

Exposure to pesticides and development of hematological cancers: a case-control study

Exposição a agrotóxicos e desenvolvimento de cânceres hematológicos: um estudo caso-controle

Exposición a plaguicidas y desarrollo de cánceres hematológicos: un estudio de casos y controles

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Abstract

The aim of this study was to analyze the association between chronic exposure to pesticides and the development of hematological cancers in a region with intense agricultural activity. This is a hospital-based case-control study. Socioeconomic, demographic, occupational and health-related aspects of patients were investigated. The univariate odds ratio (OR) of cases was verified using logistic regression analysis. In the multivariate analysis, the relevant variables in the model were maintained ($p = 0.05$). There was a predominance of males in the case (54.0%) and control (53.0%) groups. The mean age was 58.8 ± 14.5 years in the case group and 55.6 ± 12.9 years in the control group. It was found that 38.7% of the cases were farmers, and that contact for more than five years with pesticides increases the chances of developing hematological cancers by 2.19 times (OR = 2.19; 95% CI 1, 19 - 4.06). It was also found that the higher the family income, the lower the chances of these neoplasms to appear (OR = 0.26; 95% CI 0.11 - 0.65). In addition, patients who did not have a family history of cancer were 96% less likely (OR = 0.04; 95% CI 0.02 - 0.08) to develop the disease. Chronic exposure to pesticides, family history of cancer and socioeconomic status are associated with greater chances of developing hematological neoplasms. Rural workers exposed to these substances for periods of more than five years are more vulnerable.

Keywords: Hematological neoplasms; Occupational exposure; Pesticides; Toxicology.

Resumo

Objetivou-se neste estudo analisar a associação entre a exposição crônica a agrotóxicos e o desenvolvimento de cânceres hematológicos em uma região de intensa atividade agrícola. Este é um estudo caso-controle de base hospitalar. Aspectos socioeconômicos, demográficos, ocupacionais e relacionados à saúde dos pacientes foram investigados. A razão de chances (OR) univariada dos casos foi verificada por meio de análise de regressão logística. Na análise multivariada, as variáveis relevantes no modelo foram mantidas ($p = 0,05$). Houve predomínio do sexo masculino nos grupos caso (54,0%) e controle (53,0%). A média de idade foi de $58,8 \pm 14,5$ anos no grupo caso e $55,6 \pm 12,9$ anos no grupo controle. Verificou-se que 38,7% dos casos eram agricultores, e que o contato por mais de cinco anos com agrotóxicos aumenta em 2,19 vezes as chances de desenvolver câncer hematológico (OR = 2,19; IC95% 1,19 - 4,06). Verificou-se também que quanto maior a renda familiar, menores são as chances de surgimento dessas neoplasias (OR = 0,26; IC95% 0,11 - 0,65). Além disso, os pacientes que não tinham histórico familiar de câncer tiveram 96% menos probabilidade (OR = 0,04; IC95% 0,02 - 0,08) de desenvolver a doença. A exposição crônica a agrotóxicos, o histórico familiar de câncer e o nível socioeconômico estão associados a maiores chances de

desenvolver neoplasias hematológicas. Os trabalhadores rurais expostos a essas substâncias por períodos superiores a cinco anos são mais vulneráveis.

Palavras-chave: Exposição ocupacional; Neoplasias hematológicas; Pesticidas; Toxicologia.

Resumen

El objetivo de este estudio fue analizar la asociación entre la exposición crónica a plaguicidas y el desarrollo de cánceres hematológicos en una región con intensa actividad agrícola. Este es un estudio de casos y controles basado en un hospital. Se investigaron los aspectos socioeconómicos, demográficos, ocupacionales y relacionados con la salud de los pacientes. La razón de posibilidades (OR) univariante de los casos se verificó mediante análisis de regresión logística. En el análisis multivariado, las variables relevantes en el modelo se mantuvieron ($p = 0,05$). Predominó el sexo masculino en los grupos caso (54,0%) y control (53,0%). La edad media fue de $58,8 \pm 14,5$ años en el grupo de casos y de $55,6 \pm 12,9$ años en el grupo de control. Se encontró que el 38,7% de los casos eran agricultores, y que el contacto durante más de cinco años con plaguicidas aumenta 2,19 veces las posibilidades de desarrollar cánceres hematológicos (OR = 2,19; IC 95% 1, 19 - 4,06). También se encontró que cuanto mayor es el ingreso familiar, menor es la probabilidad de que aparezcan estas neoplasias (OR = 0,26; IC del 95%: 0,11 - 0,65). Además, los pacientes que no tenían antecedentes familiares de cáncer tenían un 96% menos de probabilidades (OR = 0,04; IC del 95%: 0,02 - 0,08) de desarrollar la enfermedad. La exposición crónica a plaguicidas, los antecedentes familiares de cáncer y el nivel socioeconómico se asocian con mayores posibilidades de desarrollar neoplasias hematológicas. Los trabajadores rurales expuestos a estas sustancias durante períodos de más de cinco años son más vulnerables.

Palabras clave: Exposición ocupacional; Neoplasias hematológicas; Plaguicidas; Toxicología.

1. Introduction

Cancer remains a disease with a high incidence and high mortality rates (Bray *et al.*, 2018). The cause of cancer is multifactorial and involves internal and external factors. Internal factors such as heredity, hormonal action and individual immunological conditions have an influence on oncogenesis. However, 80% to 90% of cancer cases are associated with external causes, and it is important to monitor the factors present in the environment (INCA, 2021).

In addition to ionizing radiation, infections and lifestyle, environmental and occupational exposures to chemical substances with carcinogenic potential, such as pesticides, are being increasingly studied (Moura *et al.*, 2020; Vucenik & Stains, 2012). These products, widely used in agriculture and in the domestic environment, are considered human carcinogens, since they act as tumor initiators and / or promoters (International Agency for Research on Cancer, 2015).

Chronic intoxication by organophosphate, pyrethroid and organochlorine pesticides, has been identified as a factor associated with the occurrence of hematological cancers, such as leukemias, lymphomas and myelomas (Lopes & Albuquerque, 2018; Zakerinia, Namdari & Amirghofran, 2012). Diazinon, chlorpyrifos, phosphorus and malathion are examples of active principles associated with the increase of these neoplasms (Hu *et al.*, 2012; Moase & Chan, 2012; Schinasi & Leon, 2014; Weichenthal).

Hematologic cancers concern a heterogeneous group of malignancies that affect hematopoietic precursors in the bone marrow. The organs most involved in this process are blood, bone marrow, lymph nodes, spleen, and liver. In oncological hematology, the main cancers are leukemias, lymphomas and myelomas. These cancers cause immunosuppression, which generally results from a combination of factors that determine the disease itself, as well as antineoplastic treatment (Búrigo *et al.*, 2007).

Since 2008, the Brazilian market has been ranked first in the world ranking of pesticide consumption (Carneiro *et al.*, 2015), and studies have associated morbidity and mortality from cancer with the indiscriminate use of these substances in some regions (Curvo *et al.*, 2013; Dutra *et al.*, 2020). Establishing causal links between the use of pesticides and the occurrence of cancer is a complex process, due to the heterogeneity of the compounds used in agriculture (Dutra & Ferreira, 2019), the difficulties in determining their concentrations in organisms and performing biomonitoring.

However, developing epidemiological studies that relate individual exposures to pesticides with the occurrence of cancer remains essential for public health. In this context, the aim of this study was to analyze the association between chronic exposure to pesticides and the development of hematological cancers in a region with intense agricultural activity.

2. Methodology

2.1 Study design and location

This is an observational, case-control, hospital-based study (IPTSP, 2017). The study was conducted in the municipality of Chapecó, located in the western region of Santa Catarina state, Brazil. The western region covers about 118 municipalities in the state, which together have an estimated population of approximately 1.2 million inhabitants (IBGE, 2010). The region's economy has agricultural activities as one of the main ones, with agriculture having a prominent position (EPAGRI/CEPA, 2019).

2.2 Definition of the sample and study groups

360 patients were included in the present study, 120 cases and 240 controls. The sample was calculated considering a proportion of exposed among the cases of 35.6%, and among the controls of 23.4%, with an odds ratio estimated at 1.8. The level of significance adopted was 5%, the test power 80%, and the ratio of two controls for each case (2:1).

The case group consisted of patients admitted to a referral hospital for haemato-oncological treatment in western Santa Catarina. Patients of both sexes aged over 18 years, with hematological cancer were selected for this group. To make up the control group, twice as many patients, matched for age and sex, over 18 years old, were admitted to the same hospital for different treatments, except for cancer. Patients with a clinical history of other cancers were excluded from the case and control groups, as well as those who did not accept to participate in the study.

2.3 Data collection

After signing the Free and Informed Consent Form, a questionnaire was applied, in the form of an interview, to patients in both groups, containing variables related to socioeconomic, demographic, occupational, toxicological, and health-related aspects. The occupation of the participants was classified according to the Brazilian Classification of Occupations (CBO) of the Ministry of Labor and Employment (MTE), which considers groups from the level of competence and similarity in the activities carried out (MTE, 2010).

Figure 1. Brazilian Classification of Occupations of the Ministry of Labor and Employment.

GG0	Armed Forces, police, and military firefighters
GG1	Senior members of the government, directors of public interest and press organizations and managers
GG2	Professionals in science and the arts
GG3	Mid-level technician
GG4	Administrative service workers
GG5	Service workers, salespeople in stores and markets
GG6	Agricultural, forestry, hunting and fishing workers
GG7	Workers in the production of industrial goods and services*
GG8	Workers in the production of industrial goods and services**
GG9	Maintenance and repair workers

*GG 7 production system workers who tend to be discreet and who deal more with the shape of the product than with its physical-chemical content. ** GG8 workers in production systems that are or tend to be continuous (chemical, steel, among others). Source: MTE (2010). Source: Authors.

To diagnostic confirmation, the analysis of the medical records of each patient was carried out concurrently with the interview by the researchers involved. The data collected through medical records referred to information such as: sex, age, skin color, education, socioeconomic level, place of residence, work activity, lifestyle, type of cancer (primary) and presence of metastasis.

2.4 Ethical aspects

Ethical aspects, aiming to preserve the dignity, rights, safety, and well-being of the research subject were strictly observed, and the study was approved by the Research Ethics Committee involving Human Beings of the Community University of the Region of Chapecó (Unochapecó), under number of opinion 2.942.429.

2.5 Statistical analysis

Descriptive statistics mean and standard deviation and frequency distribution (%) were used. The variables were organized to consider the need for at least 10 cases in each group. Only variables that met this requirement were included in the regression analyzes. The age group variable was subcategorized in thirds. After the descriptive analysis, the data were analyzed to check the univariate odds ratio (OR) of cases with each independent variable, individually, using univariate logistic regression analysis.

The first multivariate model considered the predictor variables 'contact with pesticides' and 'time of contact with pesticides', and the confounding variable 'history of cancer in the family'. This model explained 31.5% of the total variation of the dependent variable (R² of Cox and Snell). Then, there was a correlation between both predictor variables (Spearman's correlation coefficient = -0.492; $p < 0.001$) and the variable 'contact with pesticides', which had the lowest Wald coefficient of the two, was excluded.

Subsequently, the multivariate model was subjected to sensitivity analysis, individually removing and reinserting each independent variable and observing the coefficients and 95% confidence intervals (95% CI), compared with the first adjusted model. Relevant variables were maintained in the model ($\alpha = 0.05$). The final model presented a Cox and Snell R² of 0.333. The results were presented as odds ratio (OR) and its 95% confidence interval (95% CI). The analysis was conducted using the Statistical Package for Social Sciences (SPSS) 20.0 software.

3. Results

3.1 Characterization of cases and controls

The study sample consisted of 360 individuals, 120 cases and 240 controls. The socio-demographic and economic characteristics of the case and control groups are shown in Table 1. In both groups, there was a predominance of males, white skin color, primary education level and married marital status. The mean age of the sample was 50.2 ± 16.2 years, with 58.8 ± 14.5 years in the case group and 55.6 ± 12.9 years in the control group. In the case group, patients aged over 61 years and with a minimum wage prevailed. In the control group, there was predominance of individuals aged 44 years or less, and with an income corresponding to two or three minimum wages.

Table 1. Sociodemographic and economic variables of patients seen at a referral hospital for haemato-oncological treatment in western Santa Catarina, Brazil, 2020.

Variables	Case Group		Control Group	
	N	%	N	%
Gender				
Male	68	54.0	128	53.0
Female	52	46.0	112	47.0
Age (age range)				
≤ 44 years	30	25.0	104	43.3
45 to 60 years	40	33.3	74	30.8
> 61 years	50	41.7	62	25.9
Skin color				
White	96	80.0	187	77.9
Black	5	4.2	2	0.8
Brown	16	13.3	48	20.0
Yellow	3	2.5	2	0.8
Indigenous	0	0.0	1	0.4
Marital status				
Single	16	13.3	63	26.2
Married	84	70.0	153	63.8
Divorced	7	5.9	14	5.8
Widowed	13	10.8	10	4.2
Education level				
Illiterate	5	4.1	6	2.5
Primary	68	56.7	93	38.8
Lower and upper secondary	36	30.0	86	35.8
Post-secondary	11	9.2	55	22.9
Family income				
1 minimum wage	58	48.3	67	27.9
2 or 3 minimum wages	49	40.8	121	50.4
Above 3 minimum wages	13	10.9	52	21.7
Currently working				
Yes	44	36.7	172	71.7
No	76	63.3	68	28.3
Current address				
Urban	80	66.7	181	75.4
Rural	40	33.3	59	24.6
Previous address				
Urban	44	36.7	114	47.5
Rural	76	63.3	126	52.5

Source: Authors.

Regarding professional activity, in contrast to 71.1% of controls who reported working, 63.3% of cases reported that they did not have a professional occupation. Although most cases and controls resided in the urban area at the time of the interview, it is important to highlight the prevalence of the rural area as the previous address for both studied groups (Table 1).

3.2 Life habits, occupation, and workload

When asked about life habits, most cases declared that they were not smokers. Only three patients in the case group (2.5%) and thirteen patients in the control group (5.4%) reported smoking. As for occupation, it was found that 38.7% of cases belonged to the large group 6 of the Brazilian Classification of Occupations, which are characterized as agricultural, forestry,

hunting and fishing workers.

In the control group, 24.7% of the participants were workers in the large group 7, characterized as workers in the production of industrial goods and services, who work more with the shape of the product than with its physical-chemical content.

Regarding the weekly workload, the interviewees in the case group reported working more than 44 hours a week, while those in the control group worked 40 to 44 hours a week. It is noteworthy that rural workers also had a workload of more than 44 hours.

3.3 Exposure to pesticides and cancer

It was found that 70.8% of cases and 81.3% of controls had no current contact with pesticides. However, when evaluating the participants' exposure time to these compounds, it was observed that 9.2% of cases reported exposure for a period of one to five years and 55.0% for six or more years. In the control group, 55.8% of patients did not report exposure to pesticides, as shown in Table 2.

Table 2. Current contact with pesticides and intoxication in patients seen at a referral hospital for haemato-oncological treatment in western Santa Catarina, Brazil, 2020.

Variables	Case group*		Control group**	
	N	%	N	%
Current contact with pesticides				
Yes	35	29.2	45	18.7
No	85	70.8	195	81.3
Contact length				
None	43	35.8	134	55.8
1 up to 5 years	11	9.2	26	10.8
6 or more years	66	55.0	80	33.4
Intoxication symptoms				
Yes	15	12.5	20	8.3
No	105	87.5	220	91.7

Source: Authors.

Among patients with occupational exposure to pesticides, 63.6% of cases and 61.3% of controls reported not using personal protective equipment. Regarding poisoning, 12.5% of cases and 8.3% of controls reported having suffered poisoning from these substances. Of these, 11 cases reported only one episode of intoxication, while four patients had two or more episodes. Intoxications occurred during work activities and only one event was accidental.

When questioned about the family history of neoplasms, 60.0% of the cases stated that they had cancer cases in the family, with 47.2% of these neoplasms in first-degree relatives (parents and children), followed by 43.0% in second degree (grandparents, grandchildren and siblings). In the control group, it was observed that only 15 individuals in this group (6.3%) reported cases of neoplasms in the family.

Among the hematological cancers diagnosed in the cases, there was a predominance of non-Hodgkin's lymphoma, followed by Chronic Myeloid Leukemia and Multiple Myeloma, as shown in Table 3.

Table 3. Types of hematological cancers diagnosed in patients seen at a reference hospital for haemato-oncological treatment in western Santa Catarina, Brazil, 2020.

Diagnosis	N	%
Acute Myeloid Leukemia	12	10.0
Chronic Myeloid Leukemia	26	21.7
Acute Lymphoid Leukemia	4	3.3
Chronic Lymphoid Leukemia	13	10.8
Hodgkin's Lymphoma	14	11.7
Non-Hodgkin's Lymphoma	33	27.5
Multiple Myeloma	18	15.0

Source: Authors.

3.4 Variables analyzed between the case and control groups and their respective odds ratios (OR)

In the univariate logistic regression analysis, statistically significant differences were observed for most of the variables analyzed between the case and control groups, as shown in Table 4.

Table 4. Univariate regression analysis of the main variables with the respective odds ratios (OR), confidence intervals (95% CI) and p values of patients seen at a reference hospital for haemato-oncological treatment in western Santa Catarina, Brazil, 2020.

Variables	Cases		Control		OR (IC 95%)	P
	N	%	N	%		
Gender						0.55
Male	68	34.7	128	65.3	1	
Female	52	31.7	112	68.3	0.87 (0.56-1.36)	
Age (Average = 50,2; DP = 16,2)						
≤44	30	22.4	104	77.6	1	
45-60	40	35.1	74	64.9	1.87 (1.07-3.28)	0.03*
61+	50	44.6	62	55.4	2.79 (1.61-4.85)	<0.001*
Education level						
Primary	73	42.4	99	57.6	1	
Lower and upper secondary	36	29.5	86	70.5	0.57 (0.35-0.93)	0.02*
Post-secondary	11	16.7	55	83.3	0.27 (0.13-0.55)	<0.001*
Family income						
1 Minimum wage	58	46.4	67	53.6	1	
2-3 Minimum wages	49	28.8	121	71.2	0.47 (0.28-0.76)	0.002*
+3 Minimum wages	13	20.0	52	80.0	0.29 (0.14-0.58)	0.001*
Current place of residence						0.08
Urban	80	30.7	181	69.3	1	
Rural	40	40.4	59	59.6	1.53 (0.95-2.48)	
Previous place of residence						0.052
Urban	44	27.8	114	72.2	1	
Rural	76	37.6	126	62.4	1.56 (0.99-2.45)	
Cancer cases in the family						<0.001*
Yes	72	82.8	15	17.2	1	
No	48	17.6	225	82.4	0.04 (0.02-0.08)	
Current occupational risk						0.001*
Yes	47	47.0	53	53.0	1	
No	73	28.1	187	79.9	0.44 (0.27-0.71)	
Previous occupational risk						<0.001*
Yes	64	45.1	78	54.9	1	
No	56	25.7	162	74.3	0.42 (0.27-0.66)	
Workload						<0.001*
≤44 Hours per week	41	22.2	144	77.8	1	
Above 44 hours per week	78	44.8	96	55.2	2.85 (1.81-4.51)	
Current pesticides contact						0.03*

Variables	Cases		Control		OR (IC 95%)	P
	N	%	N	%		
Yes	35	43.8	45	56.3	1	
No	85	30.4	195	69.6	0.56 (0.34-0.93)	
Pesticides contact length						
None	43	24.3	134	75.7	1	
Between 1 and 5 years	11	29.7	26	70.3	1.32 (0.60-2.88)	0.49
Above 5 years	66	45.2	80	54.8	2.57 (1.60-4.13)	<0.001*
Use of EPI (n=360)						
No pesticide contact	45	24.7	137	75.3	1	
Contact with pesticide and PPE use	18	31.6	39	68.4	1.41 (0.73-2.69)	0.31
Contact with pesticide and no PPE use	57	47.1	64	52.9	2.71 (1.66-4.43)	<0.001*
Previous intoxication						0.25
Yes	14	42.4	19	57.6	1	
No	106	32.4	221	67.6	0.65 (0.32-1.35)	

Source: Authors.

3.5 Time of contact with pesticides, family history of cancer and family income: significant association with the development of hematological cancers

For the multivariate analysis, three variables relevant to the model were maintained: time of contact with pesticides, cancer in the family and family income. The results showed that all the variables analyzed showed a significant association with the development of hematological cancers, as shown in Table 5.

Table 5. Final model of the multivariate analysis of the association between the study covariates and development of hematological cancers of patients seen at a reference hospital for haemato-oncological treatment in western Santa Catarina, Brazil, 2020.

Variables	Gross OR (IC 95%)	p	R ²	Adjusted OR (IC 95%) 33,3%	P
Family income		<0.001*	0.05		<0.001*
Minimum wage	1			1	
2-3 Minimum wages	0.47 (0.29-0.76)			0.50 (0.27-0.93)	
+3 Minimum wages	0.29 (0.14-0.58)			0.26 (0.11-0.65)	
Cancer cases in the family		<0.001*	0.30		<0.001*
Yes	1			1	
No	0.04 (0.02-0.08)			0.04 (0.02-0.08)	
Pesticide contact length		<0.001*	0.04		<0.001*
No contact	1			1	
1 to 5 years contact	1.32 (0.60-2.89)			1.56 (0.60-4.05)	
Above 5 years	2.57 (1.60-4.13)			2.19 (1.19-4.06)	

Source: Authors.

4. Discussion

Considering the literature to which we had access, this is the first case-control study carried out in southern Brazil to assess risk factors for the development of hematological cancers. The results showed that prolonged exposure to pesticides, family history of cancer and socioeconomic condition increase the chances for the development of this type of cancer.

In this study, an adjusted odds ratio of 2.19, 95% CI (1.19 - 4.06) was found for participants who had been in contact with pesticides for five years or more. Chronic exposure to these compounds is considered one of the factors associated with the development of cancer, due to the genotoxic, mutagenic, and carcinogenic potential for cells (IARC, 2015). Therefore, this result corroborates the positive association between prolonged exposure to pesticides and the increased chances of occurrence of hematological cancers, found in national and international literature in the last decade (Moura, 2019; Navaranjan *et al.*, 2013).

According to a survey conducted in the studied region, it was shown that organophosphate and carbamate pesticides are widely used and affect the health of rural workers who suffer intoxications, demonstrated by decreased activity of the erythrocyte acetylcholinesterase enzyme (Lorenzatto *et al.*, 2020). Prolonged exposure to compounds belonging to these chemical groups can also increase the risk of hematological cancers (Moura, 2020).

As in the studied region, intoxication of rural workers by pesticides is common in several regions of Brazil Lara *et al.* (2019), Lorenzatto *et al.* (2020), and Moura (2020) due to the intensive use of these products in agriculture, which corresponds to approximately 20% of total use worldwide. Among the active ingredients used, we can mention: glyphosate, 2,4-D, atrazine, carbendazim, cypermethrin, metamidophos and acephate (IBAMA, 2017), all classified as endocrine disruptors (Mnif *et al.*, 2011). The risks associated with cancer have also been evidenced, mainly by the use of glyphosate and 2,4-D, the most consumed pesticides in the country (IARC, 2015).

Among the most prevalent hematological cancers in this study, non-Hodgkin's lymphoma stands out, whose development may also be at greater risk in individuals who use pesticides (Balasubramaniam *et al.*, 2013; Karunanayake, Dosman & Pahwa, 2013; Rudant *et al.*, 2007; Vajdic *et al.*, 2007). In addition to lymphomas, multiple myeloma, which obtained a prevalence of 15% in this study, can be associated with occupational exposure to pesticides Merhi *et al.* (2007) and Perrotta *et al.* (2013), the longer the exposure periods, the greater the chances of developing multiple myeloma (Kachuri *et al.*, 2013; Landgren *et al.*, 2009; Lope *et al.* 2008).

The risks associated with contact with pesticides are difficult to clarify due to the involvement of several factors, such as the period and level of exposure, the age group of individuals, the physical properties of the substances involved (volatility, toxicity and persistence), in addition to the environmental characteristics of contaminated areas (Alavanja *et al.*, 2003; Kim, Kabir & Jahan, 2017). Another important factor is that the chronic effects become apparent after years of exposure and, sometimes, it is not possible to relate the exposure by these substances to the diagnosis of cancer (Londres, 2011).

As exposure to pesticides can be associated with greater chances of developing hematological neoplasms, they are also related to higher mortality rates among rural workers (Coggon *et al.*, 2015). In this case, the work environment becomes conducive to prolonged exposure to carcinogenic substances, which increases the risk of cancer (INCA, 2015). In this study, there was a predominance of agricultural workers in the group (38.7%), which includes farmers, considered the most vulnerable to exposure to pesticides. The farmers have been exposed over the years to different types of pesticides, preparing and applying them. In addition, it can be exposed in the residence itself, through storage, inappropriate disposal and handling of the clothes used during application (Preza & Augusto, 2012; Santos *et al.*, 2017).

As pointed out in this study, out of patients occupationally exposed to pesticides, more than 60% did not use protective equipment, which increases exposure. In Brazilian agriculture, the inappropriate use of personal protective

equipment is a serious problem, and it is common to find rural workers who do not use them during the handling and application of agricultural chemicals, even knowing the risks related to the use of these substances for their health (Moura, 2019; Santos, Borges-Paluch *et al.*, 2017; Viero *et al.*, 2016).

It was not possible to determine the classes of pesticides and the types of chemical substances to which the patients were exposed, since at the time of the interview, the patients were unable to report the names of the active ingredients of the pesticides or their trademarks. This fact calls attention to the lack of knowledge of rural workers about the products they use in their activities.

It is important to note that pesticide poisoning can also occur indirectly, since the environment, springs and water in regions close to agricultural areas may be contaminated with residues of these substances, as well as food (Novais, Queiroz & Seabra Júnior, 2021). In this case, the problem of contamination can extend to urban areas, constituting a risk for the population. The ingestion of contaminated water and food can predispose to the emergence of endocrine diseases and cancer due to the accumulation of pesticides in the body (Palma & Lourencetti, 2011).

Another relevant data found in this study was the significant association between the family cancer history and the risk of hematological cancers. In fact, family histories of cancer, along with age, are important risk factors for most hematological cancers (INCA, 2021). Genetic changes that promote mutations in DNA predispose to the onset of the disease. In addition, with the inherited change, there is a 50% chance that the mutation will be passed on to each of the descendants. This increased risk in people with a hereditary mutation is described as genetic susceptibility (Instituto Oncoguia, 2015).

In this study, it was also found that the lower the family income, the greater the chances of developing hematological cancers. It is known that when financial resources are available, there is an improvement in the quality of life. Lifestyle, education level, socioeconomic conditions and other factors directly interfere in the daily routine for a healthy life. The adoption of a healthy life is an objective of cancer prevention, as it comprises actions that reduce the risks of having the disease. These actions include healthy food, physical activity, maintaining adequate weight, access to health services, use of preventive measures and diagnosis of diseases, in addition to early detection of precancerous conditions (Freire *et al.*, 2019).

Of the patients in the case group, 48.3% had a family income of one minimum wage. Lower income may be associated with more stressful working conditions and greater exposure to occupational risk factors. Low-income individuals have less health concerns and greater difficulty in accessing health services and information. Consequently, it results in a higher incidence of disease and, in turn, a greater need for health care (Santos, Tavares & Barabosa, 2010).

In addition to improving the quality of life, the relationship with health is established due to the higher educational level, which provides individuals with greater capacity to participate in prevention programs, self-care and to cope with health problems (Liu & Hummer, 2008). On the contrary, the low level of education is associated with unhealthy lifestyle habits, morbidity and early mortality (IBGE, 2018).

Although the possibility of memory bias should be considered as a limitation of the study, due to the responses of patients at the time of applying the questionnaires, the results of this research are similar to the findings in other studies. Therefore, they corroborate the hypothesis of increased chances of developing hematological cancers in workers exposed to pesticides (Moura, 2019; Zakerinia, Namdari & Amirghofran, 2012).

Vulnerabilities related to work processes that can increase exposure to these compounds, such as inadequate use of PPE, lack of knowledge about handled pesticides and prolonged exposure time were also verified, as described by Moura (2019).

5. Conclusion

Our results demonstrate that chronic exposure to pesticides, family history of cancer and socioeconomic condition are

associated with greater chances of developing hematological neoplasms. Rural workers exposed to these substances for periods of more than five years are more vulnerable. These data are relevant to public health and constitute yet another warning related to the negative impacts of pesticides on human health.

New studies involving this population need to be carried out, and it is important to investigate the active ingredients of pesticides most used in cases of chronic exposure. In addition, studies involving the analysis of biomarkers would also bring interesting results, making it possible to prove intoxication by these compounds.

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