Cognitive Reserve, Incident Dementia, and Associated Mortality in the Ibadan Study of Ageing

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Abstract

Objectives—To describe factors associated with incident dementia and dementia mortality over 5 years in a large community sample of elderly persons.

Design—Longitudinal investigation of a household multistage probability sample.

Setting—Eight contiguous states of the Yoruba-speaking region of Nigeria.

Participants—Individuals aged 65 and older (N=2,149).

Measurements—Dementia was diagnosed using tools previously validated in the population. Incident cases of dementia over three follow-up waves were determined after censoring cases in the preceding wave. Information on mortality was collected from key informants in subjects' households.

Results—A dementia incident rate was found of 20.9 per 1,000 person-years (95% confidence interval (CI)=17.7–24.9). The adjusted mortality hazard for those with dementia was 1.5 (95% CI=1.1–2.1). Along with previously identified social and demographic factors, poor predementia cognitive function (hazard ratio (HR)=1.8, 95% CI=1.1–2.8) and low occupational complexity (HR=3.2, 95% CI=1.3–8.0) were associated with incident dementia.

Conclusion—The findings confirm the low incidence of dementia in this population, as previously reported. The condition is nevertheless associated with higher risk of mortality. Along with some features of social disadvantage, proxies of lower cognitive reserve were risk factors for incident dementia.

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Keywords

dementia; epidemiology; risk factors; mortality; low- and middle-income countries

It is projected that, by 2040, approximately 71% of persons with dementia globally will be resident in low- and middle-income countries (LMIC)(1), but even though the number of people with dementia in these areas is growing, empirical information about the natural course of dementia in the region remains sparse.

In Nigeria, previous studies have found annual incidence rates of dementia of between 1.4% and 2.2% (2, 3). Incident dementia was mostly associated with poor socioeconomic circumstances (2, 3). The effect of proxies of cognitive reserve, such as life-course occupational complexity and predementia cognitive functioning, (4) has not been investigated.

The present study estimated dementia incidence and mortality in a previously described cohort using data derived from multiple waves conducted over 5 years, taking advantage of a longer period of case accrual (2). The effect of several risk factors on incident dementia, including proxies of cognitive reserve such as occupational complexity and predementia cognitive function, was also investigated.

Methods

Sample selection, recruitment, and follow-up

The Ibadan Study of Aging (ISA) is a stratified multistage cluster randomized sample derived from eight neighboring states in the predominantly Yoruba-speaking region of Nigeria, with a population of approximately 25 million people at the time of the study. The details of the selection procedure have been fully described (2, 5). Up to five calls were made to contact the selected individuals, and there was no replacement for those who could not be contacted or refused to participate in the study.

Baseline assessment was conducted between November 3, 2003, and August 27, 2004, and three annual follow-up waves were implemented in 2007, 2008, and 2009.

Measures

Ascertainment of dementia—The adapted 10-Word Delay Recall Test learning list (10-WDRT) was used to screen for dementia at baseline and follow-up. A second-stage assessment was conducted using the Clinician Home-based Interview to assess Function (CHIF) (6) during each wave of follow-up. The 10-WDRT is adapted from the modified Consortium to Establish a Registry for Alzheimer's Disease(7) and has been shown to have good sensitivity and specificity for identifying persons with dementia in LMIC, including in Nigeria (8).

For the learning phase of this test, a list of 10 words, adapted as previously described (2), was read to participants, who were then asked to list all of the words they could remember. The test was repeated for a total of three administrations to allow for adequate learning. For

each test, the number of words correctly remembered was noted. For the recall phase, participants were requested to repeat as many of the 10 words as they could recall after approximately 5 minutes. A diagnosis of probable dementia was made in participants who recalled fewer than two of the 10 words.

The CHIF is a 10-item semistructured home interview that evaluates respondents' higher cognitive function by assessing their knowledge of how to perform instrumental activities of daily living(6). Each item is scored on an ordinal scale of 0 to 2, with 0 indicating inability to perform the task and 2 indicating good performance. With a score range of 0 to 20, a cut-off point of <18 provides the best trade-off between sensitivity (89.5%) and specificity (68.5%) in Yoruba respondents.

As part of the follow-up waves, different interviewers administered the 10-WDRT and CHIF independently, usually within 48 hours of one another. The 10-WDRT was the first to be administered as part of an interview lasting approximately 1 hour on average. Research supervisors administered the CHIF. A psychiatrist subsequently reviewed all available information to determine dementia. The information included 10-WDRT (<2) and CHIF (<18) scores, interviewer's observations, reported functional status, and the temporal relationship of the onset of any co-occurring depressive disorder.

Estimates of incident dementia over each of the three waves of follow-up were determined after censoring cases of dementia in the preceding wave.

Ascertainment of Mortality

Information on mortality was collected during each of the follow-up waves from a key informant in the household when a member of the cohort was not available to be interviewed. In some other instances, such information was obtained between the waves during the regular monitoring activities that the research supervisors conducted. When such information was received, it was recorded in the participant's case record. In many cases, the precise dates of death were not available, and the best approximations were recorded.

Baseline risk factors

Several demographic, health, and lifestyle risk factors and chronic conditions were assessed at baseline in 2003–04. Participants' highest occupational attainment was categorized based on the International Standard Classification of Occupations (9). Social participation was assessed using items derived from the World Health Organization Disability Assessment Schedule, version 2 (10). Participants were asked: "During the last 30 days, how much did you join in family activities such as eating together, talking with family members, visiting family members, working together?" and "During the last 30 days, how much did you join in community activities such as festivities, religious activities, talking with community members, working together?" Answers were rated as 1 (not at all), 2 (a little bit), 3 (quite a bit), and 4 (a lot). Participants who answered "not at all" to either question were rated as having poor social participation.

Predementia cognitive function was based on performance on the learning phase of the 10-WDRT and dichotomized as poor for dementia-free participants who scored less than 1

standard deviation (SD) below the mean score for three administrations of the 10-WDRT and good for the other dementia-free participants(11). Economic status was rated by relating each participant status to the median of the entire sample using a listing of the number of household items(12, 13). Depression was assessed using the Composite International Diagnostic Interview(14).

Statistical methods

The sample included individuals who provided baseline data in 2003–04. A participant was considered to have reached an endpoint when they had completed assessments in 2009 or when the research interviewer was reliably informed about their death. Participants with no reports of death and who did not complete 2009 assessments were censored.

The demographic characteristics of those who provided complete information or were reported dead at the end point of the study in 2009 were compared with those who were censored using the chi-square test for categorical variables, with appropriate corrections to account for the survey design (15).

Person-years at risk were calculated as the period between baseline and follow-up assessments for those who did not develop dementia during follow-up and between baseline and the midpoint of each interval for those who developed dementia in the corresponding wave, were censored because of being lost to follow-up, or had died by the corresponding wave of follow-up. This corresponds to the actuarial adjustment approach of a life table. To explore the sensitivity of the analysis to this assumption, person-years were calculated for participants who developed dementia or were censored using the interval from baseline to the last wave in which the person was followed up. This corresponds to the product limit estimator assumption for Kaplan-Meier analyses. The incidence rates with 95% confidence interval (CIs) for actuarial and Kaplan-Meir approaches are presented in the relevant table.

Specific incidence estimates for each baseline risk factors were calculated by dividing the number of incident dementia cases by the person-years contributed. Similar methods were used in the estimation of person-years at risk and specific rates for dementia mortality.

The entire dementia-free (2003–04) cohort was used to estimate the effect of baseline risk factors on incident dementia during the follow-up period. For the purpose of estimating the effect of predementia cognitive decline on incident dementia and mortality, a category was generated for poor predementia cognitive functioning according to a previously defined procedure (11). The Cox regression model for time-invariant explanatory variables was applied to derive estimates of hazard ratios (HRs, with 95% CIs), assuming proportional hazards.

Because of the quality of the survival data, the discrete time version of the Cox regression model for time-invariant explanatory variables was used to derive estimates of HRs for dementia mortality, assuming proportional hazards. An unadjusted analysis was first conducted. Then, the effects of age, sex, socioeconomic status, place of residence, occupational attainment, and predementia cognitive functioning were adjusted for. These were factors that might have significantly affected survival to the end point of 2009 and

incident dementia. A significance level of .05 was used throughout the analyses. Coefficient estimates and 95% CIs are presented for the regression models.

Data were analyzed using Stata version 13.0 (16). The survey commands in Stata were used to account for the study sampling scheme.

Results

Two thousand one hundred forty-nine individuals consented and participated in 2003–04. Of these, 1,894 were free of dementia at baseline and were successfully followed up, giving 6,502 total risk years. The mean age of those who were followed up was 74.4±8.8. Table 1 compares participants who were followed up with those who dropped out of the study before the last follow-up assessment in 2009. Eighty-five incident cases of dementia were identified in the 2007 waves, 39 in the 2008 wave, and 12 in the 2009 wave, producing annual incidence rates of 20.9 per 1,000 person-years (95% CI=17.7–24.7) using the actuarial approach or 21.8 per 1,000 person-years (95% CI=18.4–25.8) using the Kaplan-Meier approach (Table 2). The two approaches produced similar results.

In addition to age, female sex, low socioeconomic status, rural place of residence, proxies of cognitive reserve such as lower occupational complexity, and low predementia cognitive function were associated with incident dementia (Table 2).

Annual mortality for individuals with dementia was nearly twice the rate of dementia-free participants (Table 3). The mortality hazard for dementia is also shown in Table 3.

Discussion

In this large prospective cohort study conducted in communities spread over a geographical area in which was nearly one-quarter of the Nigerian population resided at the time of study, an annual dementia incidence rate over 5 years of 2.1% or 2.2% was found, depending on the method used. Older age, female sex, rural residence, lower economic status, occupational complexity, and predementia cognitive function were associated with incident dementia. Mortality for participants with dementia was nearly twice that of those without at baseline.

The annual incidence of dementia in this report is consistent with, and confirms, a previous estimate from this population (2). The rate of 2.2% (95% CI=1.8–2.7) in that report was based on a risk period that was about half the total risk years of the present study. Estimates in the present analysis are higher than the 1.4% annual incidence of dementia observed in a population of elderly persons residing in Idikan, a densely populated inner-city community of Ibadan(3). In addition, the relative risk for dementia mortality of 2.8 (95% CI= 1.1–7.3) derived from that study (17) is higher than the rate of 1.8 found in the present cohort. Rates derived from different samples can be expected to differ, especially when there are differences in methodology. The peculiarities of such a setting may influence dementia incidence and mortality risks derived from a densely populated inner-city environment. For instance, high levels of social stimulation in a densely populated environment may lead to a lower incidence of dementia (18). Alternatively, poverty, deprivation, and limited availability

of quality health care, which are common in more-deprived communities, may result in high differential mortality from the disease. Despite methodological differences, the mortality hazard of 1.8 found in this study lies within the range of relative risks reported previously (17).

Life course higher occupational complexity and predementia cognitive function have been demonstrated as indices of protective biological (19) and socioeconomic (20) factors against the neurodegenerative changes that may result in dementia in elderly adults. This phenomenon is often viewed as being indicative of cognitive reserve. Similar to reports from higher-income countries (19–21), these proxy indicators of cognitive reserve also appeared to have an important association with incident dementia in this Nigerian cohort. The absence of an association between level of formal education and incident dementia in this study is probably not unexpected given the inconsistency in the findings from several large-scale cohort studies(21, 22). More than half of the respondents had no formal education, and a minority had a few years of formal education. It is likely that this level of educational exposure, which is probably unrelated to ability, but more to social opportunity, may not be a good reflection of cognitive function.

Because of prevailing low levels of education in the study setting, informants often did not accurately estimate the mortality data according to the actual date of death. Given the possible effect of this limitation on the quality of the survival data, a discrete, rather than continuous, time approach was used for subsequent estimation of mortality risk in this study. Additional sensitivity analyses were conducted using the product limit estimator assumptions (Kaplan-Meier). The results of the analyses were not sensitive to the different approaches. Similar to every prospective longitudinal study, attrition was a problem in this study. Small size of the dementia mortality sample made statistical correction using multiple imputation difficult to implement.

In conclusion, the annual incidence rate of dementia in Nigeria may lie between 1.0% and 2.0%. This is lower than commonly reported in studies conducted in high-income countries and may not be directly explained by the observed rate of dementia mortality in the country setting.

Acknowledgments

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Table 1

Baseline Characteristics of Participants (N=2,149)

Characteristic	Completed, n=1,314	Censored, n=835	Design-Based F Statistic	P-Value
	n (%[a])			
Age 65–69 70–74 75–79 80	398 (35.4) 327 (30.8) 185 (18.7) 404 (15.1)	304 (41.8) 168 (25.2) 110 (16.2) 253 (16.9)	3.16	.04
Sex Male Female	637 (59.9) 677 (40.2)	364 (55.4) 471 (44.6)	3.21	.08
Site Urban Semi-urban Rural	339 (26.3) 541 (41.6) 434 (32.2)	216 (25.9) 329 (41.5) 290 (32.6)	0.02	.98
Education, years 13 7–12 1–6 0	103 (7.70) 164 (13.5) 332 (26.6) 715 (52.3)	63 (8.59) 102 (11.9) 201 (24.0) 469 (55.5)	0.64	.56
Economic status High High-average Low-average Low	155 (16.3) 317 (29.9) 461 (32.2) 381 (21.6)	69 (9.8) 178 (26.2) 302 (37.9) 286 (26.1)	5.59	.002
Occupational attainment Semiskilled or higher Elementary Trade	143 (14.8) 484 (43.8) 572 (41.5)	78 (12.9) 310 (46.4) 342 (40.7)	0.49	.60
Medical comorbidity[b] No Yes	922 (68.9) 392 (31.1)	599 (68.7) 236 (31.3)	0.01	.93
Functional disability No Yes	1,148 (90.6) 166 (9.4)	739 (91.1) 96 (8.9)	0.08	.78
Depression No Yes	1,223 (92.3) 91 (7.7)	775 (92.1) 60 (7.9)	0.02	.89
Ever smoked Yes No	540 (43.4) 695 (56.7)	335 (44.1) 439 (55.9)	0.06	.80
Self-reported health Poor Good	107 (8.0) 1,178 (91.9)	69 (7.0) 726 (93.0)	0.88	.35
Ever drank Yes No	562 (47.6) 693 (52.4)	345 (48.6) 407 (51.4)	0.08	.77
Weight Underweight Normal weight Overweight Obese	117 (6.8) 642 (48.4) 325 (27.6) 222 (17.2)	81 (8.9) 400 (49.0) 198 (26.2) 136 (15.8)	0.71	.53
Social participation[c] Poor Good	92 (4.9) 1,181 (95.2)	72 (6.6) 720 (93.4)	1.98	.17

Characteristic	Completed, n=1,314	Censored, n=835	Design-Based F Statistic	P-Value

Predementia cognition
  Normal
  Low
	1,071 (88.8)
	188 (11.2)
		648 (84.9)
		137 (15.1)
			4.33	.04

[a] Weighted using sampling weights.

[b] Included several chronic medical and pain conditions common in the population.

[c] Poor social participation was ascertained according to participants answering "not at all" to "During the last 30 days, how much did you join in family activities such as eating together, talking with family members, visiting family members, working together?" or "During the last 30 days, how much did you join in community activities such as festivities, religious activities, talking with community members, working together?"

Table 2

Incident Rates and (Unadjusted) Hazard Ratio of Dementia Over 5 Years (N=1,894)

Baseline Characteristics	Incident Dementia, n	Actuarial Approach		Kaplan-Meier Approach	
		Incidence Rate per 1,000 Person-Years (95% CI)	Unadjusted HR (95% CI)	Incidence Rate per 1,000 Person-Years (95% CI)	Unadjusted HR (95% CI)
Overall	136	20.9 (17.7–24.7)		21.8 (18.4–25.8)	
Demographics					
Age					
65–69	16	6.9 (4.2–11.3)	Reference	7.6 (4.7–12.5)	Reference
70–74	30	18.0 (12.6–25.7)	2.6 (1.4–4.8)	18.5 (12.9–26.5)	2.4 (1.3–4.5)
75–79	28	30.9 (21.3–44.7)	4.4 (2.4–8.2)	31.0 (21.4–45.0)	4.1 (2.2–7.5)
80	62	38.3 (29.8–49.1)	5.3 (3.0–9.1)	38.2 (29.8–49.1)	5.1 (2.9–8.8)
Sex					
Male	41	12.6 (9.3–17.2)	Reference	13.2 (9.7–17.9)	Reference
Female	95	29.2 (23.9–35.7)	2.3 (1.6–3.3)	30.4 (24.9–37.2)	2.3 (1.6–3.3)
Site					
Urban	26	16.0 (10.9–23.5)	Reference	17.0 (11.6–25.0)	Reference
Semi-urban	56	20.7 (16.0–27.0)	1.3 (0.8–2.1)	21.3 (16.4–27.7)	1.2 (0.8–2.0)
Rural	54	24.8 (19.0–32.4)	1.6 (1.0–2.5)	26.0 (19.9–33.9)	1.5 (1.0–2.4)
Education, years					
≥13	10	21.5 (11.6–40.0)	Reference	22.5 (12.1–41.8)	Reference
7–12	19	22.6 (14.4–35.4)	1.1 (0.5–2.3)	23.1 (14.7–36.2)	1.0 (0.5–2.2)
1–6	35	22.2 (16.0–30.9)	1.0 (0.5–2.1)	23.0 (16.5–32.1)	1.0 (0.5–2.1)
0	72	19.9 (15.8–25.1)	0.9 (0.5–1.8)	20.9 (16.6–26.3)	0.9 (0.5–1.9)
Economic status					
High	6	7.7 (3.5–17.2)	Reference	7.9 (3.5–17.6)	Reference
High-average	26	16.0 (10.9–23.6)	2.0 (0.8–5.0)	16.8 (11.4–24.7)	2.1 (0.9–5.2)
Low-average	53	22.3 (17.1–29.2)	2.8 (1.2–6.6)	23.2 (17.7–30.4)	2.9 (1.3–6.9)
Low	51	29.5 (22.4–38.8)	3.6 (1.5–8.4)	31.0 (23.5–40.7)	4.0 (1.7–9.3)
Occupational attainment					
Semiskilled or higher	5	6.6 (2.7–15.7)	Reference	6.9 (2.9–16.5)	Reference
Elementary	53	21.2 (16.2–27.8)	3.2 (1.3–8.0)	21.8 (16.6–28.5)	3.2 (1.3–8.0)
Trade	62	23.1 (18.0–29.6)	3.5 (1.4–8.6)	24.1 (18.8–30.9)	3.5 (1.4–8.8)
Social participation[a]					
Good	119	20.2 (16.9–24.2)	Reference	21.0 (17.5–25.1)	Reference
Poor	14	33.7 (20.0–56.9)	1.6 (0.9–2.8)	34.1 (20.2–57.7)	1.6 (0.9–2.9)
Self-reported health					
Good	117	19.9 (16.6–23.8)	Reference	20.8 (17.3–24.9)	Reference
Poor	11	32.0 (17.7–57.8)	1.5 (0.8–2.9)	31.7 (17.6–57.2)	1.5 (0.8–2.9)
Past-year depression					
No	129	21.4 (18.0–25.4)	Reference	22.3 (18.7–26.5)	Reference
Yes	7	15.1 (7.2–31.7)	0.7 (0.3–1.5)	15.7 (7.5–33.0)	0.7 (0.3–1.5)

Baseline Characteristics	Incident Dementia, n	Actuarial Approach		Kaplan-Meier Approach	
		Incidence Rate per 1,000 Person-Years (95% CI)	Unadjusted HR (95% CI)	Incidence Rate per 1,000 Person-Years (95% CI)	Unadjusted HR (95% CI)
Functional disability					
No	120	20.2 (17.0–24.2)	Reference	21.3 (17.8–25.5)	Reference
Yes	16	28.0 (17.1–45.7)	1.3 (0.8–2.1)	26.1 (16.0–42.5)	1.3 (0.7–2.1)
Medical comorbidity[b]					
No	102	22.3 (18.3–27.0)	Reference	23.2 (19.1–28.2)	Reference
Yes	34	17.7 (12.6–24.8)	0.8 (0.5–1.2)	18.4 (13.1–25.7)	0.8 (0.5–1.2)
Ever smoked					
No	72	20.9 (16.6–26.3)	Reference	21.6 (17.1–27.2)	Reference
Yes	58	22.1 (17.1–28.6)	1.1 (0.8–1.5)	23.1 (17.9–29.9)	1.1 (0.8–1.5)
Ever drank					
No	78	24.0 (19.2–29.9)	Reference	24.6 (19.7–30.7)	Reference
Yes	51	17.5 (13.3–23.0)	0.7 (0.5–1.1)	18.2 (13.8–23.9)	0.7 (0.5–1.0)
Weight					
Normal	70	22.4 (17.7–28.3)	Reference	23.1 (18.2–29.2)	Reference
Underweight	14	30.0 (17.8–50.7)	1.3 (0.7–2.2)	29.7 (17.6–50.2)	1.3 (0.7–2.3)
Overweight	32	19.4 (13.7–27.4)	0.9 (0.6–1.3)	20.6 (14.5–29.1)	0.9 (0.6–1.4)
Obese	20	16.8 (10.8–26.0)	0.8 (0.5–1.2)	17.6 (11.4–27.3)	0.8 (0.5–1.3)
Predementia cognition					
Normal	110	19.3 (16.0–23.3)	Reference	20.2 (16.7–24.3)	Reference
Impaired	20	35.7 (23.0–55.4)	1.8 (1.1–2.8)	35.9 (23.2–55.7)	1.8 (1.1–2.9)

[a] Poor social participation was ascertained according to participants answering "not at all" to 'During the last 30 days, how much did you join in family activities such as eating together, talking with family members, visiting family members, working together?" or "During the last 30 days, how much did you join in community activities such as festivities, religious activities, talking with community members, working together?"

[b] Included several chronic medical and pain conditions common in the population.

CI=confidence interval; HR=hazard ratio

Table 3

Association Between Dementia and Mortality (N=2,149)

Dementia Status	Mortality per 1,000 Person-Years (95% CI)	Unadjusted	Adjusted[a]
		H.R (95% CI)	
Actuarial approach			
No dementia	42.3 (37.7–47.5)	Reference	Reference
Dementia	83.1 (65.4–105.6)	1.8 (1.4–2.4)	1.5 (1.1–2.1)
All	46.7 (42.0–51.7)	-	-
Kaplan-Meier approach			
No dementia	45.3 (40.3–50.8)	Reference	Reference
Dementia	86.2 (67.9–109.6)	1.9 (1.7–2.2)	1.5 (1.2–1.8)
All	49.7 (44.8–55.1)	-	-

Mortality hazards are based on discrete time proportional hazard model.

[a]Adjusted for age, sex, economic status, location, occupational attainment, and predementia cognitive function.

CI=confidence interval; HR=hazard ratio