



The Relationship between Pesticide Exposure and Liver and Renal Enzyme Disorders in Adults Aged 35-70: The Results of the First Phase of the Shahedieh Cohort Study

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ABSTRACT

Introduction: Liver and kidney are known as important organs in detoxification of the body and may be exposed to pesticide damage. This study aims to investigate the relationship between pesticide exposure and disorders of liver and renal enzymes.

Material and Methods: This cross-sectional study was conducted on 5637 Iranian adults aged 35-70 from the first phase of Shahedieh Cohort Study. The investigated variables included age, sex, BMI, smoking, liver enzymes (SGPT, SGOT, ALP, GGT), renal enzymes (Urea, Creatinine), and the information related to exposure to pesticides in the yard, home, and agricultural land during the last 12 months. Data were analyzed using SPSS software version 24.

Results: The findings showed that 8% of the people were exposed to pesticides/insecticides on agricultural land, 2% in yard, and 59.6% at home. The mean of liver and renal enzymes in people exposed to pesticides in agricultural land was higher than in non-exposed individuals. This relationship was significant for all the enzymes except GGT. People exposed to pesticides in the yard had significantly higher levels of renal enzymes than non-exposed individuals. People exposed to pesticides at home had significantly higher levels of liver enzymes and renal enzymes than the non-exposed ones. Moreover, the mean of liver and renal enzymes were lower in people who used personal protective equipment.

Conclusion: This study suggests that exposure to pesticides may impact liver and kidney functions, and taking precautions like using personal protective equipment can help minimize potential health risks.

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Introduction

Due to the increase in world population in recent years, the use of agricultural products has increased. In this regard, the use of pesticides has

increased the quality of agricultural products. Chemical pesticides are used in agricultural industry to control pests such as fungi, weeds, rodents, insects, etc. ¹. The most widely used

pesticides in agriculture are organic poisons (organochlorine, organophosphate) and mineral poisons². Pesticides help farmers produce more quality fruits and vegetables; as a result, it is also effective in the economic growth of countries³. Pesticides are the chemicals used to control pests, weeds, and diseases in crops, ensuring higher yields and better quality. However, their residues on food products can potentially harm human health and environment.

The presence of remaining pesticides in agricultural products is a concern that has been widely discussed in recent years. However, pesticides may be dangerous for the environment, plants, aquatic animals, and humans². Some effects of pesticides have been proven on laboratory animals⁴⁻⁶. Jamal et al. found that absorption of pesticides through the skin is more common among agricultural workers. Fat-soluble and even water-soluble pesticides can easily enter body through the skin². Pesticides with smaller droplets enter the lungs through inhalation². Some pesticides also enter body through swallowing and hands contaminated with soil or water⁷. Then, the pesticide enters the circulatory system, and can affect different organs in the body². To minimize the risk of pesticide residues worldwide, governments and regulatory agencies have established maximum residue limits (MRLs). These limits define the highest amount of pesticide residue that is legally tolerated in or on food products. According to the 2018 sampling results from EU member states, it is evident that the majority (95%) of food samples tested had pesticide residue levels below the MRL. However, a smaller percentage (4.5%) of the samples had residue levels exceeding the MRL⁸. This indicated that food products were within the acceptable range for pesticide residues. Farmers, agricultural experts, and policymakers work together to ensure that these limits are not exceeded.

When pesticides are ingested, inhaled, or absorbed through the skin, they can have various effects on the human body, including liver and kidney. The impact of pesticides on liver can vary depending on the type and concentration of the

pesticide, as well as the duration and frequency of exposure⁹. Liver is a vital organ responsible for numerous functions, including detoxification, metabolism, and protein synthesis. Liver and kidneys are the target organs exposed to pesticides⁷. These two organs are known as the main organs in body detoxification and may be exposed to the damage of pesticides^{1, 3}. Long-term exposure to pesticides may lead to the accumulation of toxins in liver and kidneys. These toxins cause changes in liver and kidney cells⁷, which lead to the release of some enzymes in blood¹⁰. Jamal et al. stated that the absorption of pesticides leads to a change in the serum level of acetylcholinesterase and liver and kidney dysfunction. As a result, there are changes in blood parameters of the exposed person². A study showed that urea and some liver parameters such as Gamma Glutamyl Transpeptidase (GGT), Total Bilirubin (TB), Alkaline Phosphatase (ALP), and Direct Bilirubin (DB) increased gradually during a 3-year follow-up among people exposed to pesticides. While, Alanine Transaminase (ALT) and Aspartate Transferase (AST) improved at the end of each harvesting season, but never returned to the initial rate; this indicated the harmful effects of pesticides on human kidney and liver⁷. A study has also pointed to the increase in blood creatine levels among agricultural workers at the end of the harvest season and its effect on kidneys¹¹. The effects of pesticides can even go beyond this. High levels of exposure to certain pesticides can cause liver damage, leading to inflammation (hepatitis) and even liver failure¹². Long-term exposure to certain pesticides has been linked to an increased risk of cancer¹³.

Investigating the effect of pesticides on liver and kidney enzymes is crucial for several reasons. First, pesticides are widely used in agriculture to protect crops from various pests and diseases. However, these chemicals can sometimes find their way into the food chain, posing potential risks to human health. In addition, Liver and kidney enzymes play vital roles in body's detoxification process and maintaining overall health. These organs are responsible for filtering out toxins and

metabolizing various substances, including pesticides. When pesticides accumulate in the body, they can alter the normal functioning of liver and kidney enzymes, potentially leading to adverse health effects. In conclusion, the importance of studying the effect of pesticides on liver and kidney enzymes cannot be overstated. It helps to protect public health, inform policy decisions, and promote a safer, more sustainable agricultural system. The area investigated in the present study is located in the center of Iran and is a tropical region. Agriculture is the primary occupation of the rural population in most areas of this province. Given that the possibility of pests and plant diseases increases in tropical regions, the use of pesticides in agriculture is more common³. Considering that these people are exposed to pesticides at home, yard, or agricultural land, the present study is conducted to investigate the relationship between exposure to pesticides and liver and renal enzyme disorders in adults.

Material and methods

Design

This cross-sectional study was conducted using the data collected from the enrollment phase of Shahedieh Cohort Study (SHCS). SHCS data were collected from three cities in Yazd province (Shahdieh, Zarch, and Ashkazar). The SHCS is a part of Persian cohort study¹⁴, which examines the risk factors of non-communicable diseases in Iranian population adults of between 35 and 70. The enrollment phase of SHCS was started in April 2015 and finished in September 2017, which involved four stages of data collection. Initially, individuals were invited to visit the study center, were assigned a unique code (IRCT), and were registered for future visits after giving informed consent. Appointments were then scheduled for subsequent data collection stages. In the next step, a blood test was taken from the participant at the scheduled appointment. Sampling was measured after 12 hours of fasting through a blood test (25 ml). The test results were entered into Excel software after preparation by a laboratory technician. After blood sampling, individuals'

anthropometric measurements such as height, weight, and waist circumference were taken in a fasting state by a trained person using standard methods¹⁴. These measurements were recorded simultaneously in the Excel software. Following the measurements, the questionnaire was completed by trained personnel through face-to-face interviews. Each section of the questionnaire (general, medical, and nutrition section) was asked by a separate person while responses were simultaneously recorded in software.

Participants

Of 10,000 individuals who participated in the SHCS, 153 people with incomplete questionnaires and 4210 with diabetes, hypertension, fatty liver, renal failure, or alcohol use were excluded. Finally, 5637 people were included in the study. In this study, the subjects with diseases that may affect liver or renal enzymes were excluded (diabetes, high blood pressure, and liver and kidney disease). Moreover, people who consume alcohol were excluded from the study.

Research instrument

By referring to SHCS Center, the required data included age, gender, BMI, smoking, liver enzymes (serum glutamic-pyruvic transaminase (SGPT), serum glutamic oxalacetic transaminase (SGOT), ALP, GGT), renal enzymes (Urea, Ceratinine), and information about exposure to pesticides in the yard, home, and agricultural land during the last 12 months. Regarding exposure to pesticides, people were asked "During the last 12 months, have you been exposed to pesticides in the farmland (agricultural land, greenhouse), at home and in yard?", separately. If the people answered "yes", they were asked to indicate the number of exposures in the past 12 months, and then, to indicate the duration of each exposure. In addition, they were asked, "Did you use personal protective equipment (PPE) such as protective clothing (windbreaker or full plastic clothing), protective shoes (boots), gloves, apron, respirator, protective glasses, or head protection while performing that activity?". Liver and renal enzymes in blood serum were measured after 12 hours of fasting state

through a blood test (25 ml). After transferring the samples to the laboratory, biochemical analysis was performed using a BT-1500 autoanalyzer (BT-1500, Biotechnica, Italy)¹⁵. The test results (SGPT (IU/l), SGOT (IU/l), ALP (IU/l), GGT (IU/ml), Urea (mg/dl), Ceratinine (mg/dl)) were entered into the Excel software after preparation by the laboratory technician. This study was approved by Ethics Committee of Shahid Sadoughi University of Medical Sciences, Yazd with code IR.SSU.SPH.REC.1401.046.

Statistical analysis

Data were analyzed using SPSS version 24 software and descriptive tests, Chi-square, T-test, Pearson correlation coefficients, and linear regression model. Independent T-test was used to compare the mean of liver and renal enzymes based on exposure to pesticides in the yard, home, and agricultural land, separately. Also, the mean of liver and renal enzymes was compared using an independent T- test based on the use or non-use of PPE when exposed to pesticides in the yard, home, and agricultural land, separately. The linear regression model was fitted to investigate the

effect of the average duration of exposure on pesticides in the farm, yard and home. This study examined the connection between liver and kidney enzymes and factors like sex, smoking status, age, and body mass index (BMI). It used T-tests for sex and smoking variables and Pearson correlation coefficients for age and BMI relationships. A significance level of less than 0.05 was considered.

Results

All the participants were aged between 35 to 70 and had a mean age of 45.67 ± 8.7 years. The results showed that 21% of people were smokers, and more than 70% were overweight and obese. According to Table 1, 8% of the participants reported that they were exposed to pesticides in greenhouses or on agricultural lands; in addition, 4.2% of them used PPE when exposed to pesticides. 2% stated that they were exposed to pesticides in the yard; 59.6% used insecticides at home in the last 12 months, 4.7% of whom used PPE when exposed to pesticides. The relationship between demographic and social variables and liver and kidney enzymes is shown in Tables 2 and 3.

Table 1: Frequency of exposure to pesticides in yard, farm, and home and the use of personal protective equipment (PPE) during exposure

Variables		Frequencies	Percent
Exposure on the farm	No	5188	92.0
	Yes	449	8.0
Using PPE on the farm	No	5400	95.8
	Yes	237	4.2
Exposure in the yard	No	5527	98.0
	Yes	110	2.0
Using PPE in the yard	No	5611	99.5
	Yes	26	0.5
Exposure at home	No	2241	39.8
	Yes	3396	60.2
Using PPE at home	No	5374	95.3
	Yes	263	4.7

Table 2: Mean liver and kidney enzymes according to gender and smoking status

Variable	Gender		Smoker	
	Male (n = 2895, 51.4%)	Female (n = 2742, 48.6%)	Yes (n = 1186, 21%)	No (n = 4451, 79%)
SGOT	21.19 ± 8.3	17.27 ± 8.5	19.85 ± 8.1	19.14 ± 8.8
P-value*	0.001		0.01	
SGPT	27.68 ± 1.7	17.89 ± 1.4	24.33 ± 5.5	22.54 ± 7.3
P-value*	0.001		0.001	
ALP	187.83 ± 52.5	175.92 ± 52.7	30.7 ± 3.5	25.94 ± 2.2
P-value *	0.001		0.001	
GGT	31.86 ± 2.8	21.78 ± 1.8	192.13 ± 54.4	179 ± 52.2
P-value *	0.001		0.001	
Urea	29.9 ± 7.1	24.44 ± 6.3	29.28 ± 7.1	26.71 ± 7.2
P-value *	0.001		0.001	
Ceratinine	1.2 ± 0.18	1 ± 0.15	1.22 ± 0.18	1.09 ± 0.19
P-value *	0.001		0.001	

* T-test, SGPT: serum glutamic-pyruvic transaminase, SGOT: serum glutamic oxalacetic transaminase, GGT: Gamma Glutamyl Transpeptidase, ALP: Alkaline Phosphatase

Table 3: Correlation between liver and kidney enzymes and gender and smoking status

		Urea	Ceratinine	SGOT	SGPT	ALP	GGT
Age	Pearson correlation	0.070*	0.053*	0.003	- 0.008	- 0.016	0.006
	P-value	0.000	0.000	0.777	0.431	0.123	0.549
BMI	Pearson correlation	- 0.055*	- 0.052*	0.041*	0.077*	0.035*	0.046*
	P-value	0.000	0.000	0.000	0.000	0.001	0.000

* P-value<0.01, SGPT: serum glutamic-pyruvic transaminase, SGOT: serum glutamic oxalacetic transaminase, GGT: Gamma Glutamyl Transpeptidase, ALP: Alkaline Phosphatase

Table 4 shows that the mean of all liver enzymes (SGPT, SGOT, ALP, GGT) and renal enzymes (urea, creatinine) in people exposed to pesticides in the greenhouse or agricultural land was higher than unexposed people. This relationship was significant for all the enzymes except GGT. The results also revealed that subjects exposed to

pesticides in the yard showed significantly higher levels of renal enzymes (urea, creatinine) than those who were not exposed. Also, people exposed to insecticides at home had significantly higher levels of liver enzymes (SGPT, SGOT, ALP, GGT) and renal enzymes (urea, creatinine) than unexposed participants.

Table 4: The mean of liver and renal enzymes based on exposure to pesticides in the yard, on the farm, and at home

Variable	Farm		P-value*	Yard*		P-value*	Home		P-value*
	Exposed	Unexposed		Exposed	Unexposed		Exposed	Unexposed	
SGOT(IU/l)	21.17 ± 7.87	19.12 ± 8.73	0.000	19.19 ± 7.08	19.29 ± 8.71	0.90	20.11 ± 8.70	18.75 ± 8.63	0.000
SGPT (IU/l)	26.12 ± 17.19	22.64 ± 16.98	0.000	23.62 ± 13.20	22.91 ± 17.09	0.66	25.14 ± 18.21	21.46 ± 16.03	0.000
ALP(IU/l)	186.25 ± 45.63	181.67 ± 53.53	0.04	184.43 ± 48.89	181.99 ± 53.04	0.63	184.29 ± 52.66	180.55 ± 53.11	0.01
GGT (IU/ml)	28.87 ± 21.75	26.79 ± 24.62	0.08	28.95 ± 26.34	26.92 ± 24.37	0.38	29.07 ± 26.63	25.56 ± 22.72	0.000
Ceratinine(mg/dl)	1.21 ± .17	1.11 ± .20	0.000	1.18 ± .21	1.11 ± .20	0.001	1.15 ± .20	1.09 ± .19	0.000
Urea(mg/dl)	30.44 ± 7.08	26.97 ± 7.24	0.000	29.03 ± 8.03	27.21 ± 7.27	0.01	28.33 ± 7.28	26.53 ± 7.20	0.000

* T-test, SGPT: serum glutamic-pyruvic transaminase, SGOT: serum glutamic oxalacetic transaminase, GGT: Gamma Glutamyl Transpeptidase, ALP: Alkaline Phosphatase

Table 5 showed that people who used PPE when exposed to pesticides in agricultural lands or greenhouses had significantly lower SGPT and ALP than people who did not use PPE during exposure. Moreover, people who used PPE in agricultural lands or greenhouses had significantly lower SGPT than people who did not use PPE. People who used PPE at home when exposed to

insecticides had significantly lower liver enzymes (SGPT, SGOT, and GGT) and renal enzymes (urea, creatinine) compared to people who did not use PPE during exposure. After adjusting the effect of age, smoking status, BMI and gender, linear regression model did not reveal significant relation between enzymes and exposure (Table 6).

Table 5: The mean of liver and renal enzymes in people exposed to pesticides in the yard, on the farm and at home based on the use of personal protective equipment (PPE)

Variable	Farm		P-value*	Yard		P-value*	Home		P-value*
	Unused	used		Unused	used		Unused	used	
SGOT(IU/l)	30.00 ± 15.55	15.25 ± 3.30	0.40	30.00 ± 15.55	15.25 ± 3.30	0.40	19.45 ± 8.80	18.36 ± 8.43	0.04
SGPT (IU/l)	28.00 ± .00	14.50 ± 4.35	0.01	28.00 ± .00	14.50 ± 4.35	0.01	23.32 ± 17.37	20.55 ± 14.73	0.003
ALP(IU/l)	175.50 ± 16.26	132.75 ± 12.99	0.02	175.50 ± 16.26	132.75 ± 12.99	0.10	182.52 ± 52.95	184.95 ± 61.41	0.46
GGT (IU/ml)	23.50 ± 7.77	16.75 ± 2.21	0.43	23.50 ± 7.77	16.75 ± 2.21	0.43	27.40 ± 24.74	25.53 ± 25.96	0.000
Ceratinine(mg/dl)	1.35 ± .07	1.12 ± .12	0.08	1.35 ± .07	1.12 ± .12	0.08	1.13 ± .20	1.06 ± .19	0.000
Urea(mg/dl)	37.00 ± 12.72	27.75 ± 4.78	0.23	37 ± 12.72	27.75 ± 4.78	0.23	27.36 ± 7.29	26.35 ± 7.42	0.02

* T-test, SGPT: serum glutamic-pyruvic transaminase, SGOT: serum glutamic oxalacetic transaminase, GGT: Gamma Glutamyl Transpeptidase, ALP: Alkaline Phosphatase

Table 6: The effect of average duration of exposure to pesticides on the farm, in the yard and at home by linear regression model

Dependent variable	Predictors	Beta	Std. error	P-value
Urea	MTH	0.0001	0.001	0.903
	MTY	0.007	0.010	0.452
	MTF	0.0003	0.0002	0.140
	Using PPE on the farm	0.510	0.449	0.256
	Using PPE in the yard	- 1.203	1.392	0.387
	Using PPE at home	0.253	0.415	0.543
Creatinine	MTH	2.96	0.0001	0.204
	MTY	0.0001	0.0002	0.474
	MTF	9.41	0.0001	0.133
	Using PPE on the farm	- 0.011	0.012	0.366
	Using PPE in the yard	- 0.040	0.036	0.269
	Using PPE at home	- 0.011	0.011	0.291
SGOT	MTH	0.002	0.001	0.143
	MTY	- 0.021	0.012	0.081
	MTF	- 0.0002	0.0003	0.448
	Using PPE on the farm	0.507	0.577	0.379
	Using PPE in the yard	2.085	1.789	0.244
	Using PPE at home	- 0.056	0.534	0.916
SGPT	MTH	0.002	0.002	0.462
	MTY	- 0.025	0.023	0.287
	MTF	- 0.0003	0.001	0.583
	Using PPE on the farm	0.038	1.086	0.972
	Using PPE in the yard	1.922	3.371	0.569
	Using PPE at home	- 0.076	1.006	0.940
ALP	MTH	0.010	0.007	0.163
	MTY	- 0.067	0.077	0.381
	MTF	- 0.003	0.002	0.173
	Using PPE on the farm	- 1.626	3.595	0.651
	Using PPE in the yard	- 0.013	11.157	0.999
	Using PPE at home	6.236	3.329	0.061
GGT	MTH	0.004	0.003	0.266
	MTY	- 0.035	0.035	0.312
	MTF	- 0.001	0.001	0.304
	Using PPE on the farm	0.167	1.626	0.918
	Using PPE in the yard	7.989	5.045	0.113
	Using PPE at home	1.243	1.505	0.409

MTH= the mean time of exposure at home, MTY= the mean time of exposure in the yard
 MTF= the mean time of exposure on the farm, SGPT: serum glutamic-pyruvic transaminase,
 SGOT: serum glutamic oxalacetic transaminase, GGT: Gamma Glutamyl Transpeptidase,
 ALP: Alkaline Phosphatase

Discussion

This study showed that more than half of the participants used insecticides at home for one year, but less than 0.5% used PPE during exposure. The findings related to the use of pesticides in the yard and on the agricultural land and the use of PPE during exposure indicated the unfavorable situation of using PPE when exposed to pesticides. The findings suggested that the mean of liver enzymes (urea-creatinine) in people exposed to pesticides or

insecticides in the farm, yard, or home were significantly higher than the unexposed people. Further analysis showed that the level of renal enzymes was lower in people who had used PPE during exposure, which was significant for use at home. Interventional animal studies have shown the effect of herbicides and pesticides on animal kidney tissue ^{6, 16}. Selmi et al. showed that pesticide exposure increased creatinine and urea levels in rats ⁶.

Some human studies also show the effect of pesticides on the kidneys. A study on farmers showed that long pesticide exposure had a significant relationship with chronic kidney diseases¹⁷. Some studies also showed that pesticides can be a precursor to chronic kidney disease^{18,19}. Martin et al. in their study found that pesticides may cause chronic kidney disease, but confirming this relationship requires more research²⁰. The results of a study indicated that exposure to pesticides in childhood increases the potential for kidney failure in future¹⁸. A Wan et al. also provided evidence of change in kidney function in individuals exposed to pesticides. They introduced organophosphorus pesticides as a potential cause of kidney damage²¹. Of course, some studies did not show a relationship between renal enzymes and pesticides. A prospective cohort study that considered the level, intensity, and type of pesticides, and duration of exposure did not address the relationship between pesticides and kidney failure¹⁷. In Manfo et al.'s study, none of the biochemical markers of kidney (urea, creatinine) in the farmers changed after pesticide exposure³.

Although the pathogenesis of kidney failure related to pesticides is still not fully understood, pesticides may lead to kidney damage through damage to tubular cells or changes in kidney blood flow²⁰. The findings of a study showed the presence of deformed lysosomes in the tubular cells in the kidney in people exposed to pesticides¹⁸. However Wan et al. believe that Kidney damage caused by pesticides and its pathological path depends on the class, type, and dose of pesticide²¹. Improper handling of pesticides, high toxicity of some pesticides, and lack of use or incorrect use of PPE cause damage to the kidney^{6, 22, 23}. Shearer et al. emphasize the importance of using PPE to reduce possible risks of pesticides²⁴. The findings of this study indicated the low use of PPE when exposed to pesticides and insecticides. Although PPE is not 100% effective against the toxic effects of pesticides, its use is necessary to minimize the risk of poisoning²⁰. Prado et al. believe that PPE does not have ergonomic conditions for farmers'

use, because PPE is designed for industrial use. Therefore farmer cannot use this equipment due to their working conditions (high heat and shortness of breath)²⁵. On the other hand, improper ergonomics of personal protective equipment, high heat, and increased sweating reduce body water, and as a result, dehydration damages the kidneys²⁶. Therefore, it seems necessary to design personal protective equipment suitable for the working conditions of farmers.

The findings of this study also showed that the mean of liver enzymes in subjects who had used insecticides at home was higher than the unexposed subjects. The findings also showed that SGOT, SGPT, and GGT enzymes were higher in individuals who did not use PPE during exposure. Also, the mean liver enzymes of people exposed to pesticides on agricultural land were higher compared to the unexposed people. Moreover, animal studies showed hepatotoxicity in laboratory animals after pesticide exposure^{27, 28}. A study on animals showed that tissue changes in liver cells may lead to severe liver dysfunction and cell death²⁹. According to Jellali et al.'s study, damage to liver depends on the pesticide dose. Liver steatosis, inflammation, and cell death of the liver are common damages caused by exposure to high pesticide doses. They also showed that mixing several pesticides increases its destructive effects³⁰.

The results of some studies were in line with liver changes after exposure to pests^{2, 31}. Li et al.'s study showed that exposure to organophosphate pesticides may be related to liver function biomarkers and liver damage; their findings showed the toxic effect of pesticide exposure on the human liver³². Karami et al. also reported that organophosphorus pesticides had significant and harmful effects on liver; they recommended that people with long-term exposure to pesticides or insecticides due to their jobs should have a regular evaluation for liver's health³³. Some researchers interpreted the results of their studies with caution. Lozano et al. believed that exposure to pesticides caused little damage to the liver and could not be the cause of severe liver dysfunction³⁴. In some

studies, some liver biochemical indicators had a significant correlation with pesticides. Award et al. showed that ALT, AST, and ALP enzymes were partially affected by pesticides. In addition, with increase in pesticide dose, the level of these enzymes in the serum increased significantly³⁵. ALT in Manfo et al.'s study³, AST in Lozano et al.'s study³⁴, and GGT in Sang et al.'s study³⁶ had a statistically significant relationship with liver diseases.

Although the path of the effect of pesticides on liver is not yet fully known, it is clear that pesticides accelerate the transformation of steatosis into liver inflammation or fibrosis³⁷. Damage to the liver caused by pesticides can also occur through disruption of liver metabolism, tissue damage, apoptosis, genetic damage, or cell toxicity³³. A study on the effect occupational exposure to pesticides on liver cancer showed increased DNA damage and telomere shortening regarding the people exposed to pesticides. Moreover, there was a high level of tumor biomarkers among the subjects exposed to pesticides²⁶. Therefore, farmers must become sensitive and aware of the toxicity of pesticides, liver disorders caused by pesticide exposure, and the importance of using PPE. Farmers should follow label instructions and guidelines for pesticide application, ensuring that the right amount of pesticide is used at the appropriate time during the crop's growth. Furthermore, teaching people about washing fruits and vegetables thoroughly before consumption can help remove most of the surface residues. Encouraging consumers to buy and eat products labeled as "organic" or "pesticide-free" can help drive the market towards more sustainable agricultural practices.

One of the limitations of the present study was that the type and dose of pesticides were not known in SHCS data. Moreover, SHCS data were collected by self-report, which may cause information bias. This was done because there was a possibility that people did not remember their past information. Another limitation of the current study was that it was cross-sectional. Therefore, it was not possible to definitively determine the

causal relationship based on it.

Conclusion

In summary, the study found that individuals exposed to pesticides, whether in agricultural land, yards, or homes, had higher levels of liver and renal enzymes compared to those who were not exposed to such chemical materials. Additionally, using PPE led to lower mean levels of these enzymes. This suggests that exposure to pesticides may impact liver and kidney functions, and taking precautions like using PPE can help minimize potential health risks. Considering that pesticide exposure is a modifiable risk factor, it is reasonable to sensitize at-risk individuals (such as farmers and greenhouse workers), and screen their body and monitor their health periodically. Considering that the use of PPE during exposure to pesticides in the present study was low, it is necessary to inform people, especially those who work with pesticides, about the benefits of using PPE. It is also better to encourage farmers to produce organic products to minimize the need to use pesticides. In conclusion, while there pesticides are still used in agricultural products, regulatory measures, and responsible farming practices can help keep these residues within safe limits. Consumers can also play a role by supporting sustainable agriculture and following proper food handling practices.

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Conflict of Interest

The authors declared no conflict of interest.

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Ethical Considerations

The authors obtained permission from the Ethics Committee of Shahid Sadoughi University of Medical Sciences.

Code of Ethics

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Authors' contributions

Mahdieh Momayyezi was responsible for conceptualization, investigation, methodology, project administration and writing of the original draft. Kosar Zardosht and Reyhane Sefidkar were responsible for investigation, methodology, software, review, and revision of the manuscript. Hossein Falahzadeh, Mohammad Momayyezi, and Ali Asghar Ebrahimi were responsible for conceptualization, methodology, review, and revision of the manuscript.

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References

- Sharma R, Goyal A. Agro pesticides and andrology. *Int J Pharm Pharm Sci.* 2014; 6(10): 12-9.
- Jamal F, Haque S, Singh S, et al. The influence of pesticides on hepatic and renal functions in occupational sprayers of rural Malihabad, Lucknow (India). *Toxicol open access.* 2015;1(01): 2.
- Manfo FPT, Mboe SA, Nantia EA, et al. Evaluation of the effects of agro pesticides use on liver and kidney function in farmers from Buea, Cameroon. *Journal of toxicology.* 2020;2020:1-10.
- Li B, Ma Y, Zhang YH. Oxidative stress and hepatotoxicity in the frog, *Rana chensinensis*, when exposed to low doses of trichlorfon. *Journal of Environmental Science and Health, Part B.* 2017; 52(7): 476-82.
- Mahugija JA, Chibura PE, Lugwisha EH. Residues of pesticides and metabolites in chicken kidney, liver and muscle samples from poultry farms in Dar es Salaam and Pwani, Tanzania. *Chemosphere.* 2018; 193: 869-74.
- Selmi S, Rtibi K, Grami D, et al. Malathion, an organophosphate insecticide, provokes metabolic, histopathologic and molecular disorders in liver and kidney in prepubertal male mice. *Toxicology reports.* 2018; 5: 189-95.
- Ismail AA, Henny O, Abdel Rasoul G, et al. Acute and cumulative effects of repeated exposure to chlorpyrifos on the liver and kidney function among Egyptian adolescents. *Toxics.* 2021; 9(6): 137.
- Authority EFS, Medina-Pastor P, Triacchini G. The 2018 European Union report on pesticide residues in food. *EFSA J.* 2020; 18(4): e06057.
- Upadhyay J, Rana M, Juyal V, et al. Impact of pesticide exposure and associated health effects. *Pesticides in crop production: physiological and biochemical action.* 2020: 69-88.
- Miller MA, Zachary JF. Mechanisms and morphology of cellular injury, adaptation, and death. *Pathologic basis of veterinary disease.* 2017: 2.
- Kupferman J, Ramírez-Rubio O, Amador JJ, et al. Acute kidney injury in sugarcane workers at risk for Mesoamerican nephropathy. *American Journal of Kidney Diseases.* 2018; 72(4): 475-82.
- Cano R, Pérez JL, Dávila LA, et al. Role of endocrine-disrupting chemicals in the pathogenesis of non-alcoholic fatty liver disease: a comprehensive review. *Int J Mol Sci.* 2021; 22(9): 4807.
- Cavalier H, Trasande L, Porta M. Exposures to pesticides and risk of cancer: evaluation of recent epidemiological evidence in humans and paths forward. *International Journal of Cancer.* 2023; 152(5): 879-912.
- Poustchi H, Eghtesad S, Kamangar F, et al. Prospective epidemiological research studies in Iran (the PERSIAN Cohort Study): rationale, objectives, and design. *Am J Epidemiol.* 2018; 187(4): 647-55.
- Momayyezi M, Fallahzadeh H, Fakhravari L, et al. The association between sleep pattern with lipid profile and obesity among adults in Yazd: Cross-Sectional analysis of Shahedieh Cohort Study. *Journal of Nutrition and Food Security.* 2022; 7(3): 331-9.
- Tanvir E, Afroz R, Chowdhury M, et al. A model of chlorpyrifos distribution and its

- biochemical effects on the liver and kidneys of rats. *Human & Experimental Toxicology*. 2016; 35(9): 991-1004.
17. Lebov JF, Engel LS, Richardson D, et al. Pesticide use and risk of end-stage renal disease among licensed pesticide applicators in the agricultural health study. *Occupational and environmental medicine*. 2016;73(1):3-12.
 18. Vervaeke BA, Nast CC, Jayasumana C, et al. Chronic interstitial nephritis in agricultural communities is a toxin-induced proximal tubular nephropathy. *Kidney international*. 2020; 97(2): 350-69.
 19. Jacobson MH, Wu Y, Liu M, et al. Organophosphate pesticides and progression of chronic kidney disease among children: a prospective cohort study. *Environment international*. 2021; 155: 106597.
 20. Martins GKdM, Pereira NC, Cunha NVd, et al. Exposure of patients with chronic kidney disease on dialysis to pesticides. *J Bras Nefrol*. 2022;45:169-79.
 21. Wan ET, Darssan D, Karatela S, et al. Association of pesticides and kidney function among adults in the US population 2001–2010. *Int J Environ Res Public Health*. 2021; 18(19): 10249.
 22. Wesseling C, Aragón A, González M, et al. Heat stress, hydration and uric acid: a cross-sectional study in workers of three occupations in a hotspot of Mesoamerican nephropathy in Nicaragua. *BMJ Open*. 2016; 6(12): e011034.
 23. Badr AM. Organophosphate toxicity: updates of malathion potential toxic effects in mammals and potential treatments. *Environmental Science and Pollution Research*. 2020; 27(21): 26036-57.
 24. Shearer JJ, Sandler DP, Andreotti G, et al. Pesticide use and kidney function among farmers in the biomarkers of exposure and effect in agriculture study. *Environmental research*. 2021; 199: 111276.
 25. Prado JAF, Sieglach AE, Silva B, et al. Exposição de trabalhadores rurais aos agrotóxicos. *Gaia Scien*. 2021; 15(1): 141-57.
 26. Saad-Hussein A, Beshir S, Taha MM, et al. Early prediction of liver carcinogenicity due to occupational exposure to pesticides. *Mutat Res Genet Toxicol Environ Mutagen*. 2019; 838: 46-53.
 27. Chapman E, Haby MM, Illanes E, et al. Risk factors for chronic kidney disease of non-traditional causes: a systematic review. *Rev Panam Salud Publica*. 2019; 43.
 28. Abdou HM, Hussien HM, Yousef MI. Deleterious effects of cypermethrin on rat liver and kidney: protective role of sesame oil. *Journal of Environmental Science and Health, Part B*. 2012; 47(4): 306-14.
 29. Rasgele P, Oktay M, Kekecoglu M, et al. The histopathological investigation of liver in experimental animals after short-term exposures to pesticides. *Bulgarian Journal of Agricultural Science*. 2015; 21(2): 446-53.
 30. Jellali R, Jacques S, Essaouiba A, et al. Investigation of steatosis profiles induced by pesticides using liver organ-on-chip model and omics analysis. *Food and Chemical Toxicology*. 2021; 152: 112155.
 31. Nahhal YE. Biochemical changes associated with long term exposure to pesticide among farmers in the Gaza Strip. *Occupational Diseases and Environmental Medicine*. 2016; 4(03): 72-82.
 32. Li W, Xiao H, Wu H, et al. Organophosphate pesticide exposure and biomarkers of liver injury/liver function. *Liver International*. 2022; 42(12): 2713-23.
 33. Karami-Mohajeri S, Ahmadipour A, Rahimi H-R, et al. Adverse effects of organophosphorus pesticides on the liver: a brief summary of four decades of research. *Arh Hig Rada Toksikol*. 2017; 68(4): 261-75.
 34. Lozano-Paniagua D, Parrón T, Alarcón R, et al. Evaluation of conventional and non-conventional biomarkers of liver toxicity in greenhouse workers occupationally exposed to pesticides. *Food and Chemical Toxicology*. 2021; 151: 112127.
 35. Awad O, El-Fiki S, Abou-Shanab R, et al. Influence of exposure to pesticides on liver enzymes and cholinesterase levels in male agriculture workers. *Global Nest Journal*. 2014; 16(5): 1006-15.

36. Sang H, Lee KN, Jung CH, et al.. Association between organochlorine pesticides and nonalcoholic fatty liver disease in the national health and nutrition examination survey 2003–2004. *Scientific Reports*. 2022; 12(1): 11590.
37. Laothong U. Pesticides and non-alcoholic fatty liver disease. *Thai Journal of Toxicology*. 2016; 31(2): 97-107.