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Original Article

Stomach cancer mortality among agricultural workers: results from a death certificate-based case-control study

Mortalidade por câncer de estômago em agricultores: resultados de estudo caso-controle baseado em certificado óbito

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Abstract

Introduction: Pesticide consumption is very high in Brazil. Objective: The present study investigated the stomach cancer mortality among Brazilian agricultural workers in Rio de Janeiro state. Methods: In this case-control study, cases were individuals of both genders, aged ≥20 years, for whom cause of death was ascertained as stomach cancer. Controls were individuals with causes of death other than neoplasm and diseases of the digestive system. Crude and adjusted analyses were carried out. Stomach cancer mortality risk was then estimated for the agricultural workers according to the pesticide expenditures per municipality. Results: Agricultural workers showed an elevated risk of stomach cancer mortality (adjusted OR=1.42; 95%CI: 1.33–1.78). This risk was higher among male workers, aged 50–69 years, white, and among workers with 1–7 years of education. Results also showed increasing stomach cancer mortality along with the increase of pesticide expenditure per agricultural worker. Conclusion: Stomach cancer risk among agricultural workers may be associated with pesticide exposure.

Keywords: mortality; stomach neoplasms; agriculture; epidemiology.

Resumo

Introdução: O consumo de agrotóxicos é muito alto no Brasil. Objetivo: O presente estudo teve por objetivo investigar o risco de morte por câncer de estômago em trabalhadores agrícolas residentes no estado do Rio de Janeiro. Métodos: Neste estudo do tipo caso-controle, casos consistiram em indivíduos de ambos os sexos com 20 anos ou mais, cuja causa de morte foi câncer de estômago. Controles foram indivíduos cuja causa de morte não tenha consistido em qualquer neoplasia ou doenças do sistema digestivo. Análises brutas e ajustadas foram realizadas. O risco de morte por câncer de estômago foi, em seguida, estimado para trabalhadores agrícolas de acordo com a exposição a agrotóxicos e local de residência. Resultados: Trabalhadores agrícolas apresentaram um aumento no risco de morte por câncer de estômago: OR ajustada=1,42 (IC95%: 1,33–1,78). Esse risco foi ainda maior entre homens brancos entre 50 a 69 anos e entre trabalhadores agrícolas com 1 a 7 anos de estudo. Os resultados também mostraram um aumento no risco de morte por câncer de estômago em trabalhadores agrícolas com o aumento da exposição a agrotóxicos. Conclusão: O risco de morte por câncer de estômago entre trabalhadores agrícolas pode estar associado com exposição a agrotóxicos.

Palavras-chave: mortalidade; neoplasias gástricas; agricultura; epidemiologia.

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INTRODUCTION

Exposure to pesticides is a major public health issue, especially in rural areas of developing countries[1,2]. In Brazil, pesticide sales increased 624% between 1992 and 2008, rising from 0.98 to 7.1 US$ billion[3]. This amount of pesticide use makes Brazil one among the top users of pesticides worldwide. During the same period, active farmland increased 25% in Brazil[4], whereas the number of agricultural workers dropped by about 33%, from 33.4 to 22.4 million[5]. These numbers together suggest that pesticide exposure experienced by the Brazilian agricultural workers is likely to be increasing.

Several studies indicate that agricultural workers are at higher risk of several types of cancer[6-10]. Stomach cancer is one of the most implicated ones[11-14], and elevated exposure to pesticides, experienced by this group of workers, is suspected to play a central role in such risk[15,16]. However, such an association is still a matter of debate[17].

The incidence of stomach cancer has declined in recent decades, which has been attributed to improvements in food storage and preservation, reduction of smoking prevalence and adoption of a more diversified diet by the general population[18,19]. However, epidemiologic studies show that, despite this decline, stomach cancer is still the second leading cause of cancer deaths in the world[19]. The highest rates are observed in Asia (37.0 and 23.0/100,000 among men and women, respectively) and the lowest in North America (2.9 and 1.7/100,000 among men and women, respectively). In Brazil, stomach cancer is the third most frequent neoplasm among men (16.2/100,000) and the fifth among women (6.6/100,000). In 2008, 16,832 Brazilians died from stomach cancer, which led to a mortality rate of 8.9/100,000 (13.2 and 5.4/100,000 among men and women, respectively)[20].

Despite evidence of a possible association between agricultural work, pesticide exposure and stomach cancer, this topic has been rarely studied in Brazil. Previous study of the authors of the present study designed to evaluate cancer mortality among agricultural workers from a specific area of the State of Rio de Janeiro, showed that such workers were at 1.14–2.27 times higher risk of stomach cancer mortality, depending on the age and the comparison population[13]. In the present study, death certificates were assessed to investigate the association between agricultural work, pesticide exposure, and mortality for stomach cancer.

METHODS

Cases

In this case-control study, cases were defined as all individuals of both sexes, aged ≥20 years, resident in the State of Rio de Janeiro at the time of death, for whom the main cause of death was ascertained on the death certificate as stomach cancer (International Classification of Disease - ICD -10: C16) from January 1, 1996 to December 31, 2005. Since 1979, the Brazilian Ministry of Health maintains an electronic database, from which mortality data were retrieved, with detailed records of each death that occurred in the country.

Controls

For each case, one control was randomly selected from the universe of all deaths among both sexes, ≥20 years, among residents in the State of Rio de Janeiro at the time of death and for whom the underlying main cause of death was any diagnosis other than a neoplasm (ICD-10: C00–D48) or any disease of the digestive system (ICD-10: K00–K93). Controls were matched with their cases by sex, age (5 years frequency matched) and year of death. Frequency pairing was used only on age.

Any potential cases and controls without occupation listed in the death certificate were excluded from analysis.

Data analysis

Distribution frequency of sex, age strata, race and educational level between cases and controls was compared by the chi-square test. To estimate the risk of death by stomach cancer among the agricultural workers, odds ratios (ORs), and their respective 95% confidence intervals (95%CI), were calculated.

First, crude OR of being agricultural worker among cases against controls was calculated. Logistic regression analysis was then used to calculate the OR adjusted for sex, ethnicity (white *versus* non-white), education (illiterate, 1–7 years of study and ≥8 years of study) and age (20–49, 50–69 and ≥70 years). To evaluate the possible influence of pesticide exposure on the magnitude of stomach cancer mortality risk among agricultural workers, a pesticide exposure index was calculated by dividing the amount of money expended on pesticides in each city of the State of Rio de Janeiro in 1985 by the number of agricultural workers in the respective cities[4]. This index was used in the present study as a surrogate of the agricultural workers' exposure to pesticides. Workers were then grouped in four categories of exposure (low exposure, medium exposure, high exposure and very high exposure), based on the quartiles of pesticide expenditure per agricultural worker. Adjusted ORs were calculated for the stomach cancer mortality among agricultural workers during 1996–2005, using the lowest quartile of pesticide consumption as a reference group. Time lag between data on pesticide expenditures and stomach cancer mortality was purposely used to observe a minimum latency time between exposure to the risk factor (pesticide exposure) and death from a cancer such as stomach cancer[21].

Ethics consideration

As provided in Resolution 196/96, only projects involving survey/research and bibliographic databases originate from public access and use — e.g. Departamento de Informática do Sistema Único de Saúde (DATASUS), excludes the necessity of submission to the Ethics Committee in Research.

RESULTS

Main characteristics of cases and controls are presented in Table 1. Matching of cases and controls resulted in equal proportions of men (61,8%) and women (38%) in both groups. Frequency pairing regarding age led to a similar age distribution among cases and controls. Most cases (52.2%) and controls (55.3%) were white. Moreover, among cases, 11.5% were illiterate, whereas such lack of education was observed among 11.3% of controls. Cases and controls had similar levels of education (Table 1). There were no statistically significant differences between cases and controls on these characteristics.

Crude and adjusted stomach cancer mortality ORs are presented in Table 2. Adjusted OR revealed that stomach cancer mortality was 42% higher among agricultural workers (OR: 1.42; 95%CI: 1.33–1.78) than among non-agricultural workers. Stratification by sex showed that the Agricultural workers magnitude of such risk was higher for male agricultural workers (OR: 1.88; 95%CI: 1.31–2.70) than for female ones (OR: 1.16; 95%CI: 0.49–2.74). The magnitude of stomach cancer mortality risk was also considerably higher among middle-aged agricultural workers (aged 50–69 years) (OR: 1.88; 95%CI: 1.31–2.70). Regarding race, white agricultural workers were the ones to display the highest magnitude of stomach cancer mortality risk (OR: 1.61; 95%CI: 1.20–2.17). Finally, the risk to die by stomach cancer was more evident among agricultural workers with 1–7 years of schooling (OR: 1.47; 95%CI: 1.04–2.09), than among those with >8 years of schooling (OR: 1.17; 95%CI: 0.34–4.06), but only slightly higher than that displayed by illiterate (OR: 1.38; 95%CI: 1.01–1.89) agricultural workers.

There were important modifications in the magnitude of the adjusted OR, when compared to those obtained from crude analysis. Most notably, although the magnitude of the crude stomach cancer mortality risk was much closer for male and female agricultural workers, adjusted OR showed a much more pronounced risk among males. Likewise, crude OR suggested that younger agricultural workers (aged 20–49 years) were at the highest risk to die by stomach cancer, followed by middle-aged, and then by the older agricultural workers (aged ≥70 years). However, adjustment by sex, ethnicity and education produced an important decrease in the magnitude of the risk among the younger agricultural workers, to levels below that observed for middle-aged workers. Modifications in the magnitude of the risk in the other strata were less important.

Table 3 shows ORs of stomach cancer mortality for agricultural workers by level of consumption of pesticides in the locale where the subjects resided. Stomach cancer mortality among agricultural workers was similarly elevated in the 2nd, 3rd and 4th quartiles of pesticide expenditures. Finally, when the risk of death by stomach cancer was estimated only among agricultural workers themselves, using those who resided in the 1st quartile as the comparison group, the highest magnitude of risk was observed among agricultural workers who resided in the highest pesticide-consuming areas (4th quartile), which displayed an excess risk of 35%, though this elevation only achieved borderline of statistical significance (p=0.06).

Table 1. Main characteristics of cases and controls, stomach cancer and agricultural work

	Cases n (%)	Controls n (%)	p-value (χ^2)
Sex			
Men	7,276 (61.8)	7,158 (61.9)	
Women	4,476 (38.0)	4,399 (38.1)	0.970
Age (years)			
20–49	1,413 (12.0)	1,285 (11.1)	
50–69	5,169 (43.9)	5,199 (45.0)	
70+	5,184 (44.1)	5,057 (43.8)	0.062
Ethnicity			
White	6,141 (52.2)	6,392 (55.3)	
Non-white	3,830 (32.6)	4,122 (35.7)	0.244
Education (years of study)			
Illiterate	1,356 (11.5)	1,311 (11.3)	
1–7	3,738 (31.8)	3,419 (29.6)	
8+	1,614 (13.7)	1,618 (14.0)	0.080
Total	11,766 (100)	11,557 (100)	

DISCUSSION

In the present study, the Brazilian death certificate database allowed to investigate the association between agricultural work, pesticide exposure and stomach cancer mortality through a case-control study. The use of mortality databases to investigate health problems, such as a cancer, potentially associated with an occupation has been extensively explored, although only recently in Brazil[10,22-26]. However, there are some potential issues regarding the quality of data registered in such databases that need to be addressed. Underreporting and misclassification of deaths still represent a problem in the Brazilian Mortality Information System[27], but in a much less extent in the most developed states of the country, such as Rio de Janeiro. Misclassification could also have been introduced regarding information about occupation. In the Brazilian Mortality Information System, the last

Table 2. Crude and adjusted risks of stomach cancer mortality among agricultural workers of Rio de Janeiro State, 1996–2005

	Cases	Controls	Crude OR (95%CI)	Adjusted OR (95%CI)
Total				
Agricultural workers	384	237	1.61 (1.37–1.90)	1.42 (1.33–1.78)*
Non-agricultural workers	11,382	11,320		
Gender				
Male				
Agricultural workers	356	219	1.63 (1.37–1.94)	1.88 (1.31–2.70)**
Non-agricultural workers	6,920	6,939		
Female				
Agricultural workers	27	18	1.48 (0.81–2.69)	1.16 (0.49–2.74)**
Non-agricultural workers	4,449	4,381		
Age (years)				
20–49				
Agricultural workers	35	15	2.15 (1.17–3.96)	1.42 (0.52–3.89)***
Non-agricultural workers	1,378	1,270		
50–69				
Agricultural workers	165	91	1.85 (1.43–2.40)	1.88 (1.31–2.70)***
Non-agricultural workers	5,004	5,108		
70+				
Agricultural workers	184	131	1.38 (1.10–1.74)	1.15 (0.85–1.56)***
Non-agricultural workers	5,000	4,926		
Race				
White				
Agricultural workers	193	130	1.56 (1.25–1.96)	1.61 (1.20–2.17)****
Non-agricultural workers	5,948	6,262		
Non-white				
Agricultural workers	118	91	1.41 (1.07–1.86)	1.17 (0.83–1.67)****
Non-agricultural workers	3,712	4,031		
Educational level (years of school)				
Illiterate				
Agricultural workers	129	82	1.58 (1.18–2.10)	1.38 (1.01–1.89)*****
Non-agricultural workers	1,227	1,229		
1–7				
Agricultural workers	88	54	1.50 (1.07–2.12)	1.47 (1.04–2.09)*****
Non-agricultural workers	3,650	3,365		
8+				
Agricultural workers	5	5	1.00 (0.29–3.47)	1.17 (0.34–4.06)*****
Non-agricultural workers	1,609	1,613		

*adjusted by sex, age, ethnicity and education; **adjusted by age, ethnicity and education; ***adjusted by sex, ethnicity and education; ****adjusted by sex, age and education; *****adjusted by sex, age and ethnicity.

Table 3. Crude and adjusted risk to die by stomach cancer among agricultural workers of the State of Rio de Janeiro, according to the level of pesticide use, 1996–2005

	Cases	Controls	Crude OR (95CI)	Adjusted OR (95%CI)[1*]	OR (95%CI) Agriculture workers only
1st quartile					
Agricultural workers	103	72	1.36 (1.01–1.84)	1.12 (0.76–1.66)	
Non-agricultural workers	7,196	6,848			
2nd quartile					
Agricultural workers	69	49	1.56 (1.07–2.27)	1.59 (0.93–2.73)	0.98 (0.60–1.63)
Non-agricultural workers	1,143	1,268			
3rd quartile					
Agricultural workers	77	46	1.67 (1.15–2.42)	1.81 (1.08–3.05)	1.17 (0.71–1.93)
Non-agricultural workers	1,788	1,784			
4th quartile					
Agricultural workers	120	62	1.82 (1.32–2.51)	1.58 (0.99–2.53)	1.35 (0.86–2.13)
Non-agricultural workers	963	907			
p_{Trend}			0.02	0.28	0.06

*Adjusted by sex, age, ethnicity and education.

and main job is the one that is registered. Therefore, for certain occupations, the high mobility between different jobs, which may represent exposure to different potential risk factors, may not be adequately evaluated in studies such as the present one. However, unlike the urban population, farming is a lifetime job in Brazil, especially in areas where small-to-medium properties are worked by family members, such as in the mountain region of Rio de Janeiro State[13].

Another limitation of the study is the fact that death certificates contain no information about the number of years that individuals worked as agricultural workers. Such information would have helped to improve the evaluation of the association between agricultural work and stomach cancer, as it could have been explored if larger periods as agricultural worker could increase the magnitude of the stomach cancer mortality risk.

Despite these limitations, the results suggest that agricultural workers were at higher risk to die by stomach cancer, when compared with non-agricultural workers. Such risk was even higher when adjusted for sex, age, ethnicity and education. Similar results were observed in a study conducted in Sweden, where agricultural workers were also at higher risk to die by gastric cancers[28]. Although this increase has not been observed in some other studies[17,29], a meta-analysis observed a significant association between pesticide exposure and stomach cancer among agricultural workers[11].

In the present study, male agricultural workers had a 1.88 greater likelihood to die by stomach cancer compared with non-agricultural workers. This finding is consistent with the international literature, which shows that stomach cancer is more common in men than women. In addition, illiterate agricultural workers were at considerably higher risk to die by stomach cancer than illiterate non-agricultural workers. Once more, several studies support these results as they clearly indicate an inverse correlation between education level and the risk of death by stomach cancer[30-32]. However, in a study performed in Japan such an association was not observed[33].

The results also showed that white agricultural workers had 61% more chance of dying from stomach cancer when compared with white non-agricultural workers. According to a study conducted in USA[34], rates of gastric cardia cancer were higher among non-Hispanic white men. In addition, survival of gastric cancer was also poorer among non-Hispanic whites than among individuals from any other ethnic group, according to another study conducted in USA[35]. Moreover, agricultural workers aged 20–49 years had a 2.15 greater risk of dying from stomach cancer compared with non- agricultural workers in the same age group. Other studies have similarly found elevated risks of stomach cancer among young subjects[36,37].

Agricultural workers are not solely exposed to pesticides. In fact, due to their professional activities, life style and living environment, they may be exposed to several other risk factors for stomach cancer. For instance, besides the use of pesticides, agricultural workers use large amounts of fertilizers to increase productivity. An important class of fertilizers comprises nitrate compounds, and some studies present evidences that exposure to these compounds may increase the risk of stomach cancer, presumably through the endogenous formation of nitrosamine compounds from nitrate[38-41]. Ingestion of food conserved in salt, which is also a known risk factor for stomach cancer, may be quite high in rural areas[18,42,43]. A similar situation is observed for the infection by the bacterium *Helicobacter pylori*, which is another important risk factor for stomach cancer[44-46]. Prevalence of such infection is considerably more frequent in rural than in urban areas[47].

In this current study, the higher the pesticide use, the higher was the magnitude of the stomach cancer mortality risk among agricultural workers, whether compared with agricultural or non-agricultural workers who resided in the lowest pesticide-consuming quartile. These results are similar to others obtained in different countries. In 40 districts of Ontario, Canada a study observed that the levels of atrazine in the drinking water were positively associated with the incidence of stomach cancer[48]. In a case-control study conducted in Sweden, a positive association between pesticide exposure, mainly phenoxyacetic acids, and stomach cancer was observed[49]. Another case-control study found that Hispanic farm workers from California, USA, exposed to the 2,4-dichlorophenoxyacetic acid, chlordane, propargite and triflurin were more likely to develop stomach cancer[39]. Finally, stomach cancer mortality risk was also significantly elevated among residents of Sardinia, Italy, who were exposed to dichlorodiphenyltrichloroethane[9].

CONCLUSIONS

Results of the present study suggest that agricultural workers were at significantly higher risk of death by stomach cancer, when compared with non-agricultural workers. The magnitude of such risk was higher among male workers, aged 50–69 years, white and with 1–7 years of schooling. In addition, the magnitude of stomach cancer mortality risk was also higher among those agricultural workers who resided in areas where pesticide use was more intense.

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