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# Farmers Affected by Hematological Neoplasms and Exposed to Pesticides: A study in southern Brazil

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***Keywords*— Hematologic Neoplasms, Farmers, Agrochemicals, Occupational Health.**

***Abstract*—** *The study analyzed the relationship between the variables of the sociodemographic, clinical and occupational profile of farmers exposed to pesticides undergoing treatment at a reference unit in oncology in southern Brazil with the presence of hematological neoplasms. 72 farmers participated, mostly female, elderly, low education level and rural residents. Leukemia, non-Hodgkin's lymphomas and multiple myeloma prevailed. There was statistical significance between the variables tobacco cultivation and health region with the existence of the disease and when comparing the initial age in agriculture and the daily working hours with the use of different types of pesticides, pointing to a possible relationship between these variables with the presence of hematological neoplasms. Changes in lifestyle and work become important for promoting the health of the rural population.*

## I. INTRODUCTION

Rural workers, in their occupational activity, may be exposed to pesticides, being vulnerable to the harm that contact with these chemicals can cause, making it difficult to measure the effects of chronic exposure on health.[1,2] Pesticides are used on a large scale in the world, including in Brazil, considered one of the world's largest consumers of these products and Rio Grande do Sul is among the states with the highest consumption in the country.[3-5] This excessive use causes numerous damages to the environment and impacts on human health, especially to farmers, since these products are present in the spaces of life and work of these professionals.[2]

Cancer cases have been increasing significantly, especially in developing countries, being considered by the World Health Organization as one of the most significant public health problems today.[6] This disease is characterized by the proliferation of altered cells, which can reach organs and tissues of the human body and become fatal to individuals.[7] In the same proportion, there is also an increase in the worldwide incidence of hematological cancers. [8] In Brazil, leukemia, Hodgkin's

lymphomas (LK) and Non-Hodgkin's lymphoma (NHL), are among the 10 most prevalent types of cancers in the population, with an estimated 12,790 cases in men and 10,720 in women. In the Southern Region, the estimate is 4,790 new cases, 2,720 in men and 2,070 in women, and in the state of RS alone, the projection is 2,170 new cases of the disease, 1,220 in men and 950 in women.[9]

Recent studies are evaluating the association of occupational exposure of farmers exposed to pesticides during their activities with the incidence of cancer, especially with hematological neoplasm.[10-13] Carvalho[14] pointed out the importance of investigating the social and economic factors of rural workers and how they influence the health / disease process, taking into account the occupational risks of this class.

A case-control study, conducted in Brazil, investigated the association between being an agricultural worker and the risk of mortality from (NHL) and found that farmers aged 20-39 years had a 31% higher chance of death from NHL when compared to non-farmers of the same age group.[15] Another study evaluated agricultural use of insecticides, fungicides and specific fumigants and the risk of NHL subtypes, chronic lymphocytic leukemia and multiple myeloma (MM), and demonstrated that pesticides of different chemical and functional classes were associated with the risk of NHL subtypes.[16]

Although the number of cases of hematological neoplasm is not representative when compared to other types of cancer, in Brazil, the increase of the neoplasm is observed, representing an increase of more than 100% in the number of cases in the last 10 years.[9] This fact calls for the investigation of the variables involved in the causes of this increase; however, there are not many studies carried out in the country involving this theme.[8, 15]

Farmers are seen as a group that is vulnerable to cancer. They are considered as a risk group, due to the environment in which they work and because of their work activities, they demand greater exposure to pesticides, since they involve the application of products, transportation, mixing of syrups, handling and disposal of packaging.[14,17] Taking into account that in the South region and in the state of Rio Grande do Sul the pesticide market represents a significant amount in Brazil[18], it is important to study the social demographic and occupational characteristics of the population living in the region, since it is known that there is cultivation of agricultural products, such as tobacco, vegetables and grains, which require the use of pesticides, as already reported in other studies. In addition, in Rio Grande do Sul, cancer is the main cause of death in 140 of its municipalities.[19]

In this context, the objective of this study was to analyze the relationship between the variables of the social demographic, clinical and occupational profile of farmers exposed to pesticides with the presence of hematological neoplasm.

## II. MATERIAL AND METHODS

This is a prospective, quantitative, descriptive, cross-sectional study. This was carried out in a Unit of High complexity in oncology (UNACON) in the interior of the state of Rio Grande do Sul, reference in cancer treatment by the Unified Health System, offering surgical treatment, chemotherapy and radiotherapy. This unit is a reference for 62 municipalities in the 8th, 13th and 16th Regional Health Coordinators (CRS) of the state of Rio Grande do Sul (Figure 1) comprising a population of 852,834 people (SES RS, 2018).

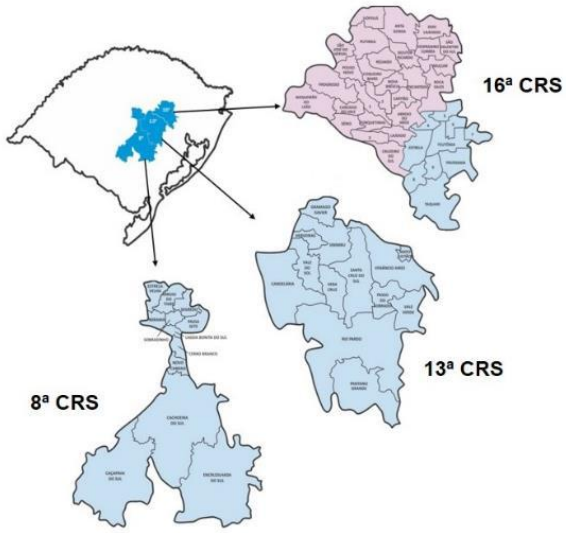


*Fig.1. Map of the 8th, 13th municipalities and 16th Regional Health Coordinators (CRS) of Rio Grande do Sul.*

Source: State Health Secretariat of Rio Grande do Sul, 2020.

The 8th CRS is made up of 12 municipalities, with a population of 200,264 inhabitants. Trade services and activities predominate, corresponding to 42.8% of the Gross Domestic Product (GDP), as well as agricultural activities (36%) and industry (15.8%). Rice, corn, beans, tobacco, soybeans, among others, predominate. The 13th CRS is made up of 13 municipalities, with a population of 327,158 inhabitants, of which 63% live in urban areas and 37% in rural areas. In this region, with regard to products from temporary crops, tobacco stands out in a greater proportion, also the breeding of dairy and beef cattle and

the cultivation of grains, such as rice and wheat, in addition to silviculture and forest exploration. Regarding the Gross Added Value of the Manufacturing Industry, 80% of this is linked to the cultivation of tobacco in the agriculture sector. The 16th CRS is made up of 37 municipalities, with a population of 325,412 inhabitants. The municipalities in this region are responsible for 25% of chicken production, 15% of pig production and 8% of dairy production in RS. The rural properties are small, with an average of 13.50 hectares and are characterized by low grain production in the region.[21] Regarding products from temporary crops, tobacco planting is responsible for 9.3% of the total and for permanent crops, the predominant cultivation is yerba mate, corresponding to 2.7%. The region is second in the state in terms of rural productivity, with a predominant feature in agribusiness activities, with emphasis on the food sector.[22]

The study participants were farmers aged ≥ 18 years, of both sexes, being treated at UNACON during the period of data collection - April and July 2019 -, with a diagnosis of hematological cancer, according to the International Classification of Diseases (ICD), as described in Chart 1. Farmers who did not have exposure to pesticides or who died during the collection period were excluded from the study.

*Chart 1. List of neoplasms according to the International Classification of Diseases (ICD)*

| CODE ICD-10* | NEOPLASM |
|---|---|
| C81 | Hodgkin'sdisease |
| C82 | Non-Hodgkin's lymphoma, follicular (nodular) |
| C83 | Diffuse non-Hodgkin'slymphoma |
| C84 | Cutaneous and peripheral T cell lymphomas |
| C85 | Non-Hodgkin's lymphoma of other types and unspecified types |
| C90 | Multiple myeloma and plasma cell malignancies |
| C91 | Lymphoidleukemia |
| C92 | Myeloidleukemia |
| C93 | Monocyticleukemia |
| C94 | Other cell leukemias of specified type |
| C95 | Leukemia of unspecified cell type |
| C96 | Other and unspecified malignancies of lymphatic, hematopoietic and related tissues |

Source: DATASUS[23]* International Nomenclature of Diseases, established by the World Health Organization.

The total number of patients undergoing cancer treatment for the treatment of hematological neoplasm at UNACON during the study period was 210 patients. Figure 2 shows the patient selection process.

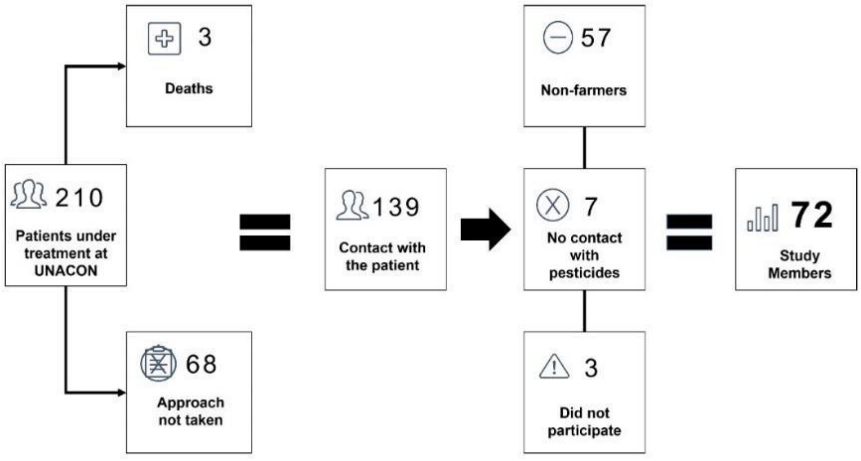


*Fig.2. Selection of the sample of farmers participating in the study.*

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Data collection took place in two stages: in the first, a report was extracted from the institution's computerized management system with the list of patients diagnosed with hematological neoplasm being treated and some information from the electronic medical record, which included the data identification of the subjects, treatment data and the number of services at the institution. Subsequently, in the second stage, the data were collected directly with the patient, through a questionnaire with 42 questions, completed by the collector, which included the following data: social demographic, behavioral, clinical, occupational and referring to previous poisoning by pesticides. The collection instrument was developed by the researcher, based on the adaptation of other research instruments, carried out by Rocha[24], Martins[25] and Faria[17], who used a questionnaire adapted from the international cohort study of the Agricultural Health Study.[26]

The approach to patients took place on the premises of the institution's chemotherapy outpatient clinic, while waiting for the consultation with the doctor or for the application of chemotherapy. An invitation to participate in the research was carried out and, if agreed, the patient signed the Free and Informed Consent Form. The questionnaire was administered to patients individually, on the premises of a multi-professional, comfortable and adequate office, with a table and chair available for the collector, participant and family and / or responsible person.

The questionnaire was applied by the researcher and by two pharmacists from the multi-professional Residency Program in Health - Attention to the Cancer Patient, a proposal developed by the UNACON institution, which aims at the technical training of health professionals to work in the oncology area. The residents received training regarding the application of the questionnaire by the researcher before the collection started.

The data were tabulated and later analyzed using the software Statistical Package for the Social Sciences (SPSS - version 23.0). The analysis consisted of descriptive statistics, with the results expressed as mean and standard deviation, frequency and percentage. The normality of age was verified by the Shapiro-Wilk test. One-Way ANOVA (normal distribution) and Kruskal-Wallis test (non-normal distribution) were used to compare means. For categorical variables, the Chi-Square test was used, considering $p < 0.05$. Multinomial Logistic Regression was used to calculate the odds ratio (odds ratio) between the groups.

The study was approved by the Research Ethics Committee of the University of Santa Cruz do Sul, under opinion number 3.017.507.

## III. RESULTS

The characteristics of the social demographic and lifestyle profile of the farmers participating in the study are described in table 1.

*Table 1. Social demographic and lifestyle profile of farmers*

| **Variable** | **n = 72**<br>**n (%)** |
|---|---|
| **Sex** | |
| Male | 29 (40.3) |
| Female | 43 (59.7) |
| **Age*** | 63.0±12.8 |
| **Marital Status[a]** | |
| Married | 51 (71.8) |
| Widower | 13 (18.3) |
| Others | 7 (9.9) |
| **Skin color** | |
| White | 63 (87.5) |

| | |
|---|---|
| Brown | 7 (9.7) |
| Black | 2 (2.8) |
| **Health region[a]** | |
| 8th HRS | 12 (16.9) |
| 13th HRS | 20 (28.2) |
| 16th HRS | 39 (54.9) |
| **Residencearea[a]** | |
| Rural | 36 (50.7) |
| Urban | 35 (49.3) |
| **Education** | |
| Illiterate | 8 (11.1) |
| IncompleteElementarySchool | 55 (72.2) |
| Complete ElementarySchool | 7 (9.7) |
| Complete high school | 5 (7.0) |
| **Family income** | |
| ≤ R$ 1.000,00 | 1 (1.4) |
| R$ 1.001,00 a 2.000,00 | 26 (36.1) |
| R$ 2.001,00 a 5.000,00 | 28 (38.9) |
| > R$ 5.000,00 | 6 (8.3) |
| Notinformed | 11 (15.3) |
| **Physicalactivity** | |
| Yes | 32 (45.1) |
| No | 40 (54.9) |
| **Bodymass index** | |
| Lowweight | 1 (1.6) |
| Eutrophic | 27 (42.9) |
| Overweight | 19 (30.2) |
| Obese | 16 (25.4) |
| **Smoking** | |
| Neversmoked | 28 (38.9) |
| Yes | 4 (5.6) |
| Ex-smoker | 24 (33.3) |
| Passive smoking | 16 (22.2) |
| **Alcoholconsumption** | |
| Never | 51 (70.8) |
| Rarely | 17 (23.6) |
| 1 to 2 times a week | 2 (2.8) |
| Daily | 2 (2.8) |

*: average and standard deviation; a: 1 missing.

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Table 2 shows the data related to the occupational profile, as well as the exposure to pesticides when exercising the activity of a farmer. Regarding the occupational profile, 9.7% of the participants still worked in agriculture; 77.7% were already retired and / or received some type of aid. As for length of service, 95.8% started agricultural activities before turning 18 and 62.3% worked more than 30 years in agricultural activity.

*Table 2. Occupational characteristics and exposure to farmers' pesticides*

| Variable | n=72 (100)<br>n (%) |
|---|---|
| **Professional activity** | |
| Retired / sickleave | 56 (77.7) |
| Unemployed | 7 (9.7) |
| Farmer | 7 (9.7) |
| Formal employee | 2 (2.8) |
| **Employmentbond** | |
| Owner | 45 (62.5) |
| Employee | 14 (19.4) |
| Temporary | 2 (2.8) |
| Others | 11 (15.3) |
| **Age of onset in agriculture** | |
| <10 anos | 42 (58.3) |
| 11 a 18 anos | 27 (37.5) |
| >18 anos | 3 (4.2) |
| **Time of activity in agriculture[a]** | |
| <10 anos | 7 (11.5) |
| 11 a 20 anos | 9 (14.8) |
| 21 a 30 anos | 7 (11.5) |
| >31anos | 38 (62.3) |
| **Cultivation** | |
| Grains | 69 (95.8) |
| Vegetables | 55 (76.4) |
| Tobacco | 52 (72.2) |
| Yerba mate | 10 (13.9) |
| **Hours of work in the field / day** | |

| | |
|---|---|
| Upto 8h | 23 (31.9) |
| More than 8h | 49 (68.1) |
| **How do you feel after a workday** | |
| Well | 30 (41.6) |
| A littletired | 18 (25.0) |
| Verytired | 22 (30.6) |
| Don’tremember | 2 (2.8) |
| **Pesticidesused** | |
| Insecticide | 13 (18.1) |
| Herbicides | 9 (12.5) |
| Fungicides | 2 (2.8) |
| All | 48 (66.6) |
| **Disposalofpackaging** | |
| Adequate | 29 (40.3) |
| Inappropriate | 43 (59.7) |
| **Use de PPE** | |
| Yes | 38 (52.8) |
| **Frequencyof use** | |
| Sometimes | 8 (21.1) |
| Frequently | 19 (50.0) |
| Always | 11 (28.9) |
| **Whatequipment?** | |
| Closedshoes | 33 (86.9) |
| Hat | 30 (78.9) |
| Gloves | 13 (34.2) |
| Waterproofclothing | 10 (26.3) |
| **Usageguidance** | |
| Yes | 29 (40.3) |
| **Who guided?** | |
| Company | 23 (79.3) |
| Publicdepartments | 4 (13.8) |
| Others | 2 (6.9) |
| **Equipment used in the application** | |
| Coastalsprayer | 40 (55.6) |
| Coastalsprayerandtractor | 11 (15.3) |
| Manual | 11 (15.3) |
| Others | 10 (13.8) |
| **Pesticidepoisoning** | |
| Yes | 26 (36.1) |
| **Discomfortafterpesticide use** | |

| | |
|---|---|
| Yes | 29 (40.3) |
| **What?** | |
| Weakness / dizziness / tremor / headache | 25 (86.2) |
| Gastrointestinal discomfort | 18 (65.1) |
| Muscle aches | 9 (31.0) |
| Sleepdisorders | 7 (24.1) |

** PPE: personal protective equipment; a: 11 missing

Regarding the clinical profile of farmers, in relation to clinical diagnoses, the types of neoplasm were Lymphoma-Hodgkin (32%); Multiple myeloma (27.8%); Lymphoid leukemia (16.6%); Lymphoid leukemia (15.2%); Hodgkin's lymphoma (5.6%) and 2.8% corresponded to other types of leukemia. Most farmers were diagnosed between 1 and 5 years (58.6%). 39 (54.2%) of them had a family history of neoplasm, 30 (41.47) of first degree of kinship. The previous co-morbidities presented that had the highest prevalence were systemic arterial hypertension (44.4%) and depression (22.2%). Regarding the use of medicines for continuous use, 91.7% used them.

When the relation between the social demographic variables and the lifestyle of the farmers was carried out with the presence of hematological neoplasm, it was possible to identify a positive association with the health region and the cultivation of tobacco, according to data in Table 3.

*Table 3. Relationship between social demographic variables and farmers' lifestyle with hematological neoplasm*

| **Variável** | **HL* (n=4) n (%)** | **NHL* (n=23) n (%)** | **MM* (n=20) n (%)** | **Leukemias (n=25) n (%)** | **P** |
|---|---|---|---|---|---|
| **Age*** | 60,7±14,6 | 63,4±11,4 | 66,9±9,3 | 60,0±15,7 | 0.340 |
| **Breed** | | | | | |
| White | 3 (5) | 19 (30) | 18 (29) | 23 (36) | 0.767 |
| Brown | 1 (14) | 3 (43) | 1 (14) | 2 (29) | |
| Black | 0 (0) | 1 (50) | 1 (50) | 0 (0) | |
| **Health Region** | | | | | |
| 8th | 4 (33) | 5 (42) | 1 (8) | 2 (17) | <0.001 |
| 13th | 0 (0) | 4 (20) | 8 (40) | 8 (40) | |
| 16th | 0 (0) | 13 (33) | 11 (28) | 15 (39) | |
| **AreaofResidence** | | | | | |
| Rural | 3 (8) | 8 (22) | 9 (25) | 16 (45) | 0.188 |
| Urban | 1 (3) | 14 (40) | 11 (31) | 9 (26) | |
| **Education** | | | | | |
| Illiterate | 0 (0) | 2 (25) | 4 (50) | 2 (25) | 0.126 |
| Incompleteelementaryschool | 2 (4) | 18 (35) | 14 (26) | 18 (35) | |
| Complete elementaryschool | 2 (29) | 1 (14) | 0 (0) | 4 (57) | |
| Complete high school | 0 (0) | 2 (40) | 2 (40) | 1 (20) | |
| **History Family ofNeoplasm** | | | | | |
| Yes | 4 (10) | 12 (31) | 12 (31) | 11 (28) | 0.192 |
| No | 0 (0) | 11 (33) | 8 (24) | 14 (43) | |
| **Which Family Member** | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| First Grade | 2 (6) | 12 (39) | 10 (32) | 7 (23) | 0.082 |
| SecondDegree | 2 (25) | 0 (0) | 2 (25) | 4 (50) | |
| Third Grade | 0 (0) | 1 (100) | 0 (0) | 0 (0) | |
| **Physicalactivity** | | | | | |
| Yes | 3 (9) | 9 (28) | 11 (35) | 9 (28) | 0.132 |
| No | 0 (0) | 14 (36) | 9 (23) | 16 (41) | |
| **Consumptionofalcoholicbeverage** | | | | | |
| Never | 3 (6) | 16 (31) | 17 (33) | 15 (30) | 0.447 |
| Daily | 0 (0) | 2 (100) | 0 (0) | 0 (0) | |
| From 1 to 2 times a week | 0 (0) | 1 (50) | 0 (0) | 1 (50) | |
| Sporadically | 1 (6) | 4 (23) | 3 (18) | 9 (53) | |
| **Smoking** | | | | | |
| Neversmoked | 0 (0) | 8 (28) | 9 (33) | 11 (39) | 0.676 |
| Smoker | 0 (0) | 2 (50) | 0 (0) | 2 (50) | |
| Ex-smoker | 2 (8) | 9 (38) | 6 (25) | 7 (29) | |
| Passive smoking | 2 (12) | 4 (24) | 5 (32) | 5 (32) | |

*HL: Hodgkin's lymphoma; NHL: Non-Hodgkin's Lymphoma; MM: Multiple Myeloma

Table 4 shows the relation between occupational variables and exposure to pesticides in farmers with hematological neoplasm.

*Table 4. Relation between occupational variables and exposure to pesticides in farmers with hematological neoplasm*

| **Variable** | **HL* (n=4) n (%)** | **NHL* (n=23) n (%)** | **MM* (n=20) n (%)** | **Leukemias (n=25) n (%)** | **p** |
|---|---|---|---|---|---|
| **Professional activity** | | | | | |
| Retired / aid | 3 (5) | 17 (31) | 18 (33) | 18 (33) | 0.884 |
| Unemployed | 1 (14) | 2 (29) | 1 (14) | 3 (43) | |
| Farmer | 0 (0) | 3 (43) | 1 (14) | 3 (43) | |
| Formal employee | 0 (0) | 1 (50) | 0 (0) | 1 (50) | |
| **Starting age in agriculture** | | | | | |
| <10 anos | 4 (10) | 12 (28) | 11 (26) | (36) | 0.343 |
| >11 anos | 0 (0) | 11 (37) | 9 (30) | 10 (33) | |
| **Graincultivation** | | | | | |
| Yes | 4 (6) | 22 (32) | 20 (29) | 23 (33) | 0.580 |
| No | 0 (0) | 1 (33) | 0 (0) | 2 (67) | |
| **GrowingVegetables** | | | | | |
| Yes | 2 (4) | 20 (37) | 16 (29) | 17 (31) | 0.252 |
| No | 2 (12) | 3 (18) | 4 (23) | 8 (47) | |
| **TobaccoGrowing** | | | | | |
| Yes | 1 (2) | 14 (27) | 17 (33) | 20 (38) | 0.040 |
| No | 3 (15) | 9 (45) | 3 (15) | 5 (25) | |

| | | | | | |
|---|---|---|---|---|---|
| **Yerba Mate cultivation** | | | | | |
| Yes | 0 (0) | 3 (30) | 5 (50) | 2 (20) | 0.328 |
| No | 4 (7) | 20 (32) | 15 (24) | 23 (36) | |
| **Pesticideused** | | | | | |
| Formicide | 2 (15) | 7 (35) | 2 (15) | 2 (15) | 0.258 |
| Fungicide | 0 (0) | 0 (0) | 1 (50) | 1 (50) | |
| Herbicide | 1 (11) | 3 (33) | 1 (11) | 4 (45) | |
| All | 1 (11) | 13 (27) | 16 (34) | 18 (38) | |
| **Disposalofpackaging** | | | | | |
| Suitable | 0 (0) | 9 (32) | 7 (25) | 12 (43) | 0.315 |
| Inappropriate | 4 (10) | 14 (32) | 13 (29) | 13 (29) | |
| **Use of PPE*** | | | | | |
| Yes | 1 (2) | 13 (34) | 8 (21) | 16 (43) | 0.268 |
| No | 3 (9) | 10 (29) | 12 (35) | 9 (27) | |

*HL: Hodgkin's lymphoma; NHL: Non-Hodgkin's Lymphoma; MM: Multiple Myeloma; PPE: Personal Protective Equipment

When related to previous co-morbidities with hematological neoplasm, depression showed a significant difference (p=0.026). The use of the types of pesticides was also compared and a significant difference was observed regarding the initial age in agriculture (p=0.027), the daily work (p=0.035), tobacco cultivation (p≤0.01) and not Significance was observed in the area of residence (p=0.055), in the health region (p=0.133), between genders (p=0.133), education (p=0.422), referring to smoking (p=0.432), consumption alcoholic beverages (p=0.371), agricultural activity time (p=0.371), grain cultivation (p=0.83), vegetables (p=0.724) and yerba mate (0.083) and use of PPE (p = 0.368).

Multinomial logistic regression analysis was used to determine the odds ratio. In the association between different hematological neoplasm and smoking, consumption of alcoholic beverages, used pesticides, cultivation of vegetables, tobacco and yerba mate, no differences in the odds ratio were observed, since between the presence of leukemia and MM, the use of PPE showed as a protective factor (OR: 0.26; CI: 0.07-0.99), according to data in table 5.

*Table 5. Association between hematological cancer groups and characteristics of work and lifestyle*

| **Variable** | | **OR (95% CI)** |
|---|---|---|
| | | **Leukemias** |
| **Smoking** | **LNH** | 1.12 (0.21–5.91) |
| | **MM** | 1.12 (0.21–5.91) |
| **Consumptionofalcoholicbeverage** | **LNH** | 1.48 (0.41–5.40) |
| | **MM** | 4.35 ( 0.95-20.03) |
| **Type of pesticide used** | **LNH** | 4.75 (0.81-28.04) |
| | **MM** | 0.94 (0.11-7.97) |
| **Cultivation of Vegetables** | **LNH** | 2.92 (0.63-13.57) |
| | **MM** | 2.31 (0.51-10.57) |
| **TobaccoCultivation** | **LNH** | 0.41 (0.10-1.72) |
| | **MM** | 1.57 (0.28-8.76) |
| **CultivationofYerba Mate** | **LNH** | 1.42 (0.20-10.15) |

| | | |
|---|---|---|
| | **MM** | 3.92 (0.61-25.10) |
| **Use of PPE** | **LNH** | 0.76 (0.21-2.75) |
| | **MM** | 0.26 (0.07-0.99) |

NHL: Non-Hodgkin's Lymphoma; MM: Multiple Myeloma, OR: odds ratio; CI: confidence interval, PPE: personal protective equipment.

## IV. DISCUSSION

The average age found in the study population characterizes the sample as elderly, which coincides with data from the literature indicate that hematological neoplasm usually affect patients older than 59 years.[15,27] However, after relating this variable to the presence of the neoplasm, it was not statistically significant (p=0.340), suggesting that there is no implication of age in presenting or not the disease.

The female sex was predominant among farmers being treated for hematological neoplasm. In the Brazilian state of Piauí, the findings of a survey that investigated the socio-demographic data of rural workers, 63% of the participants were also women[28], contradicting some studies that claim that a large part of the population of active farmers is male.[29,30] However, it should be considered that the population investigated in the present research, for the most part, was not in professional practice and the entire sample was being treated for a malignant disease, whose female life expectancy is higher than that of the male.[9] Still, it is emphasized that the participation of women in agricultural activities, in the territories where agricultural cultivation is characterized for purposes of family subsistence is greater.[28]

Some authors[31, 32] have also shown that there has been an increase in the number of neoplasm in women farmers, particularly in ovarian, pancreatic, breast and acute myeloid leukemia. Thus, it is assumed that the data found in the present study are in line with those found in the literature and although they have not shown statistical significance (p=0.281) when sex is related to the prevalence of the disease, it is an important data since it assumes that female farmers have a better survival prognosis when compared to male farmers.

The education indexes identified reveal that the most of them do not have complete elementary school and some did not even attend school. The education level of farmers in general is low, which could be observed in other studies carried out in Brazil.[15, 28,30,33,34] It thus becomes an aggravating factor for the occurrence of poisoning and death from pesticides, which can be revealed through the notification indicators. In addition, in farmers with low education, the refusal to use Individual Safety Equipment (PPE) is greater than in those with a higher level of education.[30, 35-37] It is important to note that, not only in the health area, education is also a determining factor in people's well-being conditions, acting as a protective factor against poisoning by agrochemicals.[17]

Although education was not shown to be a variable with a significant result (p=0.126) and there was no difference in the analysis of the odds ratio of this variable with the presence of hematological neoplasm (table 5), the low level of education of the sample farmers is an important piece of data, as the lower educational level of farmers can lead to misunderstanding of the guidelines regarding the use of pesticides. The difficulty in reading the labels of the containers of these products can cause mixing and inadequate preparation of the syrups, causing risks of contamination and damage to the health of the handler.[15, 29]

The present study was carried out in a reference center in oncology, which serves a population of a region formed by several ethnic groups, of which those of German, Italian and Azorean origin stand out.[38] The study patients came, in their totality, from municipalities located in these regions and were mostly called white (87.5%). In other studies, in which the presence of hematological neoplasm in farmers was investigated, there was also a predominance of white skin color.[15] In addition, it is highlighted that the majority of farmers came from municipalities of the 16th CRS, in which European colonization is predominant, mainly of German origin.

According to the report of patients in the study, the majority no longer had an occupational activity in agriculture, but a representative part of them still resided in the rural area, a common characteristic of the municipalities in the region where the study was conducted.[39] Thus, even though this variable has not shown a significant relationship with the disease (p=0.188), it is suggested that even without direct contact with pesticides, they could still be exposed to its harmful effects, as they are found in the rural area where these products are more used.[3] A study carried out in Greece, with patients undergoing treatment for myelo-dysplastic syndromes, the findings corroborate those of the present study, in which the majority of the population remained residing in the countryside.[35]

Regarding lifestyle, it was observed that farmers had healthy lifestyle habits, with the exception of physical activity. However, despite the low frequency of alcoholic

beverages and daily consumption of fruits and vegetables prevalent among the participants, the presence of smoking was found in most participants. These data can be considered as protective factors for cardiovascular diseases and cancer, except for the recent or old presence of smoking.[15] Even so, there are studies in the literature that suggest that the rural population has a higher risk for the development of some types of neoplasm, such as hematological ones[10-13], with the greatest risk factor being overexposure to pesticides and the relationship with tobacco[15] , already investigated in this study. Another fact that is important is the prevalence of overweight among farmers, which despite not being significant (p=0.140). Studies assess the presence of obesity with the development of cancers. In the present study, it is not possible to say whether this excess weight may or may not be related to the disease or chemotherapy treatment, since these data were not collected prior to the diagnosis of the neoplasia.

Analyzing the data of the occupational profile, the extensive period of exposure to pesticides of the farmers is verified, which corroborates with other studies and also with statistics about the work activities in the field.[6, 28, 40] Another relevant fact is that 62.5% of the farmers owned the workplaces, which may justify the premature start in the activity, as well as the long period of professional practice in agriculture.

The finding of child labor in agriculture was also highlighted, since it was observed, in this study, that 95.8% of the interviewees started their activities in the sector before the age of 18 years. In the past, it was a very common practice, but a recent study still identified child labor in these places, mainly associated with tobacco cultivation.[41] The International Labor Organization reported that there are still 11% of minors in employment and 59% of them are in agriculture.[42] Since the consequences of these activities as children, they will probably only be seen as adults, when there are manifestations of neoplasms, infertility problems, respiratory, among others.

In the study by Pignati[5], the authors found that in 76% of the planted area in Brazil in 2015, agricultural production of soy, corn and sugarcane prevailed. In addition, tobacco is one of the products that represents a high percentage in the number of total exports of agricultural products in the South Region.[43] Similar data were found in the present study, in which grain cultivation predominated among farmers, followed by vegetables and tobacco. Still, it is worth mentioning the low percentage of yerba mate producers among the sample farmers, due to the lower number of resident patients in the health region where the cultivation of this product is characteristic.

According to a survey presented by Friedrich[44], the most used pesticides in agricultural activity in Brazil, are herbicides, fungicides and insecticides. It was evidenced in the present research that these were also the types of pesticides used by the sample farmers. In a study by Chagas[45], farmers with exposure to pesticides classified as herbicides and fungicides, embraced a high risk for the rise of NHL and MM.

A systematic review by Schinasi and Leon[8] evaluated the relationship between NHL and exposure of rural workers to pesticides, gathering studies, of which twenty of them indicated an association between the disease and exposure to herbicides, four with fungicides and seventeen with insecticides. Research by Rapisarda[46] also suggested the association of hematological neoplasm with exposure to these products. In a study by Avgerinou[35] it was found that patients affected by hematological neoplasm exposed to insecticides and herbicides were more numerous than those patients who had no contact with these products. Those who plant yerba mate can also plant tobacco, so a high prevalence in the use of all the types of pesticides (fungicides, herbicides and insecticides), although not significant (p=0.083). Through the results found, it is suggested that those who had a longer daily workday, used more all types of pesticides, since there was significance when related to the variables (p=0.035).

In another study, the exposure to pesticides of more than 300 thousand rural workers registered in cohort studies in France, Norway and the United States with the presence of hematological neoplasm was analyzed. And the authors' suggestion was that the associations between these variables will depend on the subtype of the pathology and the pesticide used.[47]

In the present study, when the variables health region and tobacco cultivation were related, there was statistical significance ($p \leq 0.001$ and $p=0.040$, respectively), suggesting a possible relationship between tobacco plantation and the health region belonging to the farmer and the presence of neoplasm. The health region with the highest number of cases was from the municipalities belonging to the 16th CRS. In this region, family farming is the main means of production and there are municipalities that are among the largest tobacco producers in the country, which may justify these relationships, suggesting that tobacco cultivation may be related to the presence of the disease.[48] This possible relationship has not yet been pointed out in other studies, as there were no studies on the topic in the region, only in the state and country, in which there is a concern about the excessive use of pesticides in tobacco production, as well

as a high index smoking among farmers and the relationship with the development of cancer.[15, 30, 33]

The inappropriate disposal of pesticide packaging is considered to be another public health problem, since it is waste of highly toxic chemical products, which can harm the environment. Through a survey of the socioeconomic characteristics of tobacco producers in the South, researchers from the Federal University of Rio Grande do Sul found that 52.2% of respondents performed inappropriate waste disposal, including the packaging of pesticides. [40] Similar data were observed in this study, in which 59.7% of farmers also did not correctly dispose of the packaging of the products they used as pesticides and, even though there was no statistical relationship (p=0.315) with the presence of the disease, this data it is relevant, as it points out that education and awareness measures should be carried out with this population.

Regarding the use of PPE, 52.8% responded that they used them, corroborating with data from the literature.[28] However, in relation to the frequency of use of PPE, only 28.9% reported using them always. As for the type of equipment, the most cited were closed shoes (86.9%) and hats (78.9%). It is evident that even having knowledge about the health problems that can be caused by not using PPE, farmers do not seem to perceive the risk, in addition to not being concerned with practices aimed at safety at work.[30,34,49] In the research by Riquinho and Hennington[34] it was also found that most farmers did not adhere to PPE, which is justified because it makes the harvesting process difficult and due to the very hot climate. It is important to note that when comparing leukemia with MM it was observed that farmers who do not use PPE have a higher risk of developing MM among those who use PPE and those who have leukemia.

In this study, more than half of the farmers (55.6%) used the spray sprayer as a tool for applying pesticides, as well as in other studies that assessed the occupational risk of these workers.[50,51] When using this instrument, the applicator is more vulnerable to risks of intoxication or accident, as it is fragile material, being in direct contact with the worker.[52]

Acute intoxications in farmers caused by pesticides are also reported in studies worldwide, but it is known that there is an underreporting of cases, since these workers often do not identify these diseases as related to the use of these products, they often do not seek specialized care for the treatment of symptoms.[34,36,51,53] In our study, part of the sample (36.1%) reported intoxication due to the use of pesticides and 40.3% reported feeling discomfort after applying the products, mainly related to neurological symptoms, such as weakness, dizziness, tremor and headache, corroborating with other research findings.[11,45] Despite these symptoms, the majority reported feeling good after the workday.

In this sense, it is important to intervene by the health teams of the municipalities in guiding farmers about the importance of using PPE, in addition to alerting them about the symptoms of intoxication and about the necessary procedures in cases of intoxication. It is also important that these teams are trained to provide adequate care for these situations, in addition to emphasizing the need for notification of these events in the Notified Diseases Information System (SINAN), which is a very important tool in the health field. , guiding teams in the formulation of strategies that prevent recurrence of injuries and the assessment of actions through indicators that demonstrate the impact of interventions.[28]

The most frequent hematological cancers are leukemia, lymphomas and myelo-dysplastic syndromes.[54] According to the findings of the literature, in the present study, these were also the most representative among the farmers in the sample.

In Thailand, a survey was conducted with orchid producers, which evaluated the effect of exposure to pesticides on immunological, hematological and biochemical parameters. The findings showed that some results pointed to a decrease in the production of B lymphocytes in humans.[50] Other studies have also found hematological changes in pesticide applicators, in which the dependent factors were exposure time, product used and non-use of PPE.[55-57] In the present study, patients also presented these changes, since they were diagnosed with some type of hematological malignancy, which may also be related to the findings of these studies.

Regarding the diagnosis of the disease, 55 (76.4%) of the farmers were due to specific symptoms or because they felt bad due to some clinical manifestation of the disease, while 17 (23.6%) reported that they were undergoing routine. These results may suggest that this population does not have easy access to health or, even, it may be an indicator of the farmer's own disregard for their health. Generally, in rural communities, admission to public health is not as accessible as in other locations, making it an obstacle for these workers to seek medical assistance.[34] In addition, they usually seek health care only when symptoms are already evident and not through routine or preventive exams.

There was a statistical relationship between patients who reported having depression with the presence of hematological neoplasm. This data can be justified by the fact that depression is manifested in greater numbers in patients with NHL (47%) and MM (47%), while only 6% of patients with leukemia and in no case of Hodgkin's lymphoma. There is no way to say whether the disease

manifested itself before or after chemotherapy, but studies suggest the relationship between depression in cancer patients[58, 59] and with the use of pesticides. [37,60,61]

The number of farmers who reported a family history of neoplasm was greater (54.2%) and, of these, in relation to the degree of kinship, 41.47% was first degree. In a case-control study carried out in Greece, it was found that in patients with myelo-dysplastic syndrome, the frequency of reporting a history of hematological neoplasm was higher when compared to controls.[35] It is known that genetic predisposition is a collaborative factor for the development of some diseases, including cancer and, when associated with exposure to pesticides, can contribute to its development.[11,45,62] In the present study, it is suggested that the genetic factor associated with pesticide exposure may have contributed to the development of hematological neoplasm, but not in all cases.

When comparing the use of pesticides with diseases, a significant difference was observed regarding the initial age in agriculture and in the daily work shift, suggesting that these factors may indicate that there was a greater use of all types of pesticides in those farmers who started early on agricultural activity and that fulfilled a greater daily working day, that is, the younger the age and the longer the working day, the greater the use of different types of pesticides.

There was also a significant association in those who grew tobacco, suggesting that farmers who grew tobacco used more types of pesticides than those who did not. In addition, it can be suggested that those who planted yerba mate could also grow tobacco and, therefore, a high prevalence in the use of all pesticides, despite not having statistical significance (p=0.083). These findings may suggest that the early initial age in agriculture, the amount of daily hours worked and the cultivation of tobacco are related to greater exposure to pesticides and consequently becoming risk factors for the development of hematological neoplasm, as evidenced in other studies.[30]

The use of PPE in our study was considered reasonable, but when asked about the frequency, most did not always use the equipment. Even so, when analyzing of the odds ratio between the presence of leukemia and MM, the use of PPE was a protective factor. Other studies[63-65] report on the importance of using these devices in an attempt to control farmers' exposure to pesticides, but as in this research, their adherence and frequency of use was low.

## V. CONCLUSION

Among the findings of the study, the association between tobacco cultivation, health region of the farmers' residence and the existence of the disease stands out, suggesting a possible relationship between them. In this region are located municipalities that are among the largest tobacco producers in the country, which may justify these relationships, suggesting that tobacco cultivation may be related to the presence of the disease.

The study also pointed out an association between the age of beginning work in agriculture, daily working hours and the use of different types of pesticides, suggesting that the earlier the start of work in agriculture and the longer the working day, the greater exposure to different types pesticides, due to the greater concomitant use of fungicides, herbicides and insecticides.

It is noteworthy that all individuals in the research were farmers diagnosed with hematological neoplasms and direct exposure to pesticides. In addition, even though there was no association between the other variables studied, there was evidence that they could be related to the presence of hematologic neoplasia. Since it was evidenced the low level of education of the participants, the long period of exposure to pesticides, as well as the early start in agricultural activities, the non-use of PPE frequently and the concomitant exposure to different types of pesticides.

Regarding the two agricultural products grown in the study region, a large proportion of tobacco producers were found to be affected by hematological neoplasms, in contrast to the small number of producers of yerba mate with the disease.This may suggest that the cultivation of yerba mate affects and exposes farmers less to hematological neoplasms.

It is important to note that the study did not intend to prove the direct relationship between use and exposure to pesticides with the presence of hematological neoplasms among farmers.The multiple genetic, environmental and lifestyle factors need to be considered in the origin of the disease, however, it is important to pay attention to the research results, which point out work factors that can contribute to the presence of these pathologies.

Health promotion strategies are suggested that may include education actions, with the objective of stimulating changes in the lifestyle and work of farmers, greater quality of life, less exposure to pesticides and, consequently, a decrease in the presence of hematological neoplasms.

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