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REVIEW ARTICLE

Alzheimer's Disease: Prevalence Trends, Economic Costs and Therapeutic Challenges

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ABSTRACT

Alzheimer's disease (AD) remains the most common cause of dementia as the prevalence of the disease and severe cases among older individuals continue to increase. Global trends indicate that there will be about 150 million cases of AD by 2050, and the most affected countries will be those of low and middle-income. AD is already costing the world over $1 trillion, and with the rapid growth of the disease, that cost will increase. AD has a far-reaching negative impact on all of society, including caregiving, loss of patient quality of life, mental distress, and stigma. These dual burdens on society and the economy will increase as more and more countries are affected by AD, and as more countries are affected by the disease, the health inequities caused and hidden by the disease will also be more severe. It is hoped that global policy frameworks will be developed to address more systemically the challenges posed by inequitable dementia care. The emergence of Digital AD biomarkers and the application of precision medicine in digital health are promising opportunities to address the challenges of early-stage AD and decrease the burden of inequitable dementia care. In this review, we highlight the current epidemiological trends, economic and social impacts, therapeutic challenges, and future directions in AD.

KEYWORDS: *Alzheimer's disease, Economic burden, Biomarker, LMICs.*

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INTRODUCTION

Alzheimer's disease (AD) is a progressive neurodegenerative condition and the most frequent cause of dementia worldwide that leads to significant cognitive decline, functional impairment, and increased mortality in elders.[1,2] Some of the features of AD pathology include deposition of amyloid-β plaques and development of tau neurofibrillary tangles that disrupt synapses and cause neuron death, leading to the progressive worsening of memory and the ability to carry out daily routine.[3] Neurodegenerative process also results in neuronal damage, brain shrinkage, and memory impairment in the case of AD, and increases emotional strain on the patient's family members.[4]

AD has a significant impact on society. It consumes a lot of healthcare resources and increases the strain on the world's public health systems.[5] The emotional and financial impacts of AD are significant as caregivers suffer psychological and emotional distress as well as financial strain caused by the long-term caregiving role.[6] The impact of AD on society will get worse as the disease symptoms increase. In the next few decades, there will be a rapid increase in the disability and financial burden associated with AD.[7]

Demographic shifts indicate a rapid growth in the population above the age of 65, which significantly contributes to the growing number of individuals living with AD.[8,9] Biological aging drives despairing neurodegenerative changes, with age being the most pronounced, non-adjustable risk factor for AD.[7,9] Furthermore, the correlation between age and AD is further complicated by the fact that the incidence of the disease doubles approximately every 5 years later the age of 65.[10,11]

In poor and middle-income areas, the AD cases is expected to grow fastest because of low availability of early diagnosis, treatment, or long-term care.[12] Although the healthcare system is gradually evolving along with science and technology, many people are still not diagnosed in time, because many AD symptoms appear with other types of brain disease and lack of early diagnostic tests.[13]

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This review talks about the epidemiological trends, social costs, the problems with the system, and what the future holds for AD research, rules, and care. It is very important that people in all parts of the world work together to help slow down the rising number of AD cases. This is also required to enhance the knowledge about risks we can regulate, such as heart disease, diabetes, being fat, smoking, regular exercise, and a healthy lifestyle.[13,14]

In this line, this review focuses on current epidemiological trends, economic and societal implications, systemic obstacles, and future directions in AD research, policy, and care, emphasizing the critical need for concerted worldwide effort to lessen the rising global burden of AD.

EPIDEMIOLOGICAL TRENDS AND THE GLOBAL BURDEN OF AD

Increasing Prevalence and Incidence

Over the past decades, because of the major shifts in global health and longevity trends, the prevalence of people suffering from AD and dementia has consistently grown exponentially.[15] The Global Burden of Disease framework indicates that there has been more than a doubling in the prevalence rate between 1990 and 2019 in people aged above 60 years suffering from dementia, and it is rising from 20 million to over 55 million individuals worldwide.[16]

Although the incidence and mortality rates of dementia per 100,000 people each year remain reasonably constant over the past three decades, the absolute number of incidence and death cases has grown at a remarkably rapid rate as a consequence of the increasing population size and mean age.[17]

The prevalence rates based on the standard population show a slight increase over the years. This may be due to several reasons other than the aging of the populations studied. Such reasons include accurate diagnosis and longer survival rates among patients.[18] The global age-standardized prevalence rate of dementia increased from 4,900 to over 5,100 per 100,000 population between 1990 and 2019, indicating an increase in the prevalence of the disease, even after accounting for changes in the population's age distribution.[19] Moreover, large disparities exist between regions, with a higher prevalence of dementia found in developed and developing countries, thereby reflecting better recognition rates due to better screening practices, increased longevity, and better health practices.[20] However, the rates of disability and deaths due to dementia continue to show large increases in low-income and Low- and Middle-Income Countries (LMICs), where medical resources are constrained, which makes it challenging for these patients to access required memory health care.[21]

The country-wise DALYs (Figure 2.1) are used as indicators of AD burden. The 2019 Global Burden of Diseases and other dementias estimated 1% of DALYs (0.45% to 2.19%)

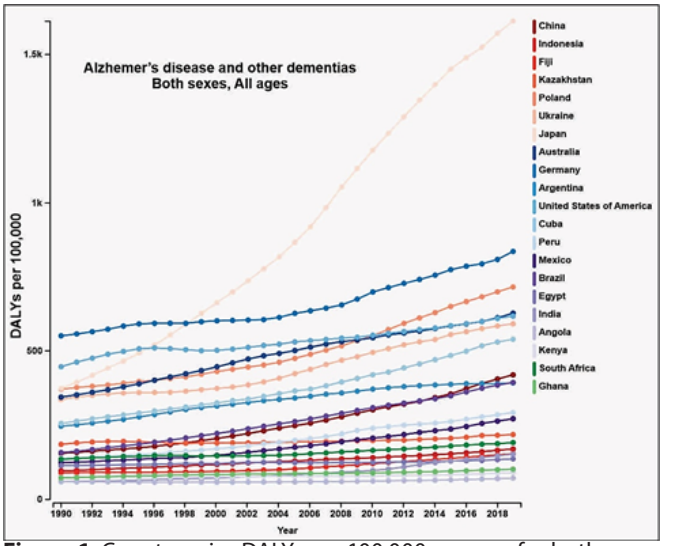

Figure 1: Country-wise DALYs per 100,000 persons for both sexes in AD and other dementias.
Source: IHME, Global Burden of Disease (2019).

along with an annual percentage of 3.39% in such patients. Furthermore, the death rate was estimated to be 1.38% of total deaths (0.32% to 3.79%) with an annual percentage of 5.34%. While the YLDs were found to be 0.31% (0.25% to 0.39%) due to AD and a 2.56% increase in the year 2018.[2,22,23]

Projections to 2050 and Beyond

Using demographic trend projections, the future for AD worldwide appears grim. The combined incidence of dementia and AD is expected to reach 152-153 million by 2050.[2,23]

Countries with rapidly aging populations, like China and several European countries, are likely to have an additional burden because a higher percentage of individuals fall under the age bracket that is highly susceptible to dementia.[24] Notably, developing countries are expected to register one of the fastest increases in dementia prevalence despite being unable to provide appropriate medical infrastructure for coping with the growing number of patients.[25,26]

ECONOMIC BURDEN OF AD

Direct and Societal Costs

Costs of AD are not limited to direct medical costs, but also include social care costs and lower labor force participation from informal (nonprofessional home provided) caregivers. In addition, the yearly cost of care per AD patient is very different in function of the stage of disease, from low costs at early stages to extraordinarily high at severe stages with need for continuous care and institutionalization.[27] The cost of AD comprises more than just direct medical costs, with a substantial amount invested in social care and huge economic losses resulting from the work performed by family members.[28] Furthermore, the annual social cost per

patient with AD is highly variable according to the stage of disease, from low costs in the early stage of cognitive impairment to extremely high costs at an advanced stage requiring full-time assistance and care.[27]

Globally, the financial toll of dementia is projected at over US $1 trillion for the year 2019 alone, portraying the substantial financial toll being exerted on respective countries' healthcare systems and their overall economies. In this respect, the medical cost component constitutes a mere fraction of total expenditure spent on dementia when compared with the social and long-term care category as a major component of total financial expenditure on a worldwide basis.[29,30] Unpaid caring is the greatest component of the overall expense incurred owing to dementia, and this huge toll has frequently been left unaccounted for in financial analyses.[31]

There are also indirect financial effects based on losses in productivity, decreased employment among caregivers, and societal effects, which contribute greatly to the total economic burden.[32] Studies have also shown that when informal care and productivity losses are taken into account in an economic model. The eventual cost is significantly higher, indicating that current estimates may underestimate the disease's actual economic potency.[33,34]

Costs in LMICs

The financial burden of dementia in LMICs is rising sharply as the financial burden exceeds the ability of the countries within the health sector.[35] In LMICs, the financial burden of dementia is not all the same; the cost of taking care of those with dementia increases significantly as the patients worsen from the initial stage to the severe stage.[36] For most countries, the burden of spending that comes with dementia has become part of the GDP of the countries; this indicates that financial growth is dwindling compared to the burden of AD.[37,38]

The influx of informal care in the support systems in LMICs is depicted, mostly because highly specialized medical support structures are difficult to come by, especially owing to financial constraints associated with these conditions.[39] Consequently, the indirect financial burden associated with caregiver support, as well as associated work-related issues, tends to overshadow the principal financial burden of medical support associated with these conditions, constituting the major portion of overall spending in these countries when it comes to the management of this condition.[40] Changes in working patterns or abandoning work altogether in a bid to support the afflicted, especially in a bid to reduce financial burdens associated with financial insecurity, tend to increase the burden associated with this condition in a bid to avert financial burden in households with low financial pockets.[41,42]

CHALLENGES IN AD MANAGEMENT

Inequities in Access to Care

The availability of diagnostics, specialist medical care, and long-term support tends to differ significantly across regions.[43] High-income nations may provide more infrastructure in terms of neuroimaging studies, cognitive function evaluation services, and sophisticated dementia speciality care programs, whereas in LMICs, there can be a lack of basic diagnostics and qualified human resources.[44,45]

If trained appropriately and provided with the tools of clinical decision support and referral systems, primary care practitioners can be involved with initial cognitive assessment and early-stage treatments while providing family support on the long trajectory of the condition.[46,47]

Late Diagnosis and Underdiagnosis

Even in settings that have well-developed healthcare systems in place, AD can be discovered late in the course of substantial loss of function. Public ignorance about the condition, coupled with a lack of screening for the condition in the general populace and the stigma associated with intellectual decline, is responsible for late diagnosis in a vast proportion of patients with AD.[48] Forgetfulness that can be attributed to early stages of the condition might be attributed to ageing by patients and their relatives, when in fact it can be the first indication of the condition.[49]

Such diagnostic gaps also limit the possibilities of optimal care planning and interventions and the participation of patients in clinical studies. Access to diagnostic biomarkers and advanced imaging in the neurosciences has not been uniform globally; in most areas, such facilities either are out of budget or are not part of the diagnostic pathways in a way that would allow for easy and quicker or earlier diagnosis.[50]

Therapeutic Limitations

Although considerable progress has been achieved in AD research, there are some therapeutic options currently available. The recently approved drugs targeting amyloid appear to have some clinical benefit and seem most effective in early AD, underlining the importance of early diagnosis.

However, management of these drugs is specialized and heavily monitored in resource-rich high-income countries (RIC) and they are costly; their real-world utility may hence be suboptimal, especially within resource-constrained settings.[51-53]

Nonetheless, many clinical trials are still showing conflicting results with the reflection of complexity nature of biological AD. Moreover, multifactorial targeted therapy is required including tau pathology, neuroinflammatory mechanisms, synaptic changes, and metabolic aspects.[53,54] Disease complexity creates significant hurdles for significant disease-modifying therapy approaches.

STRATEGIES TO REDUCE THE GLOBAL BURDEN

Early Detection and Biomarker Advances

Current diagnostic advancements hold promising power for enhancing the early detection and tracking of AD. Blood-based biomarkers, like phosphorylated tau proteins, provide an effective strategy for the prospective development of screening tests that are totally non-invasive on a larger scale.[55,56] Such tests might be applied in the primary medical evaluation in the long run. Early detection will provide individuals as well as their relatives with the opportunity to make long-term plans for their treatment, follow risk-reducing strategies, and utilize new medications that are more effective in the initial phases of AD progression.[55]

Ensuring more accessible and affordable biomarker assessments and harmonizing diagnosis procedures are key priorities for health-care systems in efforts to minimize delays in diagnosis and ensure equal dementia health outcomes in dementia management and treatment in health organizations across the globe.[57] Strategies may include harmonizing public education and screening programs.

Risk Reduction and Public Health Strategies

Increasing evidence has found that certain lifestyle and metabolic risk modifiers, like smoking and physically inactive behavior, as well as obesity and poorly managed glycemia, significantly influence the overall risk of developing dementia.[58-60] Modification of these risk factors through public health approaches aimed at adopting healthy dietary lifestyles and physical activity and managing the risk of vascular disease and smoking can potentially lower the incidence of dementia or delay symptom progression.[58,61]

Community-based efforts focusing on cardiovascular and metabolic health at the population level, in conjunction with community-based activities providing continued education and cognitive stimulation activities targeting seniors, may also be instrumental in reducing the burden of AD in the long run.[62] Long-term public health planning efforts and community-based prevention programs may also be pivotal in reducing dementia rates in the community at large.[63]

FUTURE DIRECTIONS

The care of AD in the future is likely to include precision medicine by analyzing genomics data and using biomarkers to optimize risk stratification both for individuals and at a population level. Digital health solutions such as telemedicine, cognitive monitoring wearable devices, and AI-based platforms have great potential to expand patient reach and improve the ongoing management.[64]

Digital biomarkers from speech analyses, gait analysis, or sensor data might allow early diagnosis and the development of individualized treatment approaches, especially in the areas that are difficult to reach or in disadvantaged regions worldwide.[65] Collaborative projects on a global scale for research and data sharing can lead to speed up the uncovering of AD pathophysiology, risk factors, and treatment modalities effectiveness in populations all over the world.[66,67]

Efforts to reduce stigma, educate the community, and support caregiving networks are necessary for improving the lives of people living with AD. Community, based public health interventions can, therefore, be a means of empowering the communities to recognize the early signs of dementia symptoms and implement dementia, friendly support care practices among those with dementia.[68]

CONCLUSION

AD is a mounting burden to global health, with significant effects on its epidemiology, social, and economic burden.[8,69] The situation worsens with aging population, which is putting a lot of pressure on public health measures and investment in scientific research. Besides, the cost of the disease due to direct medical expenditure and the heavy demand for caregiving is very high.[70] The disease burden can be lowered through early diagnosis, public health measures, public policy reform, and equal access to disease control, despite the numerous challenges.[71] In fact, new ways of diagnosis or disease prevention may be helpful, international collaboration and indigenous disease management practices may aid with sustainable management.[72] Combating the AD factors requires a coordinated management effort of the disease, community services, research, and health sector policies. Together and on different fronts, the escalating trend of this disease can be reversed, and better health services can be developed worldwide.

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