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Brain cancer mortality among farm workers of the State of Rio de Janeiro, Brazil: A population-based case–control study, 1996–2005

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ABSTRACT

Background: Farm workers seem to be at an increased risk of developing some cancers, notably in the brain. One of the hypotheses rose to explain such elevated risk is the intense exposure to pesticides.
Aim: To estimate the brain cancer mortality risk among agricultural workers exposed to pesticides in the State of Rio de Janeiro, Brazil.
Methods: A case–control study based on death certificates of males, 18 years or older, resident in the State Rio de Janeiro who died between 1996 and 2005. Cases ($n = 2040$) were defined as individuals with brain cancer as the underlying cause of death. For each case two controls ($n = 4140$) were randomly selected in the same database, matched for age group and region of residence. Besides the descriptive analysis, crude and adjusted odds ratios and mortality odds ratio (MOR) according to quartiles of potential exposure to pesticides, were calculated.
Results: Agricultural workers showed higher brain cancer mortality risk estimates when compared with non-farm workers (aOR: 1.82, 95% CI 1.21–2.71). In addition, the magnitude of this association was higher among white patients, with higher education, and residence in an agricultural region.
Conclusion: This study suggests an association between agricultural work and brain cancer mortality in Rio de Janeiro state. It also suggests that pesticide exposure may play a role in such risk.

Introduction

In Brazil, malignant neoplasms of the central nervous system represent an important cause of death. In 2007, these tumors were the eighth most common among Brazilian men (Brazil, 2008). Their incidence and mortality have been increasing during recent decades in many countries, motivating researchers from different areas to study their distribution and get answers for this increase. These tumors consist of a group of about twenty types of cancer divided into two major groups: gliomas and meningiomas, the former being more common in men and the latter in women (Inskip et al., 1995).

Brain cancer mortality in Brazil, as observed in other countries, accounts for a relatively small percentage of all cancer, but such distribution has been increasing (Monteiro and Koifman, 2003). Age adjusted brain cancer mortality rate increased from 2.77 per 100,000 in 1996 to 3.81 per 100,000; in Rio de Janeiro state there was an increase from 3 53 and 4.08 per 100,000, respectively (Brazil, 2008). Such increase has been partially associated to the improvement of clinical diagnosis and population aging, since age is an important risk factor for these tumors (Inskip et al., 1998).

Although there are multiple factors related to the development of brain tumors, their etiology is still poorly understood (Wrensch et al., 2002). Some studies suggest that agricultural workers are at higher risk to die by some specific cancers, including brain tumors. The main hypothesis for this excess of mortality is the more intense exposure to pesticides experienced by these workers (Blair et al., 1992; Blair and Zahm, 1995; Blair et al., 2005; Dich et al., 1997). In the United States, Lee et al. (2005) observed that agricultural workers exposed to pesticides for more than 25 years had an elevated risk of developing glioma (OR 3.9, 95% CI 1.8–8.6). Also, in India, there was a dramatic increase in the risk of death by brain tumors among workers exposed to pesticides, at a level about ten times higher than those not exposed (Bhat et al., 2010).

In Brazil, around 30% of gross domestic product is agriculture-based and the use of pesticides in the country has been growing for several decades, now becoming the largest user in the world in 2010 (Anvisa, 2010). In the highlands of Rio de Janeiro state, a study of mortality conducted by Meyer et al. (2003) found elevated risk of death from esophagus cancer, stomach cancer, liver cancer, oral cavity cancer, prostate cancer, testis cancer, leukemia, soft tissue

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sarcoma, breast cancer and prostate cancer in farm workers when compared to other occupational groups.

Although the scientific literature suggests an association between exposure to pesticides and the development of brain tumors, there are few Brazilian studies that dealt with the impact of these compounds on the cancer morbidity and mortality of rural populations (Koifman et al., 2002; Meyer et al., 2003). Thus, the association between agricultural occupation and brain cancer reported on the death certificate in males, residents in Rio de Janeiro state was the aim of this study.

Methods

Study design

This was a case–control study based on information from death certificates. The data were obtained from the Mortality Information System, made available electronically by the, Brazilian Ministry of Health (Brazil, 2008).

Classification of occupation

Mortality Information System uses the Brazilian Classification of Occupation (BCO) to identify the deceased's usual occupation (BCO, 2002). This classification is based on the *Standard Classification of Occupations* (ISCO-88), which allows comparisons with international studies (ILO, 2003). Farm workers were considered as those involved in farming and cattle raising production (BCO 61); farm workers in farming production (BCO 62), and workers of agricultural machinery (BCO 64). These activities correspond to the farming group code six in ISCO-88.

Study population

The study group comprised male individuals, 18 years or older, resident in the State of Rio de Janeiro, who died between 1996 and 2005.

Cases were defined as those who died with brain cancer as the underlying cause ascertained on their death certificate (DC). These tumors are classified according to the 10th revision of International Classification of Diseases and Related Health Problems (ICD-10) as: malignant neoplasm of cerebral meninges (C70.0), malignant neoplasm of brain (C71.0–C71.9), and malignant neoplasm of cranial nerves (C72.2–C72.5). In the present study, was considered inconclusive information regarding occupation those attested in the death certificate as retired, unidentifiable, or ignored. In that sense, among all potential cases, 278 (9.6%) had no occupational information registered at all (missing), and 571 (19.4%) were considered inconclusive. From the group of deaths from which controls were drawn, 59,775 (11.3%) had no occupational information, and 164,639 (31%) had inconclusive occupational information. Those individuals whose data on occupation were missing or inconclusive were excluded from the study. Also excluded were those whose causes of death were from other neoplasms (C00 to D48, the ICD-10) or disease of the central nervous system (G00–G99, ICD-10).

After identification of cases in the database, the controls were selected from among those remaining. Controls were randomized in the ratio of two controls for each case, being matched by year of death and by frequency of age (in decades).

Distribution of the causes of death among controls, according to the ICD-10 chapters was: diseases of the circulatory system (ICD-10: I00–I99, 35%), external causes of morbidity and mortality (ICD-10: V01–Y98, 17.1%), Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (ICD-10: R00–R99, 12.3%), certain infectious and parasitic diseases (ICD-10: A00–B99; 6.9%), diseases of the respiratory system (ICD-1-J00–J99, 6.3%), all other causes (except neoplasms and diseases of the central nervous system; 10.5%).

Study variables

The dependent variable was death from brain cancer (yes or no). The presence of pesticide exposure was measured indirectly by the occupation variable reported in the DC, as farm worker versus non-farm worker. The other independent variables considered in the study were race/ethnicity (white or nonwhite), education (without education, 1–3, 4–7, 8–11 and 12 or more years of schooling), age (18–29, 30–39, 40–49, 50–59, 60–69, 70–79 years and above 80 years of age) and micro-region of residence, according to the Brazilian Institute of Geography and Statistics (IBGE, 1990). Data from pesticide use were estimated from information on the IBGE's sales volume of pesticides in 1985, by micro-region of residence.

Statistical analysis

A descriptive analysis of the frequency of independent variables was performed. To evaluate possible differences between cases and controls, a chi-square (χ^2) was used. The risk was estimated by the Crude (OR) and Adjusted Odds Ratio (aOR) for the variables race/ethnicity, age and micro-residence, by unconditional logistical regression. Confidence intervals (95%) of OR were estimated by the Wald method, evaluating the model appropriateness the Hosmer–Lemershow test was used.

In order to verify a possible association between pesticide use and brain cancer mortality, municipalities in Rio de Janeiro state were divided into quartiles of per capita consumption of these products in 1985. Then, there was the distribution of deaths by quartile, with reference to the first, using the Mortality Odds Ratio (MOR) in accordance with the methodology suggested by Miettinen and Wang (1981).

Results

The study population included 2040 cases and 4140 controls selected in the mortality database, total of 6180 deaths among residents of Rio de Janeiro state, between 1996 and 2005. Malignant brain neoplasms had the following distribution sites: 97.4% of the brain, 2.0% of cranial nerves and 0.6% of the cerebral meninges.

Table 1 shows the distribution of deaths by age, race/ethnicity, education, occupation and place of residence. Given the strategy of matching the age distribution of cases and controls, the results were similar, with 69.2% of subjects being over 50 years of age. A statistically significant difference in the distribution of cases and controls for race/ethnicity, with higher frequency of cases among whites (71.3%, $p < 0.0001$), and also for education that was higher among cases ($p < 0.0001$). There was a statistically significant difference in geographic distribution, according to micro-region of residence or occupation (agricultural vs. non-agricultural) between cases and controls.

Table 2 shows the odds ratio of crude and adjusted mortality between cases and controls. Male individuals engaged in agricultural activities had a higher estimated risk of death from brain cancer. The analysis adjusted for variables: age, race/ethnicity, education and micro-region of residence increased the magnitude of the association to 1.82. The risk estimate was greater among white individuals, but the magnitude of such risk was slightly lower after adjustments for covariates. In the analysis of schooling, individuals who had between eight and eleven years of study had higher risk estimates in relation to those who had never studied, and the association was even in a greater magnitude, when adjusted. Compared to the illiterates, individuals with more than twelve years of education showed a brain cancer mortality risk more than three