



# 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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## ARTICLE INFO

### ORIGINAL ARTICLE

#### Article History:

Received: 18 February 2024

Accepted: 20 April 2024

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#### Keywords:

Pesticide,

Exposure,

Kidney,

Liver,

Shahedieh Cohort Study.

## 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.

**Citation:** Zardosht K, Momayyezi M, Sefidkar R, et al. *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.* J Environ Health Sustain Dev. 2024; 9(2): 2270-2281.

## 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. <sup>1</sup>. The most widely used

pesticides in agriculture are organic poisons (organochlorine, organophosphate) and mineral poisons<sup>2</sup>. Pesticides help farmers produce more quality fruits and vegetables; as a result, it is also effective in the economic growth of countries<sup>3</sup>. 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 humans<sup>2</sup>. Some effects of pesticides have been proven on laboratory animals<sup>4-6</sup>. 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 skin<sup>2</sup>. Pesticides with smaller droplets enter the lungs through inhalation<sup>2</sup>. Some pesticides also enter body through swallowing and hands contaminated with soil or water<sup>7</sup>. Then, the pesticide enters the circulatory system, and can affect different organs in the body<sup>2</sup>. 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 MRL<sup>8</sup>. 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 exposure<sup>9</sup>. Liver is a vital organ responsible for numerous functions, including detoxification, metabolism, and protein synthesis. Liver and kidneys are the target organs exposed to pesticides<sup>7</sup>. These two organs are known as the main organs in body detoxification and may be exposed to the damage of pesticides<sup>1, 3</sup>. Long-term exposure to pesticides may lead to the accumulation of toxins in liver and kidneys. These toxins cause changes in liver and kidney cells<sup>7</sup>, which lead to the release of some enzymes in blood<sup>10</sup>. 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 person<sup>2</sup>. 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 liver<sup>7</sup>. 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 kidneys<sup>11</sup>. 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 failure<sup>12</sup>. Long-term exposure to certain pesticides has been linked to an increased risk of cancer<sup>13</sup>.

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 common<sup>3</sup>. 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 study<sup>14</sup>, 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 methods<sup>14</sup>. 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)<sup>15</sup>. 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  $45.67 \pm 8.7$  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<br>(n = 2895, 51.4%) | Female<br>(n = 2742, 48.6%) | Yes<br>(n = 1186, 21%) | No<br>(n = 4451, 79%) |
| <b>SGOT</b>       | 21.19 ± 8.3               | 17.27 ± 8.5                 | 19.85 ± 8.1            | 19.14 ± 8.8           |
| P-value*          | 0.001                     |                             | 0.01                   |                       |
| <b>SGPT</b>       | 27.68 ± 1.7               | 17.89 ± 1.4                 | 24.33 ± 5.5            | 22.54 ± 7.3           |
| P-value*          | 0.001                     |                             | 0.001                  |                       |
| <b>ALP</b>        | 187.83 ± 52.5             | 175.92 ± 52.7               | 30.7 ± 3.5             | 25.94 ± 2.2           |
| P-value *         | 0.001                     |                             | 0.001                  |                       |
| <b>GGT</b>        | 31.86 ± 2.8               | 21.78 ± 1.8                 | 192.13 ± 54.4          | 179 ± 52.2            |
| P-value *         | 0.001                     |                             | 0.001                  |                       |
| <b>Urea</b>       | 29.9 ± 7.1                | 24.44 ± 6.3                 | 29.28 ± 7.1            | 26.71 ± 7.2           |
| P-value *         | 0.001                     |                             | 0.001                  |                       |
| <b>Ceratinine</b> | 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 <sup>6, 16</sup>. Selmi et al. showed that pesticide exposure increased creatinine and urea levels in rats <sup>6</sup>.

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 diseases<sup>17</sup>. Some studies also showed that pesticides can be a precursor to chronic kidney disease<sup>18,19</sup>. Martin et al. in their study found that pesticides may cause chronic kidney disease, but confirming this relationship requires more research<sup>20</sup>. The results of a study indicated that exposure to pesticides in childhood increases the potential for kidney failure in future<sup>18</sup>. 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 damage<sup>21</sup>. 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 failure<sup>17</sup>. In Manfo et al.'s study, none of the biochemical markers of kidney (urea, creatinine) in the farmers changed after pesticide exposure<sup>3</sup>.

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 flow<sup>20</sup>. The findings of a study showed the presence of deformed lysosomes in the tubular cells in the kidney in people exposed to pesticides<sup>18</sup>. However Wan et al. believe that Kidney damage caused by pesticides and its pathological path depends on the class, type, and dose of pesticide<sup>21</sup>. Improper handling of pesticides, high toxicity of some pesticides, and lack of use or incorrect use of PPE cause damage to the kidney<sup>6, 22, 23</sup>. Shearer et al. emphasize the importance of using PPE to reduce possible risks of pesticides<sup>24</sup>. 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 poisoning<sup>20</sup>. 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)<sup>25</sup>. 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 kidneys<sup>26</sup>. 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<sup>27, 28</sup>. A study on animals showed that tissue changes in liver cells may lead to severe liver dysfunction and cell death<sup>29</sup>. 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 effects<sup>30</sup>.

The results of some studies were in line with liver changes after exposure to pests<sup>2, 31</sup>. 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 liver<sup>32</sup>. 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 health<sup>33</sup>. 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 dysfunction<sup>34</sup>. 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 significantly<sup>35</sup>. ALT in Manfo et al.'s study<sup>3</sup>, AST in Lozano et al.'s study<sup>34</sup>, and GGT in Sang et al.'s study<sup>36</sup> 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 fibrosis<sup>37</sup>. Damage to the liver caused by pesticides can also occur through disruption of liver metabolism, tissue damage, apoptosis, genetic damage, or cell toxicity<sup>33</sup>. 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 pesticides<sup>26</sup>. 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.

## Acknowledgments

The researchers would like to thank Shahid Sadoughi University of Medical Sciences for financial support.

## Conflict of Interest

The authors declared no conflict of interest.

## Funding

Shahid Sadoughi University of Medical Sciences funded the project (the project No: 13028).

## Ethical Considerations

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

### Code of Ethics

Code no. IR.SSU.SPH.REC.1401.046.

### 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 Mommayyezi, and Ali Asghar Ebrahimi were responsible for conceptualization, methodology, review, and revision of the manuscript.

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