, Iraq, targeting farmers of different ages exposed to chemical pesticides along the banks of the Tigris River within the administrative borders of the province. The objective of the study was to identify the impact of alpha-cypermethrin on the health condition of farmers during spraying operations. This was achieved by measuring and identifying changes in vital indicators through biochemical tests, specifically kidney functions and liver enzymes. 200 samples were collected for the study and divided into two groups. The first group comprised 150 samples from farmers exposed to the pesticide, categorized into two age groups. The first subgroup included individuals older than 18 (100 samples), and the second included those under 18 (50 samples). The second group, the control group, consisted of 50 samples, with 25 individuals over 18 and 25 under 18. Results revealed highly significant differences ($P \leq 0.01$) in the concentrations of kidney functions (urea and creatinine) and hepatic enzymes (AST, ALT, and ALP) among individuals exposed to the pesticide compared to the concentrations in the non-exposed control group. The study's findings conclude that direct exposure to alpha-cypermethrin impacted overall body functions and affected biomarkers, particularly kidney and liver enzyme functions. Moreover, the adverse effects were more pronounced in older farmers exposed to the pesticide than their younger counterparts.

Keywords. Pyrethroids, Environmental pollution, kidney functions, liver enzymes

Significance | ALP, ALT and AST enzymes increased significantly when directly exposed to this pesticide as a result of its effect on kidney and liver functions.

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Introduction

Pesticide use in agriculture has significantly increased globally due to the growing demand for food. Pesticides are commonly used to control pests, but when they enter the body through use, inhalation, or contact, they have a toxic effect on people and can interfere with natural reactions and enzymatic function. Serious pollution issues and health risks typically accompany the extensive use of pesticides. Furthermore, the careless application of pesticides in agriculture will result in major environmental issues, including concerns for the health of those who work with pesticides and those exposed to them, particularly in this field (Sheikh et al., 2011). Organic substances called pyrethroids are applied as insecticides. There are two categories for them. The existence of a cyano group, restricted to the alpha locus, sets apart the second type of pyrethroids from the first type.

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In addition, the α-cyano group increases the toxicity of the second type of pyrethroids compared to the second type. The most common compounds of second-type pyrethroids are cypermethrin and alpha-cypermethrin (Schettgen et al., 2002).

Alpha-cypermethrin is a synthetic pyrethroid pesticide widely used in crops to control many pests because it is very effective in exterminating insects. It is widely applied in agriculture and public health programs (Sharma et al., 2014). It is one of the most widely used pesticides (M. H. Arafa et al., 2015). Recently, it was found that the cypermethrin pesticide and other pyrethroid compounds are the most widely used in Iraq (Yassin & Hadi, 2016). Therefore, it is considered one of the most dangerous environmental pollutants and toxic to all mammals, and it is one of the cypermethrin synonyms (Lewis et al., 2016). Direct exposure to pesticides is responsible for the occurrence of many health problems as well as biochemical changes with unknown long-term consequences (Damalas & Abdollahzadeh, 2016). Although pesticides are useful in improving food production, reducing farm labor needs, and improving public health, they affect human and animal health and environmental sustainability (Choudhary et al., 2018). Recent studies indicate that the alpha-cyperthrombin pesticide is highly toxic to aquatic organisms, making it questionable in agricultural uses (Hartnik et al., 2008).

Following exposure to this pesticide, elevated kidney plasma levels of urea and creatinine indicate compromised renal function linked to kidney alterations (Grewal et al., 2009). Exposure to this pesticide results in anemia and some of the previously mentioned negative effects and damages DNA (Dahamna et al., 2011; Hussien et al., 2013). Due to its composition and lipophilic qualities, tissues easily absorb it. However, when it accumulates in high concentrations in fatty tissues, the skin, kidneys, and liver, it can cause damage to tissues and nerves (Gao et al., 2016; Rehman et al., 2014). According to Hassanin et al., farmers exposed to pesticides experienced elevated urea and creatinine levels along with a kidney malfunction (Hassanin et al., 2018). Because of the high toxicity of this pesticide, research has concentrated on how it behaves in the environment (Yao et al., 2019). Additionally, it has been found that pesticides can damage heart muscle tissues, which results in cardiotoxicity in male rats (Ghazouani et al., 2020). Therefore, in this study, we determined the effect of alpha-cypermethrin during pesticide spraying operations, which might affect vital health organs such as the liver, heart, and kidney.

Material And Methods

Study Design

We have carried out this study with the Water and Environment Department of the Ministry of Science and Technology, Baghdad, between October 15, 2021, and February 15, 2022. Farmers in the Wasit Governorate of Iraq who lived near the Tigris River provided blood samples for the study. When they used the pesticide alpha-cybermethrin for control, these people were exposed to it.

Population and Study Area

The research disclosed the study's farmers exposed to alpha-cypermethrin during circulation and when this pesticide was sprayed for pest control. The Wasit Governorate's northern, central, and southern regions were included. The main focus areas were al-Hofryah, Al-Shahimiya, Al-Suwaira, Al-Aziziyah, Al-Zubaydia, Numaniyah, Al-Kut, Sheikh Saad, and Al-Hay cities. The regions are found inside the Wasit Governorate's administrative boundaries, on the banks of the Tigris River (Figure 1). Two groups of 200 samples each were used in the study. Based on age, two subgroups of the study population were created from the two groups. Individuals over the age of eighteen are included in the first group, and those under the age of eighteen are included in the second. It should be noted that study participants who smoked, drank, or received chemotherapy or radiation were not included. Those who were not farmers and did not use pesticides made up the control group.

Blood analysis

We have collected all the data using questionnaires and forms. Name, age, place and length of residence, occupation, and frequency of diseases were all included on the form. As a control group, additional residents of neighborhoods near the river also had blood drawn. After identifying the vein and taking an intravenous blood sample, about ten milliliters of venous blood samples were taken from farmers exposed to the pesticide and those without, to compare them under sterile conditions (Ombelet et al., 2019).

Enzymatic and biochemical analyses

Gell tubes held the samples for the biochemical and enzymatic tests. 3 ml of each sample was placed in the tube and labeled with numbers for biochemical analysis. After being moved to the lab, the serum was separated from the other ingredients using a centrifuge set at 3000 RPM for 10 minutes. In order to perform biochemical tests on kidney function (Urea, Creatinin) and liver function (ALT, AST, ALP), micropipettes were used to transfer blood samples into Eppendorf tubes. The Cobas C111 equipment was utilized to measure biochemical parameters related to liver enzymes and kidney function, as per a report published by Roche Company. To do this, separate the serum and measure out 200 milliliters. After this, it is put in a particular tube so the apparatus can analyze it. The apparatus will request that the tube be inserted into the slot that has been allocated for it before pressing the start button. The equipment will show up for a while after the test results are announced; for instance, it will take 12 minutes for liver enzymes, 5 minutes for urea, 9 minutes for creatinine, and so on.

Statistical analysis

The SAS, 2018 program was used to analyze the data. In this study, the T-test was employed to compare the means and identify the impact of various factors on the study parameters.

Results

Kidney functions

The findings demonstrate how alpha-cypermethrin affects kidney function by measuring urea and creatinine concentrations in pesticide-exposed individuals compared to non-exposed individuals. In contrast to 25.02 and 0.657 mg/dl, respectively, the values were 55.60 and 1.524 mg/dl (Table 1). Table (2) shows the impact of alpha-cypermethrin on kidney function for farmers exposed to the pesticide at varying ages, as indicated by urea and creatinine levels. The results in the horizontal direction seem to indicate a highly significant difference in the amount of urea between individuals exposed to the pesticide who are older than 18 and those younger than 18 ($P \leq 0.01$). In comparison to 41.17 mg/dl, the results were 62.84 mg/dl. The amounts of urea in the control groups for both groups did not differ significantly.

Liver enzymes

The results show alpha-cypermethrin's effect on the concentrations of liver enzymes (AST, ALT, ALP) in the blood serum of people exposed to this pesticide compared to non-exposed people. Significant differences ($P \leq 0.01$) in hepatic enzyme indicators were observed in people exposed to the pesticide compared to same concentrations in people not exposed to this pesticide. The results ranged 55.18, 52.99 and 142.26 u/l compared to 16.19, 14.06 and 72.16 u/l, respectively (Table 3).

Discussion

The results show that, compared to individuals not exposed to the pesticide for the same two age groups, there were significant differences in the amount of urea between farmers exposed to the pesticide over 18 and those under 18. When comparing the vertical direction, these differences were observed at ($P \leq 0.01$). Those exposed in the two age groups had values of 62.84 and 41.17 mg/dl, respectively, as opposed to 24.45 and 25.60 mg/dl. The horizontal direction of the creatinine ratio examined in Table (2) demonstrated that there were significant differences ($P \leq 0.01$) in this ratio between farmers who were over the age of 18 and those who were under the age of 18, with the former recording 1.76 mg/dl compared to the latter's 1.04 mg/dl. It was observed that there were no significant differences for the non-exposed individuals in the control groups. The individuals exposed to the pesticide, both those over 18 and those under 18, saw a highly significant difference ($P \leq 0.01$) in their creatinine percentage compared to the unexposed individuals in the control groups when comparing the vertical direction of the same Table. One of the most sensitive biochemical markers for identifying renal damage is creatinine and urea, which are entirely released by the kidneys as metabolic waste products (Garba et al., 2007).

Because of their major roles in detoxification, the removal of toxic receptors, the regulation of extracellular bodily fluids, and homeostasis, the kidneys are considered the main organs in the human body. Nephrotoxicity is characterized by an imbalance and a quick decline in kidney function; it is frequently brought on by exposure to medications and environmental contaminants (Gupta & Trivedi, 2018). According to the studies, abnormal kidney function is the cause of the increase in urea in the blood of animals exposed to pesticides (Agarwal et al., 1984). The alpha-cypermethrin pesticide alters kidney tissues, causing the Golgi apparatus and the endoplasmic reticulum of cells to proliferate and the membranes of single-cell tissues in the proximal renal tubules to deteriorate; these tubes epithelization, the lack of a cell membrane, and the thickening of the basement membrane (Luty et al., 1998).

People with high pesticide exposure might affect their kidneys due to high urea and creatinine levels. The live damage might also be obtained due to cell necrosis through the toxic effects of pyrethroid compounds. The liver damage can increase the malondial aldehyde (MDA) (Grewal et al., 2009). This observation agrees with other studies of alpha-cypermethrin adverse effects on the kidneys and liver (Sushma & Devasena, 2010). The reason behind this is the toxic effect of high concentrations of alpha-cypermethrin on liver cells' metabolic effects (Gomaa et al., 2011).

On the other hand, several studies have suggested that high urea and creatinine in farmers exposed to pesticides causes renal tubular insufficiency, poor glomerular filtration, urinary obstruction, and kidney damage (A. Arafa et al., 2013; D. A. Khan et al., 2010). This defect includes direct injury to kidney tissues and cells, pathological changes, blood circulation changes, and obstruction of renal secretion (Zhao & Lin, 2014). The kidneys are the most important target organs for pesticide attacks (Barnett & Cummings, 2018).

Serum enzyme levels, particularly those associated with liver cell damage and stress, are markers of a person's overall health (A. Khan et al., 2009). Liver damage and dysfunction may be indicated by elevated liver enzyme levels, such as ALT and AST (Rjeibi et al., 2016). Our results indicated that pesticide users in both age groups had higher blood levels of liver safety enzymes. The rise in these levels in the blood may cause this. It might result from the harmful and influential alpha-cypermethrin pesticide, which damages livers and causes oxidative damage to membranes and pathological changes in the liver. The cause is that individuals exposed to the pesticide experienced elevated levels of these enzymes in their blood serum due to oxidative stress, lipid peroxidation, pro-inflammatory symptoms, and weakened

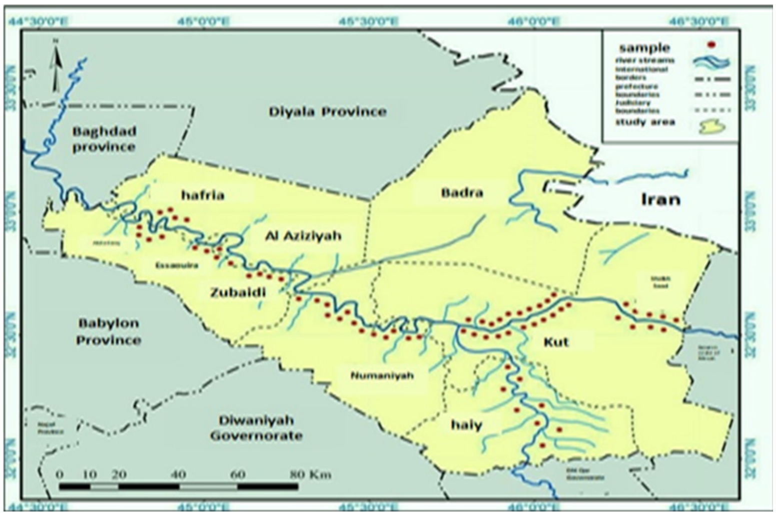

Figure 1. the map of the study samples in Wasit Governorate

Table 1. The concentration of urea and creatinine (mg/dl) in the blood serum of the exposed and non-exposed groups to the alpha-cypermethrin pesticide

Group	Mean ± SE	
	Urea (mg/ dl)	**Creatinine (mg/ dl)**
Patients (No=150)	55.60 ±0.50	1.524 ±0.02
Control (No=50)	25.02 ±0.45	0.657 ±0.01
T-test	1.781 **	0.059 **
P-value	0.0001	0.0001
O.R. (C.I.)	2.06 (1.16-4.33)	1.37 (0.86-2.51)
** (P≤0.01).		

** Indicates that there are highly significant differences at (P≤0.01) in the analysis of variance table for the groups.

Table 2. Effect of alpha-cypermethrin on kidney function (urea and creatinine) for the exposed and control groups (mean ± SE) at different ages

Parameters	Group	Mean ± SE		T-test
		>18 yr.	**<18 yr.**	
Urea	Patients	62.84 ±0.18	41.17 ±0.16	0.574 **
	Control	24.45 ±0.65	25.60 ±0.62	1.778 NS
	T-test	4.577 **	4.051 **	---
Creatinine	Patients	1.763 ±0.007	1.045 ±0.005	0.024 **
	Control	0.666 ±0.02	0.648 ±0.02	0.049 NS
	T-test	0.169 **	0.097 **	---
** (P≤0.01).				

** Indicates that there are highly significant differences at (P≤0.01) in the analysis of variance table for the groups

Table 3. The concentrations of liver enzymes AST, ALT, ALP (u/l) in the blood serum of the exposed and non-exposed group

Group	Mean ± SE		
	AST (u/l)	**ALT (u/l)**	**ALP (u/l)**
Patients (No=150)	55.18 ±0.87	52.99 ±0.75	142.26 ±1.52
Control (No=50)	16.19 ±0.22	14.06 ±0.21	72.16 ±0.88
T-test	2.977 **	2.585 **	5.285 **
P-value	0.0001	0.0001	0.0001
O.R. (C.I.)	2.82 (1.08-5.02)	1.94 (0.89-3.41)	2.77 (1.24-4.83)
** (P≤0.01)			

** Indicates that there are highly significant differences at (P≤0.01) in the analysis of variance table for the groups.

Table 4. Effect of the pesticide on the liver enzymes of the exposed and control groups (mean ± SE) in different ages

Parameters	**Group**	**Mean ± SE**		**T-test**
		>18 yr.	**<18 yr.**	
AST(U/L)	Patients	67.29 ±0.47	30.94 ±0.20	**1.358** **
	Control	16.42 ±0.28	15.96 ±0.34	**0.875 NS**
	T-test	5.492 **	3.171 **	---
ALT(U/L)	Patients	63.50 ±0.41	31.97 ±0.21	**1.180** **
	Control	13.82 ±0.30	14.29 ±0.30	**0.844 NS**
	T-test	3.893 **	2.806 **	---
ALP(IU/L)	Patients	163.68 ±0.78	99.43 ±0.22	**2.214** **
	Control	70.83 ±1.19	73.49 ±1.30	**3.501 NS**
	T-test	8.215 **	5.321 **	---
** (P≤0.01).				

** Indicates that there are highly significant differences at (P≤0.01) in the analysis of variance table for the groups

NS in the horizontal direction indicates that there are no significant differences in the analysis of variance table between groups antioxidant defense systems. Consequently, due to various illnesses, the release of these enzymes from hepatic and non-hepatic tissue sources should be increased. All of these findings suggest that the pathological effects of cypermethrin on the liver are primarily responsible for the biochemical alterations brought on by toxicity (Ghorzi et al., 2017; Nair et al., 2010). Because of using agricultural chemicals, these factors indicated the decomposition of hepatocytes and the leakage of the enzyme into the blood, and thus the cytotoxic and hepatotoxic effects. The results show alpha-cypermethrin's effect on the concentrations of liver enzymes (AST, ALT, ALP) in the blood serum of people exposed to this pesticide compared to non-exposed people. Significant differences ($P \leq 0.01$) in hepatic enzyme indicators were observed in people exposed to the pesticide compared to same concentrations in people not exposed to this pesticide. The results ranged 55.18, 52.99, and 142.26 u/l compared to 16.19, 14.06 and 72.16 u/l, respectively (Table 3). The effect of the pesticide on the liver enzymes of exposed farmers is shown in different age groups. The horizontal direction of the Table shows that the pesticide affects farmers who are older than 18 years old through a highly significant difference at ($P<0.01$) in liver enzymes represented by AST, ALT, and ALP tests compared to the farmers exposed to the pesticide who less than 18 years old. The results recorded 67.29, 63.50, and 163.68 u/l compared with 30.94, 31.97, and 99.43 u/l, respectively. In the same direction as the table, it was noted that there were no significant differences in the liver enzymes of people who were not exposed to the pesticide in the control groups.

The results showed that when comparing with the vertical direction, it notes that liver enzymes AST, ALT, and ALP were significantly increased ($P<0.01$) because of the effect of farmers of the two age groups as a result of their exposure to the pesticide compared to the control group. The increase in the blood is associated with liver injury and changes its functions (P. R. Manna et al., 2003). Also, cypermethrin pesticide causes changes in hepatocytes and increases ALT and ALP activity in the serum, indicating that cypermethrin causes pathological changes in the liver (S. Manna et al., 2004). Studies have confirmed that pesticide exposure has caused the leakage of cytosolic enzymes (ALT, AST, and ALP) from liver cells and other body organs (Dewan et al., 2004). The damage to liver cells with this pesticide has negatively affected the metabolism and many metabolic changes of protein and its composition in the liver (Kumar et al., 2009).

These are the findings from the present study. Due to their association with weak hepatic cellular function and hepatic cellular membrane rupture, the high percentages of these concentrations for the indicators (AST, ALT, and ALP) in the current study and the high concentrations of urea in the blood of farmers exposed to this pesticide at different age groups are attributed to liver functions and their excessive leakage in the blood (Table 2). (Abdel-Daim & Abdou, 2015; Abdou et al., 2015).

Conclusion

According to the current study, exposure to alpha-cypermethrin was positively correlated with higher concentrations of biochemical markers, such as liver enzymes and kidney function, at various ages. Because this pesticide affects kidney and liver functions, it was observed that the levels of urea, creatinine, ALP, ALT, and AST enzymes increased when exposed directly to it. Additional research is needed to assess the molecular toxicity of alpha-cypermethrin and investigate the damage pesticide toxicity causes to DNA.

Author contribution

S.R.S. Conceived and designed the analysis and collected the data, while M.H.M.M. performed the analysis and wrote the Paper.

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Competing financial interests

The authors have no conflict of interest.

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