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EXPOSURE TO PESTICIDES AND CANCER OCCURRENCE IN WORKERS OF TWO MUNICIPALITIES OF WEST PARANÁ[1]

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ABSTRACT

Objective: To analyze the association between exposure to pesticides and the occurrence of cancer among workers from the municipalities of Anahy and Vera Cruz do Oeste, Paraná, Brazil. **Method:** This is a quantitative and qualitative study, developed through interviews with 39 participants diagnosed with cancer residing in these cities, conducted between October 2016 and April 2017**. Results:** There was a predominance of elderly participants (84, 63%), rural workers (71.79%) and low education (94.85%). A total of 62.5% participants from Anahy and 46.15% of Vera Cruz do Oeste had a history of direct exposure to pesticides; in all cases, exposure was through agricultural activity; 56.42% the exposure was for more than 30 years. Of the pesticides mentioned by the participants, 47.36% do not have use release in Brazil. There was a prevalence of skin cancers (38.46%), prostate (17.95%) and breast (10.26%). **Conclusion:** It can be said, considering temporality, consistency and biological plausibility, that the association between cancer and exposure to pesticides cannot be denied.

Keywords: Agrochemicals. Neoplasms. Environmental exposure. Occupational exposure.

INTRODUCTION

Worldwide there is an increase in mortality rates and cancer incidence, especially among developing countries. In 2012, there were 14.1 million new cases of cancer and 8.2 million deaths[1]. In Brazil, the estimate of the National Cancer Institute (INCA) for the biennium 2018-2019, points to approximately 600 thousand new cases of cancer[(1)].

Regarding etiology, it is considered that approximately 80% of cancers are related to environmental factors, to a greater or lesser avoidable degree[(2)]. Currently, exposure to pesticideshas been highlighted as an important environmental factor, due to the increase in its use and its possible consequences for human health[(3)].

In 2008, Brazil surpassed the United States of America and became the largest user of pesticides in the world[4]. In 2010, the Brazilian market was responsible for using 19% of the global pesticide market[(4)]. In the country, an average of 12 liters/hectare/year[3] is used. The state of Paraná is the third largest user of pesticides, presenting average values of 9.6 kg/hectare/year[(3)].

According to the Dossier of the Brazilian Association of Collective Health *A warning about the impacts of pesticides on health*[3], the consequences on the use of these products in human health include allergies, gastrointestinal, respiratory, endocrine, reproductive, neurological and mental disorders, suicides and cancer.

Exposure to pesticides has been pointed as a condition potentially associated with the development of cancer by "its possible role as initiators (capable of binding to DNA) or as tumor promoters (capable of acting as cell division stimulants of a carcinogeniccell)"[(5)]. This association has been presented through several studies[(6,7,8,9,10)]. However, the more complex mechanisms of interaction between these substances and the development of cancer have not yet been fully elucidated.

Thus, considering the prevalence of cancer, as well as the high exposure and use of pesticides in the country and in Paraná, it is questioned if there is an association between exposure to pesticides and the occurrence of cancer among rural workers in this study. Thereby, the objective was to analyze the association between exposure to pesticides and the occurrence of cancer among workers from the municipalities of Anahy and Vera Cruz do Oeste, Paraná, Brazil.

[1]Work originating from the Master's thesis in Biosciences and Health, by the State University of Oeste do Paraná.

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METHODOLOGY

This is an exploratory, descriptive and quantitative field study, carried out in the municipalities of Anahy and Vera Cruz do Oeste in Paraná. The first one has a land area of 102,331 km², with 2,874 inhabitants, 73.34% of the households located in the urban and peri-urban areas, while 26.65% are in the rural area. Agricultural production is concentrated in the cultivation of manioc, corn, soybeans and wheat[11]. The second one has a land area of 326,298 km², with 8,958 inhabitants, where 76.48% of the households are in the urban and peri-urban areas, while 33.51% are in the rural area, with agricultural production of corn, soybeans, wheat and sugarcane[11].

These municipalities were chosen for being part of the *Surveillance Project of Populations Exposed to Pesticides* in municipalities of the Tenth Regional Health, of the State Health Secretariat of Paraná and have 100% coverage with Family Health Strategy (ESF) teams.

It was included in the study people older than 18 years of age who have or who had cancer, living in said municipalities, identified from records in the basic health units and crossed with information provided by the Cascavel Oncology Center (CEONC) and Paranaense West Union of Study and Fight against Cancer (UOPECCAN).

Data collection took place between October 2016 and April 2017. A total of 107 people was identified, 32 in Anahy and 75 in Vera Cruz do Oeste. Of this, 31 people were excluded: 13 were not found, 6 were not clinically able to participate, 4 died during the data collection process, 1 was arrested, 2 were under 18 and five refused to participate. participate in the study.

Thus, 76 people composed the initial sample and answered the data collection instrument validated by a pilot test, which included questions about current and previous occupation, exposure to pesticides, knowledge about the effects of pesticides on health, use of personal protective equipment (PPEs), primary anatomical location of the cancer and date of initiation of treatment. Of these, 39 (51.31%) reported direct exposure to pesticides; to whom semi-structured interviews were conducted with respect to the disease and exposure to pesticides, which were recorded and then transcribed in their entirety. Participants were identified with the letter E followed by an equivalent number in the database typing in order to ensure anonymity.

Quantitative data were analyzed based on descriptive statistics. And the interview narratives were analyzed for content and used to compose the analytical arguments.

The ethical precepts of human research were respected in accordance with Resolution 466/2012 of the National Health Council, which revoked Resolution 196/96. The study was approved by the Research Ethics Committee under opinion No. 1,696,960/2016.

RESULTS AND DISCUSSION

According to table 1, most participants (53.33% in Anahy and 54.17% in Vera Cruz do Oeste) are male, over 60 years old. The oldest age found was 83 years, and the youngest age was 48 years. The prevalent age group in Vera Cruz do Oeste was 60 to 70 years (54.16%) and in Anahy, between 70 and 80 years (46.66%). The current place of residence, both in Anahy (53.33%) and Vera Cruz do Oeste (66.67%), is the urban area. There was a low level of schooling, 86.67% participants from Anahy and 83.33% from Vera Cruz do Oeste have incomplete elementary education or are illiterate.

Schooling has been identified as one of the factors that influence the exposure and handling of pesticides[5], which can affect the perception of health and environmental risks associated with it[5]. Respondents recognized the difficulty in understanding the label information due to a lack of understanding of the instructions contained in the packaging (E6; E28; E36), as well as the non-use or inadequate use of Personal Protective Equipment (PPE), (E10, E15, E33)

> [...] since we did not study, it was difficult to read the labels, we used the dosage roughly by the eye and the application as we wished (E1).

> It was without protection, due to ignorance, because we did not understand, had no schooling (E4).

It should be noted that the difficulty of reading the labels is not only a challenge for those with low schooling, but for any worker, given the lack of clarity of the information itself.

Table 1. Characteristics of people with cancer according to gender, age, place of residence and schooling. Anahy and Vera Cruz do Oeste/Paraná, 2017.

Characteristics	Anahy		Vera Cruz do Oeste		General Total	
	N	%	N	%	N	%
Gender						
Male	8	53.33	13	54.17	21	53.85
Female	7	46.67	11	45.83	18	46.15
Total	**15**	**100**	**24**	**100**	**39**	**100**
Age						
40I—50	0	0	2	8.34	2	5.12
50I—60	2	13.34	2	8.34	4	10.25
60I—70	3	20.00	13	54.16	16	41.02
70I—80	7	46.66	4	16.66	11	28.22
80I—90	3	20.00	3	12.50	6	15.39
Total	**15**	**100**	**24**	**100**	**39**	**100**
Place of residence						
Urban	8	53.33	18	75.00	26	66.67
Rural	7	46.67	6	25.00	13	33.33
Total	**15**	**100**	**24**	**100**	**39**	**100**
Schooling						
Incomplete Elementary School	10	66.67	14	58.33	24	61.53
None	3	20.00	6	25	9	23.07
Complete Elementary School	2	13.33	2	8.33	4	10.25
Complete Higher Education	0	0	2	8.33	2	5.15
Total	**15**	**100**	**24**	**100**	**39**	**100**

Source: Researcher's database.

The main labor activity carried out by participants throughout their lives was agriculture 28 (71.79%) (Table 2) being for all of them with direct or indirect exposure to pesticides. In this context, it is considered "direct exposure", the handling of pesticides and related products in any of the stages of storage, transport, preparation, application, disposal and decontamination of equipment and clothing. While "indirect exposure" is due to being around, work or residence in areas near the places where the pesticides are handled or by the work in newly treated areas[12]. Three, besides agriculture, had contact with pesticides through cattle raising (E15, E28, E38).

As for time of exposure to pesticides, an average of 29.66 years, median of 30 years (SD= 15.06; VC = 0.98%), being two years of exposure, the minimum found and 53 the most. It is noteworthy that 11 (28.22%) of the participants claimed a time of exposure between 30 and 40 years; eight (20.51%), between 50 and 60 years and seven (17.94%), between 20 and 30 years (table 2).

Among the main factors that influence the toxicity of pesticides are the time, frequency and route of exposure[2]. The research data show that the time of exposure to pesticides was long, more than 30 years for 22 (56.42%) participants. According to the criterion of temporality (exposure for significant time and before diagnosis)[2], it is possible to estimate that this exposure has influenced, to a greater or lesser degree, the process of carcinogenesis.

In addition to working for many years in agriculture, 13 (33.33%) respondents continue to live in the rural area, which may characterize more indirect exposure through contamination of biota, water and contaminated food, as well as spray drift[3].

> [...] there would be that cloud of BHC (Hexachlorobenzene), the neighbors usually passed in the lowlands, you looked, and everything was white, you could see the excess of poison (E13).

Emphasis is given to long working hours, in which 11 (28.21%) participants claimed to work more than 10 hours a day. The circumstances of the work varied according to the crop and the number of cultivated areas, requiring the worker's dedication in almost full-time, sometimes even on weekends.

> [...] 10 hours was usual, there are days that you work up to 12, 15, 18 hours, I spent the night planting (E15).

> [...] Sometimes we worked on Sundays, in the time to harvest wheat, not to lose any (E20).

Table 2. Characteristics of people with cancer according to main labor activity throughout life, time of exposure to pesticides and primary anatomical location of cancer. Anahy and Vera Cruz do Oeste/Paraná, 2017.

Characteristics	Anahy		Vera Cruz do Oeste		General Total	
	N	%	N	%	N	%
Main work activity throughout life						
Rural worker	13	86.67	15	62.5	28	71.79
Housewife	2	13.33	1	4.17	3	7.69
Driver	0	0	3	12.5	3	7.69
Elderly caregiver	0	0	1	4.17	1	2.56
Agronomist Engineer	0	0	1	4.17	1	2.56
Carpenter	0	0	1	4.17	1	2.56
Machine operator	0	0	1	4.17	1	2.56
Pedagogue	0	0	1	4.17	1	2.56
General Total	**15**	**100**	**24**	**100**	**39**	**100**
Exposure time to pesticides (years)						
0I—10	1	6.66	3	12.5	4	10.25
10I—20	2	13.34	4	16.66	6	15.39
20I—30	3	20	4	16.66	7	17.94
30I—40	4	26.67	7	29.18	11	28.22
40I—50	0	0	3	12.5	3	7.69
50I—60	5	33.33	3	12.5	8	20.51
Total	**15**	**100**	**24**	**100**	**39**	**100**
Primary anatomical location of cancer						
Skin	7	46.67	8	33.33	15	38.46
Prostate	2	13.33	5	20.83	7	17.95
Breast	1	6.67	3	12.50	4	10.26
Intestine	1	6.67	2	8.33	3	7.69
Uterus	1	6.67	2	8.33	3	7.69
Cervix	0	0	2	8.33	2	5.13
Bladder	0	0	1	4.17	1	2.56
Stomach	1	6,67	0	0	1	2.56
Liver	1	6,67	0	0	1	2.56
Lymph nodes	1	6,67	0	0	1	2.56
Neck	0	0	1	4.17	1	2.56
Total	**15**	**100**	**24**	**100**	**39**	**100**

Source: Researcher's database.

Rural workers rarely have stable work schedules (E7; E9; E13; E16; E18; E20; E23; E28; E32; E33; E35; E39), which may aggravate work overload and time of exposure to pesticides

In addition, they are responsible most often for preparing and applying pesticides, characterizing various ways of exposure. Thus, 23 (58.97%) participants performed these tasks and applied the products with a manual spray: 24 (61.53%) cleaned the equipment and 14 (35.89%) washed contaminated clothes, activities that absorption by different routes such as dermal, inhalation and ingestion[5]. Add to this the absence of PPE use by the majority (94.87%) of the participants.

> [...] the sweat, the poison and the clothes would get sticky, it was a poison paste in the body, the poison leaves the body like chalk, the BHC. You must take a bath two or three times with soap to get it out, you stink like poison for a week. It does not leave the skin easily (E13).

> [...] it was without gloves, without a mask, without anything, we were going to work in the garden only with the shirt on top (E28).

The values found in this study on the non-use of PPE were higher than those found by Silva *et al.*[7] in a region of Rio Grande do Sul, where 54% of those surveyed did not use PPE.

There were also reports of spraying with workers nearby or even inside the plantation, exercising other activities, particularly women and rural workers.

> The men sprayed it (pesticides), sometimes they were spraying, and I was moaning weed (E34).

> Usually when we spayed it(pesticides) on cotton we would not go there, but there was corn on the aside we worked aside ... we sprayed poison, very near the corn (E9).

There is warning about the lack of protection of rural workers when reentering in plantations after the application of pesticides and the care with the washing of PPE, which is usually responsibility of women, who do it without protection, causing indirect exposure.

> [...] I would wash his clothes, they were stinky, wet, that's what I washed ... sometimes the clothes were so wet, that I would drain poison(E24).

Regarding the primary anatomical location of the cancer, the prevalence was of skin cancers with 15 cases (38.46%); followed by prostate, seven (17.95%) and breast, four (10.26%) cases (table 2).

Regarding the relationship between exposure to pesticides and the occurrence of cancer, observing the criterion of consistency (similar findings in different population groups)[2], Santos, Lopes and Koifman[13] identified a statistically high incidence Proportion Ratio for melanomas, laryngeal cancer and non-Hodgkin's lymphomas, in Acre rural workers. Silva *et al.*[14], found positive correlations between soybean and corn yields and mortality from prostate cancer in Brazil. It is also worth mentioning the increase in the incidence of alterations in the development of the reproductive tract and in male fertility, related to endocrine disrupting effects of pesticides[10,15].

Arrebola *et al.*[16] identified a potential association between exposure to organochlorine pesticides and the occurrence of breast cancer in the population of a metropolitan region of Tunisia. Silva *et al.*[17] identified cancers of the digestive system and neoplasia of the male and female genital systems as the most found in rural workers hospitalized in a university hospital in Rio Grande do Sul. Indications of long-term effects on human health, is arduous, genotoxicity being one of the important ones, considering the irreversible nature of the process[17]. In addition, other studies have associated the occurrence of cancers on exposure to pesticides[18,19,20,21].

Table 3. Type of pesticides by trade name, main active ingredient and number of citations. Anahy and Vera Cruz do Oeste, 2017

Pesticides	Main active ingredient	Anahy		Vera Cruz do Oeste		Total	
		N	%	N	%	N	%
Azodrin	Monocrotophos	13	86.66	6	25	19	48.71
Nuvacron	Monocrotophos	5	33.33	8	33.33	13	33.33
Folidol	Methyl parathion	8	53.33	5	20.83	13	33.33
Roundup	Glyphosate	3	20	6	25	9	23.07
Aldrin	Fipronil	1	6.66	7	29.16	8	20.51
BHC	*Hexachlorobenzene*	3	20	4	16.66	7	17.94
Did not know	-	1	6.66	6	25	7	17.97
Arrivo	Cypermethrin	1	6.66	1	4.16	2	5.12
Curacron	Profenofos	1	6.66	1	4.16	2	5.12
Nortox	2.4 D	0	0	2	8.33	2	5.12
Tordon	2.4 D	0	0	1	4.16	1	2.56
Trop	Glyphosate	0	0	1	4.16	1	2.56
Tamaron	Metamidophos	0	0	1	4.16	1	2.56
TrifluralinaNortox	Trifluralin	0	0	1	4.16	1	2.56
Abamectina	Abamectin	1	6.66	0	0	1	2.56
Lorsban	Clorpyrifos	1	6.66	0	0	1	2.56
Baygon	Cypermethrin	0	0	1	4.16	1	2.56
In-tec	Nonil Fonol ethoxylate	0	0	1	4.16	1	2.56
Classic	Chlorimuron Ethyl	0	0	1	4.16	1	2.56
Total		**38**	**253.28***	**53**	**220.75***	**91**	**233.26***

Source: Researcher's database.
*The percentage was greater than 100%, since each person could have been exposed to more than one product.

In addition, pesticides as chemical carcinogens can bind to the negative charge nucleus of the DNA resulting in several changes in the structure or expression of certain vital genes[5], the main ones being: alteration of DNA repair or genomic instability, electrophilic character, genotoxicity, epigenetic changes, oxidative stress, chronic inflammation,

immunosuppression, receptor-mediated modulation effects, cell immortalization, cell proliferation and cell death[17]. Thus, it is important to evaluate the impact of human exposure to these products[17].

Among the pesticides to which the participants were exposed (table 3), we highlight Azodrin, cited by 19 (48.71%) participants, Nuvacron and Folidol, both with 13 (33.33%) citations and Roundup, with nine (23.07%).

The number of products cited (19), when compared with other studies, may be considered low, mainly due to memory bias[3,5].

> [...] I have a hard time to remember, the other day I remembered the name of a poison, but now I forgot [E6].

The main pesticide class was insecticides, eight (42.10%), followed by herbicides six (31.58%), probably due to the predominant type of production in the corn, soybean and wheat field in Anahy and corn, soy and sugar cane in Vera Cruz do Oeste.

As far as toxicological classification for humans is concerned, eight (42.10%) are considered extremely toxic, six (31.58%) are moderately toxic and five (26.32%) are highly toxic.

Analyzing these pesticides through the criterion of biological plausibility (when the occurrence of cancer is considered plausible due to the toxicology of the agents under exposure)[2], Das, Shaik and Jamil[22] verified that concentrations of carbofuran, monocrotophos and endosulfan can lead to an induction of damage in the DNA, signaling the genotoxic potential of these compounds. According to IARC, methyl parathion is not classifiable as to its carcinogenicity to humans[23], whereas glyphosate was probably considered to be carcinogenic to humans[23]. Richard *et al.*[24] demonstrated that different formulations based on glyphosate may cause toxic and mutagenic effects in cells involved in reproduction.

In addition to the toxicological question, it is relevant to highlight the situation in the consumer market of the pesticides to which the population was exposed. It was identified that seven (36.84%) are prohibited, seven (36.84%) are released with restrictions of use, two (10.53%) are canceled and three (15.79%) have their use released without restrictions. That is, nine (47,36) of the 19 pesticides mentioned were considered harmful to human and/or environmental health.

Besides, several crops use more than one type of pesticide at the same time, through the cultivation of different crops concomitantly, causing multiple exposure, both the surrounding population, workers and the environment. In this study, 61.53% of the 39 participants report using two or more products, characterizing multi-chemical exposure.

> [...] in the cotton cropthere were a couple of them (pesticides) that were applied mixed (E5).

> [...] it is a mixture of poison, insecticide, fungicide [...] if you apply all the products separately, we would live in the farm [...](E18).

In view of this scenario, it is important to evaluate the biological magnification, in which molecules originating from pesticide application products in crops can recombine and form elements of greater toxicity dispersed in the environment[3]. And it is important to consider that health professionals in rural areas often relate exposure to pesticides, mainly to the occurrence of cancer, depression and intoxication in rural workers[25].

It is understood that human exposure to pesticides is complex and requires a broad knowledge of the problem, discarding the thought that the rural worker deliberately exposes himself to risks arising from the work process.

Lack of evaluation of factors such as diet, genetic factors, virus infection, smoking, alcoholism, among others, may influence the results. In addition, the evaluation based on non-specific categories of substances, obtained exclusively through interview, the small number of participants evaluated and the difficulty of estimating the time, level and intensity of exposure are limiting factors of this study. We also highlight the possible loss of individuals who have or who have had cancer due to not being identified by ESF teams and reference municipalities.

CONCLUSION

According to the results found, it can be said, considering temporality, consistency and

biological plausibility[2], that the association between cancer and exposure to pesticides cannot be denied.

Considering the pesticides that were mentioned, the association is plausible when allied to the fact that 47.36% of them were banned from the market due to their capacity to cause harm to human, animal or environmental health. In addition, 56.42% of participants were exposed for more than 30 years.

Thus, the results show that rural workers are exposed to risks from this exposure. It is associated with the vulnerability of exposure, factors such as low schooling, lack of technical information on the handling of pesticides and the indiscriminate use of these substances.

Although several *in vitro*, *in vivo*, clinical and epidemiological studies point to the association between exposure to pesticides and health hazards, further research is needed to raise awareness of a problem whose medium- and long-term consequences are still not possible to be measured properly.

EXPOSIÇÃO A AGROTÓXICOS E OCORRÊNCIA DE CÂNCER EM TRABALHADORES DE DOIS MUNICÍPIOS DO OESTE DO PARANÁ

RESUMO

Objetivo: Analisar a associação entre exposição a agrotóxicos e a ocorrência de câncer entre trabalhadores dos municípios de Anahy e Vera Cruz do Oeste, Paraná, Brasil. **Método:** Trata-se de um estudo quantitativo e qualitativo, desenvolvido por meio de entrevistas com 39 participantes com diagnóstico de câncer, residentes nos municípios citados, realizadas entre outubro de 2016 e abril de 2017. **Resultados:** Houve predomínio de participantes idosos (84,63%), agricultores (71,79%) e com baixa escolaridade (94,85%). 62,5% dos participantes de Anahy e 46,15% de Vera Cruz do Oeste tinham histórico de exposição direta a agrotóxicos; na totalidade dos casos, a exposição se deu por meio da atividade agrícola; 56,42% a exposição foi por mais de 30 anos. Dos agrotóxicos citados pelos participantes, 47,36% não possuem liberação de uso no Brasil. Houve prevalência de cânceres de pele (38,46%), próstata (17,95%) e mama (10,26%). **Conclusão:** Pode-se dizer, levando em consideração a temporalidade, a consistência e a plausibilidade biológica, que a associação entre o câncer e a exposição a agrotóxicos não pode ser descartada.

Palavras-chave: Agroquímicos. Neoplasia. Exposição ambiental. Exposição ocupacional.

EXPOSICIÓN A PLAGUICIDAS E INCIDENCIA DE CÁNCER EN TRABAJADORES DE DOS MUNICIPIOS DEL OESTE DE PARANÁ

RESUMEN

Objetivo: analizar la asociación entre exposición a plaguicidas y la incidencia de cáncer entre trabajadores de los municipios de Anahy y Vera Cruz do Oeste, Paraná, Brasil. **Método:** se trata de un estudio cuantitativo y cualitativo, desarrollado por medio de entrevistas con 39 participantes con diagnóstico de cáncer, residentes en los municipios nombrados, realizadas entre octubre de 2016 y abril de 2017. **Resultados:** hubo predominio de participantes ancianos (84,63%), agricultores (71,79%) y con baja escolaridad (94,85%). El 62,5% de los participantes de Anahy y el 46,15% de Vera Cruz do Oeste tenían histórico de exposición directa a plaguicidas; en la totalidad de los casos, la exposición ocurrió por la actividad agrícola; el 56,42% la exposición fue por más de 30 años. De los plaguicidas nombrados por los participantes, el 47,36% no posee liberación de uso en Brasil. Hubo prevalencia de cáncer de piel (38,46%), de próstata (17,95%) y de mama (10,26%). **Conclusión:** llevando en consideración la temporalidad, consistencia y plausibilidad biológica, se puede decir que la asociación entre el cáncer y la exposición a plaguicidas no puede ser excluida.

Palabras clave: Agroquímicos. Neoplasia. Exposición ambiental. Exposición ocupacional.

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