

Letter to the Editor



Case Control Study of Impulsivity, Aggression, Pesticide Exposure and Suicide Attempts Using Pesticides among Farmers*

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A case-control study was conducted to investigate associations between organophosphate pesticide (OP) exposure, aggression, impulsivity, and attempted suicide. Questionnaires were used to collect information; impulsivity and aggression were measured by the Barratt Impulsivity Scale (BIS) and the Aggression Inventory (AI). A greater number of OP symptoms was associated with an increased odds of a suicide attempt after adjusting for marital status and income (OR = 1.45; CI 1.14-1.86). Attempted suicide was significantly associated with high impulsivity scores (means: 72.4 vs. 60.6, $P < 0.0001$) and high aggression scores (means: 38.5 vs. 26.1, $P < 0.0001$). Suicide attempters had a higher number of OP exposure symptoms than controls and scored higher on scales of impulsivity and aggression.

A number of occupational studies have reported high rates of suicide in occupational groups^[1]. Farmers are among the occupational groups that have been reported to have high rates of suicide^[1]. Suicide and suicide attempts are associated with lack of impulse control, feelings of hopelessness, social isolation, and auto-aggression^[2]. In clinical studies and case reports, there is consistent evidence that acute poisoning from organophosphate pesticides may be associated with affective disorders, including anxiety and aggression^[3]. If organophosphate poisoning decreases impulse control and increases aggression in sensitive populations the result may well be increased suicidal behaviors. The purpose of this study was to use a case-control approach to investigate the relationships between attempted

suicide and levels of impulsivity and aggression. Our primary hypothesis was that suicide attempters would have higher impulsivity and aggression scores compared to non-attempters. We hypothesized that levels of impulsivity and aggression could be used to discriminate between attempters and non-attempters. Our secondary hypothesis was that high occupational exposure to organophosphate pesticide (OP) would be associated with a suicide attempt and with higher levels of impulsivity and aggression compared to non-attempters with no history of pesticide exposure.

This study was approved by both the Institutional Review Board of Jilin University and by Colorado State University. Informed consent was obtained from all participants. Cases were identified using records from the local hospital. The records indicated that the cases attempted to kill themselves using pesticides.

Criteria for inclusion of cases included: (1) being able to take care of themselves without help; (2) being able to understand the information given by the chief of the Disease Control office and being able to answer the questions about voluntary participation in the study; and (3) the mental status of the cases was stable enough to participate in the study, as assessed by a licensed psychological consultant. Controls were those who lived in another village which was the same distance to the hospital in which the case was admitted. Controls were matched to cases by gender and by age (+/-2 years). Questionnaires were used to collect information on demographic characteristics, OP exposure and 11

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symptoms of high OP exposure in the past two years, family history of mental problems and other medical conditions, and impulsivity and aggression.

The sample was 74.4% male and 25.6% female. The mean age of the sample was 46.2 (cases = 46.1 ± 13.0 ; controls = 46.2 ± 13.0 , $P = 0.682$) and did not differ due to matching. There were significant differences in marital status, family income, and duration of farm work between cases and controls (Supplement Table 1 available in www.besjournal.com). Although cases and controls were similar in their reporting of having had a pesticide illness, the median number of OP-related symptoms reported significantly differed between cases and controls (cases: 3 symptoms, range = 8; controls: 0 symptoms, range = 11; $P < 0.0001$). Each of the 43 cases reported at least one pesticide exposure symptom; this one symptom was either nausea/vomiting OR excessive sweating, indicating a high exposure to pesticides. In fact, the most frequently reported symptoms after exposure to OP pesticides were nausea and excessive sweating (Supplement Table 2 available in www.besjournal.com).

Cases were significantly more likely to report having been exposed to pesticides in the past two years than controls ($P = 0.021$). Only 44.2% of controls reported mixing, loading and applying pesticides in the past two years compared to 68.3% of cases ($P = 0.026$). Controls were significantly more likely to report removing protection (clothes, gloves, hats) before going home (50.0% vs. 4.7%, $\chi^2 = 22.1$, $P < 0.0001$) (Supplement Table 3 available in www.besjournal.com).

Suicide attempters had significantly higher impulsivity scores (means: 72.4 vs. 60.6, $P < 0.0001$) and aggression scores (means: 38.5 vs. 26.1, $P < 0.0001$) than controls in bivariate analyses. Impulsivity and aggression were significantly correlated ($\rho = 0.58$, $P < 0.0001$). Unmarried respondents had significantly higher impulsivity scores than married respondents ($P = 0.002$) and lower income respondents had higher impulsivity scores than those in the higher income category ($P = 0.002$). The same trend held for aggression scores; unmarried ($P = 0.005$) and low income ($P = 0.0003$) respondents scored significantly higher. Since being unmarried and having a low income were both associated with suicide attempts, models were adjusted for these two potential confounders. The number of OP-related symptoms was not associated with either impulsivity OR aggression, however, Barratt Impulsivity Scale (BIS) and Aggression Inventory

(AI) scores were significantly higher in those that reported at least one pesticide exposure symptom compared to those who reported none (Supplement Tables 4-5 available in www.besjournal.com).

Both BIS and AI did significantly better than chance at predicting suicide attempters (BIS: $AUC = 0.78$, $se = 0.05$, 95% CI 0.68-0.88, $\chi^2 = 29.9$, $P < 0.0001$; AI: $AUC = 0.80$, $se = 0.05$, 95% CI 0.70-0.89, $\chi^2 = 37.4$, $P < 0.0001$) (Figure 1A-B). The optimal cutoff point was 69 for BIS and 33 for AI, where both sensitivity and specificity curves intersect, although this is only one approach to identifying optimal cutpoints. Adjusting the Receiver Operating Characteristic (ROC) models for gender, income OR number of reported pesticide-related symptoms did not alter these results. The number of pesticide symptoms was significantly higher in those who scored greater than 69 on the impulsivity scale ($P = 0.01$); symptom counts were not associated with the higher category of aggression.

Farm residents reporting a higher number of OP-related symptoms had a significantly higher odds of a suicide attempt ($OR = 1.27$, CI 1.05-1.53), and the effect was stronger after adjusting for marital status and income ($OR = 1.45$, CI 1.14-1.86) (Table 1). Suicide attempts were associated with increased impulsivity ($OR = 1.09$, CI 1.04-1.14). After adjusting for being unmarried and having a low income, the effect size was only slightly reduced ($OR = 1.07$, CI 1.01-1.12) (Table 1). Similarly, the odds of a suicide attempt were significantly elevated in those with higher aggression scores ($OR = 1.10$; CI 1.05-1.16); and remained significant after adjustment ($OR = 1.08$; CI 1.02-1.14).

In impulsivity models adjusted for the number of pesticide poisoning symptoms reported, the OR for pesticide symptoms and suicide attempt was 1.23 (CI 1.01-1.50) and 1.09 (CI 1.04-1.14) for impulsivity when entered in the same model (Table 1). Similarly, the aggression model adjusted for the number of pesticide exposure symptoms had an OR of 1.23 (1.01-1.49) for symptoms and an OR of 1.10 (1.05-1.15) for aggression (Table 2). Adjusting for marital status and income strengthened the association between symptoms and suicide attempt and only slightly decreased the effect size between the personality trait and suicide attempt (Table 2). Lastly, we tested for an interaction between the main effects (OP symptoms and personality trait) but with the addition of the interaction term in the model, the main effects were not significant (Table 2). A larger sample size is needed to explore the

possibility of interactions between these associations in greater depth.

There were three important findings in our study. First, cases reported a significantly greater

number of symptoms of pesticide exposure and greater occupational exposure to pesticides than controls. Each of the 43 cases had experienced at least a nausea or an excessive sweating episode

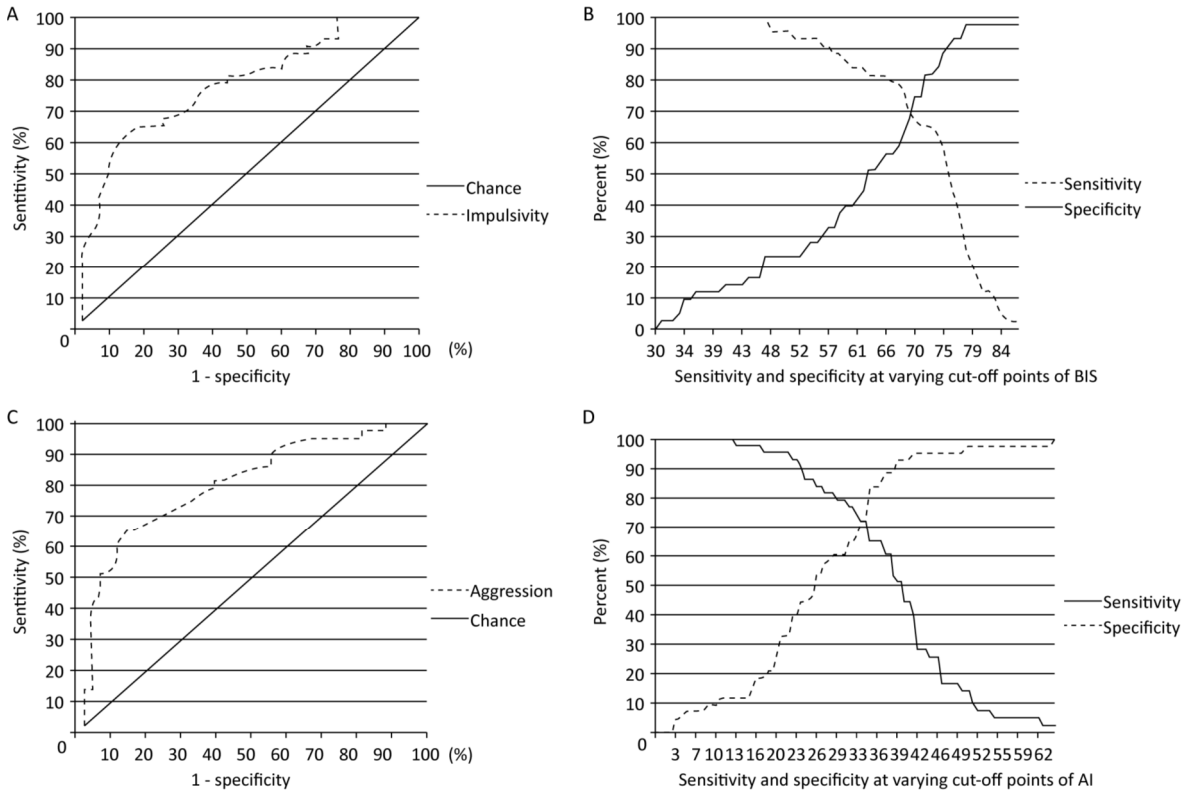


Figure 1. Receiver Operating Characteristic curve and sensitivity and specificity curve for Barrett’s Impulsivity Scale and Aggression Inventory as a diagnostic measure of suicide attempt in 43 cases of suicide attempt and 43 controls from a farm resident sample, Jilin Province, China, 2008-2010.

Table 1. Odds Ratios (OR) and 95% Confidence Interval (CI) from Logistic Regression Model for the Odds of having had a Suicide Attempt in 43 Cases of Suicide Attempt and 43 Controls

Logistic Regression Model	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)
Number of pesticide poisoning symptoms	1.27 (1.05-1.53)	1.45 (1.14-1.86)
Impulsivity	1.09 (1.04-1.14)	1.07 (1.01-1.12)
Aggression	1.10 (1.05-1.16)	1.08 (1.02-1.14)

Note. * Adjusted for income and marital status.

Table 2. Odds Ratios (OR) and 95% Confidence Interval (CI) from Logistic Regression Model with Main Effects of Symptoms and Personality Trait in 43 Cases of Suicide Attempt and 43 Controls

Logistic Regression Model	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)
Number of pesticide poisoning symptoms	1.23 (1.01-1.50)	1.43 (1.10-1.85)
Impulsivity	1.09 (1.04-1.14)	1.06 (1.00-1.12)
Number of pesticide poisoning symptoms Aggression	1.23 (1.01-1.49)	1.45 (1.12-1.89)
	1.10 (1.05-1.15)	1.08 (1.01-1.15)

Note. * Adjusted for income and marital status.

associated with pesticide exposure. Clearly, the cases had higher exposure to pesticides than the controls, over half of whom ($n = 24$) reported no symptoms. This result is consistent with previous studies supporting a causal connection between pesticide exposure and mood disorders^[4], as well as ecological studies demonstrating higher suicide rates in agricultural communities^[5]. Further, results are consistent with studies in Sri Lanka and China that reported the storage of pesticides in homes was associated with suicide attempts^[6-8], indicating that pesticides are a potent risk factor for suicide attempts.

Second, cases scored significantly higher on the BIS and AI than controls. This result is consistent with Wesseling et al.^[9] findings among OP-poisoned banana workers who had increased suicidal ideation, anxiety and hostility compared with non-poisoned controls. Impulsivity is a strong predictor for suicide intent even when controlling for anxiety and depression severity^[10]. Therefore, OP exposure is likely to be exacerbating a trait already present in the farmer that increases the risk of a suicide attempt. Thus, the OP-poisoned participants may be at risk of future suicide attempts and may require ongoing screening to reduce this risk.

Third, the symptoms participants reported after being exposed to pesticides were nausea and excessive sweating. These symptoms are consistent with exposure to OPs, which suggests that cases had a history of OP exposure before they experienced their suicide attempt. Therefore, our results support the assertion that the OP exposure likely occurred prior to the suicide attempt.

Controls were significantly more likely to remove protective clothing after working with pesticides and more likely to remove their protections before going home than were cases. OPs can be absorbed through three routes: inhalation, skin absorption, and the gastrointestinal tract. Farmers check the weather forecast before applying OPs to plants or fruits. If the weather is windy, farmers will postpone the application of pesticides. Unless farmers consume OPs on purpose, or eat before washing their hands, the gastrointestinal tract is not a major route for OP exposure. Inhalation and skin absorption are the most likely routes of exposure. The greater care taken by controls when handling pesticides may be related to their lower level of impulsivity, the fact that they handle pesticides less frequently and are less comfortable using them, or because they were less depressed

than the cases. This observation would benefit from further research because wearing protective equipment is a target of farm safety and health programs.

Although the mean scores on the BIS and AI were higher in those with pesticide symptoms, every case had one or more serious pesticide symptom. There was no way to disentangle the pesticide exposure effects from the attempted suicide. The higher scores may be related to the suicide attempt alone and not be due to the OP exposure, or the suicide attempt may be due to both the OP exposure and the presence of high impulsivity or aggression.

The study provided evidence for connections between impulse control disorders, pesticide exposures and suicide attempts. Due to local culture, potential cases not responding resulted in a low response rate, which is a serious limitation of the study. In this population, there is a strong stigma associated with suicide attempts, therefore, cases may not have been willing to reveal the reason for their hospitalizations to family and neighbors. A larger sample size would allow better control for other confounding factors, although we did not find evidence for significant confounding aside from marital status and income. In this study, OP exposure was assessed by exposure symptoms, such symptoms as excessively tired or headache which may be caused by other factors and therefore it is likely to overestimate the effects of OP exposure on suicide attempts. Moreover, questionnaire-based information was collected about OP exposure and OP-associated symptoms, which is also possible to result in recall bias. These are limitations of the study, a more physiological and toxicological assessment would improve certainty about actual exposures. The study did not assess the relationship between suicide attempts and amount of alcohol consumption nor did we assess substance abuse. Future work needs to assess these risk factors. Future work would also benefit from determining whether OP exposure mediates or moderates the association between impulsivity or aggression and suicide attempt. We could not assess BIS and AI independently from pesticide exposure and suicide attempt in this study. This information would help identify individuals who should be closely monitored for suicide ideation. Suicide attempters had a higher number of OP exposure symptoms than controls and scored higher on scales of impulsivity and aggression. Further work is needed to confirm these findings in a larger sample.

Author Contributions REN Shu Ping and STALLONES Lorann designed the study; BESELER L. Cheryl analyzed the data; REN Shu Ping, LYU Chun Ping, STALLONES Lorann and BESELER L. Cheryl all contributed in the writing process. PEI Jian Ru, LI Yu Ling, LI Jian Hui, REN Ming collected the data and interviewed the participants and helped established database.

Conflicts of Interest The authors declare that there is no conflict of interest. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention or the Fogarty International Center.

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REFERENCES

1. Kim J, Shin DH, Lee WJ. Suicidal ideation and occupational pesticide exposure among male farmers. *Environ Res*, 2014; 128, 52-6.
2. Nock M, Borges G, Bromet E, et al. Suicide and suicidal behavior. *Epidemiol Rev*, 2008; 30, 133-54.
3. Jamal GA. Neurological syndromes of organophosphorus compounds. *Adverse Drug React Toxicol Rev*, 1997; 16, 133-70.
4. Freire C, Koifman S. Pesticides, depression and suicide: a systematic review of the epidemiologic evidence. *Int J Hyg Environ Health*, 2013; 216, 445-60.
5. Parron T, Hernandez A, Villanueva E. Increased risk of suicide with exposure to pesticides in an intensive agricultural area. A 12-year retrospective study. *Forensic Sci Int*, 1996; 79, 53-63.
6. Mohamed F, Manuweera G, Gunnell D, et al. Pattern of pesticide storage before pesticide self-poisoning in rural Sri Lanka. *BMC Public Health*, 2009; 9, 405.
7. Zhang J, Stewart R, Phillips M, et al. Pesticide exposure and suicidal ideation in rural communities in Zhejiang province, China. *Bull World Health Organ*, 2009; 87, 745-53.
8. Wang BS, Chen L, Li XT, et al. Acute Pesticide Poisoning in Jiangsu Province, China, from 2006 to 2015. *Biomed Environ Sci*, 2017; 30, 695-700.
9. Wesseling C, van Wendel de Joode B, Keifer M, et al. Symptoms of psychological distress and suicidal ideation among banana workers with a history of poisoning by organophosphate *OR* n-methyl carbamate pesticides. *Occup Environ Med*, 2010; 67, 778-84.
10. Keilp JG, Goriyn M, Oquendo MA, et al. Aggressiveness, not impulsiveness *OR* hostility, distinguishes suicide attempters with major depression. *Psychol Med*, 2006; 36, 1779-88.

1. Kim J, Shin DH, Lee WJ. Suicidal ideation and occupational pesticide exposure among male farmers. *Environ Res*, 2014; 128,

Supplement Table 1. Characteristics of the 43 Cases who Attempted Suicide in 2008-2010 and 43 Controls Residing in Jilin Province, China

Characteristic	Cases N (%)	Controls N (%)	χ^2	P Value
Occupation				
Farmer	32 (74.4)	38 (88.4)	2.764	0.096
Other	11 (25.6)	5 (11.6)		
Education				
Elementary school and below	12 (27.9)	12 (27.9)	0.019	0.89
Secondary school and higher	31 (72.1)	31 (72.1)		
Family income*				
Less than 1100 dollars	39 (90.7)	10 (23.3)	39.893	0.000*
1100 dollars and above	4 (9.3)	33 (76.7)		
Marital status*				
Single	25 (58.1)	5 (11.6)	17.39	0.000*
Married	18 (41.9)	38 (88.4)		
Farm work period (year)*				
Less than 20 years	32 (74.4)	18 (41.9)	9.364	0.002*
20 years and more	11 (25.6)	25 (58.1)		
Duration of farm work in last year				
Less than 6 months	28 (65.1)	26 (60.5)	0.199	0.655
6 months and more	15 (34.9)	17 (39.5)		
Drink alcohol				
Yes	28 (65.1)	25 (58.1)	0.503	0.478
No	12 (27.9)	15 (34.9)		

Note. * $P < 0.05$.

Supplement Table 2. Pesticide Exposure Symptoms Reported after Being Exposure to Pesticides in 43 Cases and 43 Controls, Jilin Province, China, 2008-2010

Variables	Cases N (%)	Controls N (%)	χ^2	P Value
Excessively tired				
Yes	15 (35.7)	10 (23.3)	1.588	0.208
No	27 (64.3)	33 (76.7)		
Headache				
Yes	16 (38.1)	10 (23.3)	2.204	0.138
No	26 (61.9)	33 (76.7)		
Eyes irritated				
Yes	20 (48.8)	12 (27.9)	3.878	0.049
No	21 (51.2)	31 (72.1)		
Blurred vision				
Yes	3 (7.1)	5 (11.6)		0.173
No	39 (92.9)	38 (88.4)		
Nose bleeding				
Yes	1 (2.4)	4 (9.3)		0.360
No	40 (97.6)	39 (90.7)		
Nausea				
Yes	38 (88.4)	7 (16.3)	44.795	0.000*
No	5 (11.6)	36 (83.7)		
Chest discomfort				
Yes	6 (14.3)	7 (16.3)	0.065	0.799
No	36 (85.7)	36 (83.7)		
Difficulty breathing				
Yes	5 (12.5)	6 (14.0)	0.038	0.845
No	35 (87.5)	37 (86.0)		
Muscle twitches				
Yes	2 (5.0)	3 (7.1)		1.000
No	38 (95.0)	39 (92.9)		
Skin irritation				
Yes	10 (24.4)	10 (23.3)	0.015	0.903
No	31 (75.6)	33 (76.7)		
Excess sweating				
Yes	31 (73.8)	8 (19.0)	25.320	0.000*
No	11 (26.2)	34 (81.0)		

Note. * $P < 0.05$.

Supplement Table 3. Organophosphate Pesticide Exposure in 43 Cases and 43 Controls, Jilin Province, China, 2008-2010

Variables	Cases N (%)	Controls N (%)	χ^2	P Value
Exposure to pesticides				
Yes	26 (63.4)	16 (38.1)	5.321	0.021
No	15 (36.6)	26 (61.9)		
Mix, load or apply pesticide				
Yes	28 (68.3)	19 (44.2)	4.949	0.026
No	13 (31.7)	24 (55.8)		
Wear personal protection				
Yes	38 (90.5)	42 (97.7)		0.202
No	4 (9.5)	1 (2.7)		
Remove protection after pesticide use				
Yes	21 (50.0)	41 (95.3)	22.139	0.000
No	21 (50.0)	2 (4.7)		
Became ill from pesticide exposure				
Yes	30 (73.2)	26 (63.4)	0.901	0.342
No	11 (26.8)	15 (36.6)		
Sought medical attention				
Yes	8 (20)	6 (14)	0.540	0.462
No	32 (80)	37 (86)		

Note. * $P < 0.05$.

Supplement Table 4. Impulsivity and Aggression Comparison between Cases and Controls ($n = 43$) and between 86 Farm Residents Reporting No Pesticide Exposure Symptoms and Those Reporting One OR More Pesticide exposure symptoms ($\bar{x} \pm s$)

Index	Cases N = 43	Controls N = 43	P Value
Barratt Impulsivity	72.4 ± 9.9	60.6 ± 14.2	< 0.0001
Aggression	38.5 ± 11.0	26.1 ± 12.0	< 0.0001

Supplement Table 5. Impulsivity and Aggression Comparison between 86 Farm Residents Reporting no Pesticide Exposure Symptoms and Those Reporting one OR More Pesticide Exposure Symptoms ($\bar{x} \pm s$)

Index	No Symptoms (n = 24)	One OR More Symptoms (n = 62)	P Value
Barratt Impulsivity	56.8 ± 15.3	70.2 ± 10.7	< 0.0001
Aggression	23.0 ± 10.3	35.9 ± 12.2	< 0.0001