Interethnic Differences in Dementia Epidemiology: Global and Asia-Pacific Perspectives

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Key Words

Incidence • Prevalence • Alzheimer's disease • Vascular dementia

Abstract

The burden of dementia will continue to rise globally, particularly in developing countries, many of which lie in the Asia-Pacific region. It was initially thought that both prevalence and incidence of dementia showed little geographic variation. More recent work has suggested differences: migrant populations attain rates between their homelands and adopted countries, and higher rates have been found in African Americans and Hispanics compared to Caucasian Whites, and also among native Australians. The only interethnic studies in the Asia-Pacific region were performed in Singapore, which showed lower standardized prevalence among ethnic Chinese compared to ethnic Malays and Indians, independent of vascular risk factors. There was conflicting information about the relative frequencies of Alzheimer's disease and vascular dementia between ethnic groups in Singapore. More research, with careful attention to potential cultural confounders, is needed to further explore and better understand interethnic differences in dementia epidemiology.

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Introduction

The burden of dementia is rising worldwide, with major medical, social and economic impacts [1, 2]. Based on published studies and population projections, an expert panel has estimated there are 24.3 million persons with dementia in the world presently, with 4.6 million newly diagnosed cases of dementia annually, about 1 new case every 7 seconds [3]. The number of demented people is expected to double every 20 years, and reach 81.1 million by 2040 [3]. A systematic review of 36 prevalence and 15 incidence studies showed that dementia prevalence ranged from 0.3 to 1.0% among those aged 60–64 years, increasing to 42.3–68.3% among those aged 95 years and older, while incidence varied from 0.8 to 4.0 per 1,000 person-years among those aged 60–64 years, increasing to 49.8–135.7 per 1,000 person-years among those older than 95 years [4].

Approximately 60% of the world's population lives in the Asia-Pacific region. This region is home to many ethnic groups who may have differing disease patterns, even within a single country. This paper is a review of recent publications of dementia in the Asia-Pacific region, particularly those conducted in multiethnic populations. A Medline search was performed for the years 1966–2010,

combining the search term 'dementia' with the names of each of the various countries in the Asia-Pacific region, or with the phrase 'Asia-Pacific' or 'inter-ethnic' or 'multi-ethnic'. The abstracts were reviewed for relevance to the aim of this paper, and the original publications obtained where possible. The reference lists were also scrutinized for further relevant publications. All data were extracted by the first author and presented to the co-authors for comment and discussion. Conflicting views were resolved by consensus.

Dementia in the Asia-Pacific Region

Most people with dementia live in developing countries, approximately 60% in 2001, and this is expected to rise to 71% by 2040 [3]. According to forecasts, the rates of increase of persons with dementia will be nonuniform across the world [3]. The numbers in developed countries are expected to double between 2001 and 2040; however, in India, China and the surrounding Western Pacific and South Asian countries, the numbers are set to quadruple [3], which is mostly attributable to population growth, greater longevity and an exponential growth of the elderly population. Dementia is the principal cause of disability among almost all low- and middle-income countries, with a median population attributable prevalence fraction of 25.1% and intersite variation largely due to differences in socioeconomic and health characteristics [5, 6]. This will place the bulk of the global burden of dementia squarely in the developing countries of the Asia-Pacific region.

Geographical Variations in Dementia Prevalence Rates

Until recently, a controversial feature of the epidemiology of dementia is the geographical variations of prevalence rates by regions and countries across the world [3]. Compared to countries in North America and Europe, lower rates of dementia were reported in the developing world. Even within low- and middle-income countries, more recent estimates show that the dementia prevalence in 65-year-olds is high in some countries (>5%), but low in others such as India and sub-Saharan Africa (1–3%) [5]. A collaborative cross-sectional survey of 14,960 subjects aged >65 years in 11 sites in 7 low- and middle-income countries showed that the prevalence of dementia, clinically evaluated using the Diagnostic and Statistical

Manual of Mental Disorders, 4th edition, varied widely from 0.3% in rural India to 6.3% in Cuba. After age and sex standardization, dementia prevalence in urban Latin American sites was four fifths of that in Europe, but in China the prevalence was only half, and in India and rural Latin America, a quarter or less of that in Europe [7]. Dementia prevalence using 10/66 criteria was higher and more consistent across sites, but still varies significantly between 5.6% in rural China and 11.7% in the Dominican Republic [7].

Among countries in the Asia-Pacific region, the variation in dementia prevalence rates was consistent with the broad picture, as illustrated by recent publications of large studies [8–20] (table 1). Notwithstanding some differences in age among populations compared, there is a clear suggestion that dementia prevalence is higher in Japan and Korea, which are relatively higher income countries.

It was initially thought that methodological reasons rather than real differences accounted for geographic variations in dementia prevalence and incidence [4]. Especially in comparisons made with rates found in developing countries, major factors to be considered included differences among populations in age, gender and education, and the validity of case detection thresholds and responses to diagnostic assessments. Performance on neuropsychological tests used in screening and assessment for dementia is known to be education-dependent and there are likely cultural influences on the interpretation and reporting of symptoms and presentation of dementia. Case under-ascertainment in developing countries could possibly arise from the stigma attached to having a relative with dementia, or cognitive decline being attributed to normal aging. For example, because of the traditional Chinese belief that old people return to a childish state, dementia symptoms may be normalized [21]. Functional disability associated with cognitive decline may not be reported because of social acculturation of low expectation and demand for elder participation in daily functional roles and activities, or because it may be masked by more prominent coexisting physical morbidities. All these, and variations in the survival probabilities after the development of dementia, could possibly account for lower prevalence in developing countries.

A clearer picture has since emerged in subsequent studies with vastly enhanced data comparability that employed improved standardization methods for case ascertainment and statistical comparisons. These included comparative studies using dementia incidence. The inci-

Table 1. Recent publications of prevalence of dementia in Asia-Pacific countries

Country	Publication year	Sample size	Age range year	Prevalence %
India [8]	2010	2,466	>55	3.77
China [9]	2010		>55	2.99
Japan [10]	2009		>65	11.0
Korea [11]	2008	1,118	>65	6.3
Thailand [12]	2008	2,311	>45	2.35
Sri Lanka [13]	2003	703	>65	3.98
Australia [14]	2001	146		3.6
Taiwan [15]	1998	2,915	>65	3.7

Table 2. Recent publications of incidence of dementia in Asia-Pacific countries

Country	Publication year	Sample size	Age range year	Incidence reported	Incidence, % (annualized)
Japan [16]	2009	828	>65	3.23/100 person-years	3.23
China [17]	2008	1,553	>60	0.9% at 2 years	0.45
Australia [18]	2003	377	>75	16.7% at 6 years	2.78
India [19]	2001	2,698	>55	0.17/100 person-years	0.17
			>65	0.32/100 person-years	0.32
Taiwan [20]	1998	2,507	>65	1.28/year	1.28

dence rates of dementia reported in Asia-Pacific countries are shown in table 2. For example, in a comparative study of Alzheimer's disease in a rural population in India and a US population comparator that employed a standardized cognitive and functional ability screening, clinical evaluation using the Diagnostic and Statistical Manual of Mental Disorders (4th edition), and the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association criteria for the diagnosis, and the Clinical Dementia Rating scale for the staging of dementia and Alzheimer's disease showed that the age-standardized incidence rate of Alzheimer's disease in those aged ≥ 65 years (4.7 per 1,000 person-years) was substantially lower than the corresponding rate (17.5 per 1,000 person-years) in the US study population [19].

It is clearly apparent now that intercountry and intra-country regional variations in rates of dementia exist that are not simply due to differences in ascertainment protocols and lack of statistical standardization of rates. Results from the 10/66 Dementia Research Group population-based surveys are an example of many such studies that support this premise. The documentation of sub-

stantial population heterogeneity in the risks and duration of dementia suggests the importance of studying genetic, environmental risk and protective factors; cultural factors in the etiology and natural progression of dementia; and preventive approaches in reducing the burden of dementia [5, 6].

Interethnic Variations in Dementia Rates

The investigation of within-country ethnic variations in dementia rates has potentially great implications for etiological research as well as for service planning and resource allocation. Genetic and environmental factors, including lifestyle, social and cultural factors (e.g. diet, nutrition, physical, mental and social activities), and cardiovascular risk factors, as well as their complex interactions [22] are some of the important repercussions of such research [23]. There is much value from such comparative studies in uncovering the presence or higher frequencies of protective factors or the absence or relatively low frequencies of risk factors that underlies interethnic differences.

Table 3. Multiethnic community-based dementia prevalence studies in Singapore

Characteristic	Study 1 [26]	Study 2 [27]	Study 3 [28]
Publication year	1995	2008	2010
Sample size			
Total	349	14,817	995
Chinese	200	8,849	479
Malay	149	3,053	300
Indian		2,915	216
Age group, years	>65	>50	>60
Prevalence, %			
Overall	3.2	1.26	5.2
Chinese	2.5	1.19	4.2
Malay	4.0	1.56	9.4
Indian	ND	1.93	8.8
Subtype	AD	AD	–
Chinese F	1.8	Chinese 0.60	
Chinese M	1.1	Malay 0.91	
Malay F	1.5	Indian 0.89	
Malay M	1.2		
MID		VD	
Chinese F	0.9	Chinese 0.55	
Chinese M	1.1	Malay 0.52	
Malay F	4.4	Indian 0.87	
Malay M	1.2		

ND = Not done; AD = Alzheimer's disease; MID = multi-infarct dementia; VD = vascular dementia; F = female; M = male.

There are, however, few published reports of studies of interethnic differences which use population-based sampling and standardized methods of dementia case ascertainment. The handful of such interethnic studies include studies in the northern Manhattan areas of New York City of 3 ethnic groups of Caribbean Hispanics, African Americans and non-Latino Whites [24, 25], and in smaller populations in Singapore with multiethnic communities of Chinese, Malays and Indians [26–28].

North American Studies

In the northern Manhattan study in New York City, dementia prevalence was found to be higher in African Americans and Latinos than in non-Latino Whites [24]. The level of education was found to be strongly associated with rates of dementia and, when age and education were simultaneously controlled, ethnic differences in

rates were no longer consistently found. As well, in a separate study, the incidence of Alzheimer's disease was found to be increased twofold among African-American and Caribbean-Hispanic individuals compared to White individuals [25]. The disproportionate risks among the 3 ethnic groups were not entirely explained by differences in number of years of education, illiteracy or history of stroke, hypertension, heart disease or diabetes. Another study has reported that Native Americans may have a later age of onset compared to Whites [29].

Asia-Pacific Studies

Interethnic studies in other countries with different ethnic make-ups and environmental influences have been reported in Australia and Singapore. Dementia prevalence has been found to be higher among Indigenous Australians compared to the general Australian population [30]. In that study, it was not possible to determine whether factors such as education, lifestyle and cardiovascular factors explained the higher rates of dementia among Indigenous Australians.

The only other reports that have explored interethnic differences in dementia prevalence have come from studies in the multiethnic population (5 million) of Singapore. Chinese make up the major ethnic group in Singapore, comprising 74.2% of the resident population, while Malays comprise 13.4%, Indians 9.2% and other ethnicities account for 3.2% [31]. The first of these 3 population-based comparative studies of dementia was done roughly 20 years ago and the other 2 studies were completed over the last 2 years [26–28] (table 3). These studies were conducted independently by different investigators and vary in sample size, inclusion age, screening and diagnostic instruments, hence the overall prevalence of dementia varied according to the screening and diagnostic thresholds for case ascertainment. Despite these differences, all studies were remarkably consistent in finding within and across studies that dementia prevalence was lowest among ethnic Chinese, compared to ethnic Malays and ethnic Indians. Ethnic differences in dementia prevalence were not explained by differences in gender, age or education [28]. Although differences in cardiovascular factors (hypertension, diabetes, cardiovascular diseases, stroke and smoking), depression and leisure time activities contributed to the differences (but only modestly), significant ethnic differences remained. However, differences in Mini-Mental State Examination scores contributed the most in explaining almost all the

ethnic differences, suggesting that innate or acquired cognitive ability and functional reserve accounted for much of the ethnic differences in dementia prevalence [28].

Lifestyle Factors

The small number of interethnic comparison studies of dementia suggest that much remains to be understood about the onset and course of dementia, which takes decades to develop. In line with the life course approach to dementia epidemiology, environmental, social, physical and other influences throughout an individual's life span are likely to vary among ethnic groups and contribute differently to the level of cognitive functional reserve which predisposes to the development of dementia [32].

The selectively lower risks of dementia among population groups such as Japanese, Chinese and rural Indians are intriguing, and suggest that some possibly unique elements of Asian lifestyles, including traditional dietary patterns (low in calories, saturated fats, meat, full-fat dairy products, refined carbohydrates, sugar and salt, but high in vegetables and fruits, tea and spices that are phytonutrient- and antioxidant-rich) that minimize vascular risks for dementia development or confer neuroprotection, may be an important contributing factor [33]. They are paradigmatic for research in dietary and nutritional factors (such as folate, fish and omega-3 fatty acids consumption, tea, turmeric, etc.) that have been shown by a growing body of evidence to contribute to the level of cognitive functioning and the risks of cognitive decline [34].

Dementia in Migrant Populations

The important roles played by environmental factors, including diet, in dementia risks are strongly illustrated by migrant studies of Japanese who migrated from their place of birth. Reported incidence rates of dementia among elderly Japanese who emigrated to Brazil before World War II (34.2 per 1,000 person-years) [35] and prevalence rates among Japanese-Brazilians aged above 70 years (12.1%) [36], as well as among Japanese aged above 65 years in the state of Washington, USA (6.3%) [37], and among Japanese men aged above 70 years in Hawaii, USA (7.6%) [38], are higher than those found in their native homeland Japan and closer to their adopted countries.

Another study that compared dementia incidence among elderly Yoruba residing in Nigeria (i.e. Nigerian Africans) to African Americans showed a much lower incidence among the former (1.35 vs. 3.24%) [39].

APOE Genotypes

The frequency of the *APOE-ε4* allele, a known risk factor for Alzheimer's disease, is an important genetic risk factor explaining ethnic differences. This has been found to be low (7.3%) in an Indian rural population sample as compared with an American population sample (11%) [19] and other Western populations. However, the association of the *APOE ε4* allele with Alzheimer's disease or non-Alzheimer's disease dementia has been shown to vary among different ethnic groups, suggesting selective survival of carriers of different *APOE* alleles for different ethnic populations. For example, it is weaker for African Americans than for Hispanics and Whites, and was null in native Nigerians; however, the *APOE-ε2/ε3* genotype was associated with an increased risk of Alzheimer's disease in African Americans but with reduced risk in Whites [40].

Studies of ethnic differences in Singapore so far have lacked data on *APOE* status to determine its link with dementia risks among the different ethnic groups. In other nondementia-related studies, Malays have been reported to show the highest frequency of the *ε4* allele, whereas *ε2* was least common in Indians [41]. Estimates of the strength of association of the *APOE ε4* genotype with dementia and its variations among the ethnic groups in Singapore are still unavailable and should be further investigated.

The issue of how to determine race and ethnicity has significant implications on biomedical research, particularly where it is possible that biological factors may explain disparities seen in health status. Genetic studies could contribute to this particular line of research where mixed ethnicity is likely. Population stratification in association studies can be controlled for by estimating genetic ancestry, which may also help detect a biological basis for causation for population-specific differences in disease [42]. The confounding effects due to population stratification may be accounted for by using large numbers of unselected genome-wide single nucleotide polymorphisms. An alternative is to use selected panels of ancestry informative markers [43, 44]. These approaches may be further enhanced by employing appropriate statistical methods [45].

Conclusions

The societal burden due to dementia is set to grow to epidemic proportions among countries in the Asia-Pacific region. Information on possible interethnic differences are emerging, but more in-depth collaborative studies are needed to address important methodological issues, especially dementia incidence studies that pay close atten-

tion to cultural factors that can affect dementia recognition [46]. For the foreseeable future, appropriately targeted interventions for lifestyle and behavioral factors for dementia appear to hold good prospects for dementia prevention, but treatment of genetic factors are likely to remain elusive. Every effort to reduce the global impact of dementia is a worthwhile investment.

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