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Dementia: Prevalence and Risk Factors

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Abstract

The increasing prevalence of dementia already has dramatic effects on lives of millions of people across the regions and on public health costs. There is no cure yet but much can be done to improve the quality of life of people with dementia and the families who care for

them. An extensive review of the literature in several pertinent areas of inquiry that may determine and delineate the prevalence, potential risk factors related to dementia was undertaken. The overall prevalence for males and females doubled for every five years increase in age after the age of 65. It is largely a disease of older people, but 2% of those affected were under 65 years of age. Results highlight a number of risk factors associated with dementia. Inter alia, these include physical activities, education, occupation, stress, cholesterol and APOE gene. Dementia is increased in certain population and the trend is on the rise. A number of risk factors associated with dementia are modifiable and may have potential as strategies useful in preventing or delaying dementia among elderly subjects. Further research is needed to determine the validity and strength of associations of risk factors of dementia including ascertainment of its causality.

Keywords: Dementia; Prevalence; Risk factors; Risk scores; Elderly people.

1. Introduction

Dementia is a clinical syndrome under the umbrella term neurodegenerative disease. Inter alia, this term includes other diseases such as Alzheimer's disease (AD), Parkinson's disease (PD), Amyotrophic Lateral Sclerosis (ALS) or Lou Gehrig's disease, Multiple Sclerosis (MS) and Autistic spectrum disorders (ASD). Dementia is characterized by a decline in cognitive functions without impairment in consciousness. It is a non-specific illness characterized by cluster of symptoms and signs manifested by difficulties in memory, attention, language, and problem solving beyond what might be expected from normal aging. Although it is far more common in the geriatric population, it may occur in any stage of adulthood. It is global health and social crisis (Boustani et al., 2003).

Although there are more than 70 diseases that cause dementia, Alzheimer' disease (AD) is the most common cause and accounts for 50-70% of dementia, and combination of Alzheimer's disease and vascular dementia account for between 80-90% of cases (Black et al., 2001). It is a brain disorder usually in elderly, associated with slow progressive loss of brain function notably lapses in memory, disorientation, confusion, mood swings, changes in personality, language problems, such as difficulty in finding the right words for everyday objects, loss of behavioral inhibitions, loss of motivation and paranoia. Other subtypes of dementia are vascular dementia associated with vascular risk factors (Hachinski et al., 2006), lewy body dementia associated with eosinophilic cytoplasmic inclusion (Wild et al., 2003) frontotemporal dementia most commonly caused by frontotemporal degeneration (Rosen et al., 2002) and mixed dementia a combination of Alzheimer's disease and vascular dementia (Zekry et al., 2002).

Clinical features of dementia may be described in terms of as **c**ognitive which includes impaired memory (most prominent early symptom), loss of previously learnt material, language affectation and poor judgment and non-cognitive which includes verbal or physical agitation, aggressive and non-aggressive behaviour, depression (most common), sleep disturbances and psychosomatic symptoms (Clinical practice guideline, 2009).

Dementia simulates delirium and depression and these have to be differentiated (MacIntosh and Woodall, 1995). Symptoms of sleep apnea have also been reported to be associated with cognitive impairment in dementia (Ancoli-Israel and Coy, 1994). Patients with severe dementia were found to have severe obstructive sleep apnea, and those with severe obstructive sleep apnea had severe dementia (Clinical practice guideline, 2009).

Fortunately, there are some warning signs of dementia that one can look out carefully and take certain steps to reduce the risk of dementia. The warning signs are: memory loss that affects day-to-day performance, difficulty in doing familiar tasks, confusion about time and place, problems in communication, difficulty in planning or solving problems, poor judgment, misplacing things, changes in mood, changes in behaviour, changes in personality, withdrawal from work, cessation of social networking.

Notwithstanding, anyone may experience similar situations from time to time. The difference with dementia is that these characteristics will progressively get worse and affects detrimentally patient's ability to live and function safely and independently.

2. Methods

Articles and/or pertinent documents included in this review were primarily identified through a Google Scholar search of the terms dementia, prevalence, incidence, risk factors and cause. Inter alia, studies retained for reviews were generally limited to empirical investigations that provided data related to prevalence, incidence, risk factors and definitional criteria for the disorder and that specified an interval of observation.

3. Results

Prevalence of Dementia:

The world wide current prevalence of dementia was estimated to be 30 million people, with 4.6 million people affected annually which gave an estimate of about one case in every 7 seconds. The number of people affected was predicted to be over 100 million by 2050 (Wimo et al., 2003; Alzheimer's disease International, 2008) with an expectation to be double every 20 years (Ferri et al., 2005). Based on the studies in developed countries, the overall prevalence for males and females doubled for every five years increase in age after the age of 65. It is largely a disease of older people, but 2% of those affected were under 65 years of age (Table 1).

Table 1: Incidence and prevalence rates of dementia from the EURODEM meta-analyses for European studies (source: Alzheimer's disease international 2008)

Age group	Annual incidence per 100		Prevalence %	
	Males	Females	Males	Females
60-64	0.2	0.2	0.4	0.4
65-69	0.2	0.3	1.6	1.0
70-74	0.6	0.5	2.9	3.1
75-79	1.4	1.8	5.6	6.0
80-84	2.8	3.4	11.0	12.6
85-89	3.9	5.4	12.8	20.2
90+	4.0	8.2	22.1	30.8

ADI commissioned a panel of experts reached a consensus estimate of prevalence in each world region (Wimo et al., 2003; Alzheimer's disease International, 2009). The trend of for a lower prevalence of dementia in developing countries as opposed to developed countries was also supported by the consensus judgment of the expert panel (Table 2).

Table 2: ADI consensus estimates for the prevalence of dementia (%), by WHO region and age group (source: Alzheimer's disease International 2008)

WHO region	Description	60-64	65-69	70-74	75-79	80-84	85+
EURO (A)	W Europe	0.9	1.5	3.6	6.0	12.2	24.8
EURO (B)	E Europe	0.9	1.3	3.2	5.8	12.2	24.7
EURO (C)	E Europe	0.9	1.3	3.2	5.8	11.8	24.5
AMRO (A)	N America	0.8	1.7	3.3	6.5	12.8	30.1

AMRO (D)	S America	0.8	1.7	3.4	7.6	14.8	33.2
AMRO (C)	S America	0.7	1.5	2.8	6.2	11.1	28.1
EMRO (B)	Middle East	0.9	1.8	3.5	6.6	13.6	25.5
EMRO (D)	N Africa, Middle East	1.2	1.9	3.9	6.6	13.9	23.5
WPRO (A)	Japan, Australia, NZ	0.6	1.4	2.6	4.7	10.4	22.1
WPRO (B)	China and neighbours	0.6	1.7	3.7	7.0	14.4	26.2
SEARO (B)	Indonesia, SL, Thailand	1.0	1.7	3.4	5.7	10.8	17.6
SEARO (D)	India and neighbours	0.4	0.9	1.8	3.7	7.2	14.4
AFRO (D)	Sub-Saharan Africa	0.3	0.6	1.3	2.3	4.3	9.7
AFRO (E)	Sub-Saharan Africa	0.5	1.0	1.9	3.8	7.0	14.9

Note: A (lowest) to E (highest) are subgroups of the WHO world regions based on patterns of child and adult mortality.

It is evident that dementia already has dramatic effects on lives of millions of people across the region and on public health costs. There is no cure yet but much can be done to improve the quality of life of people with dementia and the families who care for them. The key is to recognize dementia as a priority health problem and in doing so, to plan the action to be taken. It is also important to promote collaboration in terms of research, data exchange which would be useful to draw the attention of governments, international organizations, and aid agencies to the dementia epidemic and the threat that it posed to public health system. It would be useful too in the development of effective health care services for people with dementia and families who care for them. The number of new cases of dementia in Asia Pacific region was projected to increase 4.3 million new cases per year in 2005 to 19.7 million new cases by 2050. The proportion of people with dementia was expected to increase from 0.38% of the total regional population to 1.4% over the next 45 years. Individual country data for the estimated old and new cases of dementia are summarized in the table below (Dementia in the Asia Pacific Region: The Epidemic is Here 2006; Alzheimer's Australia 2006; Kow, 2009).

Table 3: Estimated prevalence and incidence of dementia by the selected country and the year in Asia Pacific Region

'000 people	2005		2020		2050	
	Prevalence	Incidence	Prevalence	Incidence	Prevalence	Incidence
Australia	195.4	60.2	301.3	91.1	664.1	199.7
China	5,541.2	1,721.0	9,596.3	2,916.7	27,004.4	8,269.0
India	3,248.5	1.026.8	5,541.8	1.714.4	16,290.1	4,974.6
Indonesia	606.1	191.4	1,016.8	314.1	3,042.0	932.0
Japan	1,871.2	570.2	3,251.3	983.4	4,873.1	1,4517.7
Malaysia	63.0	20.1	126.8	39.0	453.9	138.8
Pakistan	330.1	107.3	566.6	179.3	1,916.2	584.3
Philippines	169.8	54.8	316.3	99.2	1,158.9	353.9
Singapore	22.0	6.8	52.6	15.7	186.9	56.7
Thailand	229.1	71.4	450.2	137.2	1,233.2	377.0

It appears from Table 3 that in Malaysia, the prevalence of dementia was estimated to be 63,000 people in 2005 with annual incidence cases of 20,100. This number was projected to be 126,800, annual new cases of 39,000 by 2020 and 453,900, annual new cases of 138,800 (Alzheimer's disease International, 2006). Different small scale studies give slightly different results depending on their methodologies. But the dementia epidemic is a certainty (Table 4).

Table 4: Prevalence of dementia among elderly population in Malaysia

Title and	Location	Year	Sample size	Prevalence %
Prevalence of undetected cognitive impairment and depression in residents of an elderly care home	Kedah Darul Aman	2007	167	36.5
Proportion of dementia and its associated factors among elderly patients attending outpatient clinics of Unversiti Sains Malaysia	Kubang Kerian	2006	399	2.5
The prevalence of depression among elderly in an urban area of Selangor, Malaysia	Selangor	2005	25	8.3
Prevalence of dementia among elderly Malays in an urban settlement in Malaysia	Kuala Lumpur	2006	323	6.0
Cognitive impairment among the elderly in a rural community in Malaysia	Mukim Sepang	2004	223	22.4

Risk Factors:

The risk factors of dementia maybe divided into two categories: non-modifiable and modifiable. Of the studied **non-modifiable** risk factors, age is the best-studied and strongest risk factor for dementia. Other non-modifiable risk factors include gender (more in females), genetic e.g., having a first-degree relative with a history of dementia and having the apolipoprotein E4 genotype (Boustani et al., 2003).

There are 3 causative gene mutations of dementia. These are β-amyloid protein precursor (AβPP) which is located chromosome 21, presenilline 1 (PS1) located on chromosome 14 and preseniline 2 (PS2) located on chromosome 1. 30-70% mutations are in PS1, 10-15 % in AβPP and 5% in PS2 (Patterson et al., 2008). No single genetic causation of dementia has been identified; most are complex influences of genetic risk factors. For instance, apolipoprotein E (ApoE), sortilin-related receptor 1 gene (SORL1) and environmental factors in combination gives Alzheimer's disease. Apo Eε4 is the only established single risk factor of late onset dementia (Li and Grupe, 2007). Apolipoprotein CI (apoCI) and low density lipoprotein (LDL) receptors have also been reported to modulate individuals risk to developing dementia (Retz et al., 2001).

Product of ApoE gene is a class of lipoprotein (apoE), 299 amino acids long, found in the chylomicron and intermediate density lipoproteins (IDLs) that binds to a specific receptor on liver cells and peripheral cells. It is essential for the normal catabolism of triglyceride-rich lipoprotein constituents (Entrez Gene, 2010). ApoE is essential for the normal catabolism of triglyceride-rich lipoprotein constituents. ApoE was initially recognized for its importance in lipoprotein metabolism and cardiovascular disease. More recently, it has been studied for its role in several biological processes not directly related to lipoprotein transport, including Alzheimer's disease (AD), immunoregulation, and cognition. Growing amount of studies point to apoE's interaction with many immunological processes, including suppressing T-cell proliferation, macrophage functioning regulation, lipid antigen presentation facilitation (by CD1) to natural killer T cell as well as modulation of inflammation and oxidation (Zhang et al., 2010).

The ApoE gene is mapped to chromosome 19 in a cluster with apolipoprotein C1 and the apolipoprotein C2. The ApoE gene consists of four exons and three introns, totaling 3597 base pairs. In melanocytic cells APOE gene expression may be regulated by Microphthalmia-associated transcription factor (MITF) (Hoek et al., 2008). The normal gene is apoE-ε3 while the dysfunctional genes are apoE-ε2 and apoE-ε4. The ε2 allele has a Cys at positions 112 and

158 in the receptor-binding region of ApoE, the ε3 allele has Cys at 112 and Arg at 158 while the ApoE ε4 allele has Arg at both positions 112 and 158, and these have physiological consequences (Ghebranious et al., 2005). ApoE-ε2 is associated with the genetic disorder hyperlipoproteinemia type III and with both increased and decreased risk for atherosclerosis (Breslow et al., 1982). ApoE-ε3 is found in approximately 64 percent of the population, is considered to be a neutral Apo E genotype while apoE-ε4 has been implicated in atherosclerosis and Alzheimer's disease, impaired cognitive function, and reduced neurite outgrowth. The estimated human genotype frequencies are depicted in Table 5 (Hill et al., 2007).

Table 5. Estimated human genotype frequency of apoE

Allele	ε2	ε3	ε4
ε2	~1–2%	~15%	~1–2%
ε3		~55%	~25%
ε4			~1–2%

The potentially **modifiable** risk factors of dementia include cardiovascular factors such as hypertension (National Clinical Practice Guideline, 2007), diabetes mellitus, hypercholesterolemia (Purnell et al., 2009), vitamin B12 and folic acid deficiency (Vogel et al., 2009). The life style related factors include diet (Whitmer et al., 2005). Evidence has suggested that regular physical exercise may prevent or delay the onset of dementia in older persons (Lin, 2006), such that the risk of developing dementia is higher in individuals who do not exercise. Smoking, obesity and alcohol consumption are also modifiable risk factors (National Clinical Practice Guideline, 2007).
However, tt has been reported that 15% of people with dementia have a potentially treatable cause, but the prevalence of reversible dementia is only 1% (Walstra et al., 1997).

Dementia risk score:

A pragmatic tool for predicting the risk of dementia may be considered encompassing the easily measureable characteristics as appear in Table 6.

Table 6: Risk score of dementia

Chracteristic		**Point**
Age (in year)	63	0
	64 - 84	1
	≥ 84	2
Education	≥ 11	0
	6 – 10	1
	≤ 5	2
Gender	Female	0
	Male	2
Marital status	Married	0
	Unmarried	1
Sex	Practice	0
	Don’t practice	1
Religiosity	Religious	0
	Not religious	1
Social Network	Maintain	0
	Not mantain	1
Blood pressure	Normal	0

	High	2
Body mass index (kg/m^2)	≤ 23	0
	> 23	3
Total cholesterol level	≤ 6.2	0
	> 6.2	3
Physical activity	Active	0
	Inactive	1

This risk score provide a quantitative assumption of the probability of becoming dementic but it can't be used to state certainly whether a person will develop dementia (or not develop dementia). However, it can be used to identify the personnel who are at risk most and to prioritize the target group for preventive measure.

4. Discussion

Epidemiological studies of dementia among elderly people from developing countries are scarce. In this, the systematic review of the literature on dementia in the older people, surprisingly it was found only a few small scale studies that report the prevalence and predictors of dementia. Thus, although it seems likely, it cannot be shown with numbers and/or figures conclusively that dementia is increased in certain population and the trend is on the rise. Some reports delineated the scenario of dementia country-wise based on assumptive and administrative perspective with estimated projection of incidence and prevalence of dementia. On the other hand, the small scale studies, the sample sizes were small and used screening instruments of uncertain cultural validity probably. The study with highest prevalence of dementia had the smaller number of study subjects, and the lowest prevalence had the highest sample size. The sampling technique and operational definition of dementia also differs from study to study that may have led to a erroneous estimation of the magnitude of prevalence of dementia.

The association between dementia/cognitive impairment and lifestyle determinants including plausible biochemical markers and genetic risk factors were less clear and lack in most instances. Interestingly most important predictors of dementia such as hypertension, diabetes and certain vitamins deficiency were also not examined explicitly.

5. Conclusion

The increasing prevalence of dementia as the population ages will have a dramatic impact on both provision of health care and the economy in general. A number risk factors associated with dementia are modifiable and there are potential strategies for enabling either elderly subjects to remain cognitively fit or patients with dementia to slow progression.

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References

[1] Alzheimer's Australia Dementia prevalence and incidence among Australians who do not speak English, *Access Economics*, (2006).

[2] Alzheimer's disease International factsheet, *The Prevalence of Dementia Worldwide*, (2008).

[3] Alzheimer's disease International, World Alzheimer report 2009, S. Ancoli-Israel and T. Coy, *Are Breathing Disturbances in Elderly Equivalent to Sleep apnea syndrome? Sleep*, 17(1) (1994), 77-83, Review, PubMed PMID: 8191206.

[4] K. Black, D. Logiudice, Barber Bruce and R. Smith, *Diagnosing Dementia*, (2001), Alzheimer's Association Australia.

[5] M. Boustani, B. Peterson, L. Hanson, R. Harris and K. N. Lohr, Screening for dementia in primary care: A summary of the evidence for the U.S. preventive services task force, *Annals of Internal Medicine*, 138 (2003), 927-937.

[6] J. L. Breslow, V. I. Zannis, T. R. SanGiacomo, J. L. Third, T. Tracy and C. J. Glueck, Studies of familial type III hyperlipoproteinemia using as a genetic marker the apoE phenotype E2/2, *Journal of Lipid Research*, 23(8) (1982), 1224–1235.

[7] Clinical practice guideline, *Management of Dementia (2nd Edition)*, (2009).

[8] E. Gene, Genes and mapped phenotypes, (2010), APOE apolipoprotein E [*Homo sapiens*] lineage, <http://www.ncbi.nlm.nih.gov/sites/entrez?Db=gene and Cmd=Show Detail View and Term To Search=348> (accessed 7/09/2010).

[9] C. P Ferri, M. Prince, C. Brayne, H. Brodaty, L. Fratiglioni, M. Ganguli, K. Hall, H. H. Hasegawa, Y. Huang, A. Jorm, C. Mathers, P. R. Menezes, E. Rimmer and M. Scazufca, Global prevalence of dementia: A delphi consensus study, *Lancet*, 366 (2005), 2112-2117.

[10] M. Flirski and T. Sobow, Biochemical markers and risk factors of Alzheimer's disease, *Current Alzheimer Research*, 2 (2005), 47-64.

[11] N. Ghebranious, L. Ivacic, J. Mallum and C. Dokken, Detection of ApoE E2, E3 and E4 alleles using MALDI-TOF mass spectrometry and the homogeneous mass-extend technology, *Nucleic Acids Research*, 33 (2005), 149.

[12] V. Hachinski, C. Iadecola and R. C. Petersen, National Institute of Neurological Disorders and Stroke-Canadian Stroke Network vascular cognitive impairment harmonization standards, *Stroke*, 37(9) (2006), 2220- 41, Epub 2006 Aug17, Erratum in: Stroke, 38(3) (2007Mar), 1118, Wallin, Anders [added], PubMed PMID:16917086.

[13] J. M. Hill, P. S. Bhattacharjee and D. M. Neumann, Apolipoprotein E alleles can contribute to the pathogenesis of numerous clinical conditions including HSV-1 corneal disease, *Experimental Eye Research*, 84 (5) (2007), 801–811.

[14] K. S. Hoek, N. C. Schlegel, O. M. Eichhoff, D. S. Widmer, C. Praetarius, S. O. Einarsson, S. Valgeirsdottir, K. Bergsteinsdottir, A. Schepsky, R. Dummer and E. Steingrimsson, Novel MITF targets identified using a two-step DNA microarray strategy, *Pigment Cell Melanoma Research*, 21(6) (2008), 665–76.

[15] L. H. Kow, Dementia care in Malaysia, *Alzheimer's Disease Foundation Malaysia (ADFM)*, (2009).

[16] K. W. Lin, Regular exercise reduces dementia risk, *American Family Physician*, 74(3) (2006).

[17] Y. Li and A. Grupe, Genetic of late onset Alzheimers disease: Progress and prospect, *Pharmacogenomics*, 8(12) (2007), 1747-55, Review.

[18] I. B. McIntosh and K. Woodall, Dementia: Management for, Nurses and community car workers, Edited by: G. Castledine and R. Brown, *Key Management Skills in Nursing*, (1995), Mark Allen publishing ltd.

[19] *National Clinical Practice Guideline Number 42* (2007). Dementia: NICE–SCIE Guideline on supporting people with dementia and their carers in health and social care.

[20] C. Patterson, J. W. Feightner, A. Garcia, G. Y. R. Hsiung and C. MacKnight, Diagnosis and treatment of dementia: 1, Risk assessment and primary prevention of Alzheimer disease, *Canadian Medical Association Journal*, 178(5) (2008).

[21] C. Purnell, W. S. Gao, M. Callahan, C. Hugh and M. B. Hendrie, Cardiovascular risk factors and incident, Alzheimer Disease: A Systematic Review of the Literature, *Alzheimer Disease Associated Disorders*, 23(1) (2009).

[22] W. Retz, J. Thome, N. Durany, A. Harsanyi, P. Retz-Junginger, J. Kornhuber, P. Riederer and M. Rosler, Potential genetic markers of sporadic Alzheimer's disease, P*sychiatric Geneticcs*, 11 (2001), 115-122.

[23] H. J. Rosen, K. M. Hartlkalnen and W. Jagust, Utility of clinical criteria in differentiating FTLD from AD, *Neurology*, 58 (2002), 1606-15.

[24] T. Vogel, N. Dali-Youcef, G. Kaltenbach and E. Andrès, Homocysteine, vitamin B12, folate and cognitive functions: A systematic and critical review of the literature, *International Journal of Clinical Practice*, 63(7) (2009), 1061-7.

[25] G. J. M. Walstra, S. Tunisse and W. A. Van Gool, Reversible dementia in elderly patients referred to a memory clinic, *Journal of Neurology*, 244 (1) (1997), 71–22.

[26] R. A. Whitmer, S. Sidney, J. Selby, S. C. Johnston and K. Yaffe, Midlife cardiovascular risk factors and risk of dementia in late life, *Neurology*, 64, (2005), 277–281.

[27] R. Wild Pettit TACL and A. Burns, Cholinesterase inhibitors for dementia with Lewy bodies, *Cochrane Database of Systematic Reviews*, (3) (2003), Art. No.: CD003672, DOI: 10.1002/14651858. CD003.

[28] A. Wimo, B. Winblad, H. Aguero-Torres and E. V. Strauss, The magnitude of dementia occurrence in the World, *Alzheimer Disease and Associated Disorders*, 17 (2) (2003), 63–67.

[29] Wikipedia, the free encyclopedia, Neurodegeneraytion, <http://en.wikipedia .org/ wiki/Neurodegeneration> (Accessed 25th July, 2010).

[30] R. I. Winer, *Dementia Diagnosis and Treatment*, (2007), Retrieved September 27, 2008, from Neurocare Web site: http://www.gesher.org/Neurocare/ Medical % 20Education /Dementia _Lecture.html.

[31] D. Zekry, J. J. Hauw and G. Gold, Mixed dementia: Epidemiology, diagnosis and treatment, *J. Am Geriatr Assoc*., 50 (2002), 1431-8.

[32] H. L. Zhang, J. Wu and J. Zhu, The role of apolipoprotein e in Guillain-Barré syndrome and experimental autoimmune neuritis, *Journal of Biomedicine and Biotechnology*, (2010), 357412, doi:10.1155/2010/357412, PMID 20182542.