OVERVIEW OF ALZHEIMER'S DISEASE IN NIGERIA

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ABSTRACT

Data on Alzheimer's disease (AD) in Nigeria have come largely from studies carried out by the Ibadan-Indianapolis dementia cross-cultural, collaborative research group. The age-adjusted prevalence of AD in Nigeria is 1.41% with female preponderance. The pattern of impairment is similar to documentation in other environments. The two significant risk factors are old age and female gender, while living with others appeared to be protective and there is lack of association with apolipoprotein E unlike the findings in African Americans. Further studies on disease incidence, mortality patterns and the role of vascular risk factors could provide further information on appropriate preventive measures to be undertaken to avoid an epidemic of the condition, more so as the population is ageing and the enormous resources that may be required may overwhelm our capability.

INTRODUCTION

Alzheimer's disease (AD) is a degenerative condition which slowly and progressively destroys brain cells and results in dementia. Dementia is defined as global impairment of higher cerebral function in a state of clear consciousness which ultimately necessitates assistance with activities of daily living. The synonyms include: loss of mind and brain failure. AD is the commonest type of primary degenerative dementia and accounts for between 50 and 70% of the typical late-onset cases.[1-4] The other types of primary degenerative dementias including Pick's disease (fronto-temporal dementia), Huntington's disease, diffuse Lewy body dementia, parkinson-plus syndromes are less common. Vascular dementia is the second commonest type in many countries except in Japan, Russia and parts of China where it is reported to be commoner than AD.[1] About 10-15% of the cases have treatable or reversible dementia.[2]

Alzheimer's disease was named after Alois Alzheimer, a German neuroscientist (an accomplished neurologist, psychiatrist and pathologist) who in 1907 first described the symptoms as well as the neuropathologic features of the disease. He reported the case of a 55 year-old woman who presented with paranoia, agitation, apraxia, aphasia, memory impairment and progressive motor failure.[5] At necropsy, he demonstrated the presence of abnormal proteins in the brain of that patient in the form of paired helical filaments made up of tau protein (neurofibrillary tangles) and neuritic plaques containing amyloid using the newly-available silver stains at that time. These form the pathologic basis for making the diagnosis of AD. Other features later described include the presence of granulo-vacuolar degeneration, Hirano bodies and congophilic angiopathy. In addition, there is neurotransmitter deficiency notably acetylcholine.[4,6] AD is characterised by insidious onset and progressive decline in cognition with sparing of motor and sensory functions until the late stages.[7,8] Early in the course of AD, the sufferer has memory impairment beyond what is considered acceptable for age which manifests as problem with learning and retention of new information, forgetting where things are placed and inability to use regular household items. With time, the memory loss becomes so profound that the sufferer may not be able to remember the names of family members, follow conversation or the story line of a television show. The subject may hold a key and forget how to use it. Other changes include language difficulties (aphasia), getting lost in otherwise familiar places (disorientation), lack of initiative and motivation or difficulty making decisions due to impaired judgement. Later, there is inability to cope with daily activities such as planning meals, managing finances and problems with personal care.[7] In the middle stage of the disease, there may be associated behavioural and psychiatric symptoms such as personality change, depression, hallucinations, paranoia, aggression, agitation, aimless wandering, increased irritability or anger, stubbornness, sexual disinhibition and polyphagia.[9-11] Some of these features embarrass relatives. The symptoms progress relentlessly until the sufferer becomes wholly dependent on others. The psychiatric symptoms add to the stress of the caregivers. In the advanced stages, the disease is dehumanising as the patient is confined to a wheel chair or bed, incontinent with total loss of all higher mental functions. Death usually occurs within a decade of onset as a result of urosepsis, chest infection and pulmonary embolism. The diagnosis is made when a patient presents with these features in the absence of abnormal serum constituents, anaemia or demonstrable pathology by neuroimaging and/or with neuropathological confirmation. Three diagnostic levels are recognised: definite, probable and possible.[8]

The disease has acquired a lot of attention in the last two decades for many reasons: Firstly, life expectancy is increasing and many more individuals are living to reach old age when they are at risk of developing the disease. Secondly, AD is no respecter of social status or person and many eminent personalities including presidents of powerful countries have developed the disease. Thirdly, the cost of providing care for those afflicted is enormous and beyond the reach of many countries, especially developing ones. Therefore, if the risk factors can be identified, preventive measures appropriately applied, may lower disease burden and consequently, the cost of providing care. Lastly, AD is one of the leading causes of death in western countries. Hence, it is a public health concern which can be regarded as a biosocial challenge because there is no known cure and the cause(s) is/are not known precisely yet, it affects a high proportion of elderly people.

DEMENTIA RESEARCH: THE NIGERIAN EXPERIENCE

Dementia research, and research into AD in particular, is in its infancy in Africa because the population is relatively young and communicable diseases are still overwhelming. However, changing trends are being observed because of dietary changes and assumption of western life style by affluent citizens. In addition, there is a notable change in social structure with

progressive dismantling and erosion of the extended family system which used to serve as buffer for the care of the elderly population. This has come about as a result of modernisation, economic pursuits and associated rural–urban migration. The consequence is a neglect of the elderly and many problems (including health matters) that were hitherto adequately contained within this supportive extended family system are likely to be exposed. As far back as mid 1980s, no authentic case of AD was diagnosed in Nigeria, and there was the impressionistic view that AD was more of a western disease with possible environmental predisposition.[12] Osuntokun et al found no case of AD in a community-based study of about 19,000 Nigerian subjects in Igbo-Ora.[13] Neither was any case diagnosed at Aro Neuropsychiatric Hospital at Abeokuta out of 2182 consecutive cases treated in 1984.[14] One would have expected to find that type of case if it existed at that time at Aro or other tertiary care centres in the country because of the attendant behavioural problems and/or need for supervised care. At the University College Hospital, Ibadan (UCH), one case of probable primary degenerative dementia was diagnosed in a 6-year period from 1984 to 1989 out of 37 patients managed for dementing illnesses. During this period, 57,440 cases were admitted at the UCH for care and the hospital frequency of dementia was 64 cases per 100,000.[15] This underscored the point that AD was uncommon and that in hospital series, one was more likely to encounter cases of dementia following stroke or due to other treatable causes. In another community-based study of 932 Nigerians, 31% of whom were above the age of 65 years, 34 subjects (3.8%) had age-related cognitive impairment or, at worst, questionable dementia but no AD case was diagnosed.[16] However, our preliminary neuropathologic studies showed that the substrates for AD were present in the brains of Nigerians, albeit to a less extent than in Australians. Tissue blocks from representative areas of the brain of 111 non-demented Nigerians and 99 Australians were processed for β A4 amyloid histochemistry and histologic examinations with quantitation of β A4 density. Findings were compared blind between the subjects at the two sites controlling for age. β A4 amyloid was present in the brains of 53.5% of the Australian specimens as against 25.2% of the Nigerian sample. The severity of amyloid deposition was also significantly much higher in Australians with 27.3% having moderate to severe grading as compared with only 6.3% of the Nigerian sample.[17] The study showed that Nigerians were not "immune" from developing AD. It was therefore evident that more detailed and comprehensive assessment was required for the diagnosis of AD beyond the Mini-Mental State Examination.[18] This led to the series of studies carried out by the Ibadan Dementia Research Project in collaboration with researchers from Indianapolis. The studies focused on Africans in Diaspora to tease out the possible environmental factors in dementia process. The pertinent findings as regards AD in Nigeria are presented below:

The prevalence of AD in Nigeria was determined in a cohort of 2494 subjects aged 65 years and above resident in Idikan ward, a traditional part of Ibadan city. They were recruited in a door-to-door fashion and gave informed consent. They comprised 35% males and 65% females with a mean age of 72.3 years (SD = 7.5). The level of literacy was 15%. A 2-stage study design was utilised involving a screening phase during which the Community Screening Instrument for Dementia (CSI-D) was administered followed by clinical assessment, informant's interview, neuro-psychological testing and laboratory testing in the second stage for selected subjects. Diagnosis was made along well defined criteria and consensus of investigators was strictly enforced (details described elsewhere).[19] Twenty eight demented individuals were diagnosed which comprised 18 cases of AD (64.3%), 6 of vascular dementia (28.6%) and 2 cases of other types. The age-adjusted prevalence of dementia was 2.29%, and for AD, the age-adjusted rate was 1.41%.[19] For both AD and dementia, the rates increased progressively with age as has been reported in other studies. The age-adjusted rates (overall and for each age group) were significantly lower in the Nigerian cohort than in African Americans.[19] The lower rates of AD and dementia in Nigerians agreed with findings in other developing countries[20] which may point to environmental influence in phenotypic expression of AD since the rates obtained in African Americans, who are of the same genetic heritage as Nigerians, are similar to the values in Caucasians. The Nigerian AD cases were predominantly females (16:2), were older (mean age = 82.6 years) and majority of the cases were clinically-graded to be in the mild stage (77.8%).[21] The patterns of impairment included: memory deficit (94.4%), impaired judgement (88.9%), language problems (50%) and personality change (33.3%). Problems with finances (61.1%) predominated, followed by difficulty with chores (50%), social engagements (44.4%) and personal hygiene (16.7%).[21]

The statistically significant risk factors for AD in Nigerians include: old age (odds ratio = 1.15); and female gender (odds ratio = 13.9).[22] It was also observed that social isolation was weakly associated with the development of AD (odds ratio = 0.06). The other risk factors for AD in published studies include: genetic predisposition - Down's syndrome (chromosome 21), the presenilins (chromosomes 1 & 14) and apolipoprotein E (ch.19), family history of dementia, low education, rural residence.[1,23,24] Some authors have suggested that a previous head injury could also predispose to AD. Aluminium exposure, parental age, thyroid disease and depression which were once thought to be important risk factors have not been borne out in recent studies.[1,23]

Studies in Caucasians have consistently reported the association of late-onset AD with apolipoprotein E (ε4 allele).[25] This factor is associated with cholesterol transport and repair of myelin. The frequencies of APOE ε4 alleles in Nigerians subjects were not different between the controls (20.5%) and AD cases (16.7%) quite unlike the findings in African Americans.[26] This lack of association between APOE (ε4 allele) and AD in Nigerians may be one of the factors underlying the lower prevalence of AD in this environment. It would be necessary to study vascular risk factors in details between the cohorts (African Americans and Nigerians) so as to determine the direction of preventive measures.

Management of cases is currently limited to supportive care as newer drugs like *Donepezil, Rivastigmine* etc.[27] are not available in the country and are rather expensive. Controlled trials on their usage have not been done in this country. However, in recent times, the Chinese herb *gingko-biloba* has been shown to enhance cognitive functions and may be tried when available. One must advice caution in the use of herbs because of unwanted side effects. Medications like *encephabol* and other *nootropics* have not been found to be beneficial in sustaining memory enhancement and improving functionality. Oestrogen replacement therapy has recently been shown to protect the brain from ageing by dampening amyloid production in the brain.[28] Its use is worth

trying to prevent AD in susceptible individuals although there is a risk of developing cancer. The use of antioxidants like vitamin E may reduce neuro-degeneration. Prevention of vascular disease with anti-platelet agents like *aspirin* may be contemplated along with the management of other associated medical conditions known to impair cognitive functions in the elderly. When behavioural problems become overwhelming, the use of appropriate anti-psychotic, anxiolytic and anti-depressant drugs is indicated. Education of caregivers is an essential component of management in western countries and is currently being developed. Regular, controlled exercises of cases may also confer some benefit.

CONCLUDING REMARKS

AD prevalence is currently low in Nigeria but the trend is likely to change with the ageing of the population. The association with female gender is presumed due to their older age and lower educational attainment which would result in many more of them being reassessed. There is need for incidence studies and mortality of AD cases since these could influence disease prevalence as well as further investigation of the role of vascular risk factors in the observed lower AD burden in this environment. The care of the few AD cases diagnosed is currently supportive and targeted at caregiver education as well as management of concurrent behavioural symptoms. There is a place for prophylactic therapy and trial of the newer cholinergic drugs whenever available. Public enlightenment about AD is a step in the right direction as well as planning for the care of the elderly because AD has malignant potentials and disintegrates the person afflicted.

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REFERENCES

1. Henderson AS. Dementia. World Health Organization, Geneva. 1994.
2. Morris JC. Classification of dementia and Alzheimer's disease. Acta Neurol Scand 1996; 165 suppl: 41-50.
3. Hardy J. Amyloid, the presenilins and Alzheimer's disease. Trends Neurosci.1997; 20: 154-159.
4. Katzman R. Alzheimer's disease. N. Eng J. Med 1986; 314: 964- 973.
5. Devi G, Quitschke W. Alois Alzheimer, Neuroscientist (1864-1915): profile. Alz. Dis. Assoc. Dis. 1999; 13: 132-137.
6. Doraiswamy PM. Current cholinergic therapy for symptoms of Alzheimer's disease. Primary Psychiatr. 1996; 3: 3-11.
7. Small GW, Rabin PV, Barry PP. Et al. Diagnosis and treatment of Alzheimer's disease and related disorders. JAMA 1997; 278: 1363-1371.
8. McKhan G, Drachman D, Folstein M et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group. Neurol 1984; 34:939-44.
9. Mega MS, Cummings JL, Fiorello T Gorbein J. The spectrum of behavioral changes in Alzheimer's disease. Neurology 1996; 46: 130-35.10.
10. Hendrie HC, Baiyewu O, Eldemire D, Prince C. Cross-cultural perspectives: Caribbean, Native American, and Yoruba. Int. Psychgeriat. 1996; 8 suppl 483-6.
11. Finkel S, Silva J, Cohen G et al. Behavioural and psychological signs and symptoms of dementia. Int J Geriat Psychiatr. 1997; 12: 1060-1061.
12. Henderson AS. The epidemiology of Alzheimer's disease. Brit. Med Bull. 1986; 42: 3-10.
13. Osuntokun BO, Adeuja AOG, Schoenberg BS, et al. Neurological disorders in Nigerian Africans: a community-based study. Acta Neurol Scand. 1987;
14. Gureje O, Osuntokun BO, Makanjuola JOA, Neuropsychiatric disorders in Nigerians: 1913 consecutive new patients seen in one year (1984). Afr. J Med. & med. Sci. 1989; 18: 203-209.
15. Ogunniyi A, Lekwauwa UG, Falope ZF, Osuntokun BO. Clinically-diagnosed dementing illnesses in Ibadan: features, types and associated conditions. Afr. J Med. & med. Sci. 1993; 22: 61-64.
16. Ogunniyi A, Osuntokun BO, Lekwauwa UG, Falope ZF. Rarity of dementia (by DSM-IIIR) in an urban community in Nigeria. East Afr Med J. 1992; 69:64-8.
17. Osuntokun BO, Ogunniyi A, Akang EEU, et al. BA4-amyloid in the brains of non-demented Nigerian Africans. Lancet 1994; 343: 56.
18. 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.
19. Hendrie HC, Osuntokun BO, Hall KS et al. Prevalence of Alzheimer's disease and dementia in two communities: Nigerian Africans and African Americans. Am. J Psychiatr. 1995; 152: 1485-1492.
20. 10/66 Dementia Research Group. Dementia in developing countries: a preliminary consensus statement from the 10/66 Dementia Research Group. Int. J. Geriatric Psychiatry 1999 (in press).
21. Ogunniyi A, Gureje O, Baiyewu O et al. Profile of dementia in a Nigerian community – types, pattern of impairment, and severity rating. J. Natl. Med Assoc. 1997; 89: 392-396.
22. Hall KS, Gureje O, Gao S, et al. Risk factors and Alzheimer's disease: a comparative study of two communities. Austr.& NZ J Psychiatr 1998:32: 698-706
23. Hall KS, Gao S, Unverzagt FW, Hendrie HC. Low education and childhood rural residence. Neurol 2000; 54: 95-99.
24. van Duijn CM. Epidemiology of the dementias: recent developments and new approaches. J. Neurol. Neurosurg. Psychiatr 1996; 60: 478-488.
25. Saunders AM, Strittmatter WJ, Schmechel D, et al. Association of apolipoprotein E e4 allele with late-onset Alzheimer's disease. Neurol 1993; 43: 1467-1472.
26. Osuntokun BO, Sahota A, Ogunniyi AO, et al. Lack of association between apolipoprotein E e4 and Alzheimer's disease in elderly Nigerians. Ann. Neurol 1995; 38: 463-465.
25. Farlow MR, Evans RM. Pharmacologic treatment of cognition in Alzheimer's dementia. Neurol 1998; 51 (suppl 1): S36-S44.
26. Burns A, Murphy D. Protection against Alzheimer's disease. Lancet 1996; 348: 420-421.