PREVALENCE OF EPILEPSY IN A BRAZILIAN SEMIURBAN REGION: AN EPIDEMIOLOGICAL STUDY

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ABSTRACT
Objective: WHO estimates 8/1000 individuals worldwide suffer from epilepsy, and prevalence in developing countries is usually higher than that in developed countries. According to United Nations Program for Development in Human Development Report 2013, Brazil ranks 85th in Human Development Index with a course of "high performance" in human development over the past decades. Adequate sanitary conditions indirectly indicate higher educational and health levels. This study aimed to describe the prevalence of epilepsy in the Brazilian semiurban region of Mato Grosso. Methods: A door-to-door survey was conducted in a semiurban area of Barra do Bugres in 2011. In phase 1, health agents screened participants with the Limoges questionnaire, which is a validated method used to identify patients with epilepsy in tropical regions, and in phase 2, neurological evaluation was performed on detected cases. Results: Of the 30,132 subjects who were screened, 305 were deemed positive and were advanced to phase 2 evaluation. Epilepsy was diagnosed in 241 subjects (76 children and 165 adults). The prevalence of epilepsy was 7.8/1000 inhabitants, and the overall prevalence rate of active epilepsy was 5.6/1000 inhabitants. In this study, 55.9% were male, afro-descendant ethnicity was reported by 68.7% subjects, 24.4% were declared as illiterate, and 95.5% had toilets inside their house. Conclusion: The present study is the first conducted in a semiurban region of Brazil using a population survey to evaluate epilepsy prevalence rates. These findings suggested that the association between improvements in health conditions and education are important factors for low epilepsy prevalence rates.

Keywords: Brazil; Epidemiology; Epilepsy; Prevalence; Population survey; Seizure.

BACKGROUND

Epilepsy is a chronic condition characterized by unprovoked recurrent epileptic seizures and may affect individuals of all ages(1). It is one of the most common neurological diseases, and it affects the physical and emotional health of the patient and the patient's family structure. According to Ngugi et al.(2), around 70 million individuals worldwide suffer from epilepsy, with 90% of them residing in developing countries. Around 2.4 million new cases are estimated to occur annually in developing countries all over the world, and 60% to 90% of people with epilepsy receive no treatment due to inadequate access to healthcare and the stigma associated with epilepsy(3).

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The prevalence rate of epilepsy in developing countries is usually higher than that in developed countries[4,5], and this is primarily because of conditions such as neuroinfections, inadequate prenatal care, and childbirth. The prevalence rate of epilepsy has been reported to vary substantially between developed countries (4–7/1000 individuals) and developing countries (5–74/1000 individuals)[2]. Burneo et al.[6] described in a systematic review that the median lifetime prevalence rate in Latin American countries is 17.8/1000 individuals[range, 6–43.2] . These variations may be due to different methodologies, definitions of epilepsy, and risk factors. Epidemiological studies in Latin American countries are needed to identify the source(s) of the heterogeneity within the same country, city, and regions[6]. Population-based studies, such as the door-to-door method, are considered to yield accurate data that represents the number of individuals with a disease in the overall population from the number of patients that are examined in the study.

Five epidemiological population survey studies have been conducted in Brazil, and they have found a wide variability in the epilepsy prevalence rate. A study that was conducted in the Brazilian Midwest region evaluated the prevalence rate to be 18.3/1000 in Alto Xingu, which is an Indian tribe[7]. Among the studies that have been conducted in the Brazilian Southeast region, which is the most populous and developed and primarily urban, the rates have been found to be between 9.2–18.6/1000 individuals[8–11].

According to the United Nations Program for Development in the Human Development Report 2013, Brazil ranks 85th in the Human Development Index, and it has exhibited a course of high performance in human development over the past decades. This indicates that the country was able to increase the national income and that the indicators of health and education were recorded as higher than average. Adequate sanitary conditions indirectly indicate higher educational and health levels. In particular, regarding the study of epilepsy, both educational level and sanitary conditions are of high importance with respect to its etiology and prevalence.

Because Brazil is a country with continental proportions and different socioeconomic, cultural, and environmental/climate characteristics for each region, previous studies did not necessarily reflect the reality of the country as a whole. We examined a region that is a rural area of Brazil's tropical climate and that seemed to be representative of the conditions found in most Brazilian cities. The aim of this study was to determine the prevalence rate of epilepsy in Barra do Bugres with a door-to-door survey.

METHODS

Study Population and General Design

This study was conducted in Barra do Bugres, which is a semiurban area of the Mato Grosso in Midwest Brazil. The province covers 7,228,902 km^2 and has a population of 32,124 individuals. The municipality sanitary conditions can be considered efficient because the Instituto Brasileiro de Geografia e Estatística (IBGE) 2010[12] has reported that 97.9% of all households are supplied by main water and treated sewage[13] and that only 8.44% of the population over 10 years of age have never attended school[14], indicating that the city has a good literacy rate. The health care infrastructure consists of a municipal hospital and a team of health agents, nurses, and clinics from the Health Family Program (HFP), and it covers more than 75% of the population. Neurologic attendance and electroencephalography examinations have been regular since 2001. Computed tomography scans and magnetic resonance imaging services are available in the region. Ethnically, the population is a mixture of Mestizos, mixed-race descendants of Portuguese colonists and the natives[15]. The population may be considered semiurban, and the city's economy revolves primarily around agriculture or, more specifically, the alcohol industry and cattle.

This study was approved by the ethics committee of the University of Cuiabá under number 2011/160. In the first phase of the study, health agents received verbal authorizations from subjects who agreed to participate. All subjects who refused to participate in the first phase, declined to answer a structured questionnaire and therefore were not included in this survey. In the second phase of the study, we achieved written informed consent from all individuals and / or their guardians under 18 years or cognitive impairment. We have archived all the terms of the consent of each individual evaluated in the second phase of the study. The ethics committee has approved and consented to the procedures performed well as the Barra do Bugres City Hall along with the Municipal Health. Each participant received information about the study in question and was well oriented with respect to the neurological treatments that were provided to all identified patients with epilepsy during the study period and for all the time after this research. Collected data was anonymized at all stage of the study.

All households in the period from January 2011 to August 2012 were included. In phase 1, every member of the study population or a proxy respondent who agreed to participate was

subjected to a brief screening method (Limoges questionnaire). In phase 2, the presence of epilepsy was confirmed or ruled out in subjects who were screened as positive for that condition in phase 1. Individuals who were screened as negative were not evaluated.

Phase 1: Limoges questionnaire

The Limoges questionnaire was distributed to the subjects at home or at the institution of their current residence by 57 health agents over seven micro areas coordinated by six HFP teams. Only the downtown area lacked a HFP team. All healthcare agents received training and orientations about epilepsy and its clinical manifestations. There were five meetings with presentations of the questionnaire and discussions of each of the items to be asked to the interviewees.

Subjects ≤12-years-old were screened indirectly through an interview with a close relative, usually a parent. The screening instrument used in this survey was the Limoges Questionnaire that was tested and validated in Mauritania[16,17] and was designed to detect epilepsy in tropical regions. There were five questions concerning epilepsy symptoms. All subjects with at least one positive response to any of these five questions were screened as positive for epilepsy and were invited for further evaluation in phase 2.

Phase 2: Clinical diagnosis

Two board-certified neurologists, one of whom was a pediatric neurologist, followed a standardized diagnostic protocol to evaluate all subjects who were screened positive for epilepsy in phase 1. The neurologists interviewed the subjects regarding their personal histories, performed clinical examinations, and reviewed the available laboratory data (electroencephalographic findings and brain imaging findings) to confirm or rule out the diagnoses of epilepsy and to classify the seizures.

Diagnostic Criteria

The guidelines of the International League against Epilepsy (ILAE)[18,19] were adopted as the criteria for the classification of epileptic seizures in the standard protocol. Epilepsy was defined as a condition characterized by two or more unprovoked seizures or seizure episodes. An unprovoked seizure is one without an acute underlying cause. A seizure episode is a cluster of

seizures (at least two) that occur within a 24-h period. Different events such as head trauma, stroke, intracranial infection, intoxication, or withdrawal of drugs or alcohol were considered to be acute underlying causes of seizures only when the seizures occurred within 30 days of the event[18]. Seizures that occurred more than 30 days after the event were considered to be unprovoked[19] and were accepted in this survey. We excluded subjects who had experienced only a single seizure, subjects who had only experienced neonatal seizures, febrile seizures, or seizures due to an acute underlying cause.

The diagnosis of epilepsy was definite if there was a clear description and history of seizures obtained from the subject or relatives or if there was a suggestive description and history of seizures that was corroborated by electroencephalographic findings. The diagnosis was possible if there was a suggestive description and history of seizures without electroencephalographic confirmation[18,19]. For both definite and possible cases, epilepsy was considered active if the subject was under antiepileptic medication on the day of evaluation and at least one seizure occurred in five years preceding the day of evaluation or if the subject was not under antiepileptic medication on the day of evaluation and at least 1 seizure occurred in the year preceding the day of evaluation. In all other instances, epilepsy was deemed inactive. For the seizure types reported here, we used the definitions proposed by the Commission on Classification and Terminology of the International League against Epilepsy[18].

Data Analyses

The lifetime prevalence rate was determined when active and inactive epilepsy were considered together[20]. Data analyses consisted primarily of simple comparisons of the prevalence rates for various age–sex groups, socioeconomic variables, and the history of concomitant pathologies. Prevalence rates and 95% confidence intervals (CI) were compared for each sex and age group by a Mantel–Haenszel χ^2 test. SPSS software version 17.0 was used for statistical analyses. The level of significance was 5% ($p < 0.05$) as described by Altaman (21).

RESULTS

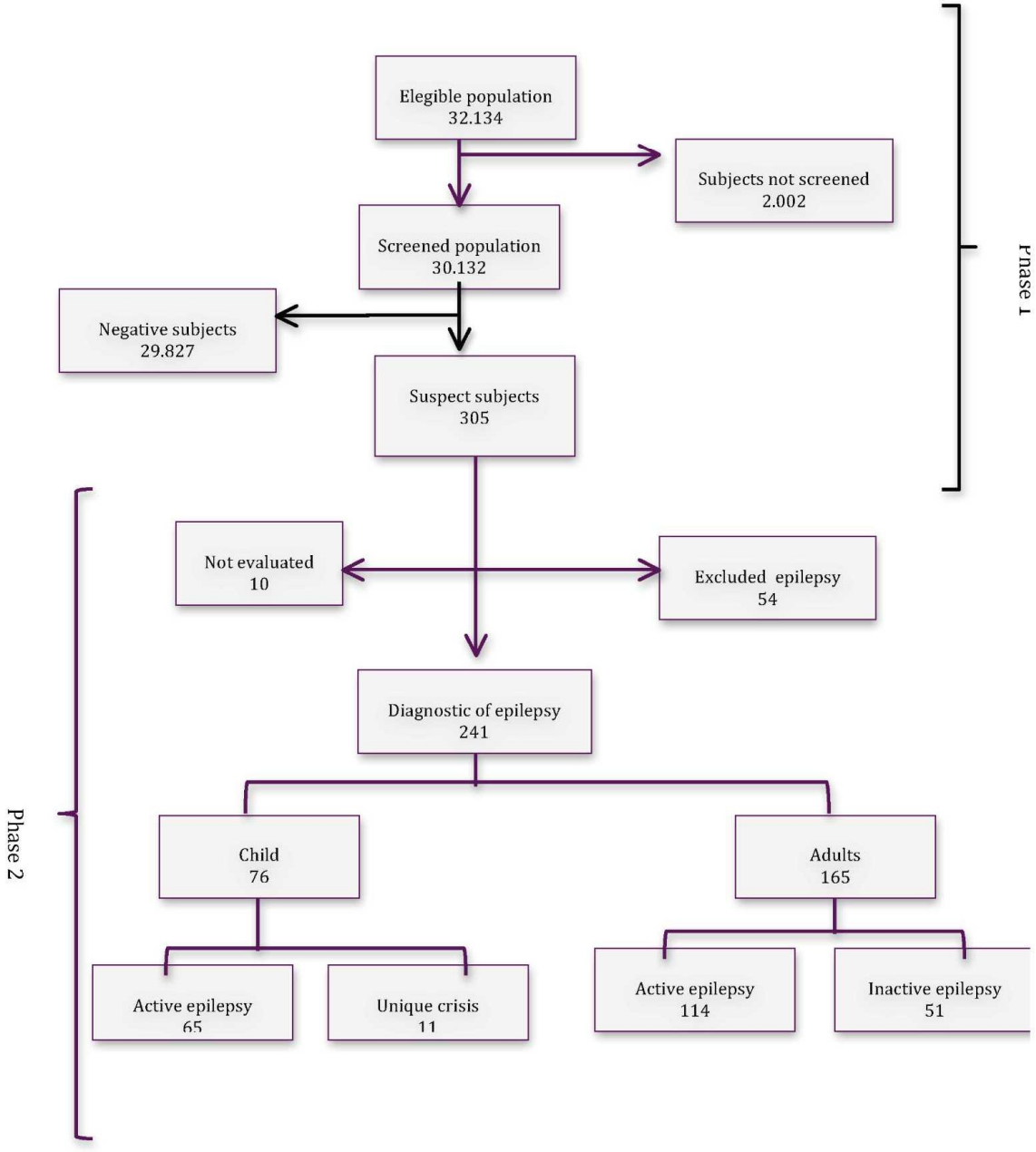
Of the 32,134 eligible subjects, we screened 30,132 (93.76%) in phase 1. Subjects comprised 15,289 men (50.8%) and 14,843 women (49.2%), of which 21,576 were adults

(71.6%) and 8,556 were children (28.4%); individuals <15-years-old were considered to be children.

Of the 30,132 subjects, 305 (1%) were deemed positive and were advanced to phase 2 evaluation (Figure 1). However, 2002 subjects who were not screened owing to a lack of agreement to participate in this research or because the health workers could not find them at home and uninsured residents for at least two visits were not evaluated further.

In phase 2, 54 non-epileptic cases were identified, and 10 individuals had moved from the city before the neurological assessment.

Figure 1. Profile of the survey



Epilepsy was diagnosed in 241 subjects (76 children and 165 adults). Active epilepsy was identified in 179 subjects (65 children and 114 adults). Inactive epilepsy was identified in 51 (21.1%), and 11 (4.5%) subjects had only one convulsive episode and therefore were excluded.

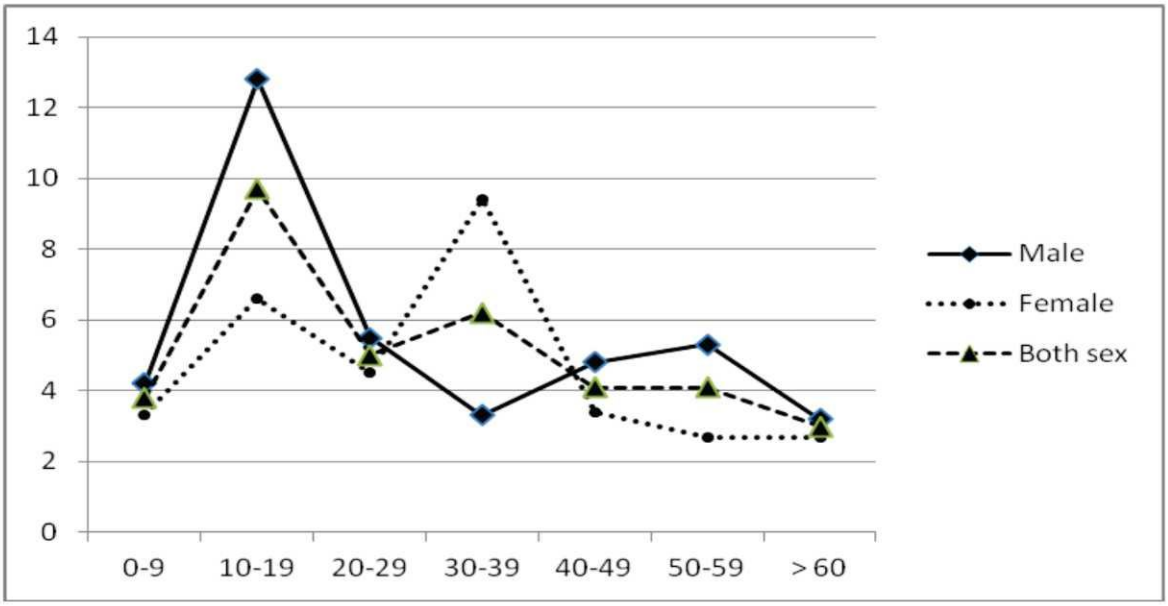
The prevalence rate of epilepsy in this study population was 7.8/1000 inhabitants with the overall active epilepsy rate as 5.6/1000, which was bifurcated as 6.0/1000 for men and 5.2/1000 for women, with no statistically significant differences ($p > 0.05$). Table 1 shows the distribution of gender- and age-based prevalence rates in the study population. The age-specific patterns of prevalence markedly differed between the both genders. In the 10–19-year-old group, the age-specific prevalence rate was higher in men than that in women ($p < 0.05$). In contrast, in the 30–39-year-old group, the age-specific prevalence rate was higher in women than that in men ($p < 0.05$), as demonstrated in Figure 2.

Table 1 - Prevalence rate of active epilepsy (cases/1000) bifurcated on the basis of age and sex.

		Male		**Female**		**Both genders**
Age	n	Prevalence/1000	n	Prevalence/1000	n	Prevalence/1000
		(CI 95%)		(CI 95%)		(CI 95%)
0–9	12	4,2 (2,3–7,5)	9	3,3 (1,6–6,5)	21	3,8 (2,4–5,9)
10–19	41	12,8 (9,3–17,5)	21	6,6 (4,2–10,3)	62	9,7 (7,5–12,5)
20–29	17	5,5 (3,3–9,0)	13	4,5 (2,5–7,9)	30	5,0 (3,4–7,2)
30–39	9	3,3 (1,6–6,5)	24	9,4 (6,2–14,2)	33	6,2 (4,3–8,8)
40–49	10	4,8 (2,4–9,1)	6	3,4 (1,4–7,7)	16	4,1 (2,4–6,8)
50–59	7	5,3 (2,3–11,4)	3	2,7 (0,7–8,5)	10	4,1 (2,1–7,8)
> 60	4	3,2 (1,0–8,7)	3	2,7 (0,7–8,6)	7	3,0 (1,3–6,4)
Total	**100**	**6,0 (4,9–7,3)**	**79**	**5,2 (4,1–6,5)**	179	**5,6 (4,8–6,5)**

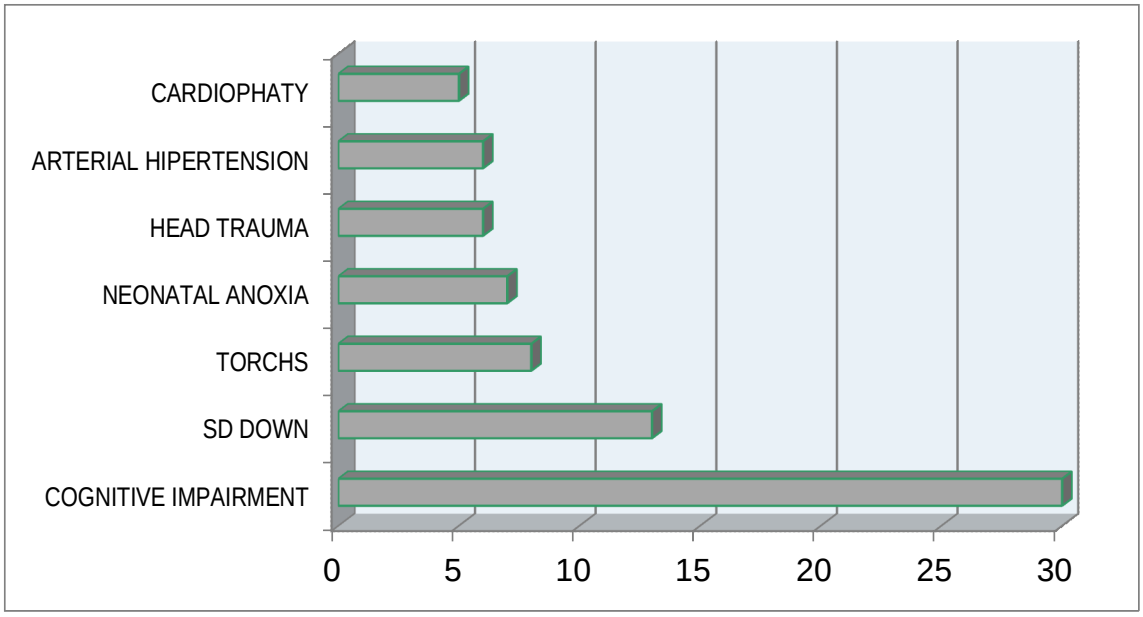
CI indicates confidence interval.

Figure 2 - Comparison of age- and sex-specific prevalence rates of active epilepsy



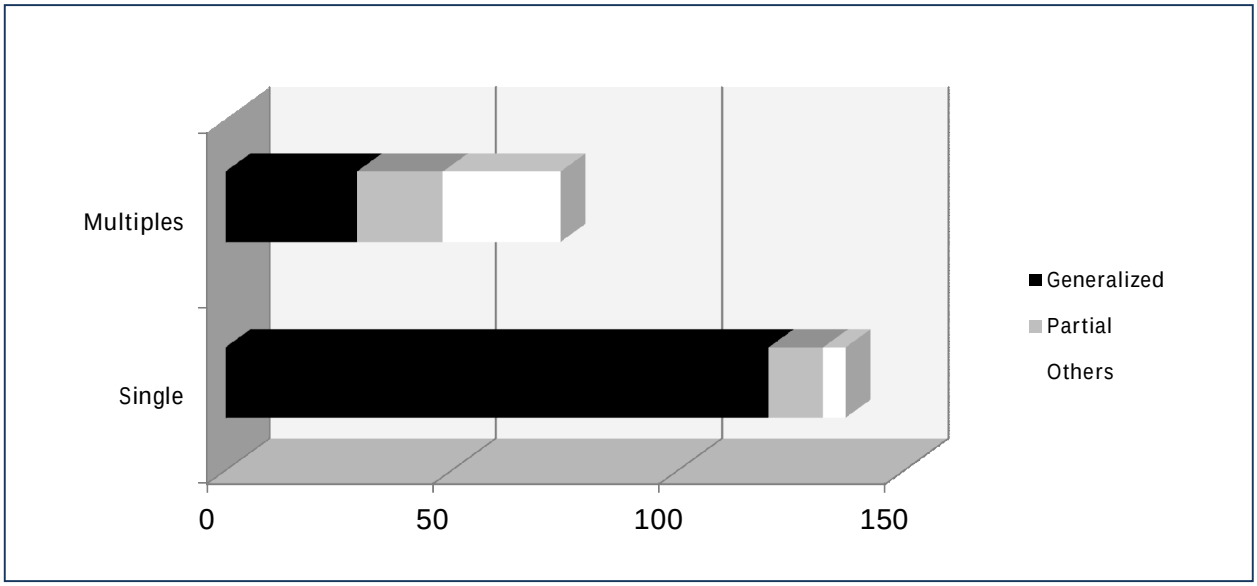
In this study population, 55.9% were male and Afro-descendant ethnicity was reported by 68.7% of the subjects. A total of 22.3% were declared illiterate, and 95.5% of the patients with epilepsy had toilets inside their house. A positive family history for epilepsy in first- and second-degree relatives was observed in 47.5% of the subjects. Figure 3 demonstrates the analysis of the comorbidities among illiterates in sample.

Figure 3 - Analysis of the Comorbidities Among Illiterates



Of the 179 patients with epilepsy, six (3.3%) were diagnosed for the first time during the survey. Seizures could not be classified in four subjects (2.9%). Figure 4 list crisis classification according amount of type of crisis. Of the patients using antiepileptic drugs, 34.6% were under treatment with more than one antiepileptic drug, 90.2% had undergone the electroencephalographic test at least one, 84.2% had undergone a computed tomography study, and 26.9% had undergone magnetic resonance imaging.

Figure 4 - Crisis classification according amount of type of crisis



DISCUSSION

In this study, we performed a door-to-door screening and clinical evaluation with a 2-phase design. House-to-house screening for epilepsy was considered feasible because we expected a high level of cooperation from the health agents and the target population. The possibility of finding undiagnosed cases is one of the advantages of this kind of study, and we diagnosed six patients (3.3%) with active epilepsy for the first time during the survey.

The lifetime prevalence rate of epilepsy in our study population was 7.8/1000 inhabitants, and the overall active epilepsy rate was 5.6/1000 individuals. A systematic review (6) has shown that the median lifetime prevalence rate for all countries in Latin America is 17.8/1000 individuals (range, 6–43.2). When comparing other rural and suburban areas in Latin America, such as Bolivia (epilepsy diagnosed in 12.3/1000 individuals (11.1/1000 for active epilepsy)] (22,23), Ecuador (epilepsy diagnosed in 14.3/1000 individuals (8.0/1000 for active epilepsy)] (24,25), and Uruguay (epilepsy diagnosed in 11.6/1000 individuals (6.4/1000 for active epilepsy)) (26,27), the results exhibited remarkably higher prevalence rates. Our data were similar to those reported by Melcon et al. (28) who found a lifetime prevalence rate of 6.2/1000 habitants and an age-adjusted rate of 6.3/1000 individuals. Survey-based studies conducted in

Brazil have reported higher prevalence rates, such as 11.9/1000 (10), 16.2/1000 (9), 18.3/1000 (7), and 18.6/1000 (8), in urban and rural areas. We believe that the low prevalence rate of epilepsy in our study population was related to the adequate sanitation, low illiteracy rates, and per capita income above the national average. Furthermore, epilepsy is a complex disease, and its prevalence depends on the interactions of environmental conditions and genetic factors (24).

Automobile accidents are common in urban areas, and poor traffic control, which is associated with a lack of a consistent seat-belt and helmet policy, is a major contributor to head injury. The prevalence of epilepsy varies according to the severity of the injury (5). However, fast access to neurosurgical services also contribute to the low prevalence rate in our study population.

Among the individuals who declared themselves illiterate, 75% had a history of associated diseases, such as cognitive impairment due to the Down syndrome or neonatal hypoxic ischemic/cerebral palsy and/or congenital infections, and 2.8% were aged 60 years. The low prevalence rate of epilepsy in our study population may be associated with a number of factors such as low illiteracy rates and adequate sanitary conditions. In fact, Nsengiyumva et al. (29) reported a positive association between epilepsy caused by parasitic disease of the central nervous system after an adjustment for other significant factors, such as sex, poor sanitation, and a past history of severe disease in childhood.

CONCLUSIONS

To the best of our knowledge, the present study is the only study conducted in a semiurban region of Brazil using a door-to-door population survey to evaluate epilepsy prevalence rates. The use of health agents as screening instruments was advantageous because they already regularly visit households and teach individuals how to prevent infectious diseases because of contamination and it was easy to educate these professionals regarding the identification of patients with epilepsy. The results of this study suggested that the association between improvements in health conditions and education are important factors contributing to the low epilepsy prevalence rates.

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