*Journal of Pharmaceutical Research International*

***30(5): 1-12, 2019; Article no.JPRI.51512***
***ISSN: 2456-9119***
*(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)*

# Chronicles of Alzheimer's Disease: A Medicinal & Therapeutic Overview in Bangladeshi Aspect

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***Author's contribution***

*The sole author designed, analysed, interpreted and prepared the manuscript.*

***Article Information***

DOI: 10.9734/JPRI/2019/v30i530282
Editor(s):
(1) Rafik Karaman, Professor, Department of Bioorganic Chemistry, College of Pharmacy, Al-Quds University, Jerusalem, Palestine.
Reviewers:
(1) Milankumar J. Kothiya, Columbia University Medical Center, USA.
(2) Yufeng Xie, University of Toronto, Canada.
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(4) Igor Iskusnykh, University of Tennessee Health Science Center, USA.
Complete Peer review History: http://www.sdiarticle4.com/review-history/51512

***Data Article***

***Received 25 July 2019***
***Accepted 01 October 2019***
***Published 23 October 2019***

## ABSTRACT

Nervous system and Neurological disorder sounds like a deep-sea of neurobiological harmony, reflecting a glorious bond and symbolizing a deep sign of interrelated linkages. Neurodegenerative diseases especially; Alzheimer's disease is a widely renowned disorder with a larger scope of research opportunities. Nowadays, there are an abundance of research activities been carried out on this specific topic. It's quite frightening to witness the ultimate outcome of Alzheimer's disease sometimes which can turn out to be the deaths of the patients. In our data analytical program, we have emphasized on Alzheimer's disease present therapeutic condition in Bangladesh, where in recent times this disorder has transformed into a household scenario. A handful number of patients been analysed through the regular observations based on their previous therapeutic history, expert opinions of scientists and physicians, as well as a smartly organized collection of medicinal and therapeutic information's been used in order to estimate and indicate an up to dated circumstance of Alzheimer's disease in Bangladesh. However, it's a matter of concern that even with the development of modern technology, this age-old innocence of the inability to treat such a class of apocalypse has raised a finger at the capability of civilized human beings. Here, we have also focused on the in-general medical therapeutics of Alzheimer's disease from which we are able to formulate a portfolio on the

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medicinal agents used in Bangladesh. Additionally, a data graphic is provided to figure out an estimated analysis of the approximate number of Alzheimer's disease affected patients in Bangladesh.

*Keywords: Neuroscience; nervous system; Alzheimer's disease; neurodegenerative disease; medication.*

## ABBREVIATIONS

| | |
|---|---|
| *APOE-4* | *: Apolipoprotein E-4 Gene* |
| *CVS* | *: Cardiovascular System* |
| *TREM-2* | *: Triggering Receptor Expressed on Myeloid Cells 2* |
| *ABCA7* | *: ATP-binding Cassette Subfamily a Member 7* |
| *SOR1* | *: SOP-2 Related Protein 1* |
| *CASS4* | *: CaS Scaffolding Protein Family Member-4* |
| *CD2AP* | *: CD-2-associated Protein* |
| *INPP5D* | *: SRC Homology2 Domain Containing Inositol Phosphate-5-Phosphate-1* |
| *MEF2C* | *: Myocyte Specific Enhancer Factor 2C* |
| *NME8* | *: N-terminal Thioredoxin Domain* |
| *PTK2B* | *: Protein Tyrosine Kinase 2 Beta* |
| *SNP* | *: Single Nucleotide Polymorphism* |
| *NMDA* | *: N-Methyl-D-Aspartate* |
| *ACI* | *: Acetylcholinesterase Inhibitors* |
| *NSAID* | *: Non Steroidal Anti-inflammatory Drug* |
| *CT* | *: Computed Tomography* |
| *MRI* | *: Magnetic Resonance Tomography* |
| *STR* | *: Short Tandem Repeat* |
| *PET* | *: Positron Emission Tomography* |
| *USD* | *: United States Dollar* |
| *AD* | *: Alzheimer Disease* |
| *SPECT* | *: Single Photon Emission Computed Tomography.* |

## 1. INTRODUCTION

Neuroscience is typically a well built and adequately balanced class of the medical realm, signifying the principles of Neurology. Though at the present time the success of scientific research focusing on Neuroscience has successfully transformed itself into a common affair, the pros and the cons of various pathways such as; signal transduction, neurological malfunctions or systemic blockages reflects the pessimism of uncertainty. Typically the dominion of Neurology cores around the nervous system. According to the generals, Neuroscience can be defined as a multidisciplinary part of the biological field concerned with the origin, structure, function, mechanism of action, classification, molecular & cellular level chemistry of neurons and the development of the nervous system.

It encompasses the complicated computational, behavioural, cognitive, voluntary and in-voluntary sections of neuroscience, which can be termed as the primary nexus between psychology, biology, neurology and health science. There are about hundred billion of neurons, with an approximate to a quadrillion units of nexus between them, yet with the development of medical technology, we are still been unable to understand or to carry out a revolutionary analytical program on single-cell molecules. In today's market, there is a wide variety of medications used in the possible treatment of Alzheimer's disease. Here we have tried to work on all of the possible classes of drugs in extended detail from the progression of Alzheimer's disease to the mechanism of actions of various drugs used through an in-depth observation.

The nervous system is a part of neuroscience. Generally, the nervous system is a class of cylindrical fibres called; Nerves. This highly complex and overly sensitive portion of our living

organism co-ordinates between the action and sensory transmission of the signals.

There are about more than 600 neurological disorders being identified, yet a large number of the disorders and their treatment policies remained to be discovered. Among them the most notorious neurological disorders are: Epilepsy, Parkinson's disease, Alzheimer's disease, Dementia, Peripheral neuropathy, Post-herpetic neuralgia, and Multiple sclerosis.

## 2. MATERIALS AND METHODS

This is a scientific data analysis, where all of the materials been used are either in the form of infographic or portfolio. With an ultimate goal is to:

- Provide a section of transparent ideas indicating the present condition of Alzheimer's disease in Bangladesh along with a comparison with other countries.
- Report about the therapeutic condition of Alzheimer's disease in Bangladesh.
- Provide a medicinal overview of Alzheimer's disease, as well as various neurological disorders in Bangladesh.
- Approximate estimation on the Bangladeshi affected patients of Alzheimer's disease (Which has never been figured out before).

Our working cycle shows an interrelated linkage in terms of our working topics. The article revolves around Alzheimer's disease and Neuroscience. Here, an empirical estimation been done on Bangladeshi aspect, as well as medicinal therapies and a definite hypothesis been developed to formulate our scientific dissertation.

## 3. DISCUSSION AND DETAILS

The main purpose of our experimental analysis is to figure out the data emblem on the present condition of Alzheimer's disease in Bangladesh and the associated therapeutics significantly utilized for the purpose of treatment as well as providing a clearer estimation of the challenging environment in Bangladesh.

For most of us, Alzheimer's disease is an ambiguous term. There is a deep sign of fear that this disease may affect everyone in its path and there is not any kind of solution to this challenge. Despite the decades of observations, we still possess no definite modifying treatment methodologies or a definite cure for Alzheimer's disease. Interestingly, an alarming statistical report suggesting a figure of 44 million of the worldwide population are suffering from this neurodegenerative disorders. This disease can occur on the synapses, where the released neurotransmitters are latterly the signals transmitted.

Dementia originally existed in the ancient Greek and Roman times. Latterly, this disease was once again been rejuvenated by the German physicist Alois Alzheimer in 1901 & the name of the disease was once again been renamed after the fame of the scientist to honour his contribution. According to scientific studies, the people aging over 65 years are at a 30 percent

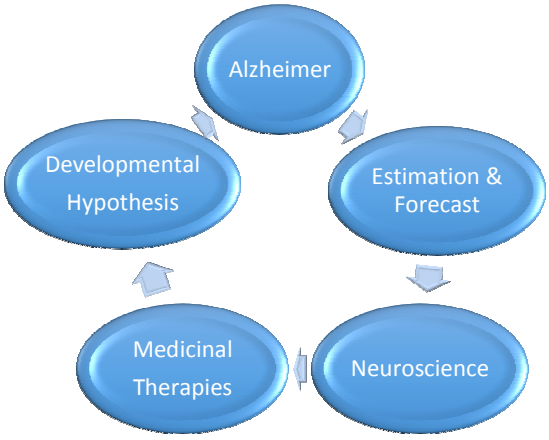


**Fig. 1. Our working cycle**

greater risk of Alzheimer's disease in comparison to other age sections. There are about 5.8 million of American's suffering from Alzheimer's disease. Additionally, the affected amount may increase from 44 million to approximately 152 million by 2050.

According to the research scientists, Alzheimer's disease occurs in the synapses. This is the place where the neurotransmitters are released and the signals are transmitted to the following synapses through the usage of the receptor protein bindings. At the same time, Amyloid-beta is released on the neurons. Continuous accumulation of Amyloid-beta proteins or lack of metabolism by the microglia would lead to the formation of sticky Amyloid plaques. As a result:

- The human brain shrinks to a certain degree.
- Neuron stops functioning loses its connection with other parts.
- At the start of Alzheimer's disease; the neurons and their connective junctions get gradually damaged. Lately, the cerebral cortex & other areas of the brain tissues are also being affected.

## 3.1 Stages of Alzheimer's Disease

Alzheimer's disease progresses quite slowly into various stages. Based on the different ways of effect, timing, & severity; Alzheimer's disease can vary into 4 stages, each of them having their own signs and symptoms.

### 3.1.1 Stage 1 [Effects of ageing on memory but no AD]

*3.1.1.1 Signs and symptoms*

In this stage, we can observe the effects of aging especially on memory, but not resulting in Alzheimer's disease.

At this stage, the signs of minor memory loss are analysed.

### 3.1.2 Stage 2 [Early stage]

*3.1.2.1 Signs and symptoms*

Early-stage or Primary stage; showing very little signs and symptoms.

Not remembering the episodes of forgetfulness.

### 3.1.3 Stage 3 [Middle stage]

*3.1.3.1 Signs and symptoms*

Mid stage; in this stage, there is an existence of a variety of signs and symptoms of Alzheimer's disease.

Patients suffering from a disturbance in sleeping and greater difficulty while remembering life events.

### 3.1.4 Stage 4 [Late stage]

*3.1.4.1 Signs and symptoms*

The extent results in a very damaging state, where the patient suffers from complete Dementia.

Poor ability to think, Becomes Paranoid.

## 3.2 Factors Affecting Alzheimer's Disease

There are several external factors resulting in the alterations leading to the initiation of Alzheimer's disease.

### 3.2.1 Factors like [1]

- APOE-4 gene variants genetically originated inside human being can lead to the accumulation of Amyloid beta [2].
- Poor sleep hygiene may resemble the main predictor of Alzheimer's disease.
- A single night's sleep deprivation can lead to the aggregation of Amyloid-beta.
- CVS diseases and the causes of CVS such as; obesity, in taking rich foods, lack of physical exercise, Hypercholesterolemia, Hypertension, Diabetes, Smoking can easily be held as the pivotal reason In Alzheimer's disease.
- Genetically inheritable genes and DNA factors can lead to the development of Alzheimer's disease in Different states of life.
- The association of Alleles with TREM2 genes can easily lead to a (3-5) times greater risks in the Development of Alzheimer's disease.
- Mutations in Amyloid beta-40 or Amyloid beta-42 factors, as well as other gene factors: ABCA7, SOR1, CASS4, CD2AP, INPP5D, MEF2C, NME8, PTK2B, SNP's,

etc. can lead to the result of Alzheimer's disease.

- Hormone replacement therapy in Menopause may increase the possibility of the risk associated With dementia to Alzheimer's disease.

#### 3.2.2 Social factors

- Smoking
- Alcohol
- Illiteracy
- Social Isolation

#### 3.2.3 Physiological factors

- Hypertension
- Hyperlipidemia
- Head Trauma
- Depression
- Elevated Homocysteine (Plasma Homocysteine level of 14 micro mole/litre or greater results in Alzheimer disease)
- Diabetes Mellitus
- Obesity

### 3.3 Experimental Details

The main purpose of our experimental analysis is to figure out the data emblem on the present condition of Alzheimer's disease in Bangladesh and the associated therapeutics significantly utilized for the purpose of treatment.

#### 3.3.1 Diagnostic tools

The presence of neurological & neurophysiological features and the advance diagnosis procedure has been figured out by the most popular following methodologies [3].

- CT-Scan (Computed Tomography Scan)
- SPECT (Single Photon Emission Computed Tomography)
- PET (Positron Emission Tomography)
- MRI (Magnetic Resonance Image) [4]
- EBT (Electron Beam Tomography)

#### 3.3.2 CT-scanner

In CT scanning methodologies, a wonderful combination of the sophisticated computer systems along with the X-ray equipment's leading to a production of vital, limbic, & axial images of the human brain. There are several factors that can play a pivotal role in this type of scanning. Such as:

- Rate of change of brain atrophy.
- Changes in brain structure.
- Initial level dilatation of the human peri-hippocampal fissure can be tagged as a useful radiologic marker. [5]
- The prominence of the choroid & hippocampal fissures.
- Enlargement of human Sylvian fissure can lead to the proper detection of Alzheimer disease.

#### 3.3.3 MRI scanner

MRI stands for "Magnetic Resonance Imaging technique". Like CT or PET scanning system, MRI doesn't involve any kind of use of ionizing radiation. It possesses the ability to depict the images of organs, soft tissues, bone and others. In the MRI scanner the fundamental revolves around the Magnetic Resonance principles. The most unique ability of MRI scanners is to produce Raw Images of its observing body. On the basis of magnetic resonance ability, the MRI machines can be divided into .3T, 1T, 1.5T, 3T, & 7T. T1, T2 weighted, & Flair is the general sequences used in usual MRI scanners**.** There is another special image called; STR is also used in MRI machines.

**Location where the MRI scan is used in the diagnosis of neurological disorder:** Hippocampus, Amygdala, Cingulate gyrus, Head of the caudate nucleus, temporal horn, Lateral ventricles, Third ventricles, cerebral perfusion.

**Note:** MRI technology shows supreme accuracy to make an appropriate forecast about the possibility of affected personnel. In this type of scenario, Diffusion tensor imaging technique is used to measure the risk of Alzheimer's.

**Spect:** "SPECT" stands for "Single Photon-Emission Computed Tomography". It mainly uses gamma rays to predict & utilizes the cross-sectional slices of the substance to measure the extent of the effect.

**Spect in Bangladesh:** Though "SPECT" as a diagnostic tool in widely popular figure throughout the whole world and has a reasonable demand in our neighbouring countries like India & Pakistan, however, there isn't any piece of reliable sources about the

Presence of SPECT machine in Bangladesh or exist for diagnostic purposes both in Governmental & Private sectors.

These radiopharmaceuticals assumed by the interactions with glutathione, which aids them to depict their active attitudes in the diagnosis of Alzheimer's disease through SPECT.

**PET (Positron Emission Tomography):** PET machines use nuclear imaging technologies to produce a 3D image of functional processes relating to the definite part of the brain, where to diagnose the existence of Alzheimer's disease. The utilization of short-lived radiopharmaceuticals along with an adequate mingle between easily available substance makes PET relatively cheaper [6].

**Application:** PET techniques mainly utilize radiotracers to observe the state of glucose metabolism in different tissues of the human brain, where the concentration of radioactive materials measured in a unit of Kilo-Becquerel per ml. PET is used to figure out the pivotal causes behind the occurrence of Alzheimer's disease. PET shows supreme accuracy in terms of diagnosis when other advance techniques completely fail to solve it out. It combines both functional information along with the anatomical details. In modern times there is two advance form of PET technique is applied [7]. Such as:

- PET-CT.
- PET-SPECT.

**How the medicines work:** The age-old or newly advanced medications used in the treatment of Alzheimer's disease targets the accumulation of Amyloid Plaques in the Synaptic junction to reduce the accumulation or to delay the accumulation on a certain position.

Type 01 Drugs mainly targets the intermediate phase before Amyloid Plaque accumulation leading to the development of Alzheimer's disease.

This type of drugs pivotally works against the inhibition of amyloid plaque accumulation in order to relief in the Alzheimer's disease.

Type 3 drugs works on the synaptic junctions ultimately aiding signal transmission and transduction to another synapse to improve the condition.

### 3.4 Mechanism of Action of Medicinal Agents

**AC inhibitor [3]:** Acetylcholinesterase inhibitor drugs works quite actively to improve acetyl signalling in the brain. These chemicals are required for the normal operation of memory functions. It works at the esoteric or ionic sites of cholinesterase receptors to exert its action.

ACI declines the breakdown of acetylcholine to make an increased supply of acetylcholine, ultimately boosting the cognition.

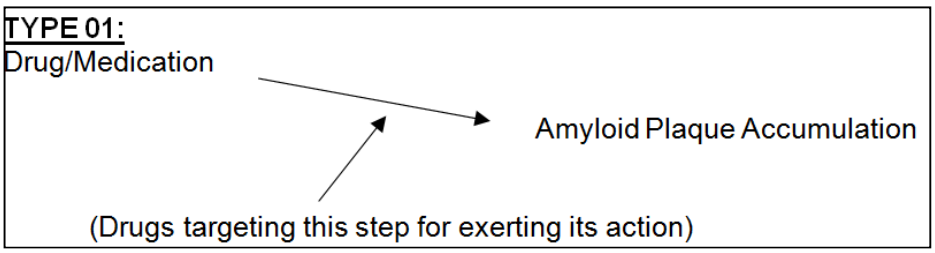


**Fig. 2. Type-1 drugs mechanism of action in Alzheimer's disease**

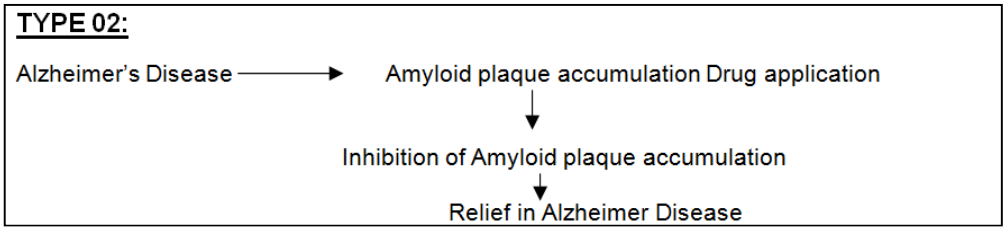


**Fig. 3. Type-2 drugs mechanisms of action in Alzheimer's disease**

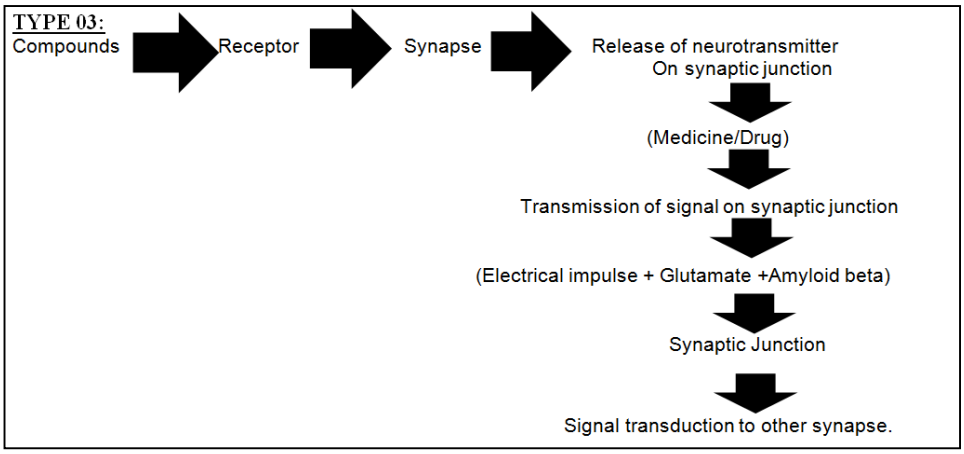


**Fig. 4. Type-3 drugs mechanism of action in Alzheimer's disease**

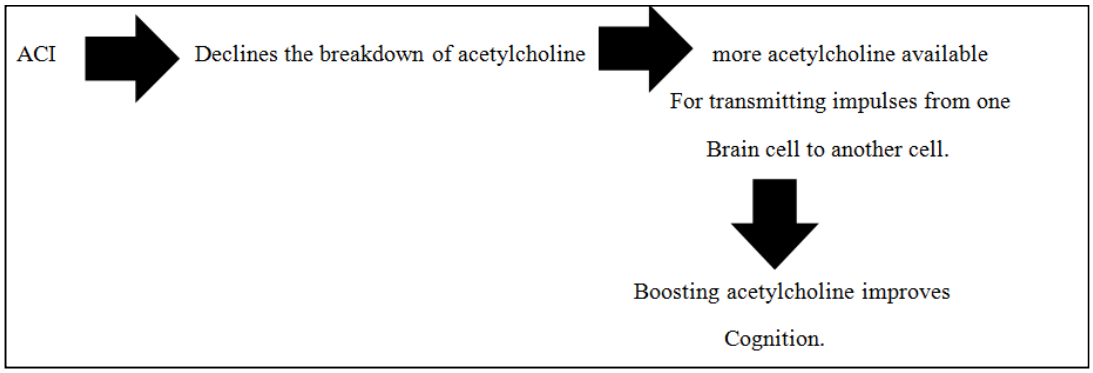


**Fig. 5. Mechanism of action of ACI**

**NMDA:** NMDA stands for N-methyl-D-aspartate, which mainly works on the NMDA receptor; an excitatory neurotransmitter at glutamate receptor, which can turn out to be toxic to nerve cells at relatively high concentration in Alzheimer disease. NMDA is used in moderate Alzheimer's disease.

**Mechanism:** NMDA has the ability to block the glutamate neurotransmitter to work against Alzheimer's disease.

**NSAID's:** NSAID's stands for non-steroidal anti-inflammatory drugs, reflecting possible active role against Alzheimer's disease. These types of drugs are also been utilized in the treatment of Alzheimer's disease.

**Mechanism of action in Alzheimer's disease:** NSAID's can exert their actions against Alzheimer by blocking the prostaglandin to lead to a better condition in Alzheimer's disease.

NSAID's can be easily classified into two of the following groups. Such as;

- Non-selective NSAID'S (COX-1)
- Selective NSAID'S (COX-2)

However, the usage of NSAID's in Alzheimer's the disease is still not FDA approved.

**Atypical anti-psychotics:** Atypical Antipsychotics is a class of medication primarily active against psychosis and used in the treatment of Alzheimer's disease.

- Atypical antipsychotics are second generation antipsychotics
- Atypical antipsychotics can work on 3 different points. Such as;
- D2 receptor
- Noradrenaline receptor
- Serotonin receptor

**Mechanism of action:** According to the schematic diagram, atypical antipsychotics can

bind to D2 receptors and various other serotonin receptors. As a result, it exerts actions such as; the blockage of the serotonin, inhibition of nor-adrenaline. Moreover, it can also possess the ability to inhibit the release of dopamine.

Here, the differences in the mechanism of actions as well as various characteristics among old atypical, new atypical and advanced atypical antipsychotics are also been shown.

**Prevention of Alzheimer's disease:** As we have previously mentioned it's nearly impossible to find a possible remedy to this burning issue. But there are several steps that we can take which may alter the development of Alzheimer's disease in the human race. Like:

- A Mediterranean diet like; eating berries and yogurt can aid us in the prevention of Alzheimer disease.
- Regularly practicing Aerobic exercise can dwindle the accumulation of Amyloid-Beta.
- Healthy lifestyle helps can help us to a certain extent against Alzheimer's disease.
- The development of neuroplasticity can help us to work on the Tipping points.
- An advance scientific study like; high level of cognitive reserve such as; learning something in new and meaning ways can help us as the source of back up memories in Alzheimer's disease affected patients.
- There are various types of medications: NSAID's, Acetylcholinesterase inhibitors, NMDA Inhibitors, Atypical antipsychotics are applied in the treatment of Alzheimer's disease.

**World-wide Alzheimer's disease:** According to some recent stats from the year 2017, there are just above 44 million Alzheimer's disease patients worldwide suffering from this disorder.

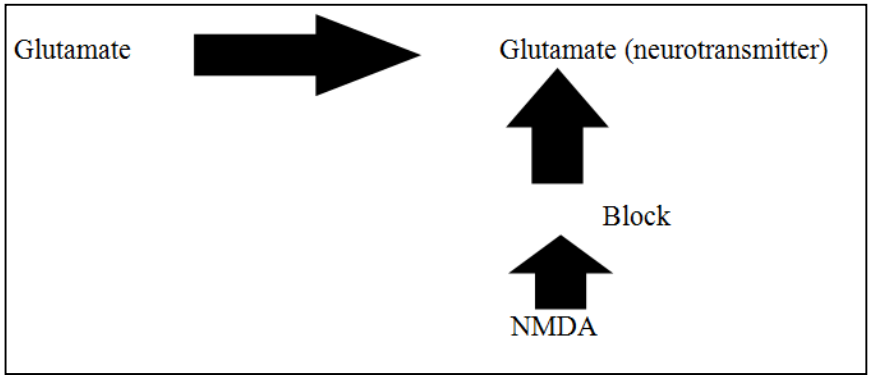


**Fig. 6. Mechanism of NMDA**

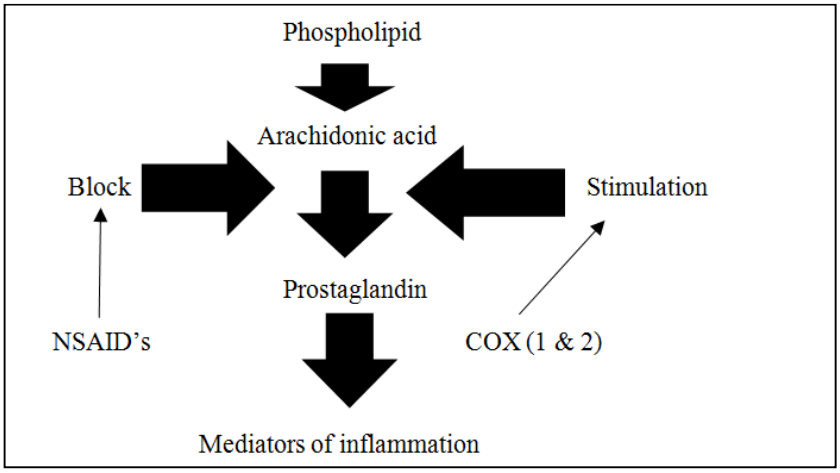


**Fig. 7. Mechanism of action of NSAID'S**

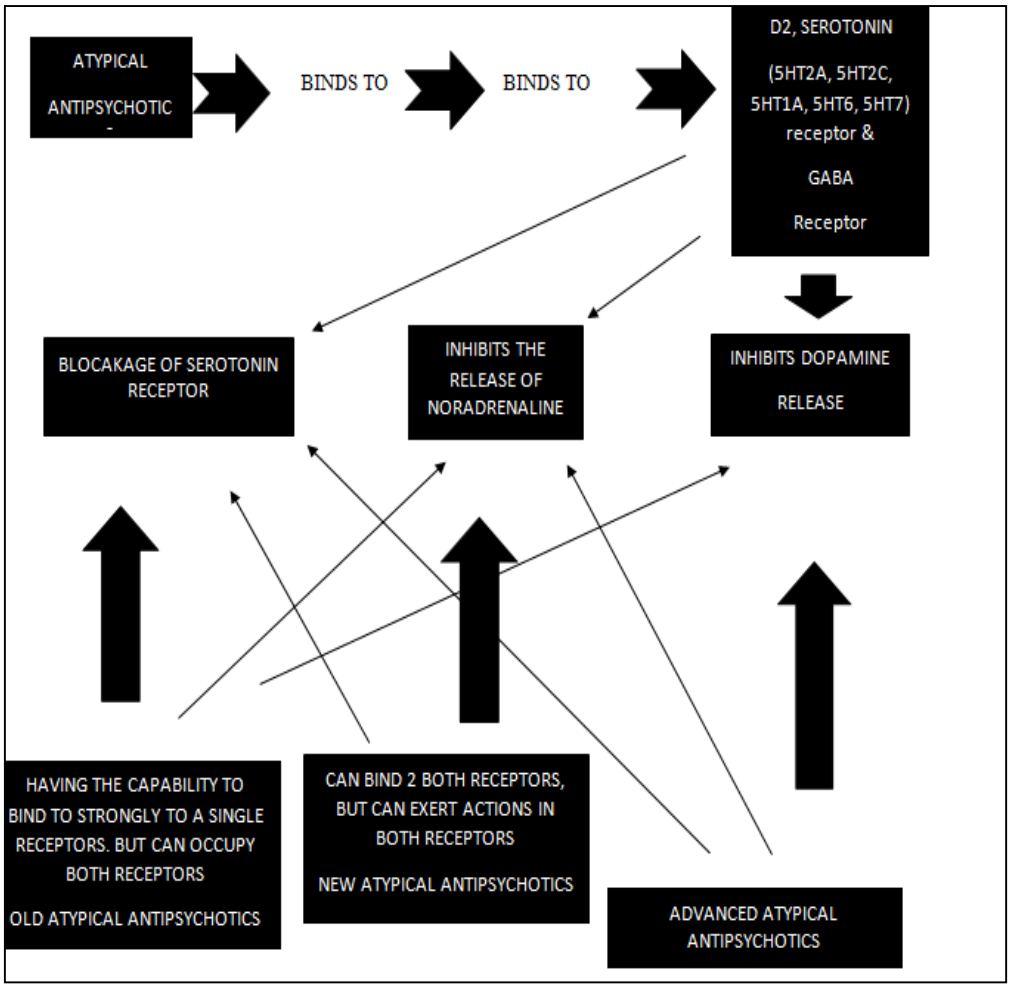


**Fig. 8. Schematic diagram showing the mechanism of action on atypical antipsychotics**

Only 1 in every 4 people through the whole realm been diagnosed. Among them, pupils living in the western part of the European continent is recognized as the most affected ones, whereas the Asians & Africans are figured out as the least affected. The total approximate cost of Alzheimer's disease and its related disease lures just above 605 Billions of USD [7], which has already risen to the figure of 290 Billion [7]. Alzheimer's disease is held as responsible as the second most leading cause of deaths, even ahead of cancer and others.

According to the Fig. 9; there is an estimation as well as a forecast been made about the possible expenditure previously been made in 2014 & and a possible figure for the upcoming 2030 and 2050, indicating an almost 4 times larger amount. **Alzheimer's disease Bangladesh:** Bangladesh is a densely populated country from the Indian subcontinent. As a result, it's quite normal to see the total number of population affected by Alzheimer's disease shows a large proportion of the population. The infographic standing below resembles a statistical view of the data analysis.

According to the infographic, it depicts that people aging over 60 contributes by an approximate 17 percentile in terms of the total number of Alzheimer's disease patients in Bangladesh in 2019.

**An estimation on the approximate number of population affected by Alzheimer's disease in Bangladesh 2019:**

**IN 2019:**

We have made an approximate study on Alzheimer's disease affected patients quite randomly throughout Bangladesh on a case

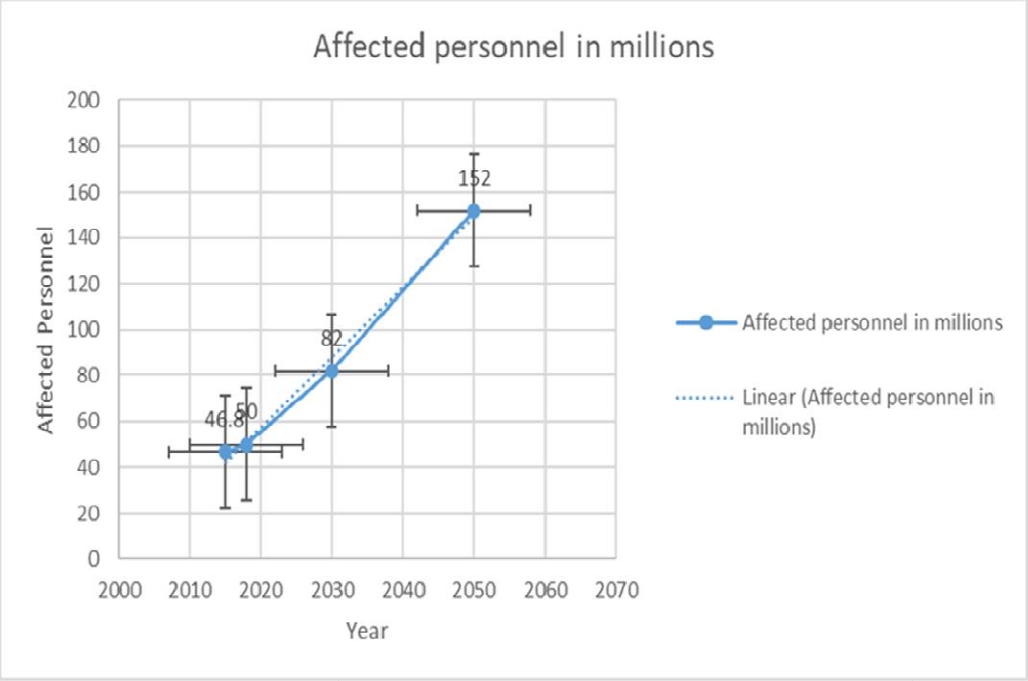


**Fig. 9. Statistical graph on the affected personnel in Alzheimer's disease in (2015, 2018, 2030 and 2050)**

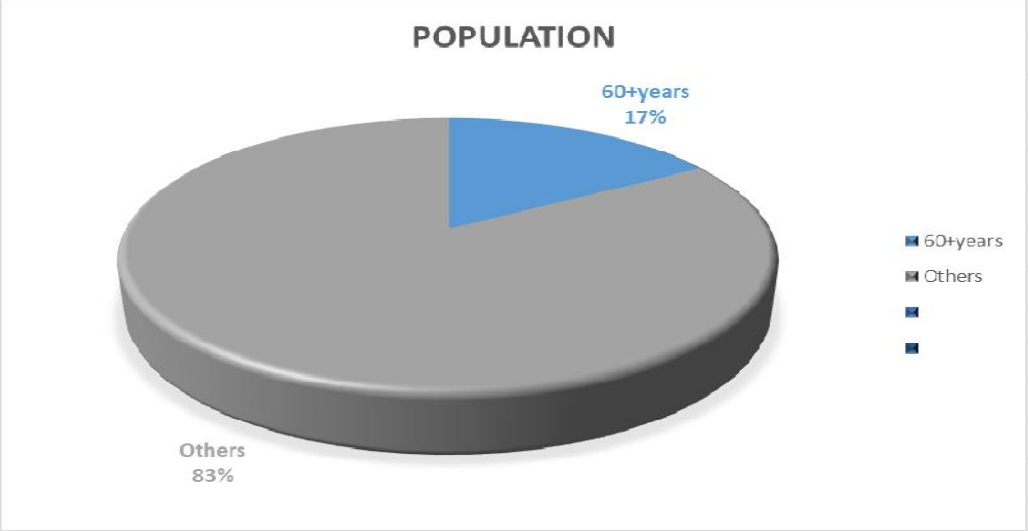


**Fig. 10. An approximate forecast about the total affected Alzheimer's disease patients in Bangladesh 2019**

study of 600 pupils, all of the pupil resulting from various age groups. The report of their previous medical history observed signs and symptoms and a series of scientific diagnostic tools been used in this observation. However, there are only 16 people termed as affected by Alzheimer's disease and many others have suffered from dementia too. Interestingly only 12 of them aging above 60 and 4 of them from other age groups and a similar assumption is been also provided for the year of 2016]. On the basis of our study, we have made an estimating forecast about the approximate number of Alzheimer's disease affected in Bangladesh.

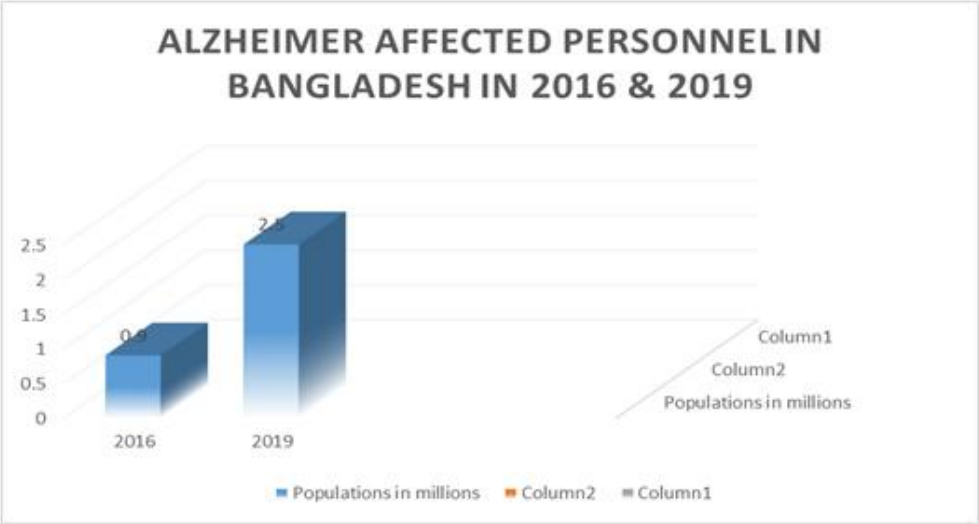


**Fig. 11. A comparison graph reflecting the Alzheimer's disease affected patients in Bangladesh in 2016 & 2019**

**Total number of population in Bangladesh:** 16, 47, 00, 000 [6]

**The approximate number of population aging more than 60 years:** 1, 02, 33, 480 [6]

**The Approximate quantity suffering from Alzheimer's disease in Bangladesh aging more than 60 years:** 2, 04, 669.6

**Rest of the population:** 15, 44, 66, 520

**Rest of the population suffering from Alzheimer's disease (Approximate):** 10, 29, 776.8

**So, the total number of people suffering from Alzheimer's disease in Bangladesh (An approximate quantity):** 1.2 million.

**An estimation on the approximate number of population affected by Alzheimer's disease in Bangladesh 2016:** According to the infographic no, it's clear to state that the approximate number of the person affected by Alzheimer's disease is between a range of (500-599) in every 100000 in 2016 [7]. When the total number of Bangladeshi Population in 2016 was: 162951560 [6].So, the probable affected Alzheimer's disease patients in 2016, was between: (.8-.9) millions.

According to Fig. 11; it indicates the amount of Alzheimer's disease patients in 2016 was about 1/3 of the total in 2019.

## 4. RESULTS

In our research analysis, we have made an empirical portfolio on Alzheimer's disease affected patients in Bangladesh. A comparison infographic has been provided in the name of Fig. 11. The number of affected patients in 2016 was: (.8-.9) millions which have increased by an approximate proportion of 1/3 to reach a figure of 1.2 million.

## 5. LIMITATION

The whole estimation is being done, throughout Bangladesh. Here, people of all over the ages have eagerly participated in this program. The only problem is that the whole process requires to be scientifically more précised and clinical. These patients should have been observed under a similar condition for a period and proper methodological observations, but because it's been a self-financed data analytical report, we were unable to ensure the quality of the analysis to a near-perfect condition. That's why we predict, if the estimation been done more strictly then, the result might have been changed.

## 6. CONCLUSION

It's an optimistic overview to observe the progression of analytical programs on the pursuit of a possible cure for the treatment of Alzheimer's disease. At present times organizations like; Alzheimer association, American brain foundation, Cure Alzheimer

foundation, Alzheimer Foundation of America are working worldwide against Alzheimer disease for decades. Still, the medicines that are widely accepted, are not useful enough in the treatment of this disease. Now we require to put a greater emphasis on this challenge with a purpose to eradicate Alzheimer's disease by the proper utilization of advanced technology at a supreme extent to ensure a the healthier numerical scenario on Alzheimer's disease treatment throughout the world and focusing on Bangladesh.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## ACKNOWLEDGEMENT

This paper is respectfully dedicated to the memory of my beloved mother, who died tragically, in 2016. We would like to thank Prof. Dr. Md. Abu Hanif Sheikh for his mental and educational support. We are also grateful to Daffodil International University for their assistance in data acquisition and interpretation. In addition, we are indebted to the reviewers to kind review and numerous perceptive comments on various drafts of the manuscript.

The author's responsibilities were as follows: data collection, data analysis and writing the whole manuscript. For the final content of the manuscript and all authors: read and approved the final manuscript. None of the authors had a conflict of interest.

## COMPETING INTERESTS

The whole data analytical program is being done with a complete Non-financial interest & all of the costs are being handled only and only by the researcher himself and it's been completed without any kind of financial assistance from any other organization. It's a data analytical the program, where the author is the only employee to perform the experimental tasks from the very beginning to the end. During this experimental journey, the author has dedicated himself for the sake of the research interest. The author announces that neither the journal nor authority has nothing to be held responsible for any kind of future conflicts. The author is also stating that this paper hasn't been published elsewhere or submitted in any other places for Publication while under submission.

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