JOBNAME: alz 18#4 2004 PAGE: 1 OUTPUT: Mon November 29 14:38:47 2004
lww/alz/88441/03-061RR

ORIGINAL ARTICLE

Incidence of Dementia in a Community-Dwelling Brazilian Population

R. Nitrini, MD, P. Caramelli, MD,* E. Herrera Jr., MD,† V. S. Bahia, MD,* L. F. Caixeta, MD,* M. Radanovic, MD,* R. Anghinah, MD,* H. Charchat-Fichman, MSc,* C. S. Porto, MSc,* M. T. Carthery, MSc,* A. P. J. Hartmann, MD,* N. Huang, MD,* J. Smid, MD,* E. P. Lima, BSc,* L. T. Takada,* and D. Y. Takahashi**

Abstract: The authors report the incidence of dementia in a community-dwelling Brazilian population. In 1997, 1656 individuals aged 65 years or more, the majority being of very low educational level, were screened at their homes in Catanduva, Brazil, and dementia was diagnosed in 118 cases. The remaining 1538 individuals were rescreened 3.25 years later applying a health questionnaire, the Mini-Mental State Examination (MMSE) and the Pfeffer Functional Activities Questionnaire (PFAQ). According to PFAQ and MMSE scores, selected subjects were submitted to clinical, neurologic, and cognitive evaluations. The subjects diagnosed with dementia underwent laboratory tests and brain computed tomography. A total of 1119 individuals were rescreened and 50 incident cases of dementia (28 with Alzheimer disease [AD]) were identified. The incidence rate of dementia was 13.8 and of AD was 7.7 per 1000 person-years for individuals aged 65 years or older. The incidence rates of dementia almost doubled with every 5 years of age. There was no difference according to gender, but women had a higher incidence of dementia, predominantly AD, in very old age. There was a trend for higher incidence of dementia in illiterates ($p = 0.07$), but multivariate analysis disclosed significant association only between age and higher incidence of dementia. The incidence rates of dementia in this Brazilian community are comparable to those reported in Western and Asian studies.

Key Words: dementia, incidence, epidemiology, education, socioeconomic level, Brazil

(*Alzheimer Dis Assoc Disord* 2004;18:241–246)

Dementia is a major social health problem because of the fast-growing elderly population. Prevalence rates of dementia have now been determined in several countries, but comparisons between populations are hampered in that they can reflect differences resulting from either incidence or survival. Incidence studies are more appropriate for assessing the burden of a disease, for the planning of health policies, for the investigation of risk factors, and for the comparison between different populations. The incidence of dementia has been determined less often than the prevalence because incidence studies require longitudinal observation to ascertain new onsets of dementing diseases.[1–4]

Incidence rates for dementia are now available for several developed countries[2–6] and for a few developing countries.[7–9] Besides age, incidence could be influenced by other demographic variables, such as educational and socioeconomic levels.[7,10,11]

In the developing world, including Latin America, a rapid increase in life expectancy has occurred in recent decades.[12] In Brazil, the group of individuals aged 60 years and older is the fastest growing age group.[13] The developing countries still have a large proportion of illiterates and individuals with low levels of schooling, especially among the elderly population. The heterogeneity of educational and socioeconomic levels in the population of developing countries could provide more information about the relative importance of ethnicity and social factors as risk factors for dementia.

The aims of this study were to determine the incidence of dementia, and of Alzheimer disease (AD), in a community-dwelling population living in an urban area in Brazil, and to correlate these data with educational and socioeconomic levels.

METHODS

Baseline Study

The study was conducted in the urban area of the town of Catanduva, in São Paulo state, southeastern Brazil, a town with 100,913 inhabitants according to the 1996 Brazilian census. In 1997, we randomly selected a quarter of the addresses from each sub-district list of addresses where individuals aged 65 years and older resided, so as to screen 25% of the domiciles. The methods and results of the baseline study were recently published.[14] Briefly, 1656 elderly individuals were screened during the months of January and February 1997, most of the individuals being white (84.5%), 9.6% of African decent, 4.3% with mixed ancestry (white, African, and indigenous) and 1.8% of Japanese origin. There were high percentages of illiterates (34.2%) and of very low educated individuals (35.6% with 1–3 years of schooling). A total of 118 cases of dementia were diagnosed, representing a prevalence of 7.1%.

Received for publication July 24, 2003; accepted April 22, 2004.
From the *Behavioral and Cognitive Neurology Unit, Department of Neurology, University of São Paulo School of Medicine, São Paulo, Brazil; and the †Department of Internal Medicine, Catanduva School of Medicine, Catanduva, Brazil.
Supported by FAPESP (Fundo de Amparo à Pesquisa do Estado de São Paulo).
Reprints: Ricardo Nitrini, MD, Rua Bartolomeu Feio, 560 04580-001 São Paulo, SP Brazil (e-mail: rnitrini@uol.com.br).

JOBNAME: alz 18#4 2004 PAGE: 2 OUTPUT: Mon November 29 14:38:48 2004
lww/alz/88441/03-061RR

Incidence Study

Screening Phase

In 2000, the 1538 without dementia in the first evaluation were informed by letter that a new home interview was being planned, in which its objectives and noncompulsory nature were explained. Seventeen graduate students of the Catanduva School of Medicine rescreened the individuals at their homes during the months of April and May 2000. Prior to this rescreening, training sessions were given by the study coordinators, including the trial application of tests and questionnaires to volunteers under the supervision of a senior neurologist (E.H.). Informed consent was obtained from all participants or from a family member, when appropriate. Screening evaluation consisted of a questionnaire assessing basic demographic data, socioeconomic level, information on the general health and mental status provided by the subject and by a family member or proxy, the Mini-Mental State Examination (MMSE),[15,16] and the Pfeffer Functional Activities Questionnaire (PFAQ).[17] The PFAQ is one of the questionnaires proposed by two consensus statements on the diagnosis of dementia,[18,19] it is answered by a family member or proxy, and it includes 10 questions about the performance in activities of daily living with scoring ranging from 0 to 3, according to the severity of disability in each activity. The maximum score is 30 and scores higher than 5 are indicative of functional impairment. For the socioeconomic level, the criteria of the Brazilian Association of the Institute of Market Research were used, where the classification is based on a score obtained from several items related to the persons' residence. These include the number of bathrooms, full-time maids, cars, TV sets, and such, combined with the educational level of the head of the household; overall levels ranging from A (highest), to E (lowest).

Diagnostic Evaluation

All subjects with PFAQ score >5 and MMSE below specific education-adjusted scores were considered to have suspected dementia and were selected for diagnostic evaluation. The MMSE cutoff scores were as follows: 27 for subjects with educational level >7 years, 24 for those with 1 to 7 years of schooling, and 19 for the illiterate. These cutoff scores were higher than those proposed by a Brazilian study,[16] to increase the sensitivity of the screening. Participants were considered illiterates when they fulfilled all of the following three conditions: they had never attended school or had attended for less than 1 year, they considered themselves as unable to read, and they were unable to read the phrase "close your eyes" from the MMSE.

For the diagnostic evaluation, 10 physicians (nine neurologists and one psychiatrist) examined those individuals having suspected dementia using a protocol consisting of medical history, information on head trauma history, smoking habits, alcohol consumption, use of anti-inflammatory drugs, use of estrogens, and family history of dementia. The individuals were also submitted to physical and neurologic examination, the Brazilian version of the CERAD neuropsychological battery,[20] a neuropsychological battery including immediate and delayed recall of 10 simple objects presented as line drawings,[21,22] semantic verbal fluency and the clock drawing test,[23] the Behave AD,[24] and the Cornell Scale for Depression in Dementia.[25]

Subjects with difficulty in performing the cognitive tests due to auditory, visual, or other physical problems that could have affected their performance were excluded from the study.

The diagnoses were established through consensus by the whole clinical team, on the same day of the diagnostic evaluation of the individual having suspected dementia, using the DSM-IV criteria for the diagnosis of dementia.[25a] Dementia severity was rated using the clinical dementia rating scale (CDR).[26] Patients with dementia underwent a diagnostic workup that included the following examinations: routine blood tests; tests for liver, kidney, and thyroid functions; serum calcium and phosphorus levels; cholesterol and triglycerides; serum B12 levels; serology for syphilis; chest x-ray; and brain computed tomography.

Based on the data from the clinical history, neurologic examination, and laboratory and brain computed tomography findings, the clinical diagnoses were established according to previously published criteria, namely, National Institute of Neurologic Communicative Disorders and Stroke-Alzheimer' Disease and Related Disorders Association (NINCDS-ADRDA) criteria[27] for AD; National Institute of Neurologic Disorders and Stroke-Association Internationale pour la Recherche et L'Enseigment en Neurosciences (NINDS-AIREN) criteria for vascular dementia and for AD with cerebrovascular disease (AD + CVD)[27a]; McKeith et al criteria[28] for dementia with Lewy body; and Neary et al criteria[29] for frontotemporal lobar degeneration.

Individuals with PFAQ score <6 and MMSE above the specific education-adjusted scores were stratified by age, sex, and educational level, and a sample of these subjects with similar age, sex, and educational level to the individuals with suspected dementia was randomly selected as a control group. These subjects were evaluated by neuropsychologists and speech therapists using the same protocol, excluding the physical and neurologic examination, and the Behave-AD. Both for the control group and for the individuals having suspected dementia, the examiners were not blind to the results of the first-stage screening.

All data collected in the screening phase and in diagnostic evaluation were transferred to the Epi-Info 6.0 computerized database (Center of Disease Control and Prevention, Atlanta, GA) with double data entry. Missing data and errors were checked and, when necessary, were followed up by a telephone call to the informant.

Data Analysis

Incidence rates were calculated by dividing the number of cases with onset of dementia in each age group over the period of 3.25 years, by the number of rescreened persons in each age group. The period of 3.25 years was defined as the time interval from the mean time of study entry to the mean time of rescreening. Either Pearson's χ^2 test for square matrix (2×2) or χ^2 for trend for rectangular matrix [$2 \times (n > 2)$] was chosen to compare demographic characteristics of groups of individuals and to determine the degree of association between variables. Multivariate analysis of dementia incidence in

relation to age, gender, literacy versus illiteracy, and socioeconomic level was undertaken by logistic regression. Age and socioeconomic levels were categorized into greater than or equal to median versus less than the median. The value of significance accepted was 0.05. The Statistical Package for the Social Sciences for Windows, version 10.0 (SPSS Inc) was used for the statistical analysis.

This study was approved by the Ethics Committee of the Hospital das Clínicas, University of São Paulo School of Medicine, Brazil.

RESULTS

The numbers participating in each phase and the general design of the study are summarized in Figure 1.

Screening Phase 1

We were able to rescreen 1119 from the target population of 1538 individuals, where 183 had died between the prevalence baseline and the incidence studies, 212 were not located, and 24 refused to participate. These 1119 individuals were not different from the target population regarding sex (Pearson's $\chi^2 = 0.064$; $p = 0.800$), educational level (χ^2 for trend = 0.4197; $p = 0.5171$), and age (χ^2 for trend = 8.265; $p = 0.1422$). The demographic features of the screened individuals are shown in Table 1.

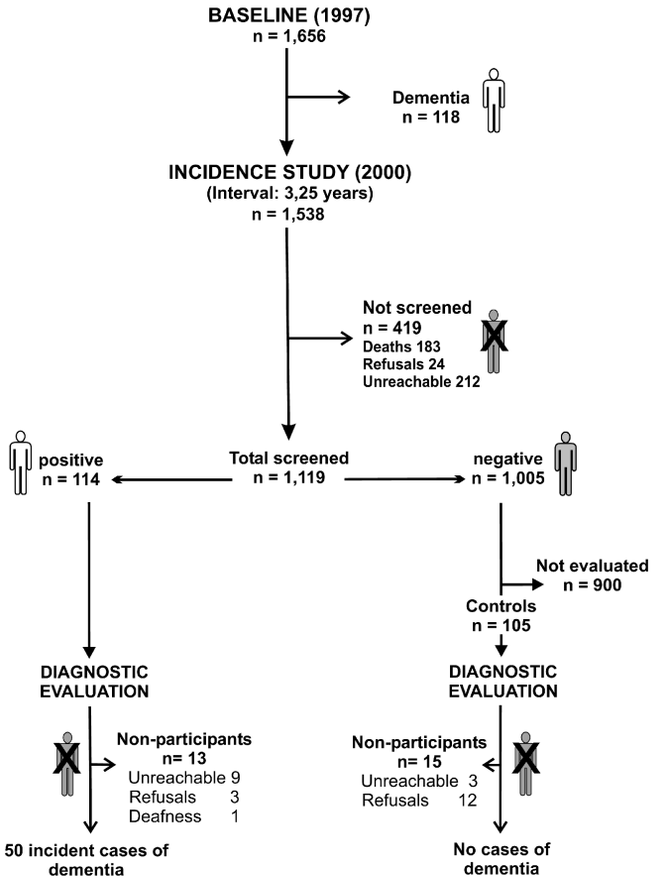

FIGURE 1. Design and participant flow chart of the study.

TABLE 1. Demographic Features of the 1,119 Screened Individuals

Age (years)	Women Schooling (years) 0	1–3	4–7	≥8	Men Schooling (years) 0	1–3	4–7	≥8	Total
65–69	33	43	34	17	17	32	21	9	206
70–74	69	86	60	15	37	91	47	24	249
75–79	68	48	33	8	25	50	22	8	262
80–84	36	20	16	7	15	19	7	3	123
85–89	19	15	11	0	14	15	4	5	83
≥90	4	0	1	2	5	2	2	0	16
Total	229	212	155	49	113	209	103	49	1,119

A total of 114 individuals were suspected to have dementia according to the MMSE and PFAQ scores, these being selected for diagnostic evaluation. A total of 105 individuals, with similar age (χ^2 for trend = 1.39; $p = 0.247$), sex (Pearson's $\chi^2 = 2.73$; $p = 0.098$), and educational level (χ^2 for trend = 2.413; $p = 0.123$) to those with suspected dementia were selected to be examined as the control group.

Diagnostic Evaluation

A total of 101 individuals (88.6%) having suspected dementia were examined (9 were not located, 3 refused to participate, and 1 had deafness). Dementia was diagnosed in 50 individuals, corresponding to the incidence rate of 13.8 per 1000 person-years for individuals aged 65 years or older. Twenty five patients were classified as CDR 1.0, 11 as CDR 2.0, and 14 as CDR 3.0. The diagnoses of the diseases causing the dementia are shown in Table 2. In the control group, 90 individuals were examined, and no case of dementia was identified.

The incidence rate of AD (including probable, possible, and AD associated with cerebrovascular disease) was 7.7 per 1000 person-years for individuals aged 65 years or older. The incidence rate of probable AD was 4.1 per 1000 person-years in this age group. Among the 25 cases of AD, 17 were women

TABLE 2. Diagnoses of the Diseases Causing Dementia in the Incident Cases

Diagnosis	*N*	%	Male (*N* = 23)	Female (*N* = 27)
Probable AD	15	30.0	4	11
Possible AD	10	20.0	4	6
AD + cerebrovascular disease	3	6.0	2	1
Vascular dementia	9	18.0	4	5
Parkinson's disease	3	6.0	2	1
Dementia with Lewy body	2	4.0	2	—
Huntington's disease	1	2.0	—	1
Frontotemporal dementia	1	2.0	—	1
Alcoholic dementia	1	2.0	1	—
Post-traumatic dementia	1	2.0	1	—
Multiple causes	2	4.0	2	2
Undetermined cause	2	4.0	1	1

JOBNAME: alz 18#4 2004 PAGE: 4 OUTPUT: Mon November 29 14:38:56 2004
lww/alz/88441/03-061RR

TABLE 3. Age-Specific Incidence Rates Per 1,000 Person-Years for Dementia by Age and Sex

Age (years)	*N*	Dementia Incidence Rates (95%CI)		
		Women	Men	Total
65–69	2	2.4 (0.52–0.725)	3.9 (0.845–11.60)	3.0 (0.4–10.7)
70–74	9	4.0 (1.74–7.77)	9.3 (5.72–15.05)	6.4 (3.0–12.1)
75–79	14	13.7 (9.36–23.87)	20.5 (14.04–32.92)	16.4 (9.1–27.1)
80–84	10	19.2 (3.87–32.05)	35.8 (21.12–58.66)	25.0 (12.2–44.4)
85–89	13	68.4 (5.13–98.60)	24.3 (11.64–45.83)	48.2 (26.5–77.8)
≥90*	2	44.0 (9.46–113.46)	34.2 (7.38–91.74)	38.5 (4.8–118.0)

Note: Chi-square for trend = 38.25; $p < 0.0001$.
CI = confidence interval.
*Only 1 patient (aged 97) was over 94.

and 8 men, but this difference was not statistically significant (Pearson's $\chi^2 = 1.087$; $p = 0.297$).

The incidence of dementia and AD was associated with age, as shown in Tables 3 and 4. Figure 2 shows the age-specific incidence rates of dementia in our study compared with meta-analysis studies.

Although sex was not associated with the incidence of dementia (Pearson's $\chi^2 = 1.25$; $p = 0.26$), the incidence of dementia was higher for women older than 85 years ($p < 0.001$; Fisher exact test). For men, the incidence was higher in the age groups younger than 85 years, but the difference was not significant ($p > 0.2$). The incidence of AD was higher for women in very old age ($p < 0.001$; Fisher exact test).

Socioeconomic levels were also not associated with the incidence of dementia (Table 5).

Incidence of dementia was higher in illiterate individuals. Twenty-one incident cases of dementia (6.1%) occurred in 342 illiterate individuals, while 29 (3.7%) occurred in 777 literate individuals (Pearson's $\chi^2 = 3.23$; $p = 0.072$). In univariate analysis, educational level was not associated with the incidence of dementia (Table 6). Logistic regression showed that only age (odds ratio = 11.7; 95% confidence interval, 3.6–37.9) was associated with higher incidence of dementia. When we introduced age by sex interaction in the logistic regression analysis, it was not significant ($p > 0.4$).

TABLE 4. Age-Specific Incidence Rates Per 1,000 Person-Years for AD by Age and Sex

Age (years)	*N*	AD* Incidence Rates (95% CI)		
		Women	Men	Total
65–69	—	—	—	—
70–74	2	1.3 (0.29–4.0)	1.55 (0.55–3.22)	1.43 (0.17–5.15)
75–79	6	7.8 (5.72–15.05)	5.86 (4.32–11.41)	7.04 (2.60–15.13)
80–84	8	19.2 (25.74–64.45)	21.47 (20.96–45.92)	20.01 (8.77–38.19)
85–89	8	41.0 (25.74–64.45)	16.2 (4.16–54.82)	29.65 (26.9–73.1)
≥90†	1	44.0 (9.46–113.46)	—	19.23 (0.5–93.0)

Note: Chi-square for trend = 37.43; $p < 0.0001$.
CI = confidence interval.
*Probable and possible AD, excluding cases with associated cerebrovascular disease.
†Only 1 patient (aged 97) was over 94.

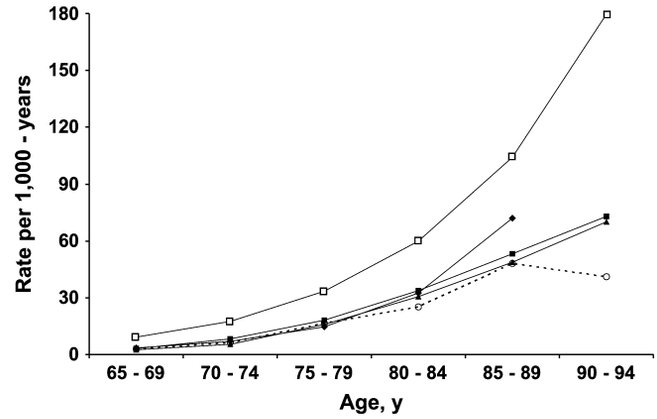

FIGURE 2. Annual incidence rates of dementia. □, Meta-analysis of European studies.[2] ◆, Meta-analysis of East Asian studies.[2] ■, Meta-analysis of Western and Asian studies.[3] ▲, Meta-analysis of European studies.[5] ○, Brazilian incidence study.

DISCUSSION

The age-specific incidence rates of dementia in this Brazilian community are close to those reported in the meta-analyses of European,[5] Western and Asian,[3] and East Asian[2] studies, up to and including the 85- to 89-year age group (Fig. 2). In another meta-analysis of nine European studies,[2] which comprise only one study also included in the meta-analysis by Fratiglioni et al,[5] the incidence rates of mild dementia were much higher than in the others, ranging from 9.1 per 1000 person-years at the ages 65 to 69 years to 104.1 at 85 to 89 years. The discrepancy between these different meta-analyses may be related to different criteria used for the diagnosis of dementia in these studies. According to Jorm and Jolley,[2] DSM criteria tend to give lower incidence rates for mild+ dementia, but higher rates for moderate+ dementia in population studies. In our study, only individuals with both low scores in the MMSE and impairment in functional activities were screened positive for dementia, a procedure that may have increased specificity to the detriment of sensitivity.

In a recent report on the incidence of dementia in Seattle,[6] the incidence rate was 4.65 per 1000 person-years at the ages 65 to 69 years, while this increased to 54.05 at 85 to 89 years; these rates are also close but slightly higher than our findings.

TABLE 5. Incidence Rates Per 1,000 Person-Years for Dementia According to Socioeconomic Level

Socioeconomic Level	*N*	Dementia (*N*)	Incidence Rate (Per 1,000 Person-Years)	95% CI
A	72	1	4.27	0.11–23.38
B	174	8	14.15	6.51–28.77
C	403	25	19.09	13.31–29.57
D	406	12	9.09	4.87–16.18
E	58	4	21.22	6.32–55.06

Note: Chi-square for trend = 0.0153; $p = 0.902$. The socioeconomic levels of 6 individuals were not known.
CI = confidence interval.

TABLE 6. Incidence Rate Per 1,000 Person-Years for Dementia According to Schooling

Schooling (years)	*N*	Dementia (*N*)	Incidence Rate (Per 1,000 person-years)	95% CI
8 or more	98	3	9.42	2.02–27.54
4–7	258	11	13.12	6.90–24.09
1–3	421	15	10.96	6.41–18.52
0 (illiterate)	342	21	18.89	12.60–30.24

Note: Chi-square for trend = 1.937; $p = 0.164$.
CI = confidence interval.

In developing countries, the incidence of dementia has been determined less often. In Ibadan, Nigeria, the mortality-adjusted incidence rate was 13.5 per 1000 person-years in individuals aged 65 or older.[9] In Beijing, the incidence rate was 5.6 per 1000 person-years, but people aged 60 years or older were included,[7] which certainly reduced the incidence rate.

The incidence rates of dementia in this community more than doubled for every 5 years of age, from the 65- to 69-year age group up to the 75- to 79-year age group. Above this age group, there was a slowing of the increase with age. In the meta-analysis of eight European studies,[5] the incidence rates of dementia ranged from 2.4 per 1000 person-years at the ages of 65 to 69 years to 48.6 per 1000 person-years at the ages 85 to 89 years, which are very similar to our findings. However, for the group aged 90 years and older, the incidence rate rose to 70.2 per 1000 person-years in the European studies while dropping to 38.46 in our study. The leveling off at older ages has been reported by others,[30–32] and it is probably due to the small number of very old individuals in the community,[2,5] although it may reflect that the acceleration of incidence rates for dementia slows down in advanced age.[3] The upper limit of the confidence interval we found is consistent with increasing incidence of dementia even in advanced ages.

Several studies have reported higher incidence of dementia in women,[4,33–35] while others did not find a difference.[36,37] Higher incidence of AD for women than for men at very old ages had already been described.[34] In our study, the incidence of dementia was higher for women older than 85 years, with most of the cases being AD. Similar findings had been reported in a meta-analysis of 23 incidence studies.[2]

We found no effects of socioeconomic levels on the incidence of dementia in this study. However, the lack of relationship with the socioeconomic level should be considered with caution because the classification we used ranks the socioeconomic level of the person at the time of study and not during childhood or early adulthood, when factors such as diet and quality of health care may well have a greater impact on the risk of developing dementia in the future.

Although there was also a trend for higher incidence of dementia in illiterates in this study, multivariate analysis did not confirm this. In a previous epidemiologic study in this same community, illiteracy was associated with higher prevalence of dementia.[14] However, the diagnosis of dementia in low-educated individuals remains a difficult undertaking. In a rural community in India, where illiterates constituted three fourths of the cohort, the incidence of dementia was very low, and the authors considered that the low sensitivity of the dementia screening instruments and the difficulties in evaluating functional decline in a "low-tech," low demanding environment were the most possible explanations for the low incidence of dementia.[8] It is possible that these circumstances occurred in our study and that the incidence in the illiterate and low educated individuals may be higher than we are reporting.

There are other factors that may have contributed toward reducing the estimate of the true incidence of dementia in this study. One of these is attrition. However, when we compared the 1119 screened individuals with the target population of 1538 individuals, there were no differences in age, sex, and educational level between them. Besides, only individuals that were screened positive for dementia and a sample of negative screened individuals were submitted to a diagnostic evaluation for dementia, and there was also attrition between screening and diagnostic evaluation phases. Although this two-stage method of case ascertainment had been used in most studies on the incidence of dementia, one-stage comprehensive diagnostic procedures have been recently proposed for population studies on dementia, a method that may prove useful for future studies in developing countries.[38]

There were 183 deaths between baseline study in 1997 and follow-up in 2000, and several of the deceased persons may have had dementia, as has been already reported.[4] We did not interview informants about deceased persons' cognitive decline, but as most of the incidence studies did not make adjustments for deceased persons, the comparison between our incidence rates with theirs probably was not affected by mortality rate.

In the Indianapolis-Ibadan Dementia Project, two populations from nonindustrialized and industrialized countries were evaluated for the incidence of dementia using identical diagnostic methods, and the incidence was lower among Yoruba than among blacks. The lower incidence of dementia in the Yoruba was assumed by the authors to be related to genetic and other environmental factors.[9] Since allelic polymorphisms of the ApoE gene is the most important risk factor for late-onset AD, it is pertinent to inform that the association of the ε4 allele with AD in the population of this Brazilian State[39] is weaker than those reported in North American,[40] Scandinavian,[41] and Northern Italian populations[42] but is similar to those of Spanish[43] and other Latin American populations.[44,45]

To summarize, all these possibilities may have contributed to reducing the incidence we found in this study, and should be taken into consideration when devising future epidemiologic studies into dementia in developing countries.

CONCLUSION

The incidence rates of dementia in this Brazilian community are comparable to those reported in Western and Asian studies, and AD is the most common type of dementia.

ACKNOWLEDGMENTS

The authors thank the medical students from the Catanduva School of Medicine for their participation in the study and the elderly population of Catanduva.

REFERENCES

1. Jorm AF. *The Epidemiology of Alzheimer's Disease and Related Disorders*. London: Chapman and Hill, 1990.
2. Jorm AF, Jolley D. The incidence of dementia: a meta-analysis. *Neurology.* 1998;51:728–733.
3. Gao S, Hendrie HC, Hall KS, et al. The relationships between age, sex, and the incidence of dementia and Alzheimer's disease: a meta-analysis. *Arch Gen Psychiatry.* 1998;55:809–815.
4. Canadian Study of Health and Aging Working Group. The incidence of dementia in Canada. *Neurology.* 2000;55:66–73.
5. Fratiglioni L, Launer LJ, Andersen K, et al. Incidence of dementia and major subtypes in Europe: a collaborative study of population-based cohorts. *Neurology.* 2000;54(suppl 5):10–15.
6. Kukull WA, Higdon R, Bowen JD, et al. Dementia and Alzheimer disease incidence: a prospective cohort study. *Arch Neurol*. 2002;59:1737–1746.
7. Li G, Shen C, Chen CH, et al. A three-year epidemiological survey of age-related dementia in an urban area of Beijing. *Acta Psychiatr Scand*. 1991;83:99–104.
8. Chandra V, Pandav R, Dodge HH, et al. Incidence of Alzheimer's disease in a rural community in India: the Indo-US study. *Neurology.* 2001;57:985–989.
9. Hendrie HC, Ogunniyi A, Hall KS, et al. Incidence of dementia in Ibadan, Nigeria, and African American residing in Indianapolis, Indiana. *JAMA*. 2001;285:739–747.
10. Ganguli M, Dodge HH, Chen P, et al. Ten-year incidence of dementia in a rural elderly US community population: the MoVIES project. *Neurology.* 2000;54:1109–1116.
11. Hall KS, Gao S, Unverzagt FW, et al. Low education and childhood rural residence: risk for Alzheimer's disease in African Americans. *Neurology.* 2000;54:95–99.
12. Mangone CA, Arizaga RL. Dementia in Argentina and other Latin-American countries: an overview. *Neuroepidemiology.* 1999;18:231–235.
13. Ramos LR, Veras RP, Kalache A. Population aging: a Brazilian reality. *Rev Saude Publica*. 1987;21:212–224.
14. Herrera E Jr, Caramelli P, Silveira ASB, et al. Epidemiological survey of dementia in a community-dwelling Brazilian population. *Alzheimer Dis Assoc Disord*. 2002;16:103–108.
15. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12:189–198.
16. Bertolucci PHF, Brucki SM, Campacci SR, et al. O mini-exame do estado mental em uma população geral. *Arq Neuropsiquiatr.* 1994;52:1–7.
17. Pfeffer RI, Kurosaki TT, Harrah CH, et al. Measurement of functional activities in older adults in the community. *J Gerontol*. 1982;37:323–329.
18. Corey-Bloom J, Thal LJ, Galasko D, et al. Diagnosis and evaluation of dementia. *Neurology.* 1995;45:211–218.
19. Small GW, Rabins PV, Barry PP, et al. Diagnosis and treatment of Alzheimer's disease and related disorders. *JAMA*. 1997;278:1363–1371.
20. Bertolucci PH, Okamoto IH, Brucki SM, et al. Applicability of the CERAD neuropsychological battery to Brazilian elderly. *Arq Neuropsiquiatr*. 2001;59:532–536.
21. Nitrini R, Lefèvre BH, Mathias SC, et al. Testes neuropsicológicos de aplicação simples para o diagnóstico de demência. *Arq Neuropsiquiatr*. 1994;52:457–465.
22. Nitrini R, Caramelli P, Herrera E Jr, et al. Performance of illiterate and literate nondemented elderly subjects in two tests of long-term memory. *J Intern Neuropsych Soc*. In press.
23. Sunderland T, Hill JL, Melow AM, et al. Clock drawing in Alzheimer's disease: a novel measure of dementia severity. *J Am Geriatr Soc*. 1989;37:725–729.
24. Reisberg B, Borenstein J, Salob SP, et al. Behavioral symptoms in Alzheimer's disease: phenomenology and treatment. *J Clin Psychiatry.* 1987;48(suppl):9–15.
25. Alexopoulos GS, Abrams RC, Young RC, et al. Cornell Scale for depression in dementia. *Biol Psychiatry.* 1988;23:271–284.

25a. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th ed. Washington, DC: American Psychiatric Association, 1994.

26. Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology.* 1993;43:2412–2414.
27. Mc Khann G, Drachman D, Folstein M, et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA work group under the auspices of department of health and human services task force on Alzheimer's disease. *Neurology.* 1984;34:939–944.

27a. Román GC, Tatemichi TK, Erkinjuntti T, et al. Vascular dementia: diagnostic criteria for research studies. Report of the NINDS-AIREN international workshop. *Neurology.* 1993;43:250–260.

28. McKeith IG, Galasko D, Kosaka K, et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. *Neurology.* 1996;47:1113–1124.
29. Neary D, Snowden JS, Gustafson L, et al. Frontotemporal lobar degeneration: a consensus on clinical diagnostic criteria. *Neurology.* 1998;51:1546–1554.
30. Manubens JM, Martinez-Lage JM, Lacruz F, et al. Prevalence of Alzheimer's disease and other dementing disorders in Pamplona, Spain. *Neuroepidemiology.* 1995;14:155–164.
31. Lobo A, Saz P, Marcos G, et al. Incidence of dementia and other psychiatric conditions in the elderly. *Neuroepidemiology.* 1992;11(suppl 1):52–56.
32. Hagnell O, Öjesjö L, Rorsman B. Incidence of dementia in the Lundby study. *Neuroepidemiology.* 1992;11(suppl 1):61–66.
33. Letenneur L, Commengs D, Dartigues JF, et al. Incidence of dementia and Alzheimer's disease in elderly community residents of southwestern France. *Int J Epidemiol*. 1994;23:1256–1261.
34. Fratiglioni L, Viitanen M, von Strauss E, et al. Very old women at highest risk of dementia and Alzheimer's disease: incidence data from the Kungsholmen Project, Stockholm. *Neurology.* 1997;48:132–138.
35. Ott A, Breteler MM, van Harskamp F, et al. Incidence and risk of dementia: the Rotterdam study. *Am J Epidemiol*. 1998;147:574–580.
36. Bachman DL, Wolf PA, Linn RT, et al. Incidence of dementia and probable Alzheimer's disease in a general population: the Framingham Study. *Neurology.* 1993;43:515–519.
37. Rocca WA, Cha RH, Waring SC, et al. Incidence of dementia and Alzheimer's disease: a reanalysis of data from Rochester, Minnesota, 1975–1984. *Am J Epidemiol*. 1998;148:51–62.
38. Prince M, Acosta D, Chiu H, et al for the 10/66 Dementia Research Group. Dementia diagnosis in developing countries: a cross-cultural validation study. *Lancet*. 2003;361:909–917.
39. Bahia VS. *Polimorfismos da região promotora e codificadora do gene APOE e do gene LRP na doença de Alzheimer em indivíduos brasileiros* [Thesis]. São Paulo, Brazil: University of São Paulo School of Medicine, 2003.
40. Strittmatter WJ, Saunders AM, Schemechel D. Apolipoprotein E: high-avidity binding to β-amyloid and increase frequency of type 4 allele in late onset familial Alzheimer disease. *Proc Natl Acad Sci USA*. 1993;90:1977–1981.
41. Lehtovirta M, Helisalmi S, Mannermaa A, et al. Apolipoprotein E polymorphism and Alzheimer's disease in Eastern Finland. *Neurosci Lett*. 1995;185:13–15.
42. Sorbi S, Nacmias B, Forleo P, et al. ApoE allele frequencies in Italian sporadic and familial Alzheimer's disease. *Neurosci Lett*. 1994;177:100–102.
43. Adroer R, Santacruz P, Blesa R, et al. Apolipoprotein E allele frequency in Spanish Alzheimer and control cases. *Neurosci Lett*. 1995;189:182–186.
44. Morelli L, Leoni J, Castano EM, et al. Apolipoprotein E polymorphism and late onset Alzheimer's disease in Argentina. *J Neurol Neurosurg Psychiatry.* 1996;61:426–427.
45. Jacquier M, Arango D, Villareal E, et al. ApoE β4 and Alzheimer disease: positive association in a Colombian clinical series and review of the Latin-American studies. *Arq Neuropsiquiatr.* 2001;59:11–17.

