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Luiza Taciana Rodrigues de Moura[a]
https://orcid.org/0000-0002-3105-228X

Cheila Nataly Galindo Bedor[b]
https://orcid.org/0000-0002-1614-7539

Guilherme Leocádio Medeiros Sobral[c]
https://orcid.org/0000-0003-2999-4179

Vilma Sousa Santana[d]
https://orcid.org/0000-0003-3399-7612

Maria Paula Curado[e]
https://orcid.org/0000-0001-8172-2483

[a] Universidade Federal do Vale do São Francisco, Colegiado de Enfermagem. Petrolina, PE, Brazil.

[b] Universidade Federal do Vale do São Francisco, Colegiado de Ciências Farmacêuticas. Petrolina, PE, Brazil.

[c] Hospital e Maternidade Santa Maria, Araripina, PE, Brazil.

[d] Universidade Federal da Bahia, Instituto de Saúde Coletiva, Programa Integrado de Saúde Ambiental e do Trabalhador. Salvador, BA, Brazil.

[e] A.C. Camargo Câncer Center, Fundação Antônio Prudente, Centro Internacional de Pesquisa e Ensino. São Paulo, SP, Brazil.

Correspondence:
Luiza Taciana Rodrigues de Moura
E-mail:
luiza.taciana@univasf.edu.br

This study was based on a doctoral thesis entitled "Risk factors associated with the presence of hematologic neoplasms in the fruticulture pole Petrolina (PE)/ Juazeiro (BA)] by Luiza Taciana Rodrigues de Moura, presented in 2019 at the Science Graduate Program at Fundação Antônio Prudente, A.C. Camargo Cancer Center, São Paulo, SP, Brazil.

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Occupational factors associated with hematological neoplasms in a fruit production pole: a case-control study

Fatores ocupacionais associados a neoplasias hematológicas em um polo fruticultor: estudo de caso-controle

Abstract

Objectives: to identify the occupational risk factors for hematological neoplasms, specifically leukemia, lymphomas, and multiple myeloma. *Methods:* this is a case-control study. Cases were individuals with hematological neoplasms and controls were individuals with other diagnoses; frequency-matched by sex and age. Individual interviews were conducted by trained researchers using a structured questionnaire. We collected information on participants' occupational history and chemicals use and exposure, in general, and pesticides, in particular. Odds ratios (OR) were used as association measurements, estimated by multivariate non-conditional logistic regression models for exploratory analysis. *Results:* 61 cases and 146 controls were included. We found that agricultural work (OR: 2.18; 95% confidence interval (95%CI): 1.10;4.30), occupational exposure to pesticides (OR: 2.37; 95%CI: 1.18;4.77), and total occupational exposure to pesticides throughout their working life (in hours) — both short (OR: 3.52; 95%CI: 1.25;9.87) and long (OR: 3.95; 95%CI: 1.54;10.14) — constituted risk factors for hematological neoplasms, when compared to those unexposed. We adjusted these measures for alcohol consumption and smoking, physical activity, income, education, and history of occupational exposure to chemicals. *Conclusion*: occupational exposure to pesticides is associated with hematological neoplasms regardless of lifestyle and socioeconomic status.

Keywords: hematologic neoplasms; agriculture; agrochemicals; occupational exposure; occupational health.

Resumo

Objetivos*: identificar fatores de risco ocupacionais para neoplasias hematológicas, leucemia, linfomas e mieloma múltiplo.* Métodos*: estudo caso-controle conduzido com casos de neoplasias hematológicas e controles recrutados do mesmo serviço, com outros diagnósticos, pareados por frequência, sexo e idade. Entrevistas individuais foram realizadas por pesquisadores treinados, utilizando um questionário estruturado. Informações sobre a história ocupacional, uso e características de exposições a substâncias químicas, em geral, e a agrotóxicos foram registradas. Foram estimadas* odds ratios *(OR), por meio de modelos de regressão logística não-condicional multivariável para análise exploratória.* Resultados*: foram incluídos 61 casos e 146 controles. Trabalho na agropecuária (OR: 2,18; intervalo de confiança de 95% (IC95%): 1,10;4,30), exposição ocupacional a agrotóxicos (OR: 2,37; IC95%: 1,18;4,77), e tempo total de exposição ocupacional a agrotóxicos na vida laboral em horas – curto (OR: 3,52; IC95%: 1,25;9,87) e longo (OR: 3,95; IC95%: 1,54;10,14) – foram fatores de risco para neoplasias hematológicas, em comparação aos não expostos. Essas medidas foram ajustadas por consumo de álcool e tabagismo, prática de atividade física, renda, escolaridade e história de exposição ocupacional a produtos químicos.* Conclusão*: a exposição ocupacional a agrotóxicos se associa a neoplasias hematológicas, independentemente de características do estilo de vida e nível socioeconômico.*

Palavras-chave: *neoplasias hematológicas; agricultura; agroquímicos; exposição ocupacional; saúde do trabalhador.*

Introduction

In 2020, estimates suggest that 1,278,362 individuals suffer with hematological neoplasms (HN) worldwide[1], of which 474,519 consisted of new cases of leukemia, 544,352 of non-Hodgkin's lymphoma (NHL), 83,087 of Hodgkin's lymphoma (HL), and 176,404 of multiple myeloma (MM). From 2006 to 2016, the annual incidence of leukemia and lymphomas increased by 26% and 45%, respectively[2], whereas the number of MM cases increased by 126% between 1990-2016[3]. This increase in HN has been attributed, among other aspects, to environmental and occupational risk factors, especially exposure to chemicals [4].

According to the International Agency for Research on Cancer, several chemical carcinogens account for the increased risk of HN. For leukemia, findings from several studies indicate that benzene, butadiene, and formaldehyde (used in industrial processes) and medications such as busulfan, cyclophosphamide, etoposide, melphalan, semustine, and chlorambucil feature among its risk factors[4,5]. Regarding pesticides, research has found diazinon as a probable carcinogen in the IARC 2A Group (due to limited evidence for it as a cause of leukemia)[6].

Specifically for lymphomas, the chemical agents butadiene, cyclosporine, azathioprine and the organochlorine pesticides pentachlorophenol and lindane are associated factors[4,5]. The literature has also found that other pesticides, such as malathion, diazinon, and glyphosate are probably carcinogens in that same group, 2A[6]. Regarding MM, pentachlorophenol and butadiene are chemical carcinogens but the literature still shows insufficient evidence for definitive conclusions about the association between benzene, ethylene oxide, styrene, 1,1,1-trichloroethane, and MM [4,5].

Brazil is the fourth largest exporter of agricultural products in the world. In 2019, its agribusiness goods and services generated R$ 1.55 trillion (or 21.4% of the Brazilian GDP)[7]. Agribusiness is the main consumer of pesticides, and the country is the third largest employer of pesticides per planted area in the world (5.95 kg/ha)[8]. Data from the 2017 agricultural census showed a total of 15 million workers in this industry[9]. Studies have found that occupational exposure to pesticides affects these workers[10] but few have focused on its association with HN.

The Petrolina-Juazeiro fruit production pole was established in the states of Pernambuco and Bahia (in Northeastern Brazil), with an export-oriented economic activity since 1960 and is considered the most developed irrigation pole and one of the most important economic centers in the hinterlands. Due to the high quality of its products (mainly grapes and mangoes), it exports more than 90% of its production to Europe, the United States, and Japan[11].

In addition to the socioeconomic development of the region, investment in irrigated fruit farming, with an emphasis on large monocultures, brought the need for the intense use of pesticides, a characteristic of its agribusiness production model[12]. According to the 2017 agricultural census, this region comprises 14,306 registered agricultural properties, of which 46% use pesticides[9]. A study conducted with small agricultural properties in this region showed that among the 108 pesticides reported, the most used were those in the insecticide class (43.9%), especially pyrethroids (18.4%) and organophosphates (17%)[13].

The impacts of this production model are unevenly distributed in the territory and people who work in rural areas are at the greatest risk of damage to their health due to their continuous and prolonged exposure to these chemical and toxic substances, which points to a process of illness directly related to work and pesticides. In addition to occupational exposure, note that the entire population surrounding agricultural areas can develop chronic consequences from cumulative exposure by drinking water and consuming contaminated food.[12,14]

This area is, therefore, opportune for the study of the association between chemical exposures in general (especially pesticides) and HN. This study aims to identify the occupational risk factors for hematological neoplasms, leukemia, lymphomas, and multiple myeloma.

Methods

Study design and setting

This case-control study was reported according to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. Study subjects were identified in local Unified Health System units, which cover municipalities in the states of Bahia and Pernambuco[15]. Participants were recruited for the case group at the High Complexity Care Unit in Oncology at the Oncology Center of the Regional Hospital of Juazeiro in Bahia, a reference in the treatment of the disease (except for gynecological and childhood cancer) in an area covering 53 municipalities in the states of Bahia and Pernambuco, which constitute the Interstate Health Care Network in the Macro-region of the Middle São Francisco Valley. The control group was recruited at the Regional Hospital of Juazeiro specialty outpatient clinic. Data was collected from October 2016 to July 2018.

Participants

All live patients whose clinical and histopathological diagnoses were recorded — coded by the International Classification of Diseases (ICD-10th Revision[16]) from C81 to C95 (C81-Hodgkin lymphoma, C82-Follicular lymphoma, C83-Non-follicular lymphoma, C84-Mature T/NK-cell lymphomas, C85-Other and unspecified types of non-Hodgkin lymphoma, C86-Other specified types of T/NK-cell lymphoma, C88-Malignant immunoproliferative diseases, C90-Multiple myeloma and malignant plasma cell neoplasms, C91-Lymphoid leukaemia, C92-Myeloid leukaemia, C93-Monocytic leukaemia, C94-Other leukaemias of specified cell type, C95-Leukaemia of unspecified cell type) and were admitted for treatment from 01/01/2013 to 02/28/2018, of both sexes, and aged over 20 years at diagnosis (due to our focus on occupational exposures) were invited to participate in this study. Our exclusion criteria were composed of age below 20 years and death.

Individuals of both sexes without a previous diagnosis of cancer or other lymphohematopoietic diseases who were aged 20 years or above and under outpatient care were considered as meeting the inclusion criteria for the control group. Patients diagnosed with any type of cancer during the research period were excluded. Participants in the control group were selected by a simple random probabilistic method in the same reference healthcare center treating acute and chronic diseases and recruited if they came from the same municipalities in which those in the case group were identified and recruited. Participants in the case group were frequency-matched to those in the control one sex and age in a ratio of 1 case:2 controls.

No sample calculation was performed because the number of patients at the center was small. On February 28, 2018, 52 patients were being actively treated for hematological neoplasms.

Data collection

Lists with the names of patients selected for previously scheduled presential interviews were given to trained interviewers (PhD student and an undergraduate researcher) who were unaware of participants' diagnoses. After discussing our research with participants, they were invited to partake in it and sign informed consent forms. Then, a semi-structured questionnaire — developed for this research by adapting the questionnaire for rural producers on the pesticides used in fruit production[17] by Moura et al. 2018[18] — was applied at a discreet place within the healthcare unit. Both the team and participants were unaware of our study hypothesis. Complementary information on the clinical aspects of the cases was extracted from patients' medical records.

Definition of variables

Our outcome variable were hematological neoplasms (1 = yes, 0 = no) comprising leukemia, lymphoma, and multiple myeloma. The variables on potential associated factors were agricultural work (1 = yes, 0 = no); occupational exposure to pesticides (1 = yes, 0 = no); history of occupational exposure to other chemicals (1 = yes, 0 = no); cumulative exposure to pesticides (in years, 0 = none, 1 =≤ 10, and 2 => 10), time of exposure to pesticides (in hours/day, 0 = none, 1 =≤7, and 2 => 7); and total time of occupational exposure to pesticides in participants' working life (in hours), categorically analyzed as unexposed, short exposure – corresponding to values up to 50% of the distribution – and long exposure (0 = unexposed, 1 =≤ 10,000, and 2 =≥ 10,001). All variables were self-reported.

The variable "other chemicals" was investigated since this study seeks to assess occupational exposure, refraining from restricting its assessment to exposure to pesticides, as its sample was small. Thus, all chemicals were grouped into a single category. Information on this variable was collected by an open question which enabled multiple answers. The most reported chemical products were wall paint, formaldehyde-based cosmetics, and sodium hypochlorite.

Analyses were adjusted for lifestyle variables, such as alcohol consumption (0 = never, 1 = ex-consumer/current consumer); smoking (0 = never, 1 = ex-smoker/current smoker); physical activity (1 = yes, 0 = no); per capita income (0 = ≥ 0.5 minimum wage, 1 = <0.5 minimum wage); educational attainment (0 =≥ 10 years, 1 =< 10 years, and 2 = none); and history of occupational exposure to other chemicals (1 = yes, 0 = no).

Bias control procedures included: 1) adjustment for confounding variables: groups were frequency-matched by sex and age group (20-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years, and 80 years and above) and analyzed via Odds Ratio (OR) by multivariate non-conditional logistic regression; 2) information bias: data was standardly collected by two trained researchers via the same collection instruments for the case and control groups. Participants were unaware of our study hypothesis; and 3) selection bias: participants in the control group were selected by a simple random probabilistic manner (lottery) in the chosen healthcare facility (a reference in the care of acute and chronic clinical diseases) and from the same municipalities as those in the case group.

Statistical analysis

In our analysis, the three assessed malignant neoplasms were pooled due to the small number of specific diagnoses. Association measures correspond to unadjusted and adjusted Odds Ratio, estimated by a non-conditional logistic regression. A stepwise forward modeling was used, starting with the exposure variables with $p<0.05$ (agricultural work, exposure to pesticides, and cumulative exposure to pesticides), analyzed in separate models. The variables considered confounding factors were selected and inserted into the multiple model; the variables "sex" and "age" were excluded from the model because the groups had been matched. In model 2, variables related to lifestyle (alcohol consumption, smoking, and physical activity), socioeconomic variables (per capita income and educational attainment) were considered adjustment variables. In model 3, in addition to the previous variables, history of occupational exposure to other chemicals was added. Missing data from the period of exposure to pesticides (in years and hours/day) in those in the control group were replaced by their arithmetic mean with valid values. A sensitivity analysis of the model was performed with and without imputed data, respectively, to assess if imputation introduced any bias. Statistical inferences were based on 95% confidence intervals, calculated by the likelihood ratio method. The general adjustment of the model was evaluated by -2 log likelihood (-2 LL). Analyses were performed in Epi Info, version 7.2.2.6.

This study was registered on Plataforma Brasil and approved by the Ethics and Deontology Committee in Studies and Research of the Federal University of Vale do São Francisco under CAAE 54635116.5.0000.5196, in 2016 jun 19.

Results

Of the 70 eligible HN patients, 61 (87%) agreed to participate in this study, whereas, of the 180 recruited volunteers in the control group, 146 (81.1%) did. Cases and controls showed a higher proportion of men aged 60 or over who had 10 or less years of schooling, per capita income of half a minimum wage, and originally came from the municipality of Juazeiro, Bahia (**Table 1**).

Table 2 shows that working in agriculture was positively associated with the occurrence of HN (OR: 1.92; 95%CI: 1.04;3.56), as was occupational exposure to pesticides (OR: 1.99; 95%CI: 1.04;3.79) — but not to other chemicals (OR: 0.95; 95%CI: 0.39;2.29). In the case of pesticides, the positive association occurred in those exposed for more than seven hours a day (OR: 2.21; 95%CI: 1.03;4.74), for longer than 10 years (OR: 3.68; 95%CI : 1.35;10.01); and who had short (OR: 3.15; 95%CI: 1.22;8.13) and long (OR: 2.91; 95%CI: 1.22;6.90) occupational exposure to pesticides during their working life (in hours) in the unadjusted model.

We observed that simultaneously adjusting for lifestyle variables, alcohol consumption, smoking, and physical activity, socioeconomic data, per capita income, and schooling failed to significantly change the positive associations with agricultural work, even when we included exposure to other chemicals at work (OR: 2.18; 95%CI: 1.10;4.30), resembling that for occupational exposure to pesticides (OR: 2.37; 95%CI: 1.18;4.77), as did total time of occupational exposure to pesticides during both short (OR: 3.52; 95%CI: 1.25;9.87) and long (OR: 3.95; 95%CI: 1.54;10.14) exposure throughout working life (in hours) (**Table 3)**.

Table 1 Sociodemographic characteristics of cases with hematological neoplasms (HN) and controls. Juazeiro (BA), Petrolina (PE), 2018

Variables	*Cases (n = 61)*		*Controls (n = 146)*	
	n	*%*	*n*	*%*
Sex				
Female	26	42.6	62	42.5
Male	35	57.4	84	57.5
Age (years)				
20 - 39	11	18.0	34	23.2
40 - 59	22	36.1	47	32.2
60 and +	28	45.9	65	44.6
Schooling (years)				
≥10 years	15	24.6	38	26.0
<10 years	32	52.4	84	57.5
Illiterate	14	23.0	24	16.5
Per capita income (minimum wages)				
≥ 0.5	35	57.4	84	57.5
< 0.5	26	42.6	62	42.5
Municipality				
Other NE municipalities	22	36.0	42	28.8
Juazeiro	27	44.3	81	55.5
Petrolina	12	19.7	23	15.7

Legend: NE - Northeast

Table 2 Unadjusted odds ratio (OR) and 95% confidence intervals (95%CI) for the variables "occupational exposure" and "hematological neoplasms" (HN) in cases and controls. Juazeiro (BA), Petrolina (PE), 2018

Variables	*Cases (n=61)*	*Controls (n=146)*	*OR*	*95%CI*
Agricultural work				
Yes	39	70	1.92	(1.04;3.56)
No	22	76	1.00	(--- ---)
Type of occupational exposure				
Pesticides				
Yes	23	34	1.99	(1.04;3.79)
No	38	112	1.00	(--- ---)
Other chemicals				
Yes	8	20	0.95	(0.39;2.29)
No	53	126	1.00	(--- ---)
Pesticides				
Exposure time (years)				
≤ 10	13	26	1.47	(0.68;3.15)
> 10	10	8	3.68	(1.35;10.01)
None	38	112	1.00	(--- ---)
Exposure time (hours/day)				
≤ 7	8	14	1.68	(0.65;4.32)
> 7	15	20	2.21	(1.03;4.74)
None	38	112	1.00	(--- ---)
Total time of occupational exposure to pesticides during working life in hours*				
≤ 10,000 (short)	10	10	3.15	(1.22;8.13)
≥ 10,001 (long)	12	13	2.91	(1.22;6.90)
Not exposed	39	123	1.00	(--- ---)

* Years X hours/day X days/week X 42 weeks per year

Table 3 Unadjusted (ORuna) and adjusted (ORa) odds ratio and association between occupational variables and hematological neoplasms (HN). Juazeiro (BA), Petrolina (PE), 2018.

Models	*Model 1*		*Model 2*		*Model 3 (Final)*	
	ORuna	*95%CI*	*ORa*	*95%CI*	*ORa*	*95%CI*
Agricultural work	1.92	(1.04;3.56)	1.92	(1.00;3.67)	2.18	(1.10;4.30)
Exposure to chemicals	----	(--- ---)	----	(--- ---)	1.12	(0.43;2.90)
Alcohol consumption	----	(--- ---)	0.39	(0.19;0.79)	0.38	(0.18;0.77)
Smoking	----	(--- ---)	0.83	(0.42;1.64)	0.75	(0.38;1.48)
Physical activity	----	(--- ---)	1.19	(0.60;2.35)	1.17	(0.59;2.32)
Per capita income	----	(--- ---)	0.74	(0.28;1.94)	0.75	(0.38;1.47)
Low schooling (<10 years)	----	(--- ---)	0.99	(0.45;2.15)	1.05	(0.47;2.32)
Illiterate	----	(--- ---)	1.57	(0.58;4.25)	1.64	(0.60;4.47)
Exposure to pesticides	1.99	(1.04;3.79)	2.37	(1.18;4.74)	2.37	(1.18;4.77)
Exposure to chemicals	----	(--- ---)	----	(--- ---)	1.02	(0.40;2.62)
Alcohol consumption	----	(--- ---)	0.36	(0.17;0.74)	0.36	(0.17;0.74)
Smoking	----	(--- ---)	0.79	(0.40;1.58)	0.79	(0.40;1.58)
Physical activity	----	(--- ---)	1.16	(0.58;2.30)	1.16	(0.58;2.30)
Per capita income	----	(--- ---)	0.78	(0.40;1.51)	0.78	(0.40;1.52)
Low schooling (<10 years)	----	(--- ---)	1.18	(0.53;2.60)	1.18	(0.53;2.61)
Illiterate	----	(--- ---)	2.06	(0.75;5.66)	2.06	(0.75;5.66)
Total occupational exposure to pesticides during working life (in hours; short)	3.15	(1.22;8.13)	3.48	(1.24;9.69)	3.52	(1.25;9.87)
Exposure to chemicals	----	(--- ---)	----	(--- ---)	1.18	(0.43;3.01)
Alcohol consumption	----	(--- ---)	0.41	(0.18;0.91)	0.41	(0.18;0.91)
Smoking	----	(--- ---)	0.89	(0.41;1.90)	0.88	(0.41;1.90)
Physical activity	----	(--- ---)	0.85	(0.40;1.80)	0.85	(0.40;1.80)
Per capita income	----	(--- ---)	0.63	(0.30;1.33)	0.64	(0.30;1.35)
Low schooling (< 10 years)	----	(--- ---)	0.42	(0.17;1.01)	0.96	(0.40;2.29)
Illiterate	----	(--- ---)	0.44	(0.15;1.26)	2.24	(0.07;6.43)
Total occupational exposure to pesticides during working life (in hours; long)	2.91	(1.22;6.90)	3.95	(1.54;10.11)	3.95	(1.54;10.14)
Exposure to chemicals	----	(--- ---)	----	(--- ---)	0.98	(0.36;2.68)
Alcohol consumption	----	(--- ---)	0.30	(0.13;0.69)	0.30	(0.13;0.69)
Smoking	----	(--- ---)	0.75	(0.36;1.56)	0.75	(0.36;1.56)
Physical activity	----	(--- ---)	1.07	(0.51;2.23)	1.07	(0.51;2.24)
Per capita income	----	(--- ---)	0.71	(0.34;1.46)	0.71	(0.34;1.47)
Low schooling (<10 years)	----	(--- ---)	0.64	(0.26;1.60)	1.26	(0.52;3.00)
Illiterate	----	(--- ---)	0.51	(0.16;1.56)	1.95	(0.63;6.02)

Legend: exp = exposure. Related categories: agricultural work (no); consumption of alcoholic beverages (never); smoking (never); physical activity (yes); per capita income (≥ 0.5 minimum wages); schooling (≥ 10 years); exposure to chemicals (no exposure); exposure to pesticides (no exposure); and total time of exposure to pesticides (no exposure).

Discussion

Other studies have already described the association of HN with agricultural activity[19,20]. Thus, our findings agree with the literature. A scope review aimed to highlight the profile of Brazilian research investigating health outcomes due to exposure to pesticides and found that studies point out to positive correlations between exposure to pesticides, hematological outcomes, and genetic damage in the analyzed subjects[12], which highlights the importance of the association between occupational exposure to pesticides and HN.

The association we found at the Petrolina-Juazeiro fruit production pole may be related to vulnerabilities during agricultural work processes, in which exposure to pesticides in unsafe conditions, without technical guidance on the correct use of these products and monitoring of exposure levels, coupled with social determinants, such as the low levels of schooling and income found among workers in this study, increased the risk of HN[4,21]. Considering other social issues, a study conducted in Mato Grosso municipalities with 4,751 individuals showed that residing between 90 and 300 meters from agricultural crops in rural areas for six to 10 years were associated with the prevalence of cancer in that population[22].

Occupational exposure to pesticides for more than seven hours a day and for longer than 10 years increased the risk of HN, when compared to those unexposed, like the findings of other authors who described an association among organophosphate pesticides, HN[23], NHL[24-27], and leukemia[23,28] in those exposed for a longer time or with greater intensity. Another study also found an association between increased exposure to organochlorines and NHL[27].

Note that other studies have reported a higher frequency of organophosphate and pyrethroid insecticide use in the fruit production pole[13,18,29]. Research has evaluated these pesticides for their carcinogenic potential, such as epigenetic alterations with changes in the expression profile of microRNAs, found in insecticides with dichlorvos and triazofos[30]. A study has showed higher DNA damage and hypermethylation in soybean crop workers exposed to a mixture of herbicides, fungicides, and insecticides (among them, the organophosphates chlorpyrifos, dichlorvos, and profenofos) than in individuals unexposed to pesticides[31].

There is evidence of a significant correlation with pesticide poisoning and oncogenic modulations. At the molecular level, pesticides can cause oxidative stress, act as endocrine disruptors, and modulate gene expression. Such changes primarily harm cells and play a key role in the pathogenesis of various disorders, including cancer[32].

In contrast, our results differ from cohort studies, which failed to find positive associations between organophosphates and a HN group[28,33-35]. These divergent results may stem from different data collection and analysis methodologies, in addition to biases related to measurement of exposure, especially if based only on participants' self-reports, who may have difficulties describing chemicals, intensity of use, and frequency of application throughout their working life[36].

Measuring pesticide exposure in workers is complex. Aspects requiring consideration are intensity of exposure, degree of agent concentration in external and environmental spaces or in doses in the body; exposure time, duration, and frequency, cumulative exposure; windows of susceptibility; and metabolic duration or persistence of the causative agent in the body. Research can also use environmental or biological monitoring data, workplace records or other sources, expert assessments, exposure-work matrices, and questionnaires or interviews with subjects or family members. However, all of these measures may be subject to error[37].

Still, a systematic review, investigating how exposure assessment influenced risk estimates for some chronic diseases, including non-Hodgkin's lymphoma, showed that the method for attributing workers' occupational exposure to pesticides failed to result in different estimates of relative risk. In general, study design, year of publication, and geographic region in which the study was conducted showed greater effects on estimated relative risk than the method to assess exposure[38].

Conclusion

Despite the limitations of this study, such as its small sample size, possibility of memory bias, joint consideration of different hematological malignancies, and its crude assessment of exposure, its statistical analysis showed acceptable confidence intervals, indicating that, despite its methodological weaknesses, it shows significant results and reinforce the hypothesis that occupational exposure to pesticides may be associated with HN, regardless of lifestyle characteristics and socioeconomic status. Thus, we believe that measures to protect workers and ban pesticides associated with increased risk should be recommended.

Research should consider the importance of our type of study, which highlights agricultural workers' occupational risks and vulnerabilities, a population that has difficulties accessing health services and suffers the effects of scarce public policies for their comprehensive health care.

Authors' contribution

Sobral GLM, Moura LTR, Bedor CNG, Santana VS, and Curado MP contributed substantially to the study design, survey, and analysis and interpretation of data. Moura LTR, Bedor CNG, Santana VS, and Curado MP participated in the elaboration, critical revisions of the manuscript, and in the approval of the final published version. All authors assume full public responsibility for the conducted research and the published content.

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