URBAN PREVALENCE OF EPILEPSY

Populational study in São José do Rio Preto, a medium-sized city in Brazil

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ABSTRACT - The aim of this study was to determine the prevalence of epilepsy in the urban population of São José do Rio Preto. This is a medium-sized city of 336000 inhabitants, located in the northwest of the state of São Paulo, Brazil. *Method*: A cross-sectional epidemiological investigation with a randomized sample was performed in two phases, a screening phase and a confirmation of the diagnosis phase. The gold standard was a clinical investigation and neurological examination. The chi-square test was used in analysis of the results and p-value value ≤ 0.05 was considered significant. Prevalence was calculated with 95% confidence interval. *Results*: The study sample size was 17293 individuals, with distributions of gender, age, and race similar to the general population. The prevalence per 1000 inhabitants of epilepsy was 18.6, of these 8.2 were active, defined as at least one seizure within the last two years. The prevalence per 1000 inhabitants for the age groups (years) was 4.9 (0-4), 11.7 (5-14), 20.3 (15-64) and 32.8 (65 or over). *Conclusion*: Prevalence of both accumulated and active epilepsy was elevated, comparable to other developing nations, in particular those of Latin America. However, the prevalence of epilepsy in childhood was low, whilst in aged individuals it was high similar to industrialized nations.

KEY WORDS: epilepsy, epidemiology, prevalence, Latin America.

Prevalência urbana da epilepsia: estudo populacional em São José do Rio Preto - cidade de médio porte do Brasil

RESUMO - *Antecedentes:* O objetivo deste estudo foi determinar a prevalência da epilepsia na população urbana de São José do Rio Preto, com 336000 habitantes, localizada no noroeste do Estado de São Paulo/ Brasil. *Método*: O estudo populacional, tipo corte transversal, em amostra aleatória, constituiu-se de uma fase de rastreamento, mediante um questionário. O padrão ouro para confirmação diagnóstica foi a história clínica e o exame neurológico. Os testes do χ^2 e intervalo de confiança de 95% (IC-95%) foram usados para análise dos resultados, tendo sido considerados significantes os de valor p$\leq$0,05. *Resultados*: A amostra estudada foi de 17293 pessoas, cuja distribuição quanto ao sexo, à faixa etária e à raça foram semelhantes à da população em geral. A prevalência de epilepsia por 1000 hab. foi 18,6, sendo 8,2 para ativa considerando-se, pelo menos, uma crise no período dos últimos 2 anos. A prevalência na faixa etária de 0 a 4 anos foi 4,9, de 5 a 14, 11,7; de 15 a 64, 20,3; e acima dos 65 anos foi 32,8. *Conclusão*: As prevalências de epilepsia acumulada e ativa foram elevadas, semelhantes às dos países em desenvolvimento, em particular, aos da América Latina. A prevalência de epilepsia na infância foi baixa, enquanto que nos idosos foi elevada, semelhantes às observadas em países desenvolvidos. Estes resultados são relevantes no planejamento de medidas sanitárias, adequação ao tratamento da população, considerando a alta prevalência encontrada, para minimizar o impacto da epilepsia na população.

PALAVRAS-CHAVE: epilepsia, epidemiologia, prevalência, América Latina.

Epilepsy is one of the most common serious chronic disorder[1] and it causes suffering for patients and families[2,3]. Epidemiological studies of the prevalence of epilepsy have produced results that vary from 1.5/1000[4] to 57/1000[5] inhabitants.

The discrepant results are explained by different etiologic risk factors and distinct methodologies employed[1,4-10].

A direct approach among the members of the community is the best method to estimate the rate of epilepsy in devel-

oping countries, as quality of data required may not be available in the form of medical records[4,8,10-15]. Brazil is a country of continental dimension located in South America with approximately 170 millions inhabitants. Two epidemiological studies were carried out in Brazil. Marino et al., (1986)[16] found a prevalence of epilepsy of 11.9/1000 in São Paulo city. However, the study does not make distinction between active and inactive epilepsy. Fernandes et al., (1992)[17] applied a screening questionnaire for epilepsy in Porto Alegre city and found a prevalence of 16.5/1000 for active and 20.3/1000 for inactive epilepsy.

This study aims to estimate the prevalence of active and accumulated epilepsy in relation to the distribution of age groups, epileptic seizure types and syndromes in a medium sized urban city in southeastern Brazil.

METHOD

Demographic data - This survey was carried out in São José do Rio Preto (SJRP) a city located in the northwest of the State of São Paulo, Brazil. The urban population according to the national census (IBGE)[18] is 336000 inhabitants where 51.3% are women. The distribution in percentages of the inhabitants for the age groups (years) is 7.3% (0-4), 17.3% (5-15), 68.8% (15-64), and 6.6% (65 or over).

Questionnaire - We first constructed a questionnaire (shown in the Appendix 1), composed of eight questions which were modified from the guidelines of the World Health Organization (WHO), and similar to the nine questions used by Placencia et al.[8]. This was applied in 100 consecutive patients with epilepsy in the outpatient clinic of the Hospital de Base (HB) Medical School in São José do Rio Preto, with the aim of improving the language and cultural terminology.

Pilot study - A pilot study was carried out to validate the questionnaire.

The chosen suburb, for this phase, was São Deocleciano (2001), with 1500 inhabitants[9]. A cross-sectional house-to-house survey was performed using this questionnaire with the aim of screening individuals with a possible history of epileptic seizures. A total of 20 students from the School of Economics of Dom Pedro Faculty performed this task, identifying the houses as positive or negative according to the questionnaire. Positive cases were considered with at least one affirmative response.

In the diagnostic confirmation phase, a specialist with experience in epilepsy visited all cases, both positive and negative to make a clinical record and a physical examination. The aim of this phase was to determine the true and false positive and negative cases, to assess the sensitivity and specificity of the questionnaire, previously described by Borges et al. elsewhere[9]. Briefly, questionnaire presented a sensitivity of 95.83% and a specificity of 97.8%. The total number of participants in the survey was 1025 where 46.9% were men. The first three questions produced the majority of the affirmative responses and were responsible for the majority of the true positive cases. The other questions produced the greatest number of false positive cases.

Field study - A large-scale cross-sectional population-based survey using a random sample and segmented depending on the fifteen administration regions of the city was planned. The sample size was defined by standard techniques using mathematical equations with correlation for finite populations[19,20]. The study was done in two phases, using the same strategy used in the pilot study: a screening phase, applying the questionnaire, and a confirmation of the diagnosis phase, done by a clinical investigation and neurological examination.

First phase - Five professionals trained in home surveys to identify the houses with positive and negative cases applied the questionnaire door-to-door in a randomly chosen sample.

Second phase - The diagnostic confirmation was performed by only one professional (MAB) in all positive cases. The information of these people was crosschecked with the archives of HB whenever available. Cases with doubts or no previous diagnoses were submitted to complementary exams as individual basis needed to confirm the diagnosis. False positive cases were determined by a mathematical model from the validation of the pilot study.

Diagnostic validation criteria of epilepsy - The guidelines of the International League Against Epilepsy (ILAE)[21,22] were adopted as the criteria for the classification of epileptic seizures in the preparation of the standard protocol. Only those individuals who had at least two non-provoked seizures at an interval of at least 24 hours between them were considered.

The etiology of the epilepsy was classified according to the proposal of the *Commission on Epidemiology and Prognosis* of ILAE[15] and Hauser et al.[2] The etiology of epilepsy was classified into three groups, as follows: *Idiopathic seizure* - epilepsy that fulfills criteria of one of the epileptic syndromes (presumably genetic) which occur in the absence of any neurological anomalies; *Symptomatic* - epilepsy that occurs in the presence of a remote aggression or to a previous disorder that is recognized as an associated risk factor before the first seizure; *Possible symptomatic (Cryptogenic)* - epilepsy in the absence of an identifiable cause and the patient does not meet the criteria for idiopathic epileptic syndrome[2].

Active epilepsy (E_{at}) at 2, 3, 4, and 5 years was defined as the occurrence of at least one seizure in one of these time intervals preceding the survey, independent of the use or not of antiepileptic drugs. Accumulated prevalence (E_{ac}) was the total prevalence, composed of both active and inactive epileptic seizures. Non-provoked and acute symptomatic (provoked) seizures and non-epileptic events were defined, according to Hauser et al.[2]. All seizures and events that did not fit into these criteria and epilepsy definitions were excluded.

The data was analyzed using Microsoft Excel and MINITAB. The chi-square test was used in the analysis of the gender and age of the individuals. A 95% confidence interval (95% CI) was calculated for the prevalence estimates.

RESULTS

The sample size was composed of 7655 domiciles. We were able to access 4815 houses, as the others were closed, after at least three returns at each address. Only 11 refusals occurred.

Appendix 1

This questionnaire was constructed and tested in Portuguese.

House nº . . . ., Number of inhabitants [   ] male [   ]; female [   ]

Name . . . . .Age . . . .

Street . . . ., nº . . . . .Apart nº . . . .

Suburb . . . . .Phone: . . . .

1.   Do you have or have you had seizures (attacks, fit, convulsion) in which you lost consciousness and fall suddenly? In this house, does anyone have? YES[   ]; NO[   ].

2.   Do you have or have you had seizures in which you lose contact with reality (surroundings) and become "off the air"? In this house, does anyone have? YES[   ]; NO[   ].

3.   Do you have or have you had seizures in which you have uncontrollable jerks/jolts of the arms, legs, mouth or the head twisted to the side? In this house, does anyone have? YES[   ]; NO[   ].

4.   Do you have or have you had fainting episodes and on recovering your senses you notice that you urinated or defecated in your clothes by accident? In this house, does anyone have? YES[   ]; NO[   ].

5.   Do you have or have you had seizures in which you feel a bad sensation such as "sinking" or a "knot" in the stomach which   rises to the throat and after you fall unconscious? Following this, witnesses say that you fidgeted with your clothes, chewed,   or looked at a distant point? In this house, does anyone have these seizures? YES[   ]; NO[   ].

6.   Did a doctor or health worker or even members of your family ever mention to you that you had febrile convulsions in your childhood or during any serious disease? In this house, does anyone have these seizures? YES[   ]; NO[   ].

7.   Do you have sudden jolts similar to a "shock" in the arms (you drop things) or legs with or without falling, mainly in the morning? YES[   ]; NO[   ].

8. Is there anyone from this house with epilepsy in an asylum in São José do Rio Preto? YES[   ]; NO[   ].

POSITIVE [   ]   NEGATIVE [   ]

NOBODY ANSWERED THE DOOR [ ]   HOUSE LOCKED [ ]   UNINHABITED [ ]

REFUSAL TO PARTICIPATE [ ]

The survey included 17293 inhabitants of 4804 domiciles of the city. The questionnaire was positive for at least one question of 894 people living in 890 dwellings. These individuals were examined by the neurologist and 308 cases were confirmed as having epilepsy. It was noticed that 40% of the identified people with epilepsy regularly attend or, at least, have been treated in the outpatient's clinic of the HB. Furthermore, all had at least an EEG, 80% had a brain CT scan, and 10% a brain MRI.

A total of 321 cases of epilepsy were evidenced, including 308 true positive cases and 13 false negative cases mathematically projected from the results of the research instrument validation (sensitivity of 95.8 [95% CI: 94.6 - 97])[9]. The average age of confirmed cases in the study was 38.4 (range from 1 to 84 years). The female gender accounted for 165 cases (51.3%), which is a similar ratio to the sample population, and the general population of São José do Rio Preto (p-value = 0.99).

Prevalence - The results showed that the accumulated prevalence of epilepsy was 18.6/1000 inhabitants (95% CI:16.6 - 20.6).

Prevalence and age range - The accumulated prevalence of epilepsy was not equally distributed among the four age groups studied, as can be seen in Table 1 (p-value = 0.0001).

Prevalence of active epilepsy (P_{ae}) - The active epilepsy was analyzed taking into account at least one seizure in the last 2, 3, 4 and 5 years. The results are shown in Table 2. The prevalence of inactive epilepsy was obtained by subtracting the active epilepsy prevalence from the accumulated and it was studied in respect to the identical time intervals.

Prevalence of types of epilepsy according to the ILAE classification - The prevalence of epilepsy according to the clinical and electroencephalographic classification of epileptic seizures (ILAE)[21] is shown in Table 3.

Prevalence of epileptic syndromes according to the ILAE classification - The prevalence of epilepsy considering its syndromic classification according to ILAE (1989)[22] was analyzed and the results are shown in Table 4.

DISCUSSION

In general, the use of the questionnaire was well accepted by the population and refusal to collaborate was minimal. In various residences the interviewers were unsuccessful in talking to the inhabitants. The investigator (MAB) himself went

Table 1. Prevalence of accumulated epilepsy with respect to age groups*.

Age range	Prevalence	
(years)	/1000 inhabitants	95%;CI
0 to 4	4.9	3.9 - 6.0
5 to 14	11.7	10.0 - 13.3
15 to 64	20.3	18.2 - 24.4
65 or more	32.8	30.1 - 35.4
Total	18.6	16.6 - 20.6

*, p-value < 0.0001

to some of these houses and verified that the reason for this was fear of robbers (the individual was alone at home) and the inconvenience of politicians, preachers, salesmen and beggars. In lower economic class neighborhoods, individuals were more collaborative to give information about diseases in the family. In the upper class communities this was more complicated and to access them, we asked the help of their neighbors to inform them about the research and also we contacted them by previous telephone calls.

Confirmation of diagnosis, based on clinical records and a physical examination, was made by a neurologist (MAB) with experience in epilepsy. As diagnosis of epilepsy is sometimes difficult[23], care was taken to crosscheck the information with records from the reference service of the HB when the data were available. These details increased the credibility and the reliability of the results, mainly in respect to classification of seizures and of causes of disease. This procedure has frequently been used by other authors[11,12,24,16].

The accumulated and active (2, 3, 4, and 5 years) prevalence of epilepsy in the city of São José do Rio Preto are high and overall they are comparable to prevalences estimated in other developing countries[5,8,13,22], specifically to Latin American countries. Placencia et al.[8] reviewed 48 studies published in the 70s, 80s and 90s about prevalence using different methodologies. They found a high prevalence particularly in developing countries, although in some countries such as India[25] and

Nigeria[11,12] there are regions in which the prevalence is low, similar to what is observed in developed countries[26].

The accumulated prevalence was not associated with gender, as had been observed in the majority of surveys, both in developed [2] and developing countries[5,16,21]. The active epilepsy rate was high with all the period intervals considered (2, 3, 4 and 5 years), with a great increase in the prevalence from two to five-year period. This may be explained by the difficulty of some patients in maintaining the adherence to treatment, already suggested by Zielinski in a study from Poland[27]. However, this increase of prevalence over the five-year period found in this study, is more accentuated, but no significant, than that in developed countries which supports findings by Fernandes et al. in Brazil[17,28] and Aziz et al. in Pakistan[24].

This design did not specifically consider the interval in which the patients did not take medicine, the so-called treatment gap. However, in respect to the occurrence of at least one seizure in the last 5 years, only 28.5% of the individuals with epilepsy controlled their seizures, suggesting that the treatment gap is high. These alarming numbers are relevant and of great importance to the local public health.

The five age groups studied, two of which are related to children, took into consideration the period in which the main symptoms of idiopathic epilepsy appear[29]. In this study, a strong association between the prevalence of epilepsy and age was demonstrated. For instance, the prevalence of active epilepsy (five-year period) among children from 0 to 14 years is low, comparable to the prevalence found by Hauser et al.[2] in the city of Rochester in the USA and Kurtz et al.[30] in Britain. In general, the recent epidemiological studies have pointed to a low rate in this age group, except for a study in India[31] in which the prevalence was high, probably due to malnutrition, perinatal problems and infections.

The prevalence of active epilepsy in school children (5 to 14 years) in this study had a significant increase similar to studies from the industrialized world[2]. This stems from the appearance of idiopathic epilepsy in infancy. However, the prevalence of epilepsy in this age group was significantly lower than the rate found in Chile[32], which was probably due to their inclu-

Table 2. Prevalence of active and inactive epilepsy with respect to at least one seizure in the last 2, 3, 4 and 5 years.

Last seizure	Active epilepsy		Inactive epilepsy	
(years)	Prevalence	95%;CI	Prevalence	95%;CI
2	8.2	6.8 - 9.5	10.4	8.9 - 11.9
3	10.9	9.3 - 12.4	7.7	6.4 - 9.0
4	12.6	10.9 - 14.3	5.9	4.8 - 7.1
5	13.3	11.6 - 15.0	5.3	4.2 - 6.4

Table 3. Percentages and prevalence of types of epileptic seizures (ILAE)[21].

Classification	Patients with epilepsy		Epidemiology	
ILAE (1981)	N	%	Prevalence/ 1000 inhabitants	95%;CI
Partial242	75.4	14.0	12.2 - 15.7	
Generalized	42	13.1	2.4	1.7 - 3.1
Non-Classified	37	11.5	2.2	1.5 - 2.9

Table 4. Percentages and prevalence of the epileptic syndromes (ILAE)[22].

Seizure type	Patients with epilepsy		Epidemiology	
ILAE (1989)	N	%	Prevalence	95;CI %
Idiopathic	27	8.4	1.5	0.9 - 2.2
Cryptogenic	179	55.9	10.4	8.9 - 11.9
Symptomatic	111	34.6	6.4	5.2 - 7.6
Undetermined	4	1.21	0.2	-
Total	321	100	18.6	16.6 - 20.6

sion of febrile seizures as epilepsy in their study.

The prevalence of accumulated epilepsy in adults was high, similar to the rates found in other developing countries in Latin America[5,16,28,33]. Thus, the most important risk factors acting in developing countries may have influenced this age group in the past and perhaps still have an influence with diseases such as neurocysticercosis, infectious diseases and sanitary health problems[34-37].

The prevalence of accumulated epilepsy in the elderly is high. According to publications, this rate is falling in industrialized countries[2,11] and even more so in underdeveloped countries[8,13], a fact that is difficult to explain. Another fact observed in relation to the accumulated prevalence in SJRP, among the elderly, was the significant tendency to be greater then in developed countries[38,39]. This is probably due to an overlapping of risk factors found both in developed and in developing countries[40].

The partial seizures were the most common, however with an elevated prevalence. These results are similar to those of several recent researches[2,40-43]. The explanation proposed for this fact may be the low rate of remission of partial seizures. Another aspect that may cause an overestimation of this prevalence is neurocysticercosis a risk factor which is endemic in this region[35,36].

Idiopathic seizures have a low prevalence, significantly lower than the results of other recent investigations in Europe[43-45]. Perhaps this fact is due to the disproportional increase in the prevalence of cryptogenic and symptomatic epilepsy, a characteristic of underdeveloped and developing countries. Thus,

if patients with epilepsy caused by avoidable circumstances were ignored in this study, the prevalence of symptomatic epilepsy would probably be significantly higher and therefore similar to results found in Europe. The percentage of symptomatic seizures was similar to the recent studies[23,43,46], perhaps due to the technological resources now available here.

The results of this research demonstrated that the prevalence of epilepsy in São José do Rio Preto is high among young people, adults and the elderly but low among children. This reflects the influences of risk factors from both industrialized and underdeveloped societies. Also more than two thirds of the individuals with epilepsy are without control of their seizures, in such a way that government public health campaigns are urgently required, with the aim of socio-economic inclusion of this important group of the population.

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