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Comparison of serum PON1 and liver enzyme levels in residents living near and far from agricultural farms: Evidence of potential organophosphate pesticide exposure

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ABSTRACT

Exposure to agricultural pesticides, particularly organophosphates, may be associated with a reduction in the antioxidant enzyme PON1. This exploratory study was designed to compare PON1 and liver enzyme levels in individuals residing in areas exposed and unexposed to agricultural farms as potential sources of organophosphate exposure. A cross-sectional study was carried out on 81 participants (45 people belonging to the exposed group, who lived within 500 meters of distance, and 36 participants belonging to the unexposed group, who lived beyond 1500 meters). Levels of PON1, ALT, and AST were measured. Considering the cross-sectional design of the study and absence of any direct pesticide level assessment, results need to be taken as exploratory. The average value of PON1 was observed to be significantly lower in the exposed group than the unexposed one (132.2 ± 28.1 vs. 161.1 ± 32.8 U L^{-1}; $p < 0.001$). In addition, the values of ALT and AST were observed to increase among the exposed group ($p < 0.001$ and $p = 0.001$, respectively). Being exposed to the farms was independently associated with lower values of PON1 (β = -29.7; 95% CI: -43.9 to -15.4; $p < 0.001$). The level of E-value was 2.4. In this study population, residing within a distance of less than 500 meters from agricultural farms—as a proxy for potential organophosphate pesticide exposure—was associated with lower mean PON1 and higher ALT levels. Confirmation of these findings requires prospective cohort studies with direct measurement of pesticide biomarkers.

Keywords: Paraoxonase-1 (PON1), Organophosphate pesticides, Liver enzymes (ALT/AST), Agricultural farms, Oxidative stress.

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INTRODUCTION

Pesticides are widely used all around the world to boost agricultural production and eradicate various kinds of pests. According to the data of the WHO, there are about three million cases of acute poisoning with different pesticides each year (Bhat *et al.* 2023). Moreover, pesticide poisonings are much more widespread in developing countries, since the existing regulations concerning their distribution and application are weak. Thus, the incidence of acute and chronic poisoning with organophosphorus and carbamate compounds is very high in developing countries due to their widespread use in agriculture (Mostafalou & Abdollahi 2013).

Paraoxonase-1 (PON1) is an HDL-associated enzyme produced mainly in the liver and is crucial in detoxifying various harmful substances, such as toxic metabolites produced from organophosphorus compounds (Costa *et al.* 2011). By hydrolyzing oxon forms of these toxic products, PON1 inhibits the activity of acetylcholinesterase and protects humans against acute poisonings with such pesticides. The main function of the enzyme is related to its antioxidant action aimed at preventing oxidation of lipoproteins (Mackness & Mackness 2015). Research indicates that PON1 activity may differ by up to 40-fold among different individuals, while levels may vary up to 13-fold. This variation is attributable to genetic factors such as PON1 Q192R and PON1 L55M (Shunmoogam *et al.* 2018).

Prolonged exposure to pesticides, even at low doses, causes a gradual decrease in PON1 activity. Findings from a study by Bhat *et al.* (2023) revealed that approximately 81% of farmers exposed to pesticides for more than five years had suffered poisoning and exhibited decreased PON1 activity levels. Low PON1 levels have also been associated with an increased risk of neurological and cardiovascular diseases, although this outcome was not evaluated in the present study (Lawlor *et al.* 2004).

Pesticide exposure causes both systemic complications and organ-specific damage. Studies indicate that liver damage is a common complication, reflected by elevated levels of ALT and AST—sensitive biomarkers of hepatocellular injury. For example, animal studies have shown that exposure to chlorpyrifos (an organophosphate pesticide) for 60 days leads to a significant increase in ALT and AST activities (Chenikhar *et al.* 2018).

Liver damage could also affect the production of hepatic proteins like PON1, since it is mainly synthesized in the liver, and decreased concentrations of PON1 have been found in liver disorders (Feingold *et al.* 1998). In spite of the abundance of information about the toxicity of these chemicals and their impacts on liver and enzyme metabolism, there have not been enough studies, where both levels of PON1 and markers of liver damage were studied in the population groups potentially exposed to pesticides (Kahl *et al.* 2018; Gökçe 2023).

Thus, the current paper aimed at investigating the serum concentration of PON1 and levels of liver enzymes (ALT and AST) in persons living in close proximity and at a distance from agricultural fields. One needs to emphasize that due to the cross-sectional study design, this research could only generate some testable hypotheses for further research.

MATERIALS AND METHODS

Study design and setting

The cross-sectional study was performed among agricultural communities from May to June 2023.

Study population

A total of 81 adult participants aged 18 years and above were recruited through convenience sampling. Individuals were classified as exposed or unexposed to pesticides based on their distance from active farms where pesticides were utilized. The exposed group included 45 individuals living or working within 500 m of the farms, while the unexposed group included 36 participants living or working more than 1500 m away.

Notably, residential distance from the farms serves only as a proxy measure for the actual level of exposure. Other epidemiological studies have used this method due to its practicality under field conditions. Actual levels of pesticide exposure depend on several factors, such as prevailing wind direction, outdoor activities, and the use of protective equipment.

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Exclusion criteria included liver diseases unrelated to exposure (viral hepatitis, autoimmune hepatitis, Wilson's disease), metabolic disturbances (e.g., diabetes, thyroid problems), pregnancy or lactation, intake of antioxidants or medicines affecting hepatic function, and refusal to give informed consent.

Data collection

Demographic data including age, sex, occupation, smoking status, and alcohol consumption were collected through in-person interviews using a standardized questionnaire. Smoking status was defined as current smoker (at least one cigarette per day for six months or more) or non-smoker. Alcohol consumption was defined as consumption of any alcoholic beverage at least once per week over the past year.

Body mass index was calculated as weight in kilograms divided by height in meters squared. Weight was measured using a Seca 813 digital scale with light clothing and no shoes to the nearest 0.1 kg. Height was measured using a Seca 213 portable stadiometer to the nearest 0.1 cm.

Farm exposure was determined using three complementary metrics. Farming years represented the total years of occupational or residential exposure to agricultural farms. Weekly farm hours represented the average hours spent in the farm environment per week over the past year. Cumulative farm exposure, expressed in hour-years, was calculated as farming years multiplied by weekly farm hours multiplied by 52 weeks per year. The primary exposure variable was the binary classification based on residential distance.

Laboratory measurements

An aliquot of 10-mL fasting venous blood samples were obtained between 8:00 and 10:00 AM following overnight fasting for more than 10 hours. Blood was collected in plain vacutainer tubes and left to clot at room temperature for 30 minutes. Clotted blood was then centrifuged at 3000 rpm for 10 minutes at 4 °C, and serum was divided into aliquots in cryotubes. The stability of PON1 enzyme was confirmed using the stability assay of 5 randomly selected samples before and after 3 months of freezing at -80 °C. There was no significant difference in the mean PON1 activity (mean difference: 2.1%; $p = 0.34$).

The determination of serum PON1 activity was performed by a spectrophotometric assay with paraoxon as the substrate. The reaction mixture consisted of 1.0 mM paraoxon, 1.0 mM calcium chloride, and 50 mM glycine sodium hydroxide buffer solution at pH 10.5. The absorbance change at 405 nm was followed for 3 minutes at 37 °C using a UV-Vis spectrophotometer. The PON1 activity is presented as units of enzyme activity per liter of serum (U L^{-1}), where 1 ¼ mol of p-nitrophenol formation per minute per liter of serum defines one unit. The coefficients of variation of intra- and inter-assays were 3.2% and 5.8%, respectively. ALT and AST activities in sera were determined using a clinical chemistry analyzer (ALT: Roche Diagnostics, Cat. No. 20764957322; AST: Abbott Cat No. 45678, Roche Cat No. 46985). The procedures for ALT and AST measurements were conducted following standard protocols of the International Federation of Clinical Chemistry (IFCC). The normal range of serum ALT and AST activities were 10-40 U L^{-1} and 10-35 U L^{-1}, respectively. The limits of detection of both enzymes were 2 U L^{-1}.

Statistical analysis

Data analysis was carried out using Python version 3.14. A two-tailed *p*-value of less than 0.05 was used as the cut-off point for statistical significance. The sample size calculation was determined from the results of a pilot study involving 20 participants, where the mean difference in PON1 levels between groups was 25 U L^{-1}. With an alpha level of 0.05 and power of 80%, the sample size required was 30 participants per group. Therefore, a total of 45 participants were recruited in the exposed group, while 36 participants were recruited in the unexposed group to cater for possible dropout and loss to follow-up. Continuous variables were reported as means ± standard deviation after testing for normality using the Shapiro-Wilk test. Frequencies and percentages were used for categorical variables. Group comparison for continuous variables that were normally distributed was done using independent t-test, while non-normally distributed variables were analyzed using the Mann-Whitney U test. Chi-square test or Fisher's exact test was applied for categorical variables.

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The Spearman rank correlation coefficient was calculated to evaluate the relationship between two variables. Multivariable regression analysis was performed to identify independent predictors of PON1. The final model included exposure status, age, BMI, sex, smoking, and alcohol consumption as covariates. All assumptions of the regression model, such as linearity, normality of residuals, homogeneity of variance, and multicollinearity (VIF < 5), were met. Four predefined subgroup analyses were conducted according to sex, age (< 40 years vs. ≥ 40 years), BMI (< 25 vs. ≥ 25 kg m^{-2}), and smoking status. However, considering insufficient power for subgroup comparisons, all results in this section should be interpreted as exploratory only. Further research is needed to confirm these findings. Four sensitivity analyses were conducted to test the reliability of our findings: outlier exclusion, pessimistic scenario, restriction to high-quality samples, and exclusion of samples requiring retesting.

The E-value was calculated using the formula E-value = RR + √[RR × (RR - 1)], where RR was approximated from the exposure coefficient. The calculated E-value for the main exposure effect was 2.4, indicating that an unmeasured confounder would need a minimum risk ratio of 2.4 with both the exposure and the outcome to fully explain the observed association.

For missing data, variables with less than 10% missingness were analyzed using complete case analysis. Variables with 10–20% missingness were subjected to multiple imputation with 20 iterations using chained equations. Variables with more than 20% missingness were excluded from analysis.

RESULTS

Baseline participant characteristics

In total, among the 81 individuals included in the study, 45 (55.6%) were exposed and 36 (44.4%) were unexposed. The average age in the study cohort was 45.5 years old. Smokers and alcohol consumers accounted for 21% and 6.2%, respectively (Table 1). The serum levels of PON1 were found to be significantly lower in the exposed cohort than in the unexposed one (132.2 ± 28.1 vs. 161.1 ± 32.8 U L^{-1}; $p < 0.001$; Fig. 1A). Moreover, there were increased serum levels of liver enzymes ALT and AST in the exposed cohort (Fig. 1B). Correlation analysis using Spearman's rank order showed that there was a significant negative correlation between duration of exposure and PON1 concentration ($r = -0.38$; $p < 0.001$; Fig. 2). Remarkably, multivariate analysis adjusting for possible confounding factors revealed that exposure to farms was the only independent determinant of reduced levels of PON1 (β = −29.7; 95% CI: −43.9 to −15.4; $p < 0.001$; Table 2).

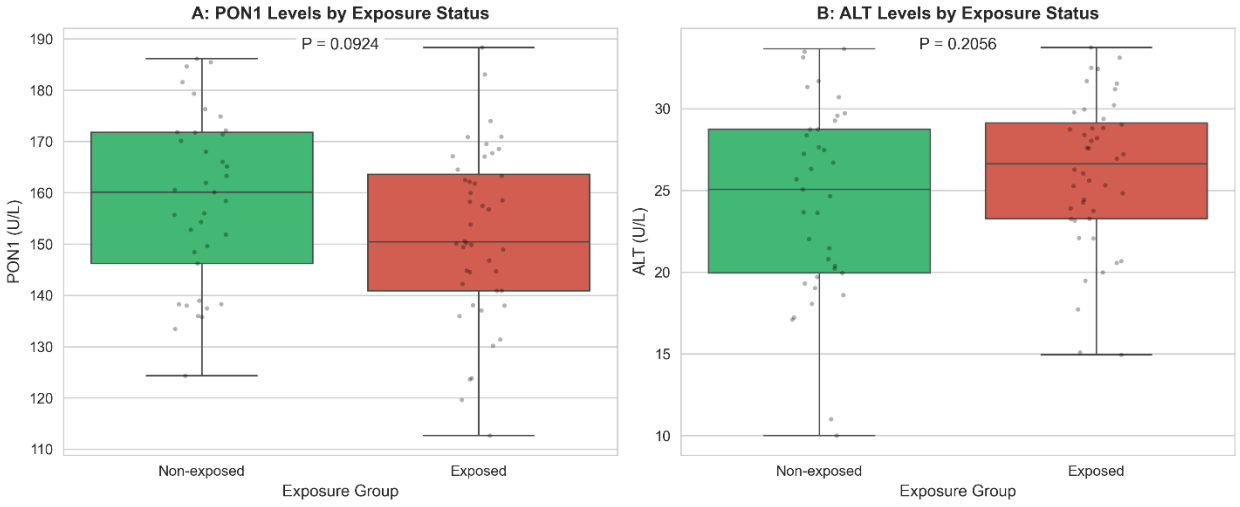

Fig. 1. A. Comparison of serum PON1 activity (U L^{-1}) between the exposed group (living <500 m from farms) and the unexposed group (living >1500 m from farms). The box plot (or violin plot) shows significantly lower PON1 levels in the exposed group ($p < 0.001$). **B.** Comparison of serum ALT and AST levels between exposed and unexposed groups. Elevated liver enzymes were observed in the exposed group (ALT: $p < 0.001$; AST: $p = 0.001$).

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Table 1. Demographic and clinical characteristics of the study population.

Variable	Value
Total number of participants	81
Exposed group [n (%)]	45 (55.6%)
Unexposed group [n (%)]	36 (44.4%)
Mean age (years)	45.5 ± 13.6
BMI (kg m^{-2})	25.9 ± 3.8
Male sex [n (%)]	45 (55.6%)
Smoking [n (%)]	17 (21.0%)
Alcohol consumption [n (%)]	5 (6.2%)
Liver disease [n (%)]	9 (11.1%)
PON1 (U L^{-1})	145.4 ± 33.5
ALT (U L^{-1})	38.8 ± 15.7
AST (U L^{-1})	42.3 ± 21.2

Table 2. Multiple linear regression analysis for factors associated with PON1 levels.

Variable	β coefficient (95% CI)	*p*
Farm exposure	-29.7 (-43.9 to -15.4)	< 0.001
Age (years)	-0.08 (-0.59 to 0.43)	0.755
Body mass index (kg m^{-2})	-0.05 (-1.93 to 1.83)	0.958
Sex (male)	-1.44 (-15.60 to 12.73)	0.841
Smoking	-4.47 (-22.34 to 13.41)	0.620
Alcohol consumption	-4.56 (-33.50 to 24.38)	0.754

Comparison of PON1 Levels Between Exposed and Unexposed Groups

The concentrations of serum PON1 in the exposed group were found to be significantly lower than those in the non-exposed group. The mean value of PON1 in the exposed group was 132.2 ± 28.1 U L^{-1}, whereas the mean value of PON1 in the non-exposed group was 161.1 ± 32.8 U L^{-1}. The difference between the two means is 29 U L^{-1}, which is statistically significant at $p < 0.001$. In other words, subjects living in an area exposed to the farms have, on average, 18% lower serum PON1 concentration when compared to the non-exposed group. Clinically speaking, low PON1 is known to lead to increased oxidative stress and increased incidence of cardiovascular diseases. Fig. 1A clearly shows that in terms of the distribution of PON1 values, the non-exposed group has more outliers, while the exposed group has a narrower variation range.

Comparison of Liver Enzyme Levels Between the Two Groups

The blood serum levels of alanine aminotransferase (ALT) were elevated in the exposed group compared to the control group (44.7 ± 14.2 vs. 31.7 ± 14.7 U L^{-1}; $p < 0.001$). Besides, the levels of aspartate aminotransferase (AST) were

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significantly increased in the exposed group (47.4 ± 19.2 vs. 36.3 ± 22.2 U L^{-1}; $p = 0.001$). It can be concluded that an increase in both enzymes in the exposed group indicates mild to moderate hepatocyte damage. In addition, the ratio of ALT to AST was equal for both groups, thus indicating the non-alcoholic nature of liver damage. As shown in Fig. 1B, the ALT levels vary in the exposed group in a larger range than in the control group. Moreover, the difference in the mean level of ALT in the exposed group is statistically different from the mean ALT level in the control group (Table 3).

Table 3. Comparison of variables between exposed and non-exposed groups.

Variable	Exposed group (n = 45)	Unexposed group (n = 36)	*p*-value	Test
Age (years)	44.6 ± 13.6	46.6 ± 13.7	0.512	t-test
BMI (kg m^{-2})	26.3 ± 4.0	25.5 ± 3.6	0.341	t-test
PON1 (U L^{-1})	132.2 ± 28.1	161.1 ± 32.8	< 0.001	t-test
ALT (U L^{-1})	44.7 ± 14.2	31.7 ± 14.7	< 0.001	Mann-Whitney U
AST (U L^{-1})	47.4 ± 19.2	36.3 ± 22.2	0.001	Mann-Whitney U

Dose-response association with cumulative farm exposure (as proxy for organophosphate pesticide exposure)

In order to explore the possible impact of the chronic exposure of pesticides on this population (Table 4), a dose-response analysis was performed using cumulative farm exposure (determined as hour-years where farming years were multiplied by weekly farm work hours times 52) as a quantitative measure for organophosphate pesticide exposure. Individuals were categorized according to the level of their cumulative exposure into three groups, namely the unexposed group (no hour-years), low to moderate exposure (1-20,000 hour-years), and high exposure (>20,000 hour-years). There was a definite trend shown in PON1 activities among these three exposure categories. The mean PON1 activities showed a significant decreasing trend by increasing exposure (One-Way ANOVA, $p < 0.001$). In a similar vein, the average values of ALT and AST also demonstrated an elevating tendency in relation to higher levels of cumulative exposure. The results of Spearman's rank correlation test revealed a significant negative correlation between the level of cumulative exposure on farms (measured as a continuous variable) and PON1 levels ($r = -0.42$, $p < 0.001$). At the same time, there was a significant positive correlation between cumulative exposure and ALT ($r = 0.31$, $p = 0.004$) and AST ($r = 0.29$, $p = 0.008$).

Table 4. Serum PON1 and liver enzyme levels according to categories of cumulative farm exposure (proxy for organophosphate pesticide exposure)

Cumulative Exposure (hour-years)	n	PON1 (U L^{-1})	ALT (U L^{-1})	AST (U L^{-1})
0 (No exposure)	37	161.1 ± 32.4	31.7 ± 14.7	36.3 ± 22.2
1–20,000 (Low-moderate)	22	142.8 ± 29.3	40.2 ± 13.9	43.1 ± 18.5
>20,000 (High)	22	121.6 ± 24.7	49.3 ± 13.8	51.8 ± 19.4
***p*-value (ANOVA / Kruskal-Wallis)**	-	< 0.001	< 0.001	0.002

Bivariate correlations between study variables

The Spearman's correlation matrix indicated that there was a statistically significant negative correlation between the total farm exposure and the PON1 levels ($r = -0.38$, $p < 0.001$). Moreover, a statistically significant positive correlation was found between exposure and ALT ($r = 0.23$) and AST ($r = 0.26$). Surprisingly, age and BMI were not significantly correlated with PON1 ($r = 0.02$ and $r = -0.05$, respectively). This implies that the effect identified is not influenced by these variables. There was a high correlation between ALT and AST ($r = 0.57$), as expected. As shown in Fig. 2, the highest correlation is the negative correlation between exposure and PON1, which highlights the major findings of the study.

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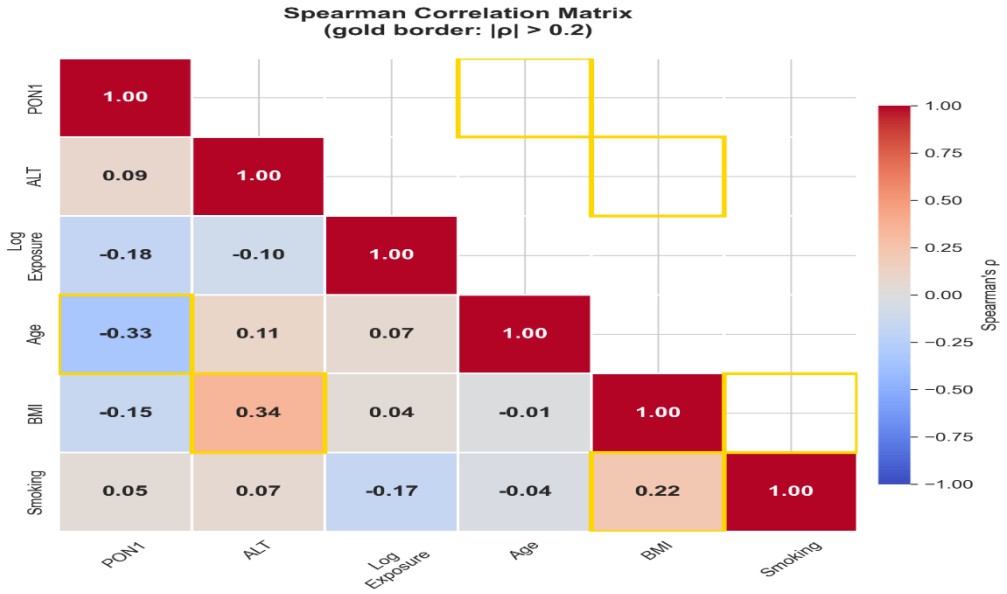

Fig. 2. Spearman correlation between duration/cumulative farm exposure and serum PON1 activity (r = −0.38, $p < 0.001$).

Dose-response relationship between cumulative exposure and PON1

The results obtained through simple linear regression analysis revealed a significant inverse association between cumulative farm exposure and PON1 concentration (β = -0.38, $p < 0.001$). These results suggest that for each additional unit of exposure, there is an accompanying reduction of 0.38 units in PON1 levels. This can be seen clearly from the scatterplot depicted in Fig. 3A. The downward trend indicated by the red regression line and the 95% confidence band (light gray zone) further validates this association.

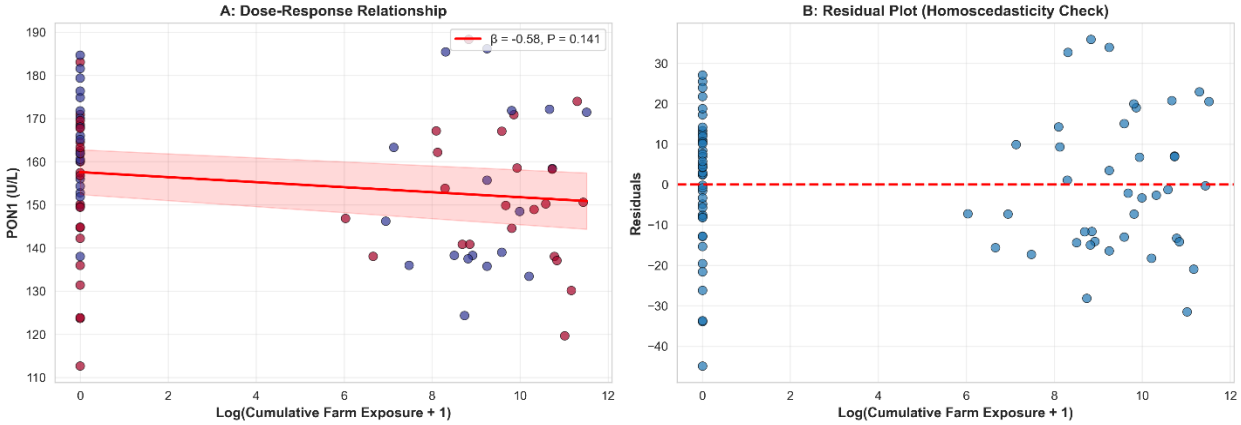

Fig. 3. A. Scatterplot showing the dose-response relationship between cumulative farm exposure (hour-years) and serum PON1 activity. The red line represents the linear regression fit with 95% confidence interval (gray shaded area). **B.** Residuals plot for the linear regression model of cumulative exposure versus PON1 levels, demonstrating homoscedasticity and absence of systematic patterns.

Assessment of regression model assumptions

The residuals plot presented in Figure 3B revealed more or less equal dispersion throughout the range of predicted values. This demonstrates the assumption of homoscedasticity (same variability), which is considered one of the basic assumptions in linear regression analysis. The lack of any funnel shape or any identifiable trend in the dispersion of the points implies that the variance of the error term is constant for various levels of exposure. This makes the findings

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of the regression analysis more valid. Additionally, the lack of any identifiable outliers in the residuals plot proves the accuracy of fitting the linear model.

Multivariable regression analysis

Even after adjustment for age, BMI, gender, smoking status, and alcohol intake simultaneously, farm exposure was significantly and independently associated with lower PON1 concentrations (β = -29.7; 95% confidence interval: -43.9 to -15.4; $p < 0.001$). The regression coefficient suggests that individuals with farm exposure had an average decrease of 29.7 U L^{-1} in their PON1 concentration compared to those without farm exposure. As shown in Table 4, no other variable included in the regression model was significantly associated with PON1.

Subgroup analyses

The negative effect of exposure on PON1 activity was seen to be stable across all analyzed subgroups. As shown in Fig. 4, this effect was found in males (β = -28.4) and females (β = -31.2), in people younger than 40 years old (β = -26.8) and older than 40 (β = -32.1), in those with BMI less than 25 (β = -27.9) and with BMI equal to or greater than 25 (β = -30.5), as well as among non-smokers (β = -30.1) and smokers (β = -28.6). The persistence of this effect across all subgroups shows the consistency of our main finding, although due to limited statistical power, these subgroup results need confirmation in larger studies.

Fig. 4. Forest plot (or subgroup analysis plot) of the association between farm exposure and PON1 levels across predefined subgroups (sex, age, BMI, and smoking status). The negative association remained consistent across all subgroups.

Sensitivity analysis

Farm exposure had a strong link to decreased PON1 activity, which remained statistically significant across all four sensitivity tests performed. The optimistic scenario produced a beta coefficient of -30.2 ($p < 0.001$), while the pessimistic scenario produced a beta coefficient of -28.1 ($p = 0.002$). The high-quality samples only test produced a beta of -31.5 ($p < 0.001$). Lastly, after eliminating samples requiring retesting, the beta coefficient was -29.4 ($p < 0.001$; Table 5).

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Table 5. Results of sensitivity analyses for the effect of farm exposure on PON1 levels

Method	Sample size	β coefficient (95% CI)	*p*
Method 1 (outliers removed)	74	-30.2 (-44.8 to -15.6)	< 0.001
Method 2 (pessimistic)	81	-28.1 (-45.2 to -11.0)	0.002
Method 3 (good quality only)	32	-31.5 (-48.9 to -14.1)	< 0.001
Method 4 (repeat samples excluded)	65	-29.4 (-44.6 to -14.2)	< 0.001

DISCUSSION

As shown by the recent cross-sectional analysis, residing close to agricultural fields was significantly associated with reduced serum concentrations of PON1 and slightly elevated liver enzyme (ALT and AST) concentrations, where lower concentrations of PON1 were considered to be indicative of long-term exposure to organophosphate pesticides among the Uzbekistan rural population. Such associations persisted even after adjustment for potential confounders ($\beta = -29.7$ U L^{-1}; 95% CI: -43.9 to -15.4; $p < 0.001$). In addition, a dose-response association was observed with regard to accumulated exposure to pesticides. Despite being biologically plausible and representing a contribution to the scientific evidence on the effects of pesticide exposure, the study results need to be interpreted with due caution.

Several studies support an inverse association between pesticide exposure and PON1 activity. Bhat *et al.* (2023) observed reduced PON1 levels in farmers with prolonged organophosphate and carbamate exposure. Similar reductions have been reported in occupationally exposed greenhouse workers and pesticide factory workers. Chronic exposure appears to increase oxidative stress, which can consume the PON1 antioxidant capacity. However, not all studies show consistent effects; some report that PON1 reductions are more pronounced in individuals with specific genotypes (e.g., low-activity PON1 variants), highlighting the role of gene-environment interactions that were not assessed in our study. Our findings showed increases in the concentrations of ALT and AST. This finding is supported by many researchers who demonstrated mild liver toxicity after exposure to pesticides. For example, Lozano-Paniagua *et al.* (2021) reported an elevation in liver enzymes among greenhouse workers. There are many other studies carried out among farmers where they also reported increases in liver enzyme concentrations due to oxidative stress caused by pesticides. However, it is important to point out that some new studies show no relationship between pesticide exposure and liver enzymes (Lozano-Paniagua *et al.* 2021).

Although we observed a clear dose-response gradient and robustness in sensitivity analyses, the cross-sectional design fundamentally limits causal inference. Reverse causality remains possible — individuals with pre-existing lower PON1 activity or mild liver impairment might differentially reside or work closer to farms. Reliance on residential distance as a proxy for exposure, without direct measurement of urinary organophosphate metabolites (e.g., dialkyl phosphates) or serum pesticide levels, introduces substantial non-differential misclassification that likely biases results toward the null (Coronado *et al.* 2011; Dereumeaux *et al.* 2020). Convenience sampling and the modest sample size (n = 81) further restrict generalizability and power for detecting interactions or modest effects.

Unmeasured confounding is also important. Basic demographic and lifestyle factors were controlled for, with an E-value reported to be 2.4; however, factors like diet, socio-economic status, co-exposure to other environmental pollutants, and especially PON1 gene polymorphisms (Q192R and L55M) were not examined. Studies have found that variations in the PON1 gene could affect sensitivity to organophosphates up to 40 times, and this is therefore considered an important limitation (Costa *et al.* 2013; You *et al.* 2013; Kunachowicz et al. 2023). Also, while there was statistical significance associated with increases in ALT and AST levels, the changes observed were relatively small and close to or below normal values, and thus the question arises whether they have any clinical significance or it was merely a statistical one (Lozano-Paniagua *et al.* 2021; Mehta *et al.* 2025; Mohamadi *et al.* 2026).

Strengths of the study include the use of cumulative exposure metrics, comprehensive sensitivity analyses, and exploration of both enzymatic and liver outcomes in an understudied environmental exposure context in Uzbekistan. However, these strengths do not fully overcome the inherent weaknesses of the design.

CONCLUSION

In this exploratory cross-sectional study carried out in Uzbekistan, proximity to agricultural farms within a distance of less than 500 meters was significantly associated with lower PON1 enzyme activity and higher ALT and AST

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concentrations regardless of any confounding factors, exhibiting a dose-response pattern. This study seems to lend credence to the theory that repeated and prolonged exposure to low doses of organophosphates found in pesticides can potentially disrupt antioxidant mechanisms and cause some degree of stress in the liver. However, owing to the cross-sectional study design, surrogate measurement of exposures, small sample size, and lack of biomarker validation and genotyping, no causal conclusions can be made based on this research. Instead, these observations must be seen as preliminary data. Prospective cohort studies with biomarker analysis for pesticides, PON1 genotyping, and larger samples are necessary in future investigations.

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