

Original Research Article

Pattern and treatment of Alzheimer's disease at different health care levels in Bangladesh: a hospital based survey

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ABSTRACT

Background: More than 25 million people in the world today are affected by Alzheimer's disease. In both developed and developing nations, Alzheimer's disease (AD) has had tremendous impact on the affected individuals, caregivers, and society. This study investigates the current status of AD in Bangladesh in terms of complications associated with AD as well as treatment strategies.

Methods: A cross-sectional design was applied in the study. It involves the formulated questionnaires in four medical namely, Department of Neurology of Bangabandhu Sheikh Mujib Medical University, Dhaka Medical College Hospital, National Institute of Neuroscience and Hospital and Alzheimer's society of Bangladesh from October 2022 to April 2023.

Results: Total 153 Alzheimer's disease patients (male 58.16% and female 41.84%) were recruited in this study. Though the causes of AD are still not fully elucidated, it may be claimed that person having a stressful profession have a high risk to develop AD. From the study, it was noticed that maximum number (73.85%) of patients were identified with manifestations at the moderate signs and symptoms. It was observed that Structural Magnetic Resonance Imaging (sMRI) (97.38%) and Computerized Tomography (CT) scan (93.46%) were most popular diagnosis procedure. It was observed that along with non-pharmacological treatment, drugs used to manage AD were combination of donepezil and memantine (47%), ginkgo biloba (38%), donepezil (9%), rivastigmine (4%) and memantine (2%). However, these drugs also have some adverse effects too.

Conclusions: Our population-based data may provide evidence to know about the conditions of AD in Bangladesh.

Keywords: Alzheimer's disease, Common types of dementia, Mild cognitive impairment

INTRODUCTION

Alzheimer's disease (AD) is defined as a multifactorial, irreversible, and progressive neurodegenerative brain disorder with a particular onset and course of cognitive and functional decline associated with age that ultimately results in death.¹ Gradually, it pushes people into mild cognitive impairment which is one type of brain failure and slowly becomes more severe and worse. Alzheimer's disease typically has a clinical lifespan of eight to ten

years, with an average from one to 25 years.² About 95% of cases of Alzheimer's disease are late-onset, affecting people older than 60 to 65 years old, and 5% are early-onset, affecting people younger than 60 to 65 years old.³ AD can be characterized by numerous features namely, cognitive decline, obliterates thinking and memory abilities, poor judgment, hallucination, eventually reduces a person's capacity for handling simple tasks and language disturbance.⁴ Dementia is considered as a notable feature (50-75%) of Alzheimer's disease which interferes with daily life, difficulty with problem solving

or problem in designing, difficulty in completing routine tasks at home, on work or during free time, confusion about time or location, difficulty in understanding visual cues and spatial relationships and new word problems in speaking and writing.¹

The first description of Alzheimer's disease was given by Dr. Alois Alzheimer on November 4, 1906, but he noticed it first in 1901 when he met one of his patients named Mrs. Auguste Deter in an asylum of Frankfurt.⁵ A German colleague of Dr. Alzheimer named Dr. Emil Kraepelin, coined the term as "Alzheimer's disease" in reference to Dr. Alzheimer's patient in the eighth edition of book, "Handbook of Psychiatrie".⁶ The causes of Alzheimer's disease are still not fully elucidated. There are many theories that seek to explain the cause, but ultimately, damage to cells in the brain results in Alzheimer's disease. In the early stage, hippocampus is damaged and the cells to carry out their normal function is impaired. Since those cells normally function in the creation and consolidation of new memories, damaged parts of the brain are affected.³ Modifiable risk factor and genetic factors are those factors which are responsible for AD. Age, obesity, family history, smoking, diet and others are the modifiable risk factors and APOE ϵ 4 gene, amyloid- β protein precursor, presenilin-1, presenilin-2, ATPBCT7, AKAP9, bridging integrator 1, CD2 associated protein, clusterin, CD33, SORL1, TREM2, tau and phosphatidylinositol binding clathrinid assembly protein are the genetic risk factors.⁷

Cognitive analysis, psychological evaluation, physiological signals, and behavioral responses are the four types of processes by which Alzheimer's disease can be diagnosed.⁸ Unfortunately, no permanent cure of AD can be found yet, but it can be controlled and managed the symptoms donepezil, rivastigmine, galantamine, memantine, combination of donepezil and memantine are drugs which are used to manage or control the symptoms of AD.⁹ It has been reported that everyday lifestyle could lower the risk of Alzheimer's disease.¹⁰ In this study, we examined the status of Alzheimer's disease in Dhaka, Bangladesh along with its treatment pattern.

METHODS

Study design

This cross-sectional study was carried out to investigate the current situation of patients with Alzheimer's disease among patients of hospitals and a caregiver center in Bangladesh from October 2022 to April 2023.

Study area

The current study was conducted at the department of neurology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka Medical College Hospital, National Institute of Neuroscience and hospital and Alzheimer's society in Bangladesh. The specific areas

were selected based on the availability of patients with Alzheimer's disease.

Participants

The patients of the study were well-versed about the aim of the study before answering the queries and it was also made clear to the participants before answering session that who were unwilling to join in the study should feel free to withdraw. The technical terms were clarified in detail for better understanding of the participants. No multi-response answers for single-response questions were considered for data analysis. Consultation with the physicians was also taken into consideration in this study.

Sample size

The survey was carried out on 153 patients with signs and symptoms of Alzheimer's disease and patients with drug therapy and non-pharmacological therapy. From which, the number of male patients were 89 and female patients were 64.

Questionnaire design

The questionnaire was categorized according to Alzheimer's Disease Assessment Scale (ADAS), Mini-Mental State Examination (MMSE), and Clinical Dementia Rating (CDR).¹¹⁻¹³ Some patient's identity, biophysical characteristics, and personal history questions was also adopted from formerly published study.¹⁴ The questionnaire was formulated which comprised statistics regarding the patient's identity, biophysical characteristics, personal history, modality of the signs and symptoms, signs and symptoms of different stages of Alzheimer's disease, diagnosis process, drug treatment, side effects of these drugs therapy.

Data collection

The questionnaires were distributed to all patients, regardless of age and sex. Any patient who developed some signs and symptoms of Alzheimer's disease and came to the studied institutions was included in the study. The patients who did not develop enough signs and symptoms were excluded from the study. All data were collected in person through the pre-defined questionnaires given to the patients.

Statistical analysis

Statistical analysis was performed using Microsoft Office Excel 2021 software.

Consent of participate

Written consent was taken from all study participants prior to interview. Information taken from participants was kept confidential.

RESULTS

General characteristics such as sex, age, living area, educational background, occupation of the studied

patients at three tertiary care hospitals and a daycare center in Bangladesh are presented in Table 1.

Table 1: General characteristics of the patients with Alzheimer's disease.

Parameter	Characteristics	Number (n = 153)	Percentage (%)
Sex	Male	89	58.16
	Female	64	41.84
Age in years	41-60	41	26.79
	61-80	95	62.09
	81-100	17	11.11
Living area	Rural	47	30.71
	Urban	79	51.63
	S-Urban	27	17.64
Educational status	Illiterate	24	15.68
	Can read only	11	7.18
	Can write a letter	14	9.15
	Secondary School Certificate (SSC) or equivalent	35	22.87
	Higher Secondary School Certificate (HSC) or more	69	45.09
Occupational status	Clerical	03	1.96
	Professional	21	13.72
	Managerial	23	15.03
	Housewife	47	30.71
	Business	51	33.33
	Skilled worker	06	3.92
	Technical	02	1.3

Table 2: Biophysical characteristics of the patients with Alzheimer's disease.

Parameter	Characteristics	Number (n=153)	Percentage (%)
Weight (kg)	31-40	09	5.88
	41-50	11	7.18
	51-60	29	18.95
	61-70	56	36.60
	71-80	38	24.83
	81-90	06	3.92
	91-100	04	2.61
Pulse rate	Normal (60-100 beats per minutes)	89	58.16
	Abnormal (below 60 or over 100)	64	41.83
Body temperature	Normal (36.5°C-37.2°C)	121	79.08
	Abnormal (below 36.5°C or over 37.2°C)	32	20.91
Blood pressure	Normal (120/80 mmHg)	89	58.16
	High (130-140/ 85-90 mmHg)	48	31.37
	Low (90/ 60 mmHg)	16	10.45

Biophysical characteristics (i.e. weight, pulse rate, body temperature and blood pressure) of the studied patients at three tertiary care hospitals and a daycare center in Bangladesh are presented in Table 2.

Stages of signs and symptoms, modality of the symptoms, diagnosis process, physiological signals analysis tests, behavioral responses tests of AD observed during the survey at three tertiary care hospitals and a daycare center in Bangladesh are presented in Table 3.

Donepezil, a medication from the N-benzylpiperidine family, was analyzed by Japanese pharmaceuticals industry and was approved for treating the symptoms of Alzheimer's patient in 1996. This noncompetitive inhibitor of AChE is highly selective, reversible and has little side effects while considerably improving AD symptoms.¹⁵ It works by preventing the breakdown of acetylcholine in the brain.¹⁶ From this study, it can be analyzed that 9% of AD patients were treated with donepezil.

Memantine (1-amino-3,5-dimethyl adamantane), a noncompetitive NMDA receptor antagonist, approved in May 2002 by the European Union and licensed by the FDA in October 2003. It is used to treat mild to severe Alzheimer's disease and has a half-life of less than 60 hours. This medication reduces excitotoxicity and neurodegeneration induced by excessive glutamate

activity.¹⁵ Memantine can attenuate glutamatergic neurotransmission, hyperphosphorylation of Tau proteins, and protect against Abeta peptide toxicity.¹⁷ According to this analysis, 2% of AD patients were pharmacologically managed with memantine.

Rivastigmine, a physostigmine-derived medication, inhibits AChE and BChE irreversibly and pseudo-selectively. This medicine is effective and well-tolerated in AD patients. It does not use the cytochrome P450 system for metabolism, lowering the risk of drug-drug interactions.¹⁵ It also improves cognition and has neuroprotective effects.¹⁸ It prevents the breakdown of acetylcholine and butyrylcholine (a brain chemical similar to acetylcholine) in the brain.¹⁶ In this study analysis, 4% of Alzheimer's patients used rivastigmine as their symptomatic relief.

Table 3: Stage of signs and symptoms and diagnosis of Alzheimer's disease.

Parameter	Characteristics	Number (n=153)	Percentage (%)
Stages of signs and symptoms	Signs and symptoms of early or first stage	17	11.11
	Signs and symptoms of middle stage	113	73.85
	Signs and symptoms of last or final stage	22	14.37
Modality of the symptoms	Physiological	116	75.81
	Psychological	143	93.46
	Cognitive	104	67.97
	Behavioral	143	93.46
Diagnosis process	Cognitive analysis	96	62.74
	Psychological evaluation	119	77.78
	Physiological signals	143	93.46
	Behavioral responses	107	69.93
Physiological signal tests	Cerebrospinal fluid (CSF)	89	58.17
	Blood test	117	76.47
	CT scan	143	93.46
	Positron emission tomography (PET) Scan	76	49.67
	sMRI	143	97.38
	Eye dynamics	93	60.78
Behavioral responses tests	General behavior assessment test	129	84.31
	Activity daily living (ADL) test	117	76.47
	Speech	137	89.54

Table 4: Adverse/ side effects of the drugs which are used to manage or control the symptoms of Alzheimer's disease.

Parameter	Characteristics	Number (n=153)	Percentage (%)
Adverse/side effects	Headache	136	88.89
	Vomiting	14	9.15
	Confusion	122	79.73
	Muscle cramps and weakness	43	28.10
	Insomnia	04	2.61
	Weight loss	34	22.22
	Dizziness	144	94.11
	Nightmares	82	53.59

Ginkgo biloba extract contains EGb 761, which is used to treat mild to moderate Alzheimer's disease. It's

comparable to donepezil. It improves symptoms, lowers thrombosis, and improves cognition, working memory,

and short-term visual memory in Alzheimer's disease with few side effects.¹⁹ In this study, 38% of patients were treated with Ginkgo biloba.

The combination of memantine and donepezil for individuals with severe AD demonstrated a significant improvement in cognitive function, ADL, and behavioral. The reasoning behind mixing memantine with donepezil stems from their complementing methods of action. While donepezil increases acetylcholine levels to improve synaptic transmission, memantine protects neurons from glutamate-induced damage. This dual approach addresses two distinct elements of the illness process, potentially providing more benefits than each medicine alone.²⁰ According to this study, 47% of AD patients were pharmacologically managed with the combination of memantine and donepezil.

Side effects of these drugs which are used to manage or control the symptoms of AD represented in the observed during the survey at three tertiary care hospitals and a daycare center in Bangladesh are presented in Table 4.

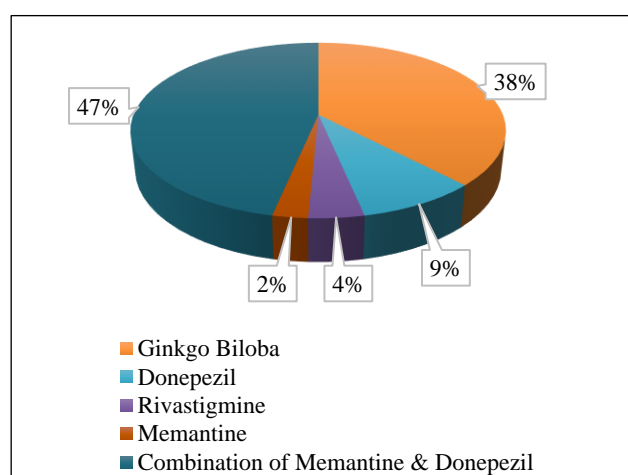


Figure 1: Medication used for the management of AD in Bangladesh.

DISCUSSION

Nowadays, the number of people with Alzheimer's disease is rapidly increasing in prevalence, and merely a quarter of individuals suffer from this disease. According to Alzheimer's statistics for 2019, AD affects up to 50 million individuals worldwide.²¹ According to world Alzheimer's report 2022, the percentage of male and female patients are 37% and 62%, respectively. The average age of these patients is 70 ± 12 years old.²² In this survey, the signs and symptoms, diagnosis process, pattern and treatment were observed of Alzheimer's patients of Bangladesh. In this study, age distribution showed that 62.09% of patients between (61-80) age group are highly affected by Alzheimer's disease. Here, it was observed that the male patients (58.16%) have been commonly suffered by Alzheimer's disease than female patients (41.84%). It was also noticed that the majority of

Alzheimer's disease patients have normal pulse (58.16%), whereas 41.83% of patients have abnormal pulse. Furthermore, it was noticed that 79.08% of AD patients have normal body temperature and 20.91% of AD patients have abnormal temperature. As a result, it is possible to conclude that most patients have a normal body temperature. From the study analysis, it can also be observed that 58.16% of patients have normal blood pressure. It was also shown that many people with Alzheimer's disease had finished HSC or higher education levels (45.09%). From the analysis, it also found that, large number of patients had related to business in their professional life. In their professional life, 33.33% of patients were doing different businesses, 30.71% of patients were housewife, 15.03% of patients related to managerial jobs. Therefore, it may be claimed that people having a profession which is too stressful have a high risk to develop Alzheimer's disease.

According to world Alzheimer's report 2022, 49% of patients were in the mid/ moderate stages of AD, 39% were in early stage and 8% were in advance stage. From the study analysis, it was noticed that maximum number of patients are identified that they are having AD when they have been facing the problems of middle stage of signs and symptoms or moderate signs and symptoms are rarely identified via themselves because maximum of them basically used to ignore the signs and symptoms of AD until they faced moderate stage of signs and symptoms. According to the findings of this study, 73.85% of patients had middle or moderate signs and symptoms, 11.11% had first or mild stage signs and symptoms, and 14.37% had last or severe stage signs and symptoms. From modality analysis, it can be said that most of the patients of AD have been facing psychological and behavioral symptoms and the number is 93.46%. In the meantime, 75.81% of patients have been facing physiological problems and 67.97% of patients have been facing cognitive problems. In Bangladesh, sMRI and CT scan are the most popular physiological signal tests used to diagnose AD. It was noticed that 97.38% of patients were detected using the sMRI test, and 93.46% of patients were identified using the CT scan. In behavioral responses, 89.54% of patients had identified via speech, 84.31% of patients had identified by general behavior assessment and 76.47% of patients had identified by activity of daily living test (ADL).

AD is one of those diseases which are not permanently curable, but it can be controlled by taking some pharmacological and non-pharmacological treatment. Non-pharmacological treatment is more popular procedure to keep AD in control in Bangladesh. Cognitive training, cognitive rehabilitation, and cognitive stimulation therapy (CST) confer modest but significant benefits in the treatment of cognitive symptoms in people with AD. Cognitive training is one type of training for the patients with AD which is directed by any individuals or computer and has some evidence to overcome the situation of cognitive symptoms in healthy older peoples.

Moreover, Cognitive rehabilitation also seems to have positive functional effects but brain training games like sudoku, chess etc. have no advantages in the improvement of cognitive symptoms of AD.²³ However, pharmacological treatment is also preferable. Now-a-days, there are some drugs that are used to treat AD or keep control on AD. According to this study findings, 47% of patients were treated with a combination of memantine and donepezil, 38% with ginkgo biloba, 9% with donepezil, 4% with rivastigmine, and 2% with memantine. However, these medications do have certain adverse effects. The most common side effects of these medicines include dizziness, headache, confusion, and nightmares. This study revealed that 94.11% of patients experienced dizziness, 88.89% experienced headache, 79.73% experienced confusion, 53.59% experienced nightmares, 28.10% experienced muscle cramps and weakness, 22.22% experienced weight loss, 9.15% experienced vomiting, and 2.16% experienced insomnia.

Alzheimer's disease is a progressive brain disorder that affects memory, thinking and behavior. It is one form of dementia, which is a general term for the mild cognitive impairment that can occur in a person's aged life. In Bangladesh, Alzheimer's disease is becoming an increasingly common health concern for the ageing population like many other regions. But maximum of the population of Bangladesh are not aware of Alzheimer's disease. In fact, many people never hear the name of this disease too. The exact causes of Alzheimer's disease are not fully understood yet. But it is believed to result from a combination of genetic, environmental and lifestyle factors. Age is the greatest risk factor for developing Alzheimer's disease, with the likelihood of the disease increasing as a person gets older.

The signs and symptoms of Alzheimer's disease can't be identified in the early stage easily. Maximum of patients used to find their problems in the middle stage or moderate stage of signs and symptoms. Actually, in mild or first stage, they ignored the signs and symptoms because they are not aware of AD. The diagnosis process of AD is made through a combination of medical and cognitive assessment, along with brain imaging tests. CT scan, MRI scan, PET Scan, CSF test and blood test are most popular diagnosis process in Bangladesh. General behavior assessment, speech and ADL tests are also common diagnosis process to identify AD. Currently, there is not permanent cure for Alzheimer's disease, but treatment and support are available that can help to manage and control its signs and symptoms and improve the quality of life for the patients who are affected by AD.

Some drugs are used to treat or control the symptoms. Most popular drugs are ginkgo biloba, combination of memantine and donepezil, rivastigmine, donepezil and memantine. However, the diagnosis and management of AD is challenging due to several factors, including limited resources, inadequate training of healthcare professionals and social stigma. Additionally, a lack of

awareness among the general population among the general population regarding this disease and its management further complicates the situation.

CONCLUSION

Alzheimer's disease is a growing concern in Bangladesh, and it is important to raise awareness about the condition and provide support to those who are affected by AD. In Bangladesh, it is crucial that efforts must be taken to prevent and manage Alzheimer's disease due to the aging population and rising life expectancy.

The current survey might have the potential contribute for better understanding of Alzheimer's disease pattern in Bangladesh and will be a foundation for in-depth research in this area. More research is required so that the characteristics of the disease in the Bangladeshi population can be understood which might bring a treatment and management strategy.

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