Mortality rates in community-dwelling Tanzanians with dementia and mild cognitive impairment: a 4-year follow-up study

STELLA-MARIA PADDICK1,2, ALOYCE KISOLI3, CATHERINE L. DOTCHIN1,4, WILLIAM K. GRAY1, PAUL CHAOTE5, ANNA LONGDON6, RICHARD W. WALKER1,7

1Northumbria Healthcare NHS Foundation Trust, Department of Medicine, North Tyneside General Hospital, Tyne and Wear, UK
2Institute of Neuroscience, Newcastle University, Newcastle Upon Tyne, UK
3Hai District Hospital, Boman’gombe, Kilimanjaro, Tanzania
4Institute for Ageing, Newcastle University, Newcastle-upon-Tyne, UK
5District Medical Office, Hai District Hospital, Boman’gombe, Hai, Tanzania
6South Devon Healthcare NHS Foundation Trust, Torquay, UK
7Institute of Health and Society, Newcastle University, Newcastle upon Tyne, UK

Address correspondence to: S-M. Paddick. Tel/fax (+44) 191 293 2709. Email: stellamaria@doctors.org.uk

Abstract

Background: we have previously conducted a community-based prevalence study of dementia in older adults living in the rural Hai district of Tanzania. The aim of this study was to record mortality rates at 4 years post-diagnosis, of those with dementia, mild cognitive impairment (MCI) and no cognitive impairment.

Methods: during Phase I of the prevalence study, 1,198 people aged 70 years and over were screened, and a stratified sample of 296 was assessed for the presence of dementia or MCI in Phase II. Seventy-eight people had dementia and 46 had MCI. Four years after diagnosis, we attempted to follow-up all those seen in Phase II and record all deaths.
Results: of the 296, follow-up data were available for 287 (97.0%), including 77 with dementia and 45 with MCI. Of the 172 with no cognitive impairment, 165 (95.9%) were followed up and a sample of 89 people selected as representative of the background population. Forty-eight people with dementia (62.3%), 19 with MCI (42.2%) and 11 with no cognitive impairment (12.4%) had died at 4-year follow-up. After adjusting for the effects of age, gender and education, the hazard ratio was 6.33 (95% CI 3.19–12.58) for dementia and 3.57 (95% CI 1.64–7.79) for MCI relative to people with no cognitive impairment. Mortality rates were highest in those with vascular dementia.

Conclusion: dementia and MCI were associated with excess mortality relative to those with no cognitive impairment.

Keywords: dementia, Alzheimer’s disease, mortality, Tanzania, Africa, older people

Methods

This study was approved by the National Institute of Medical Research, Dar-es-Salaam, Tanzania. Signed informed consent was obtained, with a thumbprint for those that could not read and write. The purpose and implications of the study were verbally explained. In cases where patients were unable to give valid consent, written assent was obtained from a close relative.

Study population

The Hai district in northern Tanzania is part of Kilimanjaro region and is largely rural. The economy is based around agriculture with most people reliant on small farms as a source of income and food. Part of Hai district has been used as a demographic surveillance site (DSS) since the 1990s. There are regular population censuses within the DSS. On the 1st of June 2009, the population of all 52 villages of the DSS was 161,119. We aimed to interview and assess all those aged 70 years and over living in six randomly selected villages. Full details of the study recruitment process have been published [8].

Assessment for the presence of dementia and MCI

Phase I

A census enumerator visited subjects who met the study inclusion criteria. Prior to commencement of the study, workshops were held for all enumerators, and the concept of dementia was discussed at length with local case studies used as teaching aids. Screening was conducted on 1,198 subjects using the Community Screening Instrument for Dementia (CSI-D) [9], which has been used extensively in low- and middle-income countries (LMICs), and validated in Swahili [10]. The screening interview has two sections, with an interview for the person suspected of having dementia and an informant section for which a close family member is interviewed. CSI-D scores were categorised as ‘good performance (n = 910)’, ‘moderate performance (n = 104)’ or ‘poor performance (n = 184)’ [9]. Supplementary data, Appendix S1 available in Age and Ageing online summarise the recruitment process.
Phase II
All cases identified as having poor performance on the CSI-D, who could be followed-up, were fully assessed for the presence of dementia by a study doctor (S.-M.P. or A.L.) in Phase II. We also aimed to assess 50% of those with moderate performance and 5% of those with good performance on the CSI-D. People with moderate and good CSI-D performance were selected for assessment using a random number generator. This resulted in a Phase II cohort of 296 (168 poor performance, 56 moderate performance and 72 good performance), see Supplementary data, Appendix S1 available in Age and Ageing online.

The point-prevalence date was 12th April 2010. Dementia diagnosis was based on the DSM-IV criteria [11] and MCI on international consensus criteria [12]. Computerised tomography scanning was used where clinically indicated. Dementia sub-type diagnosis used the NINDS-AIREN (National Institute of Neurological Disorders and Stroke—Association Internationale pour la Recherche et l’Enseignement en Neurosciences) criteria and Hachinski score for VAD, and NINCDS-ADRDA (National Institute of Neurological and Communicative Disorders and Stroke—Alzheimer’s Disease and Related Disorders Association) criteria for AD [13]. Seventy-eight cases of dementia (including 38 cases of AD and 32 cases of VAD) and 46 cases of MCI were diagnosed [8, 14].

Demographic and educational data were collected from the patients and informants. Data were also collected relating to the approximate date of dementia or MCI onset. Patients and informants were prompted by being asked to recall the date of onset of a particular functional impairment related to cognitive impairment. In some cases, an accurate date of symptom onset could not be identified.

Follow-up
Cases were followed-up at 2, 3 and 4 years, with 12th April 2014 set as the cut-off. Thus, data were available for a full 4 years from the point prevalence date. Data were collected relating to mortality status at each follow-up by a study nurse accompanying the census enumerator. It is customary in Hai to record date of death on a memorial stone near to the family home, providing a means of triangulating these data. Furthermore, data collected at 2, 3 and 4 years were compared to provide an additional integrity check. We were unable to collect data in relation to cause of death, as this information is not recorded routinely in Hai.

Statistical methods
Data were analysed using standard statistical software, PASW-18 for windows (PASW, Chicago, IL, USA). Follow-up mortality data were available for 287 (97.0%) of the 296 people fully assessed for dementia in Phase II of the study. Seventy-seven of these followed up had dementia, 45 had MCI and 165 had no cognitive impairment. Those with no cognitive impairment were likely to be unrepresentative of the background population of the Hai district, given the stratification used in Phase II of the prevalence study. To construct a cohort that was broadly representative of the background population with no cognitive impairment, we randomly selected a cohort from those followed up that was representative of the original background population of people aged 70 years and over living in the six villages, based on CSI-D performance. Thus, the cohort contained all 67 people in the good performance on CSI-D group for whom follow-up data were available, 8 people randomly selected from the moderate performance group and 14 people randomly selected from the poor performance group. The selection procedure is shown schematically in Supplementary data, Appendix S1 available in Age and Ageing online and gave a background population cohort of 89 people. No attempt was made to age-match the selected background population, and adjustment for age was done using regression modelling.

Hazard ratios (HRs) were calculated using Cox proportional hazards regression modelling with adjustment for the effects of age, gender and education. Age was categorised into 5-year age bands for this analysis, since the age data violated the assumptions of proportionality. Education was dichotomised as some formal education and no formal education, reflecting the low levels of education in the background population [8].

Results
Two-hundred and eleven people were followed up, 77 with dementia, 45 with MCI and 89 with no cognitive impairment. Deaths by age and gender at 4-year follow-up are presented in Table 1. A cumulative survival curve from the point prevalence date, showing the trend over time, is shown in Figure 1.

Table 1. Mortality rates at 4-year follow-up by diagnosis, age and gender

<table>
<thead>
<tr>
<th></th>
<th>Dementia (n = 77)</th>
<th>Mild cognitive impairment (n = 45)</th>
<th>Background population (n = 89)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
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<tr>
<td>Males</td>
<td>15/25 (60.0%)</td>
<td>6/10 (60.0%)</td>
<td>2/33 (6.1%)</td>
</tr>
<tr>
<td>Females</td>
<td>33/52 (63.5%)</td>
<td>13/35 (37.1%)</td>
<td>9/56 (16.1%)</td>
</tr>
<tr>
<td><strong>Age bands</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70–74 years</td>
<td>9/18 (50.0%)</td>
<td>2/6 (33.3%)</td>
<td>4/35 (11.4%)</td>
</tr>
<tr>
<td>75–79 years</td>
<td>9/12 (75.0%)</td>
<td>1/6 (16.7%)</td>
<td>3/26 (11.5%)</td>
</tr>
<tr>
<td>80–84 years</td>
<td>4/9 (44.4%)</td>
<td>4/12 (33.3%)</td>
<td>1/13 (7.7%)</td>
</tr>
<tr>
<td>85 years and over</td>
<td>26/38 (68.4%)</td>
<td>12/21 (57.1%)</td>
<td>3/15 (20.0%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>48/77 (62.3%)</td>
<td>19/45 (42.2%)</td>
<td>11/89 (12.4%)</td>
</tr>
</tbody>
</table>
Data on age of onset of MCI or dementia symptoms were not available for all cases followed up due to the informant or patient being unable to provide a reliable onset date. For the 73 dementia cases and 29 MCI cases for whom data were available, the median time from symptoms being first noticed by a close relative or friend (symptom onset) to baseline was 3 years (inter-quartile range (IQR) 1–5, range 0.33–10) and 2 years (IQR 0.5–5, range 0.33–8), respectively.

In those known to have died, the median time from symptom onset to death was 4.3 years (IQR 2.6–6.4, range 0.9–12.4) in 45 dementia cases and 3.9 years (IQR 3.4–4.8, range 1.5–7.8) in 11 MCI cases.

The lower crude mortality rate in the background population may be partly explained by their younger age structure. The median age at baseline in the dementia group was 83 years (inter-quartile range IQR 75–90), in the MCI group was 82 years (IQR 78–90.5) and in the background population was 76 years (IQR 72–81). A Cox regression model, with adjustment for the effects of age, gender and education, was developed to calculate HRs relative to the background population (Table 2); people with dementia and MCI had a significantly increased HR even after adjustment.

Mortality and dementia sub-type

Thirty-seven of the 38 cases (97.4%) of AD and all 32 cases of VAD had 4-year follow-up data available. There was no significant difference in time from onset of symptoms to baseline in those with AD and VAD, 3 years (inter-quartile range (IQR) 1–5, range 0.5–10) and 2.75 years (IQR 1–5, range 0.66–10), respectively. U = 485.0, χ² = 0.531, P = 0.596. There were 19 (51.4%) deaths from 37 AD cases and 24 (75.0%) deaths in 32 VAD cases. Twenty-three of the 32 VAD cases had had a stroke prior to dementia diagnosis. The survival curve for each sub-type is shown in Figure 1. In regression modelling, those with VAD had a significantly greater risk of death at 4 years than those with AD (Table 2).

Discussion

There have been very few previous studies of dementia-associated mortality SSA, and none previously in an East African population. Case-fatality rates were high, and rates of excess mortality associated with dementia were higher than those reported in Ibadan, Nigeria and many HICs [5–6, 15]. The overall mortality rate was similar to that reported in Botswana [7]. The Ibadan study found higher mortality rates in those with VAD, compared with AD, though in our Tanzanian cohort the difference was significant. The lack of significance in Ibadan partly reflects the fact that only 28 dementia cases were identified in the original prevalence study (18 with AD and 8 with VAD), limiting the statistical power of the analyses. The relatively high HR reported in our study may be due to the relatively high number of VAD cases, over 70% of whom had also had a stroke [14]. We have previously demonstrated high
stroke incidence rates [16] and high post-stroke mortality [17] in this population; therefore, this may partially account for the increased mortality. Moreover, rates of hypertension are high with most cases undiagnosed, and if diagnosed, poorly controlled in this population [18]. Uncontrolled hypertension will increase the prevalence of VAD and is the most important risk factor for stroke [19]. The fact that many chronic conditions are frequently undiagnosed in many areas of SSA can only add to the overall disease burden and the complexity of managing conditions such as dementia [20–21].

Existing data from HICs suggest that stroke is a common cause of death in VAD and AD, with bronchopneumonia frequently leading to death in both sub-types [22–23]. Data from systematic reviews on causes of mortality in dementia remain limited [22–23].

The relatively high mortality in MCI cases is notable and only slightly lower than seen in people with AD. Although the reasons for this are not clear, it may be that, in this resource-poor setting, where community-based medical care is extremely limited, people with MCI are generally frail and have a greater number of untreated co-morbidities and vascular risk factors compared with people with MCI living in HICs. Given that MCI is potentially reversible, further investigation of the progression of the condition in this setting is merited. We also recognise that some of those with MCI will have gone on to develop dementia during follow-up and this will have impacted upon survival rates [24].

Studies from other LMICs report similar findings to our own. A number of studies from China record significantly higher mortality in people with dementia [25]. Katzman et al. [26] reported higher mortality in those with VAD compared with those with AD in Shanghai. A 3-year follow-up of an urban Brazilian population of 1,393 older adults reported un-adjusted and adjusted HRs of 5.16 and 3.92, respectively, for dementia [27]. As in our population, dementia was the single strongest predictor of mortality, with age and non-cognitive health status markers less influential.

A study from the Chicago Health and Ageing Project published in 2009 reported higher risk of death in those with MCI (HR 1.48) and AD (HR 2.84) compared with the background population [28]. Interestingly, there was no difference in HRs between white and African-American subjects. The observation that MCI was associated with significant excess mortality is interesting, since previous studies had been inconclusive [29–30]. The influence of MCI on survival is likely to be greater in our cohort where interventions to reduce the burden of cognitive impairment are lacking.

Limitations

The Phase II cohort was a stratified sample of the background population, with over-sampling of those with cognitive impairment. However, a cohort was selected from those without dementia or MCI that was thought to be broadly representative of people aged 70 years and over in HAI without cognitive impairment. If any bias has affected the estimation of HRs, it is likely that this will be an under-estimation, rather than an over-estimation. We acknowledge that, despite adjustment for the direct influence of age on outcomes using regression, some age-related differences may not have been accounted for.

We are unable to present data on cause of death. Due to resource limitations, we were unable to use verbal autopsy to collect these data. We acknowledge that data on approximate date of symptom onset may be unreliable in some cases. Prompts were used to try to obtain as accurate an estimate as possible, although in some cases no estimate was available.

Conclusions

Dementia and MCI are associated with increased rates of mortality, in comparison with the background population of people without cognitive impairment. Further work on causes of death in people with cognitive impairment in SSA is needed to inform secondary prevention initiatives. Prevention of stroke and nutritional deficiency may be targets for intervention. The relatively short survival after symptom onset in this population indicates a need for palliative care initiatives and carer education programmes. Longer term, targeting vascular risk factors for dementia, such as hypertension, may be an effective method of reducing the incidence, and therefore the overall disease burden, of dementia.

Key points

- There are few previous data on mortality rates for people with dementia living in sub-Saharan Africa.
- We investigated mortality rates at 4 years post-diagnosis in a cohort of people aged 70 years and over living in rural Tanzania.
- Of 77 with dementia, 48 (62.3%) had died at follow-up. This compared with 11 of 89 (12.4%) with no cognitive impairment.
- The adjusted HR was 6.33 (95% CI 3.19 to12.58) for dementia relative to people with no cognitive impairment.
- Interventions for people with dementia and their carers are greatly needed in this setting.

Acknowledgements

We acknowledge the help of all healthcare workers, officials, carers and family members who assisted in identification of cases, examination and assessment and in data collection.

Conflicts of interest

None declared.

Funding

This study was part funded by a British Geriatric Society SpR start-up grant and an Academy of Medical Sciences (UK)
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clinical lecturer start up grant. The sponsors of this study had no role in designing the study; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

Supplementary data
Supplementary data mentioned in the text are available to subscribers in Age and Ageing online.

References

Received 3 September 2014; accepted in revised form 31 December 2014