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Depressive symptoms and suicide attempts among farmers exposed to pesticides

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ABSTRACT

Pesticides safeguard crop health but may diminish cholinesterase activity in farmers, potentially leading to psychiatric disorders like depression and suicide attempts. This study, with 453 participants (225 pesticide-exposed farmers, 228 non-farmers) in Almería, Spain, aimed to investigate the presence of depressive symptoms and suicide attempts, the decrease acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) activity, and their relationship with pesticide exposure in farmers. Depressive symptoms were evaluated using the Spanish adaptation of the Beck Depression Inventory, and blood samples were analyzed for AChE and BChE activity. Farmers showed significantly increased risk of moderate/severe depression and suicide attempts compared to non-farmers (OR = 2.18; p = 0.001), with highest risks observed among mancozeb users (OR = 2.76; p = 0.001 for depression) and malathion users (OR = 3.50; p = 0.001 for suicide attempts). Findings emphasize elevated depression and suicide risks among pesticide-exposed farmers, particularly associated with chlorpyrifos, mancozeb, and malathion exposure.

1. Introduction

Ensuring an optimum state of mental well-being is crucial for overall happiness and fulfillment, laying the foundation for a satisfying and productive life (OECD and European Union, 2018). However, more than a billion people worldwide experience psychiatric disorders (Sunkel, 2022), and these conditions, especially depression, constitute a significant contributor to disability-adjusted life years in high-income nations (Arias et al., 2022; GBD, 2019). In the European Union, approximately 17.3% of the population, equivalent to around 84 million people, is affected by psychiatric disorders (OECD and European Union, 2018). In Spain, approximately 10% of the surveyed population acknowledges experiencing psychiatric disorders, with depression (6.7%) being a prominent factor (Ministerio de Sanidad, 2019). In addition, the economic burden of these disorders exceeds 45 billion euros annually in Spain, making it a substantial challenge to the health system (OECD and European Union, 2018). At the same time, suicide is a serious global public health issue that takes the lives of more than 700,000 people each year (World Health Organization, 2021). A previous meta-analysis highlighted specific occupations associated with an increased risk of suicide (Milner et al., 2013). Despite limited research, previous studies suggest significantly elevated rates of depression (Jones-Bitton et al., 2020; Rudolphi et al., 2020) and suicide (Norrod et al., 2023; Purc-Stephenson et al., 2023) among farmers compared to the general population.

Farmers face various stressors that predispose them to a higher risk

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of depression and suicide, including economic difficulties (Jones-Bitton et al., 2020; Rudolphi et al., 2020; Zanchi et al., 2023), social isolation (Reed and Claunch, 2020), chronic health issues (Ringgenberg et al., 2018; Scheyett et al., 2019; Zanchi et al., 2023), limited access to healthcare (Brew et al., 2016; Jones et al., 2010), adverse weather conditions (Ayal et al., 2021), procedures and regulations (Truchot and Andela, 2018), as well as exposure to pesticides (Campos et al., 2016; Stallones and Beseler, 2016; Zanchi et al., 2023). Over the past 15 years, various pesticides were used in intensive agriculture, including organochlorines, organophosphates, and inorganics (García-García et al., 2016). In 2021, Spain led pesticide sales in the European Union, with approximately 76,448 tons. Of these, 10,091 tonnes (13.2 per cent) were used in the southern Spanish region of Almería, recognized for its intensive agricultural practices, both in greenhouses and outdoors (Ministerio de Agricultura, 2021). Farmers, regularly exposed through inhalation and skin contact, face risks of intoxication (Mackenzie Ross et al., 2010). Recent research suggests that these intensive pesticide practices increase the risk of diseases, including neuropsychiatric disorders (Farnham et al., 2021; Fuhrimann et al., 2021; Gangemi et al., 2016; Lozano-Paniagua et al., 2021; Zhang et al., 2016). Thus, pesticides, with neurotoxic properties, can impact physiological functions with prolonged exposures (Corsini et al., 2013; Mrema et al., 2013), implying inhibition of acetylcholinesterase (AChE), a fundamental enzyme for neuromuscular and cerebral function (Altinyazar et al., 2016). Although there are few studies addressing the neurotoxic effects of long-term exposure to low doses of pesticides (Antonangeli et al., 2023).

Currently, some studies link pesticide exposure to a variety of effects on neurological health (Ong-Artborirak et al., 2022; Parrón et al., 2011), including hormonal disorders (Leemans et al., 2019), symptoms of ADHD in adolescent pesticide applicators (Rohlman et al., 2019), neurodevelopmental disorders (van Wendel de Joode et al., 2016), a higher risk of dream-enacted behaviors (Yuan et al., 2022), irritation, erection and sensorimotor dysfunction (Rohlman et al., 2019; Zhang et al., 2016). Despite these findings, there is a lack of information about the psychological well-being of farmers concerning their exposure to pesticides, prompting a call for increased attention to the psychological well-being of this population and the conduct of more comprehensive studies on occupational pesticide exposure (Zanchi et al., 2023). Understanding this relationship could be crucial for intervening before the onset of psychiatric disorders such as depression, thereby contributing to the reduction of hospitalization rates and the use of psychotropic medications, improving psychological well-being and quality of life. Furthermore, since suicide in the agricultural population is widespread and constitutes a significant public health issue, it is imperative to comprehend the risk and protective factors associated with it to design and implement specific interventions targeting those with higher vulnerability. Therefore, this study aimed to investigate the presence of depressive symptoms and suicide attempts, the decrease AChE and BChE activity, and their relationship with pesticide exposure in farmers.

2. Materials and methods

2.1. Study design and area of study

A cross-sectional research was conducted to explore the potential relationship between occupational exposure to pesticides and potential psychiatric disorders, such as depression and suicide attempts, in the region of Almería, situated in the southeastern part of Spain. Almería is the first horticultural production area of intensive agriculture under plastic greenhouse in Spain, where an area encompassing 32,827 ha is specifically allocated for the implementation of intensive agriculture conducted within plastic greenhouses (Instituto Nacional de Estadística INE 2020; Ministerio de Agricultura, 2021).

2.2. Study population

The research enlisted 453 individuals, aged 18–65, within the timeframe spanning from February 2022 to October 2023. The exposed group comprised 225 farmers engaged in intensive agriculture, specifically working in greenhouses. These workers were engaged in different agricultural tasks (40 hours per week) such as pruning, weeding, or thinning, so they encountered pesticides through both direct and indirect means. The growth cycles of greenhouse crops in the study area encompassed various stages, each necessitating specific tasks such as plant staking, pruning, weeding, thinning, preparation of the fumigation broth and pesticide application. These tasks were performed at different stages of the crop growth cycle, so that all greenhouse workers carried out the same task during each stage. According to the details provided by agronomists overseeing the study region, the pesticides most frequently used during the study period were insecticides (Methyl chlorpyrifos [Organophosphate], Formetanate [N-methylcarbamate], Malathion [Organophosphate]) and fungicides (Mancozeb [Dithiocarbamate]). Subsequently, each worker was asked individually which of these pesticides they used.

The criteria for inclusion in the exposed group were being a farmer working in greenhouses, male, aged 18 years or above, having more than 2 years of experience as farmers, residing at the current address for a minimum of 5 years and who had signed the informed consent. These farmers were enlisted directly within the confines of the greenhouses, capitalizing on the scheduled routine of their occupational health monitoring, which involved the gathering of blood samples. The rate of participation approached almost 100%. The control group consisted of 228 male individuals (public administration workers and primary and secondary school teachers). The inclusion criteria for the control group were: workers with no history of occupational contact with pesticides, age 18 years or older, and who had signed the informed consent form. This group was composed of healthy residents of the same geographic area (municipality) who had no history of occupational exposure to pesticides, which served as exclusion criteria. They were recruited through the Occupational Risk Prevention Centre, an organization responsible for supervising the health and safety of workers, including the conduct of health assessments and the gathering of blood samples. Residing in the same municipality as the farmers, located in the province of Almería, they were recruited simultaneously with the greenhouse workers during the same period of the year. This timing was strategically aligned with their scheduled visits to the Centre, ensuring that occupational health assessments and dietary exposure to pesticides were comparable in both groups. Consequently, the principal disparity between the two groups is found in pesticide exposure resulting from engagement in agricultural activities within greenhouses.

Exclusion criteria for both groups were: participants with a clinical diagnosis of chronic disease (e.g., cancer, renal, neurological, liver disease) and those who refused to sign informed consent.

2.3. Data collection

Workers were interviewed through a survey. This survey included sociodemographic data such as age, body mass index (BMI), level of education, monthly household income, smoking habit, and place of residence. Through this same survey, data related to agricultural activity were also collected, such as the duration of their agricultural work experience (in years) and types of pesticides used individually in the last year. The interviews were conducted by a skilled interviewer and a psychiatry specialist.

The residential locations of both the exposed and control groups were categorized into two zones based on pesticide usage levels. This classification considered the percentage of land allocated to intensive agriculture within plastic-covered greenhouses during the 2020–2021 crop year. The high pesticide use zone encompassed 96% of the greenhouse area in Almería, specifically Campo del Poniente and Campo de

Níjar, whereas the low pesticide use zone comprised the remaining 4% of the greenhouse area in Levante Almeriense (Ministerio de Agricultura, 2021).

Enzyme markers such as erythrocyte AChE and BChE were analyzed in the blood samples taken during the health surveillance examination of all workers in both groups. Blood samples were obtained via venipuncture following a 10-hour fasting period during the health surveillance examination of all workers in both groups. These samples were immediately placed in a portable refrigerator and transported to an external laboratory within 4 hours. Upon arrival, the blood was centrifuged at 400 ×g for 20 minutes to separate the plasma and erythrocyte components, which were subsequently stored at − 40 °C for the determination of enzyme markers such as erythrocyte AChE and BChE. AChE activity was assessed using the modified Ellman method as described by Worek et al. (1999), while BChE was determined following the protocol outlined by Whittaker (1984).

The evaluation of depression levels in both farmers and non-farmers was conducted through the Beck Depression Inventory-II (BDI-II). The Spanish adaptation of the BDI-II, a self-administered tool designed to gauge depressive symptoms, was employed for this purpose. The inventory comprises 21 items, with each item being assessed on a scale ranging from 0 to 3 points. This scoring method yields a total score that spans from 0 to 63. In individuals with a psychological disorder, a score between 0 and 13 may be considered indicative of minimal depressive symptomatology, 14–19 as mild, 20–28 as moderate, and 29–63 as severe, as established by Beck et al. (Beck et al., 1996). The internal consistency reliability of the BDI-II is reported to be a Cronbach's alpha of 0.87. In our investigation, we calculated Cronbach's alpha coefficient value of 0.88.

They were also asked if they had ever suicide attempt. Both the BDI-II questionnaire and the information related to suicide attempts in the study population was gathered through in-person interviews facilitated by the psychiatric specialist.

2.4. Ethical considerations

This study received approval from the Ethics and Research Committee of the University of Almeria (EFM 96/2021). Involvement in the study was voluntary, and participants provided written informed consent after being briefed on the study's objectives. All procedures adhered to the ethical guidelines outlined in the Declaration of Helsinki. Each participant was assigned a unique personal code to safeguard the confidentiality of the data.

2.5. Statistical analysis

The IBM SPSS statistical software package (SPSS 29.0 for Windows) was employed for statistical analysis.

Descriptive analysis included the computation of means and standard deviations for continuous variables, while categorical variables underwent the calculation of absolute and relative frequency distributions. The distribution of categorical variables related to the study's outcome was assessed using Chi-square tests. Since the distribution of the age, AChE, BChE, and years working in agriculture did not meet the normality criteria, as confirmed by the Kolmogorov-Smirnov test, the non-parametric Mann-Whitney U test was employed to compare these variables between farmers and controls. Effect sizes were indicated using Rosenthal's r, categorized as small (0.10), medium (0.24), and large (0.37) (Rosenthal and Rubin, 1982). The risk of depression and suicide attempt, both in the overall population and the subgroup of farmers, was determined by odds ratios (OR) and 95% confidence intervals (CI) through the Chi-square test. Multiple logistic regression analysis was applied to evaluate the risk of depression and suicide attempts in both the entire study population and the subgroup of farmers. The models underwent adjustment for independent variables displaying statistically significant differences in the bivariate analysis. These variables encompassed labor status (distinguishing between groups), place of residence (distinguishing between areas with low and high pesticide use), AChE and BChE. Furthermore, in the model specific to the subgroup of farmers, we incorporate factors like AChE and BChE, along with considerations for the type of pesticides used in the previous year: chlorpyrifos (yes/no), formetanate (yes/no), malathion (yes/no), mancozeb (yes/no). In the logistic regression analysis of suicide attempts, the factor assessing the degree of depression was additionally integrated into the model for both the entire population and the subgroup of farmers. In the analysis, potential confounding variables such as age, educational level, BMI, and household monthly income were also taken into account. The dependent variables included the occurrence of depression (moderate/severe depression vs. minimal/mild depression) and suicide attempt (yes/no). The threshold for statistical significance was established at a p-value < 0.05.

3. Results

A collective of 453 participants partook in this study, comprising 225 farmers and 228 non-farmers.

The characteristics of the participants are presented in Table 1. No differences were noted concerning age, BMI, education level, household monthly income, smoking habit, place of residence, and length of residence (years) on the current farm. All participants were citizens of Spain.

Table 2 shows the distribution of depression levels and suicide attempts as well as the mean scores for Beck Depression and enzyme activity (AChE, BChE) in farmers and non-farmers. In the farmers, there was a statistically significant increase in depression levels compared to non-agricultural [22.06 (6.12) vs. 19.01 (4.85), Rosenthal r: 0.29; p < 0.001]. 11.1% of the farmers had severe levels of depression compared

Table 1
Comparison of sociodemographic data between 'farmers' and 'non-farmers'.

Characteristic		Farmers (n=225)	Non-farmers (n=228)	p-value
Age (years) †		38.38 (8.17)	38.85 (4.56)	0.210*
BMI	Normal (18.5–24.9)	151 (67.1%)	134 (58.8%)	0.121**
	Low (<18.5)	24 (10.7%)	37 (16.2%)	
	High (≥25.0)	50 (22.2%)	57 (25.0%)	
Education level	No studies	53 (23.6%)	36 (15.8%)	0.167**
	Low	82 (36.4%)	83 (36.4%)	
	Medium	71 (31.7%)	85 (37.3%)	
	High	19 (8.3%)	24 (10.5%)	
Household monthly income	<1.200 €	13 (5.8%)	10 (4.5%)	0.570**
	1.200–2.500 €	201 (89.3%)	199 (87.2%)	
	>2.500 €	11 (4.9%)	19 (8.3%)	
Tobacco	Yes	85 (37.9%)	109 (47.8%)	0.093**
	No	111 (49.6%)	98 (43.0%)	
	Former smoker	28 (12.5%)	21 (9.2%)	
Place of residence	Areas with high pesticide use	167 (73.2%)	180 (80%)	0.090**
	Areas with low pesticide use	61 (26.8%)	45 (20.0%)	

†Data expressed as mean (standard deviation)
p-value obtained using the * Mann–Whitney U test for continuous variables or the ** Chi-square test for categorical variables.

Table 2
Comparison of the depression levels, suicide attempt and mean scores for AChE and BChE between 'farmers' and 'non-farmers'.

Disorders		Farmers (n=225)	Non-farmers (n=228)	Rosenthalŕ	p-value
Depression Level	Minimal	22 (9.8%)	29 (12.7%)	-	<0.001*
	Mild	62 (27.6%)	91 (39.9%)		
	Moderate	116 (51.6%)	103 (45.2%)		
	Severe	25 (11.1%)	5 (2.2%)		
Beck Depression Total		22.06 (6.12)	18.91 (4.75)	0.29	0.001*
Suicide attempt	Yes	75 (33.3%)	42 (18.4%)	-	0.01*
	No	150 (66.7%)	186 (81.6%)		
AChE		12.36 (1.87)	14.03 (2.04)	-0.37	<0.001**
BChE		4624.83 (876.21)	4812.51 (909.72)	-0.13	0.022**

Abbreviations: AChE: erythrocyte acetylcholinesterase; BChE: butyrylcholinesterase
p-value obtained using the * Chi-squared test for categorical variables or * Mann–Whitney U test for continuous variables.

to 2.2% of the non-farmers group. In addition, 33.3% of farmers had made a suicide attempt compared to 18.4% of non-farmers. Both results were statistically significant.

The AChE activity was lower in farmers than in non-farmers (Rosenthalŕ: −0.37; p = 0.001), as was BChE activity (Rosenthalŕ: −0.13; p = 0.034).

When comparing AChE and BChE activity in farmers and non-farmers, according to the level of depression and whether they had had any suicide attempts, a significant decrease in AChE activity was observed in farmers with moderate/severe depression with respect to those with minimal/mild depression symptoms (Rosenthal'r: −0.56; p = 0.040). In non-farmers, although AChE activity was also slightly lower in those with moderate/severe depression, this decrease was not statistically significant (Table 3).

Farmers who had had a suicide attempt showed significantly lower AChE and BChE activity relative to those who had not had suicidal attempts (Rosenthal'r: −0.39; p = 0.003; Rosenthal'r: −0.34; p = 0.008, respectively). No significant changes in AChE and BChE values were observed for non-farmers.

Table 4 shows the risk of depression and suicide attempt in farmers, expressed as OR, adjusted for use of chlorpyrifos, formetanate, malathion and mancozeb vs. no use in the last year. A significantly increased risk of moderate/severe depression and suicide attempt was found for farmers who had been exposed to chlorpyrifos, malathion and mancozeb. The most prominent statistically significant risks were identified among farmers exhibiting moderate/severe levels of depression who used mancozeb compared to those who did not (OR: 3.24; p = 0.001). In farmers with suicide attempts, the highest risk was observed for farmers using malathion compared to those not using malathion (OR: 2.51; p = 0.002). No statistically significant disparities were noted in the likelihood of depression and suicide attempts between farmers who utilized formetanate and those who did not.

Farmers who showed moderate/severe symptoms of depression and had had some attempt suicide, had been working in agriculture for more years, being these results statistically significant.

The results of the multiple logistic regression analysis, exploring factors linked to the onset of depression (moderate/ severe depression vs. minimal/ mild depression) and suicide attempt (yes/no) in a) the overall study population and b) specifically for farmers, are outlined in Table 5. The model for the total population underwent adjustments for age, BMI, educational level, household monthly income, labor status, place of residence, AChE and BChE, serving as independent variables. Among the total population, farmers exhibited a markedly higher risk of experiencing moderate/severe depression and attempting suicide (OR 2.18 and 1.70, respectively, p < 0.05). The model designed for farmers underwent adjustments for age, BMI, educational level, household monthly income, place of residence, AChE, BChE and use of chlorpyrifos, formetanate, malathion and mancozeb, as independent variables. Farmers utilizing mancozeb displayed the highest risk of moderate/severe depression (OR = 2.76; p = 0.001). The highest risk of attempted suicide was observed in farmers who had moderate/severe depression and used malathion (OR = 3.50; p = 0.001).

4. Discussion

The aim of this research was to investigate the presence of depressive symptoms and suicide attempts, the decrease AChE and BChE activity, and their relationship with pesticide exposure in farmers. To the best of our understanding, as of now, there are no existing studies in Spain that explore these psychiatric disorders in farmers with pesticide exposure. The obtained results indicate an association between occupational exposure to various pesticides and the presence of depressive symptoms, as well as suicide attempts. In the surveyed sample of farmers, an increase in moderate to severe levels of depression was observed, accompanied by a notable decrease in AChE and BChE activity. A more detailed analysis revealed that those farmers with moderate to severe depression had even lower AChE activity. Furthermore, exposure to certain pesticides, such as chlorpyrifos, malathion, and mancozeb, significantly associated with an increased risk of depression and suicide in farmers.

The well-being of individuals is influenced by most pesticides, primarily because of their effects on neurological functions (Jokanović et al., 2023; Kim et al., 2017; Meyer-Baron et al., 2015). This study revealed significant differences between farmers and non-farmers

Table 3
Comparison of mean scores for AChE and BChE based on the level of depression and suicide attempt in the two study groups, 'farmers' and 'non-farmers'.

		Farmers (n=225)	Rosenthalŕ	p-value*	Non-farmers (n=228)	Rosenthalŕ	p-value*
AChE	Moderate/ severe depression	12.37 (1.99)	-0.56	0.040	13.86 (2.02)	-0.17	0.091
	Minimal/ mild depression	13.39 (1.65)			14.22 (2.06)		
BChE	Moderate/ severe depression	4574.15 (873.57)	-0.15	0.136	4764.19 (856.13)	-0.10	0.282
	Minimal/ mild depression	4708.21 (880.79)			4849.72 (952.17)		
AChE	Suicide attempt	11.88 (1.94)	-0.39	0.003	14.03 (2.01)	-0.01	0.460
	No suicide attempt	12.60 (1.79)			14.06 (2.14)		
BChE	Suicide attempt	4422.62 (884.65)	-0.34	0.008	4933.36 (890.17)	-0.16	0.051
	No suicide attempt	4725.93 (857.84)			5081.63 (936.80)		

Data expressed as mean (standard deviation)
Abbreviations: AChE: erythrocyte acetylcholinesterase; BChE: butyrylcholinesterase
p-value obtained using the * Mann–Whitney U test.

Table 4
Risk of depression and suicide attempt by type of pesticides in farmers.

		Farmers							
		Moderate/ severe depression (n=141)	Minimal/ mild depression (n=84)	OR (95% C.I.)	p-value*	Suicide attempt (n=75)	No suicide attempt (n=150)	OR (95% C.I.)	p-value *
Chlorpyrifos	Yes	91 (64.5%)	40 (47.6%)	2.02	0.013	53 (70.7%)	78 (52.0%)	2.23	0.007
	No	50 (35.5%)	44 (52.4%)	(1.15–3.47)		22 (29.3%)	72 (48.0%)	(1.23–4.01)	
Formetanate	Yes	65 (46.1%)	40 (48.0%)	0.85	0.571	31 (41.3%)	76 (50.7%)	0.88	0.186
	No	76 (53.9%)	44 (52.0%)	(0.49–1.46)		44 (58.7%)	74 (49.3%)	(0.59–1.20)	
Malathion	Yes	87 (61.7%)	36 (42.9%)	2.14	0.006	52 (69.3%)	71 (47.3%)	2.51	0.002
	No	54 (38.3%)	48 (57.1%)	(1.24–3.72)		23 (30.7%)	79 (52.7%)	(1.40–4.52)	
Mancozeb	Yes	89 (63.1%)	29 (34.5%)	3.24	0.001	48 (64.0%)	70 (46.7%)	2.03	0.014
	No	52 (36.9%)	55 (65.5%)	(1.84–5.71)		27 (36.0%)	80 (53.3%)	(1.14–3.59)	
Years working in agriculture		14.40 (6.83)	11.17 (6.77)	-	0.03**	14.12 (6.81)	11.73 (6.79)	-	0.02**

p-value obtained using the *Chi-squared test for categorical variables and **Mann–Whitney U test for continuous variables.

Table 5
Stepwise multiple binary logistic regression analysis of the risk of depression and suicide attempt in the total population and in farmers, adjusted for potential risk factors.

		Parameters	OR	95% C.I.	p-value
Moderate/ severe depression	Total population[a]	Farmers	2.18	1.43–3.31	0.001
	Farmers[b]	Use of chlorpyrifos (yes)	1.68	1.09–3.06	0.048
		Use of malathion (yes)	1.78	1.13–3.18	0.031
		Use of mancozeb (yes)	2.76	1.54–4.98	0.001
Suicide attempt	Total population[a]	Farmers	1.70	1.16–2.71	0.026
	Farmers[c]	Moderate/severe depression	2.78	1.42–5.44	0.003
		Use of chlorpyrifos (yes)	2.32	1.23–4.36	0.009
		Use of malathion (yes)	2.62	1.40–4.91	0.003
		Use of mancozeb (yes)	2.16	1.13–4.11	0.019
		Moderate/severe depression*Use of malathion (yes)	3.50	1.68–7.29	0.001

[a] The final regression model was adjusted for labour status (0: non-farmers; 1: farmers).
[b] The final regression model was adjusted for use of chlorpyrifos (0: yes; 1: no), use of malathion (0: yes, 1: no) and use of mancozeb (0: yes, 1: no).
[c] The final regression model was adjusted for depression levels (0: minimal/ mild depression; 1: Moderate/ severe depression), use of chlorpyrifos (0: yes; 1: no), use of malathion (0: yes, 1: no), use of mancozeb (0: yes, 1: no) and interaction moderate/severe depression*Use of malathion (yes).

regarding levels of depression and suicide attempts. Farmers exhibited a significant increase in depression levels, with a substantial percentage experiencing much higher severity levels compared to the non-agricultural group. Moreover, the percentage of farmers who had attempted suicide was double that of non-farmers. These results are consistent with prior studies suggesting that pesticide exposure induces mood disorders such as depression (Conti et al., 2018; Harrison and Mackenzie Ross, 2016; Koh et al., 2017), leading farmers to unconsciously attempt suicide (Junior et al., 2021). These findings emphasize the significance of examining and mitigating the risks linked to pesticide exposure concerning depression in adults (Wu et al., 2023). A distinctive aspect of this study was the assessment of enzymatic activity, specifically focusing on AChE and BChE. Lower AChE and BChE activity were identified in farmers, and this decline was more pronounced in those with moderate/severe depression. Additionally, farmers who had attempted suicide exhibited lower AChE and BChE activity compared to those who had not made any attempts. Organophosphate and carbamate pesticides inhibit AChE (Kaur et al., 2023), leading to measurable physiological changes in exposed individuals (Dasgupta et al., 2007; Suarez-Lopez et al., 2013). Furthermore, significant inhibition of AChE in the hippocampus of rats has been reported following exposure to these pesticides (Johnson et al., 2009), a structure with crucial functions in depression, suicidal occurrences, memory, and imagination (Li et al., 2015).

Additionally, a significant increase in the risk of moderate/severe depression and suicide attempts was observed in farmers exposed to specific pesticides, specifically chlorpyrifos, malathion, and mancozeb, compared to those not exposed in the past year. The highest risks were found in farmers with moderate/severe depression levels who used mancozeb. In the study conducted by Kaur et al., a comparable association was noted, indicating significantly elevated rates of severe depression among farmers exposed to organophosphate pesticides compared to the control group (Kaur et al., 2023). Recently, researchers indicated a relationship between depression in farmers and exposure to organophosphates, especially chlorpyrifos, a product also used in our study area (Kori et al., 2020). Furthermore, farmers who used malathion had the highest risk of suicide attempts compared to non-users. Elevated rates of suicide were similarly documented in regions where organophosphates were employed (Parrón et al., 1996). No statistically significant differences were observed in the risk of depression and suicide attempts between farmers who used formetanate and those who did not.

The neurotoxic effects of organophosphates and carbamates are closely related to the inhibition of the enzyme AChE, which causes excessive stimulation of muscarinic and nicotinic receptors, resulting in cholinergic overstimulation and an increased risk for the development of neuropsychiatric disorders (Harrison and Mackenzie Ross, 2016). Our results also showed a decrease in BChE activity, despite farmers not reporting any acute intoxication symptoms when questioned. This emphasizes that chronic exposure to low levels of pesticides can cause damage, even in the absence of acute intoxication (Zanchi et al., 2024).

The findings from the multiple logistic regression analysis indicated a notable elevation in the likelihood of moderate/severe depression and suicide attempts among farmers in comparison to the general population. These findings are supported by the most recent scientific literature documenting elevated levels of depressive symptoms (Petarli et al., 2022) and suicide (Phalp et al., 2022; Reed and Claunch, 2020; Weichelt et al., 2021) in farmers. It is important to note that the greatest likelihood of experiencing moderate/severe depression was identified in farmers utilizing mancozeb. Recently, Frengidou et al. supported the connection between pesticide poisoning and depressive symptoms, also reinforcing the hypothesis that pesticide exposure constitutes a risk factor for depression (Frengidou et al., 2024), and confirming the positive association observed in this study. Moreover, farmers exposed to pesticides have shown elevated levels of renal and hepatic stress markers, alongside indicators of oxidative stress and heightened inflammatory cytokines, when compared to controls, suggesting a potential association between inflammation, oxidative stress, and depression in this population (Zanchi et al., 2024). Furthermore, scientific evidence supports adverse effects of mancozeb on reproductive health (Bianchi et al., 2020), neurochemical and morphological alterations in the hypothalamus during development (Morales-Ovalles et al., 2018), and exacerbation of liver diseases (Pirozzi et al., 2016), among others. Regarding suicide attempts, farmers with moderate/severe depression who used malathion presented the highest risk. According to Jung et al., exposure to pesticides is linked to a heightened risk of suicide (Jung et al., 2019). Despite clear evidence of the potential toxic effects of malathion on health, affecting the central nervous system, reproductive system, lungs, liver, kidneys, pancreas and blood, and being genotoxic and carcinogenic (Badr, 2020), its specific relationship with suicide attempts still remains unknown. To the best of our knowledge, this is the first study associating the use of mancozeb and malathion with the risk of depression and suicide attempts, respectively.

This study holds significant implications for clinical practice and the development of various health policies. Greater attention should be given to the mental health status of agricultural workers, and efforts should be made to enhance their knowledge regarding the proper use and health risks associated with pesticides. Considering that the development of depression is linked to poor health, understanding the factors leading to it is crucial. Developing health policies with effective interventions and providing quality services for individuals with depression could reduce suicide attempt rates. However, there are several limitations in this study that must be considered. Given that this is a cross-sectional study, it is not possible to establish a cause-and-effect relationship. The collected data may be subject to recall bias and information bias among respondents, as they are based on their memories. It is important to consider that data collection through self-reported surveys could result in inaccurate information from participants. Although the majority of interviewed participants, both farmers and non-farmers, had at least primary education and exhibited a similar household monthly income, to minimize these biases, interviews were conducted by trained specialized personnel and a psychiatrist. For future studies, alternative data collection methods such as medical records could be utilized, alongside conducting regular follow-ups with participants to verify response consistency and minimize long-term memory errors. Despite being informed that the purpose of the study was to assess their mental health for preventive measures rather than evaluating safety measures used during work hours, all farmers reported using gloves as PPE, thus raising the possibility that some might have been reluctant to admit non-use due to social desirability bias.

5. Conclusion

The results of this study highlight a higher risk of depressive symptoms and suicide attempts among farmers exposed to pesticides, specifically those exposed to chlorpyrifos, mancozeb, and malathion, common pesticides in the study region for crops grown under plastic coverings. It was observed that farmers with moderate/severe depressive symptoms and exposure to malathion had the greatest risk of suicide attempts. Additionally, a significant decrease in the activity of the enzyme AChE was found in farmers with moderate/severe depressive symptoms, while those who had attempted suicide showed a decrease in both AChE and BChE activity. These findings underscore the importance of investigating the neurotoxic effects of pesticides and their relationship with mental disorders, emphasizing the need to implement appropriate preventive and protective measures in agriculture to preserve the mental health of farmers.

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CRediT authorship contribution statement

Jessica Garcia-Gonzalez: Writing – review & editing, Writing – original draft, Investigation, Data curation. **Mar Requena-Mullor:** Visualization, Methodology, Formal analysis, Conceptualization. **Fátima Ruiz-Moreno:** Writing – original draft, Validation, Data curation. **Ruirui Zheng:** Writing – original draft, Validation, Supervision, Investigation, Data curation. **Raúl Romero del Rey:** Writing – review & editing, Supervision, Investigation, Data curation, Conceptualization. **Ángela Navarro-Mena:** Writing – original draft, Visualization. **Antonia López-Villén:** Supervision, Investigation, Conceptualization. **Raquel Alarcon-Rodriguez:** Writing – review & editing, Validation, Supervision, Methodology, Formal analysis, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

The authors do not have permission to share data.

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