# Pesticide exposure and risk of Parkinson's disease: A case-control study in Northeastern Brazil

## Exposição a agrotóxicos e risco de doença de Parkinson: Um estudo caso-controle no Nordeste do Brasil

## Exposición a pesticidas y riesgo de enfermedad de Parkinson: Un estudio de casos y controles en el Noreste de Brasil

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**Abstract**
Parkinson's disease (PD) is an idiopathic neurodegenerative disease, and it has been linked to long-term pesticide exposure. In this study, we aimed to determine whether pesticide exposure was associated with the risk of PD and other neurological manifestations. We conducted a pilot case-control study in patients from two neurology outpatient clinics. PD cases (n = 29) were matched with controls (n = 83) randomly selected from the same outpatient clinics. For data collection, telephone-based interviews were performed using a structured questionnaire. Overall, PD cases were proportionally more exposed to pesticides than the control group, but the association was not statistically significant (OR= 1.92; 95%, CI: 0.77–4.66; p = 0.15). We identified a high prevalence of neurological and psychological symptoms among the study participants, especially among the individuals who reported pesticide exposure. Our results reinforce the importance of further studies investigating the relationship between PD and pesticides to better understand this phenomenon.
**Keywords:** Pesticides; Parkinson disease; Neurodegenerative diseases; Environmental exposure.

**Resumo**
A doença de Parkinson (DP) é uma doença neurodegenerativa idiopática e tem sido associada à exposição prolongada a pesticidas. Neste trabalho, nosso objetivo foi determinar se a exposição a pesticidas estava associada ao risco de DP e outras manifestações neurológicas. Realizamos um estudo piloto de caso-controle com pacientes de dois ambulatórios de neurologia. Casos de DP (n = 29) foram pareados com controles (n = 83) selecionados aleatoriamente nos mesmos ambulatórios. Para a coleta de dados, entrevistas por telefone foram realizadas usando um questionário estruturado. No geral, os casos de DP foram proporcionalmente mais expostos a pesticidas do que o grupo controle, mas a associação não foi estatisticamente significativa (OR= 1,92; 95%, IC: 0,77–4,66; p = 0,15). Identificamos alta prevalência de sintomas neurológicos e psicológicos entre os participantes do estudo, principalmente entre os indivíduos que relataram exposição a agrotóxicos. Nossos resultados reforçam a importância de mais estudos que investiguem a relação entre DP e agrotóxicos para melhor entender esse fenômeno.
**Palavras-chave:** Pesticidas; Doença de Parkinson; Doenças neurodegenerativas; Exposição ambiental.

**Resumen**
La enfermedad de Parkinson (EP) es una enfermedad neurodegenerativa idiopática y se ha relacionado con la exposición prolongada a pesticidas. En este estudio, nuestro objetivo fue determinar si la exposición a pesticidas estaba asociada con el riesgo de EP y otras manifestaciones neurológicas. Realizamos un estudio piloto de casos y controles en pacientes de dos clínicas ambulatorias de neurología. Los casos de EP (n = 29) se emparejaron con controles (n = 83) seleccionados al azar de las mismas clínicas ambulatorias. Para la recolección de datos, se realizaron entrevistas telefónicas mediante un cuestionario estructurado. En general, los casos de EP estuvieron proporcionalmente más expuestos a pesticidas que el grupo control, pero la asociación no fue estadísticamente significativa (OR= 1,92; 95%, IC: 0,77–4,66; p = 0,15). Identificamos una alta prevalencia de síntomas neurológicos y psicológicos entre los participantes del estudio, especialmente entre las personas que reportaron exposición a pesticidas. Nuestros resultados refuerzan la importancia de realizar más estudios que investiguen la relación entre PD y pesticidas para comprender mejor este fenómeno.
**Palabras clave:** Plaguicidas; Enfermedad de Parkinson; Enfermedades neurodegenerativas; Exposición ambiental.

## 1. Introduction

Pesticides are a broad group of compounds extensively used in agriculture to control pests and diseases that cause crop damage and economic yield loss. They are toxic for several biological targets and have differences according to chemical structure. Given the growing use of these products worldwide, epidemiological data have shown the side effects of pesticides on non-target species, including humans (Richardson et al., 2019; Lushchak et al., 2018).

Many pesticides can cross the blood brain barrier and interfere with the activity of central nervous system (CNS). Some pesticides have neurotoxic effects, and they can damage the brain cells and induce neurodegeneration (Islam & Malik, 2018). Some studies have been linked pesticide exposure to neurotoxicity and human neurodegenerative diseases such as Parkinson’s disease (Richardson et al., 2019; Gunnarsson & Bodin, 2019; Narayan et al., 2017).

Parkinson's Disease (PD) is characterized by a clinical syndrome resulting from a dysfunction of the nigrostriatal dopaminergic system, and it has been linked to chronic management of pesticides in previous studies (Takahashi & Hashizume, 2014; Moisan et al., 2015). For this reason, farmers and individuals living in rural communities represent groups at high risk. They are routinely directly or indirectly exposed to high levels of pesticides. Notably, epidemiological studies have reported an increased risk of PD in farmers exposed to pesticides (Pouchieu et al., 2018).

In Brazil, agriculture has been one of the main economic activities over the centuries, which have led to an increase in the pesticide use. In the Northeast region, family farmers are responsible for most of the agricultural production, and they stand out as a population that is highly vulnerable to the effects of pesticide exposure. However, little is known about associations between PD and pesticide exposure in Brazilian population. Hence, we conducted a pilot case-control study with outpatients of Neurology clinics at the Federal University of Sergipe, Brazil, to determine whether pesticide exposure increase the risk of developing PD.

## 2. Methodology

### 2.1 Study setting and design

We conducted a pilot case-control study among patients from neurology outpatient clinics situated in two municipalities (Lagarto and Aracaju) in the Sergipe state, Northeast Brazil, using electronic medical records and telephone interviews. The study period was from January 20, 2022, to July 14, 2022.

First, a structured questionnaire was developed, tested, and revised by our team. Second, a trained researcher administered a telephone-based interview to each participant. The questionnaire included a survey of sociodemographic data, medical and labor history, and the history of direct or indirect exposure to pesticides. Oral consent was obtained from all interviewed participants. The Ethics Committee of the Federal University of Sergipe approved this study (CAAE 48534621.0.0000.5546).

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**2.2 Study population**

As cases, we included individuals of both genders, aged 18 years or older, diagnosed with idiopathic Parkinson's disease and followed up by the Neurology outpatient clinics of the Federal University of Sergipe. Controls without PD were randomly selected from the same outpatient clinics in the proportion of up to 4 controls for every 1 case. The controls were matched to cases by age (±5 years), sex, and region of residence. We excluded individuals under 18 years old and those with missing or incorrect telephone numbers in the medical records that prevented contact for the interview.

**2.3 Statistical analysis**

Data were analyzed using Graph Pad Prism, version 8.0. Descriptive data were presented as frequency, percentages, mean and standard deviation (SD). Fisher's exact test and odds ratio (OR) were used to evaluate association between variables. For statistical significance, p-value <0.05 and a 95% confidence interval (CI) were considered.

## 3. Results

A total of 36 patients met all inclusion criteria and were eligible for case group, but only 29 (83%) were included, all of them with a clinical diagnosis of PD. Among patients previously matched as controls (n = 117), only 83 were included in the study. Most participants were male, either among cases (68.9 %) or controls (59.0 %). On average, PD cases were 68.7 years old (SD= 8.9), and controls patients were 66.4 years old (SD = 9.5). The main demographic characteristics of the participants are shown in Table 1.

**Table 1 -** Demographic characteristics of the study participants.

| | | ***Cases (N=29)*** | ***Controls (N=83)*** |
|---|---|---|---|
| | | **Mean (SD)** | **Mean (SD)** |
| *Age (years)* | | 68.7(8.9) | 66.7(9.4) |
| | | **N (%)** | **N (%)** |
| *Sex* | | | |
| | *Male* | 20 (68.9) | 49 (59.0) |
| | *Female* | 9 (31) | 34 (40.9) |
| *Marital status* | | | |
| | *Married* | 24 (82.7) | 38 (45.7) |
| | *Single* | 3 (10.3) | 18 (21.6) |
| | *Divorced* | 0 (0) | 6 (7.2) |
| | *Ignored* | 2 (6.8) | 19 (22.8) |
| *Color* | | | |
| | *Brown* | 23 (79.3) | 61 (73.4) |
| | *White* | 5 (17.2) | 11 (13.2) |
| | *Black* | 0 (0) | 8 (9.6) |
| | *Indigenous* | 0 (0) | 0 (0) |
| | *Ignored* | 1 (3.4) | 3 (3.6) |
| *Scholarity* | | | |
| | *Illiterate* | 6 (20.6) | 6 (7.2) |
| | *1st grade complete* | 4 (13.7) | 10 (12) |
| | *2nd grade complete* | 2 (6.8) | 5 (6) |
| | *1st grade incomplete* | 7 (24.1) | 18 (21.6) |
| | *2nd grade incomplete* | 0 (0) | 0 (0) |
| | *Graduation complete* | 0 (0) | 4 (4.8) |
| | *Graduation incomplete* | 0 (0) | 0 (0) |
| | *Ignored* | 10 (34.4) | 40 (48.1) |

Source: Authors.

In this study, the most frequent comorbidities were hypertension, diabetes mellitus, dyslipidemia and depression in both groups. We found a significant association between hypertension and PD (OR 0.38, 95% CI 0.15-0.90; p=0.03), but this was not observed for the diabetes (OR 0.37, 95% CI 0.12-1.11; p=0.09), dyslipidemia (OR 0.88, 95% CI 0.34-2.29; p>0.99), and depression (OR 1.71, 95% CI 0.58-5.80; p=0.35) (Table 2).

**Table 2 -** Summary of the measured comorbidities and lifestyle factors.

| | | Cases (n=29) N (%) | Controls (n=83) N (%) | OR (CI 95%) | P Value |
|---|---|---|---|---|---|
| **Comorbidities** | | | | | |
| **Hypertension** | No | 19 (65.5) | 35 (42.2) | 0.38 | 0.03* |
| | Yes | 10 (34.5) | 48 (57.8) | | |
| **Diabetes Mellitus** | No | 25 (86.2) | 58 (69.8) | 0.37 | 0.09 |
| | Yes | 4 (13.79) | 25 (30.1) | | |
| **Dyslipidemia** | No | 21 (72.4) | 58 (69.9) | 0.88 | >0.99 |
| | Yes | 8 (25.6) | 25 (30.1) | | |
| **Depression** | No | 24 (82.8) | 74 (89.2) | 1.71 | 0.35 |
| | Yes | 5 (17.2) | 9 (10.8) | | |
| **Lifestyle factors** | | | | | |
| **Smoking** | No | 26 (86.7) | 65 (78.3) | 0.41 | 0.27 |
| | Yes | 3 (10.3) | 18 (21.7) | | |
| **Alcohol intake** | No | 23 (79.3) | 41 (49.4) | 0.25 | 0.008* |
| | Yes | 6 (20.7) | 42 (49.4) | | |
| **Physical activity** | No | 27 (93.1) | 74 (89.2) | 0.61 | 0.72 |
| | Yes | 2 (6.9) | 9 (10.8) | | |
| **Rural living** | No | 8 (27.6) | 29 (34.9) | 1.41 | 0.50 |
| | Yes | 21 (72.4) | 54 (65.1) | | |
| **Farming occupation** | No | 11 (37.9) | 43 (51.8) | 1.76 | 0.28 |
| | Yes | 18 (62.1) | 40 (48.2) | | |
| **Pesticide Exposure** | No | 18 (62.1) | 63 (75.9) | 1.92 | 0.16 |
| | Yes | 11 (37.9) | 20 (24.1) | | |

Source: Authors.

We sought to investigate the association between modifiable lifestyle factors and PD risk (Table 2). Overall, we did not find any association of PD with smoking (OR 0.41, 95% CI 0.12-1.54; p=0.27) and physical activity (OR 0.60, 95% CI 0.12-2.64; p=0.72). In contrast, we found a significant association between alcohol intake and PD (OR 0.25, 95% CI 0.09-0.68; p=0.008). Considering the significant effect of gender on PD development and prevalence, we also conducted a data analysis separately for males and females. The association between decreased PD and alcohol intake was more significant in males (OR 0.09, 95% CI 0.02-0.30; p<0.0001), but no differences were found between PD risk and other variables.

Out of all participants of our sample, 37.9% of the PD cases and 24.1% of the control patients reported pesticide exposure during working in agricultural occupations, although no significant relationship was found between self-reported pesticide exposure (OR 1.92, 95% CI 0.77-4.66; p=0.16), rural living (OR 1.41, 95% CI 0.55-3.54; p=0.50), farming work (OR 1.76, 95% CI 0.75-4.09; p=0.28) and risk of PD, as shown in Table 2. The duration of pesticide exposure was higher between PD cases than control group, since 63.6% of cases reported a time of exposure more than 20 years in comparison to 45 % of control group that reported a duration of exposure between 10 and 20 years.

Regarding using personal protective equipment (PPE) during pesticide application, 36% of PD cases and 20% of controls reported never used PPE. We found no significant association between use of PPE and the occurrence of PD (OR 0.43, 95% CI 0.10-1.90; p=0.40). Nevertheless, individuals of both groups were aware that pesticide exposure increases risks to their health, although most of them did not know how to specify any specific risk involved.

Pesticide applicators from both groups reported purchasing the products mainly from farmhouses, cooperatives, or directly from self-employed sellers. However, only 5 (45%) of the applicators among the PD cases and 11 (55%) of the applicators among the controls group were able to specify the type (or name) of pesticide they used. The most used pesticides were the herbicides glyphosate and paraquat, in both groups. When we asked whether, during the purchase of the products, they received technical guidance (on the correct handling and forms of protection against intoxication), only 45% of all applicators responded affirmatively.

Among 11 PD cases who applied pesticides, we asked whether they thought the disease was related to exposure to these products, and 7 of them answered affirmatively. Among 18 PD cases that did not report direct exposure to pesticides, we observed that 9 of them also thought that the disease was related to pesticides, 7 of them were living or have lived in rural areas.

We did not identify cases of pesticide poisoning in either group (either affecting the participants or involving any of their family members), not even seeking medical assistance due to signs and symptoms suggestive of intoxication. However, when we asked if they knew how to recognize the signs and symptoms of pesticides poisoning, individuals of both groups demonstrated not knowledge about it, and the lack of knowledge was proportionally more significant in the control group (30% versus 10.3%).

Finally, we identified a high prevalence of neurological and psychological symptoms among the study participants (table 3). When we analyzed the symptoms only among the individuals who reported previous pesticide exposure, we observed in both groups that the most commonly reported symptoms were body ache (81% in cases and 85% in controls), sleep disorders (81% in cases and 75% in controls) and memory impairment (72% in cases and 80% in controls). In addition, we observed that headache was reported by 72% of cases exposed to pesticides. Meanwhile, in the control group, olfactory impairment and fatigue were among the most common symptoms in those individuals, reported by 70% and 65%, respectively (Table 4).

**Table 3 -** Prevalence of neurological and psychological symptoms among participants (cases=29, controls=83).

| Symptoms | Number among cases | Prevalence % (CI) | Number among controls | Prevalence % (CI) |
|---|---|---|---|---|
| Headache | 23 | 79.3 (0.6-0.9) | 62 | 74.7 (0.6-0.8) |
| Body ache | 24 | 82.7 (0.6-0.9) | 66 | 79.5 (0.7-0.9) |
| Muscle weakness | 23 | 79.3 (0.6-0.9) | 58 | 69.8 (0.6-0.8) |
| Cramps | 25 | 86.2 (0.7-1.0) | 71 | 85.5 (0.8-0.9) |
| Mood disorders | 25 | 86.2 (0.6-0.9) | 65 | 78.3 (0.7-0.9) |
| Irritability | 20 | 68.9 (0.5-0.8) | 73 | 87.9 (0.8-0.9) |
| Sleep disorders | 26 | 89.6 (0.7-1.0) | 58 | 69.8 (0.6-0.8) |
| Olfactory impairment | 23 | 79.3 (0.6-0.9) | 58 | 69.8(0.6-0.8) |
| Memory impairment | 24 | 82.7 (0.6-0.9) | 68 | 81.9 (0.7-0.9) |
| Fatigue | 26 | 89.6 (0.7-1.0) | 73 | 87.9 (0.8-0.9) |

Source: Authors.

**Table 4 -** Prevalence of neurological and psychological symptoms among participants that reported pesticide exposure (cases=11, controls=20).

| Symptoms | Number among cases | Prevalence % (CI) | Number among controls | Prevalence % (CI) |
|---|---|---|---|---|
| Headache | 8 | 72.7 (0.39-0.94) | 10 | 50.0 (0.27-0.73) |
| Body ache | 9 | 81.8 (0.48-0.98) | 17 | 85.0 (0.62-0.97) |
| Muscle weakness | 7 | 63.6 (0.31-0.89) | 11 | 55.0 (0.31-0.77) |
| Cramps | 5 | 45.4 (0.17-0.77) | 12 | 0.60 (0.36-0.81) |
| Mood disorders | 6 | 45.4 (0.17-0.77) | 9 | 0.45 (0.23-0.68) |
| Irritability | 5 | 45.4 (0.17-0.77) | 10 | 50.0 (0.27-0.73) |
| Sleep disorders | 9 | 81.8 (0.48-0.98) | 15 | 75.0 (0.51-0.91) |
| Olfactory impairment | 5 | 45.4 (0.17-0.77) | 14 | 70.0 (0.46-0.88) |
| Memory impairment | 8 | 72.7 (0.39-0.94) | 16 | 80.0 (0.56-0.94) |
| Fatigue | 5 | 45.4 (0.17-0.77) | 13 | 65.0 (0.41-0.85) |

Source: Authors.

## 4. Discussion

It is widely believed that environmental factors, including pesticide exposure, may play a role in the development of Parkinson's disease (PD). In this case-control study, we investigated the association between occupational exposure to pesticides and some lifestyles factors with the risk of PD. Overall, we observed that individuals with a clinical diagnosis of PD were proportionally more exposed to pesticides than individuals of control group, however, no significant association between pesticide exposure and PD risk was found.

It is important to note that among the study participants, some constraints were noticed during the interviews. It occurred primarily when they were asked questions about the application of pesticides, ways of obtaining the products, the frequency of application, and the commercial name of the pesticides used. In addition, due to physical and/or cognitive limitations imposed by the underlying disease and/or age, to answer the questions, five respondents among the PD cases and 19 respondents among the controls group were close relatives or caregivers of the participants in this research.

Our results showed a higher frequency of male individuals over 50 years old, in both groups, proving that, in most cases, agricultural work is predominantly performed by men, who are usually older (Takahashi & Hashizume, 2014). There was no significant difference in sex, age, schooling, color, or marital status variables between groups of our sample. However, it is worth to consider that social inequities are part of the complex spectrum known as 'social determinants of health', which directly influence the occurrence of outcomes of interest to the health public, such as PD (Brucker, 2017).

Common comorbidities, such as hypertension, diabetes, dyslipidemia appeared to be frequent among patients with PD and have been associated with an increase the risk of PD (Martínez-Horta et al., 2021; Santiago, Bottero, & Potashkin, 2017). Our results showed no significant association between diabetes and dyslipidemia and PD. In contrast, we found a decreased risk of PD among patients with hypertension, as shown in table 2. There are contradictory data regarding the association between these comorbidities and PD risk. It is well documented that the prevalence of PD and aforementioned comorbidities, as well as the relationship between those, vary widely due several factors, which can explain divergent observations (Martínez-Horta et al., 2021; Hou et al., 2018; Ng et al., 2021).

Depression and other types of psychological distress are part of the clinical manifestations of patients with PD (Saadat et al., 2020; Weintraub et al., 2022). Depression may occur as a pre-motor symptom or at any stage of PD (Reichmann, 2017). Our results showed no significant association between depression and PD, perhaps due the small sample size or because was underrecognized. Nevertheless, 17.24% of our cases had depression as one of their symptoms. Depression is one of the most common non-motor symptoms in PD patients, present in almost 50% of them (Yapici et al., 2017). However, unfortunately, it is still underrecognized in some patients and, when identified, sometimes it is not properly treated (Marsh, 2013).

Epidemiologic studies have suggested that lifestyle factors play a role in the development of PD (Andrew et al., . Smoking may have a protective effect on PD development, since an inverse association between smoking status and PD risk has been shown by previous studies (Gallo et al., 2019; Gu et al., 2022). Alcohol consumption (Shao et al., 2021) and regular physical activity (Llamas-Velasco et al., 2021) also appear play a protective effect for PD development. We did not find any association between PD risk and smoking and physical activity. Nonetheless, alcohol consumption was associated with a decreased risk of PD (Table 2).

Evidence suggests that certain environmental factors can increase the risk of PD development (Marras et al., 2019) . Our results found no link between some environmental factors (rural living, farming work and self-reported pesticide exposure) and PD risk, which can be explained by the discrepancies among PD cases and controls in terms of the history of living and/or working in rural areas as well as regarding the pesticide exposure. Although this finding did not turn up statistically significant in our analyses, evidence suggests that exposure to pesticides from working in rural areas and/or living in agricultural communities increases the chances of developing a neurodegenerative disease. Nevertheless, associations between rural living, farming work and pesticide exposure are still inconsistent across previous studies (Gunnarsson & Bodin, 2019; Andrew et al., 2021; Breckenridge et al., 2016).

Regardless of pesticide type or toxicity, people who are both directly and indirectly exposed to pesticides can be intoxicated and suffer acute and/or chronic toxic effects (Richardson et al., 2019; Islam & Malik, 2018). For this reason, personal protective equipment (PPE) helps to minimize pesticide exposure and reduce the risk of pesticide poisoning. Although, no significant association was found between the PPE and PD risk in our sample, the low adherence to PPE use was evident. It's worth to highlighting that all our PD cases who reported previous pesticide exposure, 36 % also revelead that never used PPE during application and 67% used them only sometimes. While among controls individuals, 20% reported never used PPE and 65% used just sometimes. There are many cases of poisoning in people who use pesticides, mainly due to poor commitment to the use of PPE. Pesticides can be absorbed via dermal, oral or inhalation routes, however, in most work situations, dermal exposure in the principal route for pesticides applicators or even for people who clean the work equipment's (Macfarlane et al., 2013). Consequently, acute (headache, dizziness, fainting, seizure) and chronic (neurodegenerative diseases, including parkinsonian syndrome) neurological effects may arise from pesticide intoxication (Naughton & Terry, 2018; Eriguchi et al., 2019).

Our results revealed a lack of instruction regarding the correct handling of pesticides and protection measures when purchasing the products. In addition, we observed an inability of some individuals to recognize signs and symptoms of pesticide poisoning, which can explain the absence of self-reported or notified case of intoxication in our sample. The effects of intoxication can appear immediately or only for a few weeks, depending on the active ingredient (Islam & Malik, 2018; Naughton & Terry, 2018), so the individuals may not correlate the symptoms with the pesticide exposure. Therefore, our findings shed light on the importance of adoption of measures to raise awareness of the population, directly and indirectly exposed to agrochemicals, about the impact of these substances on human health. Previous studies have suggested that pesticide exposure can cause brain damage and could be a significant risk factor for neurological disorders, such as cognitive deficits, behavioral and neurodegenerative disease, such as Parkinson's disease (Gunnarsson & Bodin, 2019; Narayan et al., 2017; Medeiros et al., 2020; Negatu et al., 2018).

We identified a high prevalence of neurological symptoms among those individuals exposed to pesticides, where symptoms such as body ache, sleep disorders and memory impairment were often reported by the PD cases and controls (Table 3). These symptoms have also been frequently reported in previous studies that evaluated the impact of occupational pesticide exposure on farmers (Kori et al., 2018; Ong-Artborirak et al., 2022). The high frequency of olfactory dysfunction between cases and controls was also highlighted, this alteration is a recognized prodromal sign of neurodegenerative diseases, such as Parkinson's Disease, occurring at the beginning of the disease process and are commonly found after long-term exposure to pesticides (Benarroch, 2010; Quandt et al., 2017). Thus, health professionals should investigate the relationship between pesticide exposure and neurological symptoms in individuals of groups with occupational exposure, such as agricultural workers. A special attention should be given to the family farmers, which usually are responsible for most of the agricultural production in northeast Brazil. Therefore, they stand out as a population that is highly vulnerable to the effects of pesticide exposure and a higher risk for development of neurological disorders, such as Parkinson's disease.

This study has some limitations. First, by design, case-control studies are prone to recall bias. We used questionnaires to investigate the various aspects of pesticide exposure because of the practicality and low cost that this method represents. Collection through questionnaires and, primarily, via telephone, increases the risk of causing omission of answers or even false information, in addition to the refusal to participate, resulting in underestimated exposure or the absence or weak association between exposure to pesticides and occurrence of PD, as observed in our work. Second, the small simple size can reduce the power of the study. Further research needs to be conducted to increase the sample size and avoid the type II error. Third, the high prevalence of cognitive impairment in the participants due to different clinical conditions prevented a more accurate collection of data, especially those related to work history, as a necessary intermediary of a relative or caregiver.

There also strengths of this study. Although we did not find a significant association between pesticide exposure and PD, our study contributes to exploring the possible toxic effects of pesticides on the central nervous system of rural workers and residents of agricultural communities. The lack of monitoring of pesticide exposure among family farmers can contribute to increase the morbidity risk and mortality of these individuals, due the toxicity and impact of pesticides in their health. Thus, additional studies are needed to elucidate the relationship between pesticide exposure and neurological disorders, such as PD.

## 5. Conclusion

In summary, although a statistically significant association was not found between the pesticide exposure and PD risk, our findings provide new insights into the importance of monitoring the neurological symptoms in individuals exposed to pesticides, since new pesticides continue to be introduced in Brazil with low level of knowledge about safe use practices and population health status. Further studies should be conducted using larger samples, preferably population-based, as well as addressing the risk of PD and other neurological conditions according to the type of pesticide.

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