

STUDY OF EPIDEMIOLOGICAL FACTORS ASSOCIATED WITH A NEUROCYSTICERCOSIS IN PATIENTS OF PIEDADE CITY, BRAZIL

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ABSTRACT

Neurocysticercosis is a parasitic disease that affects the central nervous system. Its main clinical manifestation are seizures. The objective of this study was to investigate the prevalence of neurocysticercosis and its epidemiological factors in epileptic patients seen in the emergency department of the municipality of Piedade, São Paulo. A total of 136 patients with a history of seizures observed in the Municipal Emergency Department of Piedade/SP were evaluated. There were 24 confirmed cases of neurocysticercosis among the 136 patients with seizures, corresponding to a prevalence of 17.65%. The main associated factors were age older than 60 years (PR=4.9; p=0.008), open sewer (PR=8.14; p=0.002), consumption of unwashed fruits or vegetables (PR=9.9; p=0.004), and type of drinking water source [urban untreated, urban treated but unfiltered, and rural] (PR=11.4; p=0.048). An important prevalence of neurocysticercosis was observed in the sample studied. Measures raising awareness of the disease in the population and preventive strategies must be taken by the competent authorities.

KEYWORDS: Neurocysticercosis, seizures, Epidemiological Factors.

1. INTRODUCTION

Neurocysticercosis (NCC) is a term used to define the involvement of the central nervous system (CNS) by larval forms of *Taenia solium*. This disease is the most common cause of epilepsy in adults worldwide and one of the parasitic infections most commonly associated with chronic morbidity on all continents, including North America. In addition to seizures, other clinical manifestations are dementia, intracranial hypertension, and meningitis. A number of studies suggest that, in its vesicular form, the cysticercus can persist for many years in the CNS while the patient remains asymptomatic.^[1,2]

Despite its importance, global morbidity due to NCC is underappreciated. The financial resources for research are scarce, a fact that impedes researchers to make the necessary advances in the prevention and treatment of this neuroinfection and thus to prevent the millions of patients with epilepsy. It is estimated that 50 million people worldwide have NCC, with 50,000 annual deaths.^[3]

Brazil is one of the countries strongly affected by the taeniasis/cysticercosis complex. In most states and municipalities, precarious hygiene habits, diets and basic sanitation facilities, among other factors, contribute to the occurrence of this disease. The State of São Paulo, the richest state in Brazil, faces the same problem in all

regions, regardless of socioeconomic situation. Among the few studies on this topic conducted in Brazil, an incidence of 74.1 cases of NCC per 100,000 inhabitants was demonstrated in Ribeirão Preto, northeastern region of the state.^[1,4]

Within this context, the objective of the present study was to investigate the current situation in the municipality of Piedade, State of São Paulo, Brazil, evaluating the prevalence of NCC and its epidemiological factors in epileptic patients seen in the Municipal Emergency Department.

2. MATERIALS AND METHODS

2.1. Patients

A cross-sectional study was conducted on 136 patients of both sexes with a history of seizures at least once in their life. The patients were referred by physicians of the Municipal Emergency Department for neurological assessment by the responsible researcher. Neurocysticercosis was diagnosed according to the criteria of Del Bruto et al.^[5]

2.2. Study area and period Piedade (São Paulo)

History: Piedade has been known as the onion capital and used to be the largest producer in Brazil. Today, the municipality's agriculture is diverse, producing fruits and

vegetables, especially artichokes, strawberries and onions.

Geography: The municipality is located between mountains, within the Serra do Mar, in an ecological preservation area. Several rivers and streams of the Tietê, Paranapanema and Ribeira de Iguape river basins cross Piedade. The municipality comprises an area of 745.52 km².

Demography: The population descended from pioneers and native people and did not receive significant slave labor. Foreign immigration only occurred in the middle of the 20th century, with the arrival of Japanese and Italians. In view of its very cold and humid climate and due to its reserves, the city has received numerous German, Swiss and Austrian immigrants, but also Dutch, Belgian, Danish, Swedish and Norwegian immigrants and therefore no relevant colonies have been formed.

The total population consists of 52,214 inhabitants; of these, 23,782 live in the urban area and 28,432 in the rural area. There are 26,602 men and 25,612 women (Source: CENSO 2010/IBGE).

2.2.2. Study period

The study was conducted from May 2014 to August 2015 and included all residents of the urban and rural areas of the municipality of Piedade/SP.

2.3. Data collection

A questionnaire was developed according to the objectives of the study. The data were collected by personal interview using the structured and pre-tested questionnaire after the subjects signed the free informed consent form for voluntary participations. The data were collected exclusively by the responsible researcher.

The participants received information about the objective of the study and confidentiality, and were identified by their initials and surname. Subjects younger than 12 years and pregnant women were excluded. In the case of subjects younger than 18 years, the questions were answered by the parents or legal representative. Cranial computed tomography (CT) and/or magnetic resonance imaging (MRI) scans were available for all cases studied.

2.4. Ethical approval

The study was approved by the Ethics Committee of the School of Medicine of the University of São Paulo (2013/1068-FMUSP).

2.5. Statistical analysis

The data were analyzed using the STATA 10.0 software. Analysis consisted of the description of absolute and relative (%) frequencies for the categories of the variables studied. The prevalence of NCC and its respective prevalence ratio (PR) and 95% confidence interval were calculated for the categories of each variable by simple (for NCC and a given factor) and multiple (for NCC and different factors simultaneously) Poisson regression. The association between the presence of NCC and the other variables was evaluated adopting a level of significance of <0.05.^[6] All variables were entered in the initial multiple regression model and those with $p > 0.05$ were excluded step-by-step in decreasing order of p . Thus, only variables with $p < 0.05$ remained in the final model.

3. RESULTS

The questionnaire was applied to 136 patients, including 54 (39.71%) males and 82 (60.29%) females ranging in age from 13 to 86 years.

Among the participants with parasites detected by the imaging methods, 29.2% lived in the urban area and 70.8% in the rural area (Fig. 1). Only calcified parasites were found in 100% of the contaminated cases. The percentage of patients with parasites was 29.2% among men and 70.8% among women (Fig. 2).

All 136 patients had a history of seizures, with at least one episode in their life, and were submitted to cranial CT and/or MRI. All patients were informed about the imaging results, received prescriptions for medications if necessary, and were advised to continue treatment with a specialist. The results were analyzed by the principal researcher together with two other Researchers. The prevalence of NCC in the sample was 17.65% (24 out of 136 patients), with a 95% confidence interval of 11.16 to 24.13%.

Table 1 shows the results of univariate analysis of the association of the sociodemographic factors studied with cases of NCC. A significantly higher prevalence was observed among patients older than 60 years (PR=3.04; $p=0.042$). The prevalence did not differ significantly by sex, skin color, education level, income, or occupation.

Table 1: Univariate analysis of the association of sociodemographic factors with the prevalence of neurocysticercosis.

Variable	Category	NCC + N (%)	NCC - N (%)	PR	95% CI	p
Age (years)						
	13-30	5(13,2)	33(86,8)	1		
	31-45	4 (9.5)	38 (90,5)	0.73	0.19-2.69	0.630
	46-60	5 (16.1)	26 (83.9)	1.23	0.35-4.23	0.748
	61 or +	10 (40.0)	15 (60.0)	3.04	1.04-8.89	0.042

Sex						
	Female	17 (20.7)	65 (79.3)	1.60	0.66-3.85	0.296
	Male	7 (12.9)	47 (87.1)			
Skin color						
	White	23 (19.2)	97 (80.8)			
	Black or brown	1 (6.2)	15 (93.8)	0.33	0.04-2.41	0.273
Education level						
	Illiterate or elementary school	18 (20.2)	71 (79.8)			
	High school (complete or incomplete) and higher education	6 (12.8)	41 (87.2)	0.63	0.25-1.59	0.329
Household income						
	0-0.8 minimum wages	14 (20.9)	53 (79.1)	1.44	0.64-3.25	0.377
	0.81 or + minimum wages	10 (14.5)	59 (85.5)			
Occupation						
	Agriculture or no occupation	16 (18.2)	72 (81.8)	1.09	0.47-2.55	0.20
	Commerce or industry	8 (16.7)	40 (83.3)			

NCC: neurocysticercosis, PR: prevalence ratio; 95% CI: 95% confidence interval; p: significance.

Table 2 shows the results of univariate analysis of the association of household characteristics with cases of NCC. The prevalence of NCC was significantly higher for households with an open sewer (PR=4.71; p=0.012).

No significantly different prevalence was observed for the variables type of property, presence of pig breeding, rearing other animals, or waste disposal.

Table 2: Univariate analysis of the association of household characteristics with the prevalence of neurocysticercosis.

Variable	Category	NCC + N (%)	NCC - N (%)	PR	95%CI	p
Property						
	Owned	2 (7.41)	25 (92.6)	0.36	0.9-1.56	0.175
	Rented or leased	22 (20.2)	87 (79.8)	1		
Sewage disposal						
	Public sewer or septic tank	21 (15.9)	111 (84.1)	1		
	Open sewer	3 (75.0)	1 (25.0)	4.71	1.41-15.8	0.012
Pig breeding						
	Yes	13 (18.9)	56 (81.1)	1.15	0.51-2.56	0.737
	No	11 (16.4)	56 (83.6)			
Rearing other animals						
	Yes	19 (19.8)	77(80.2)	1.58	0.59-4.24	0.361
	No	5 (12.5)	35 (87.5)			
Waste disposal						
	Adequate	1 (12.5)	7 (87.5)	0.69	0.09-5.15	0.722
	Inadequate	23 (18.0)	105 (82.0)			

NCC: neurocysticercosis, PR: prevalence ratio; 95% CI: 95% confidence interval; p: significance.

The results of univariate analysis of the association between eating and hygiene habits and the prevalence of NCC are shown in Table 3. No significant association was observed with the type of drinking water, production

of vegetables or fruits, consumption of unwashed fruits or vegetables, type of meat consumed, frequent meals eaten away from home, hand washing, history of stool tests, or history of worm infection.

Table 3: Univariate analysis of the association of eating and hygiene habits with the prevalence of neurocysticercosis.

Variable	Category	NCC + N (%)	NCC - N (%)	PR	95%CI	p
Drinking water						
	Urban treated, filtered	1 (6.7)	14 (93.3)	1		
	Urban untreated, urban treated but unfiltered, and rural	23 (19.0)	98 (81.0)	2.43	0.33-18.0	0.385

Production of vegetables and fruits						
	Yes	12	50			
	No	12	62	0.84	0.38-1.86	0.665
Fruit and vegetable consumption						
	Washed (filtered or boiled or chlorinated water or vinegar)	21 (16.4)	107 (83.6)	1		
	Unwashed	3 (37.5)	5 (62.5)	2.29	0.68-7.66	0.18
Type of meat consumed						
	Raw or undercooked	17 (20.7)	65 (79.3)	1.60	0.66-3.86	0.296
	Well-cooked or roasted	7 (13.0)	47 (87.0)			
Frequently eating out						
	Yes	15 (18.8)	65 (81.2)			
	No	9 (16.1)	47 (83.9)	0.86	0.38-1.96	0.715
Washing hands before eating						
	Yes	12	59	0.92	0.41-2.04	0.829
	No	12	53			
Washing hands after eating						
	Yes	9	49	0.81	0.35-1.84	0.611
	No	15	63			
History of stool tests						
	Yes	7	45	0.67	0.28-1.60	0.364
	No	17	67			
History of worm infection						
	Yes	14	58	1.22	0.55-2.80	0.597
	No	10	54			

NCC: neurocysticercosis, PR: prevalence ratio; 95%CI: 95% confidence interval; p: significance.

Table 4 shows the results of multiple regression analysis of the association between the factors studied and the prevalence of NCC. The data reveal the strength of the independent association of each factor with NCC. A significantly higher prevalence was observed for the

categories age older than 60 years (RP=4.9; p=0.008), open sewer (RP=8.14; p=0.002), consumption of unwashed fruits and vegetables (RP=9.9; p=0.004), and type of drinking water [urban untreated, urban treated but unfiltered, and rural] (RP=11.4; p=0.048).

Table 4: Final Poisson multiple regression model between the factors studied and the confirmed diagnosis of neurocysticercosis.

Variable	Category	PR	95%CI	p
Age (years)				
	13-30	1		
	31-45	0.73	0.19-2.79	0.645
	46-60	1.57	0.44-5.60	0.490
	61 or +	4.90	1.50-15.97	0.008
Sewage disposal				
	Public sewer of septic tank	1		
	Open sewer	8.14	2.18-30.4	0.002
Fruit and vegetable consumption				
	Washed (filtered or boiled or chlorinated water or vinegar)	1		
	Unwashed	9.90	2.18-47.13	0.004
Drinking water				
	Urban treated, filtered			
	Urban untreated, Urban treated but unfiltered, and rural	11.4	1.02-127.7	0.048

PR: prevalence ratio; 95%CI: 95% confidence interval; p: significance.

4. DISCUSSION

Cross-sectional studies only allow analysis of the association between factors and outcomes present on that occasion, a fact that limits investigation of the topic since NCC can take several years until the emergence of relevant symptoms, including seizures. Another limitation of the present study that should be mentioned is the sample size which, although adequate to estimate the prevalence of NCC among patients with seizures of the emergency service, was insufficient to scrutinize risk factors, providing conclusive results only for some factors that exhibited a very strong association. With these premises in mind, we can carefully interpret the main results of this study. The prevalence of NCC in the sample was 17.65% and was strongly associated with age older than 60 years, open sewer, deficient drinking water treatment, and inadequate washing of fruits and vegetables for consumption. These results are a valuable contribution since the prevalence of NCC in Brazil is unknown because of the absence of obligatory notification in most states and the inaccessibility to diagnostic tests for the majority of the population. The clinical findings are variable and the polymorphic manifestations of NCC depend not only on the location, but also on the number of parasites, stage of cysticercus development (viable or calcified), and host characteristics.

The cerebral calcifications observed in the present study are a serious health problem since they can cause irreversible alterations in the patient and may require treatment and medication use throughout life. The diagnosis of NCC is made by a combination of immunological methods and neuroimaging techniques.^[9-12] The totally misguided view of the world population, including health professionals, that the calcified forms are mostly inoffensive must be revised.^[7,8,13,14] In the area studied here, other asymptomatic individuals might be contaminated, carrying different forms of the parasite that may have persisted in the CNS for many years without causing clinically exuberant symptoms.^[1,2] Unfortunately, many health services are ineffective in reporting cases, a fact that renders geographic mapping deficient and consequently undermines efforts to eradicate the disease. The factors that contribute to the endemic nature of the taeniasis/cysticercosis complex are multiple and complex, and are intimately related to personal hygiene habits and to family and environmental factors.

Within this context, it is necessary to raise the awareness of government agencies for broad investment in collective health programs and to attribute to health education the importance it deserves in the control of the taeniasis/cysticercosis complex, considering the severe consequences of this disease for collective health and the lack of access of the majority of the population to diagnostic methods. An effective control program of the disease should include rigorous quality control of pork meat and instructions for the population regarding the

need to consume well-cooked pork products since the parasite can lodge itself in any part of the animal's body. The animal or its products must be bought in reliable establishments submitted to health inspections by the competent authorities. Vegetables and fruits must be very well washed with filtered or boiled water before consumption. Drinking water must also be filtered or boiled. Instructions about washing hands before eating, during food preparation, and after bathroom use are imperative. Considering the biological cycle of the parasite, adequate disposal of human feces through septic tanks and septic tanks would be an important step for control of the disease. Raising awareness of the population and resource mobilization by the competent authorities for research and control of cysticercosis are urgently needed not only in the area studied but around the world.

Conflicts of interest

The authors declare that they have no conflict of interest.

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