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ANALYSIS OF MEDICATION AND PHARMACOLOGY OF ALZHEIMER'S DISEASE COMMONLY USED IN PAKISTAN

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Abstract:

Introduction: *Alzheimer's disease (AD) is the most common form of dementia accounting for 60–80% of dementia diagnosis and affects nearly 50 million people worldwide. Two classes of medications are FDA approved for the treatment of Alzheimer's disease (AD), acetylcholinesterase inhibitors and an NMDA receptor antagonist.* ***Aims and objectives:*** *The basic aim of the study is to analyze the medication and pharmacology of Alzheimer's disease commonly used in Pakistan.* ***Methodology of the study:*** *This study was conducted at Services institute of medical sciences, Lahore during 2017. We collect the data from doctors and patients both because we want to find the therapeutics of AD in local population of Pakistan.* ***Results:*** *To provide early and accurate diagnosis of AD, extensive efforts have been made into developing sophisticated methods to assess pathology in the living human brain. However, to date, no test or combination of tests that could accurately diagnose AD is available for broad clinical use outside of AD research centers.* ***Conclusion:*** *It is concluded that there are no clear and perfect medication for AD. The current diseased approach for AD consists of optimizing modifiable risk factors to reduce and delay symptom onset as well as symptomatic treatment after disease onset.*

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INTRODUCTION

Alzheimer's disease (AD) is the most common form of dementia accounting for 60–80% of dementia diagnosis and affects nearly 50 million people worldwide. Two classes of medications are FDA approved for the treatment of Alzheimer's disease (AD), acetylcholinesterase inhibitors (AChEI: donepezil, rivastigmine, galantamine, tacrine) and an NMDA receptor antagonist. Extant research has shown that race and ethnicity is a factor in the reported use of AD medications [1]. However, these have generally been drawn from data encompassing either a single center or geographically limited centers so that national trends and regional variability have been hard to discern. Since minority populations participate to a small degree in AD research, larger samples are necessary to determine if there is differential usage by these groups. The worldwide number of affected individuals is expected to reach 66 million by 2030, and 131 million by 2050 as the number of older adult's increases [1]. One in 10 people over age 65 and every third person over age 85 in the US has a diagnosis of AD. The global financial toll of dementia was estimated to be 818 billion US dollars in 2015, an increase of 35% since 2010 and this cost is expected to further rise together with the prevalence of AD. The majority of the costs are related to family and social care of patients, rather than medical care. About 5% of all AD patients show cognitive symptoms before age 65 and are classified as early onset Alzheimer's disease (EOAD). Patients showing clinical symptoms after age 65 are classified as having late onset Alzheimer's disease (LOAD) [2]. Here, we provide a summary of the clinical, neuropathological, fluid, and imaging biomarkers of AD along with a more comprehensive review of genetic findings in both Mendelian and sporadic forms of AD[3]. We discuss how genetic analysis as applied in Mendelian randomization (MR) may be helpful in validating causality of modifiable risk factors that could advance preventive measures. Moreover, genetic data may be useful to facilitate precision medicine. The goal of precision medicine is to integrate clinical, genetic, and life style data to enable clinicians to efficiently and accurately predict the most appropriate course of action for a patient. We emphasize the ways genetics may facilitate precision medicine in AD: (1) identifying at risk individuals through risk prediction, (2) improving diagnostic precision, and (3) expediting the discovery of targetable disease mechanisms for drug development[4]. Due to the large number of published articles in biomedical research of AD, we refer to more recent comprehensive reviews written by domain experts and supplement these with other findings [5].

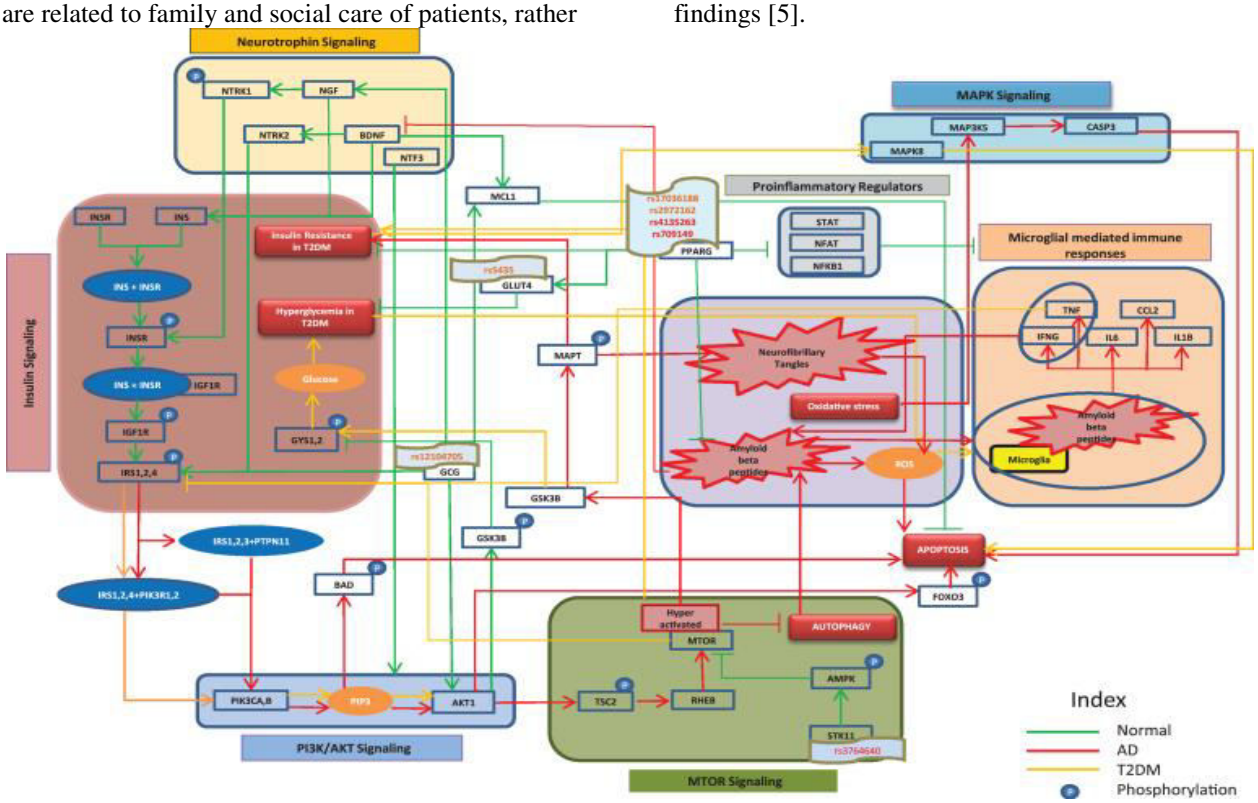

Figure 01: Significant pathways between AD and T2D

Aims and objectives

The basic aim of the study is to analyze the medication and pharmacology of Alzheimer's disease commonly used in Pakistan.

METHODOLOGY OF THE STUDY:

This study was conducted at Services institute of medical sciences, Lahore during 2017. We collect the data from doctors and patients both because we want to find the therapeutics of AD in local population of Pakistan.

Data collection

We conduct the interviews and questionnaire for analysis. We included publications of the Mendelian AD genes as well as publications that were referred and curated by the National Human Genome Research Institute-European Bioinformatics Institute (NHGRI-EBI) Catalog of published genome-wide association studies (GWAS Catalog). In addition, we included high-quality association studies reporting rare variants that meet the "analytically rigorous" criteria for GWAS or are otherwise statistically thorough.

Statistical analysis

All *P* values presented in the results are two-sided, and all analyses were performed by using SAS software.

RESULTS:

To provide early and accurate diagnosis of AD, extensive efforts have been made into developing sophisticated methods to assess pathology in the living human brain. However, to date, no test or combination of tests that could accurately diagnose AD is available for broad clinical use outside of AD research centers[6]. CSF levels of Aβ42, tau, and hyperphosphorylated tau as markers for amyloid, neuronal injury, and tangles, respectively, have been the main fluid biomarkers used in AD research. In CSF of AD patients, a decreased level of Aβ42 has been consistently found. Interestingly, a reduction of CSF Aβ42 had been shown to correlate with brain atrophy in non-demented elderly indicating a potential preclinical stage[7].

Drugs analysis

We collect the data and form a precise table regarding medications which are used for the therapeutic approach and medication of AD. (Table 01).

Table 01: Drugs used for AD

CR Best Buy	Drug/Strength/Form	Brand	Average Monthly Cost [2]	Frequency of Use Per Day [3]
	Donepezil 5 mg tablet	Aricept	$363	One
	Donepezil 5 mg tablet	Generic	$208	One
	Donepezil 10 mg tablet	Aricept	$352	One
	Donepezil 10 mg tablet	Generic	$203	One
	Donepezil 23 mg tablet	Aricept	$309	One
	Donepezil 5 mg dissolvable tablet	Generic	$240	One
	Donepezil 10 mg dissolvable tablet	Generic	$210	One
	Galantamine 4 mg tablet	Generic	$196	Two
	Galantamine 8 mg tablet	Generic	$183	Two
	Galantamine 12 mg tablet	Generic	$180	Two
	Galantamine 8 mg sustained-release capsule	Generic	$177	One
	Galantamine 16 mg sustained-release capsule	Generic	$179	One
	Galantamine 24 mg sustained-release capsule	Generic	$183	One
	Memantine 5 mg tablet	Namenda	$269	Two
	Memantine 10 mg tablet	Namenda	$266	Two
	Memantine 10 mg/5 mL oral solution	Namenda	$489	Two

DISCUSSION:

Generally speaking, it is challenging and time-consuming to isolate, identify, and screen the bioactive components in natural medicines. In addition, the components may be metabolized to phase I and II derivatives following absorption. Therefore, the bioavailability and access of metabolites or natural components to brain tissues are absolutely critical factors in predicting the potential for those compounds as CNS drugs [6]. A large number of epidemiological, preclinical and pathophysiology studies indicate that AD and T2DM share cellular and molecular mechanism [6]. The classical approaches in measuring comorbidity that are based on clinical readouts, patient data, and electronic health records cannot reason over the dysfunctional molecular activity or the impaired biological pathway involved in the diseased state [7]. On the contrary, deciphering comorbidity at a mechanistic level could well explain the outcomes of clinical readouts and patient examinations establishing a link between proteomic/genomic and phenotypic aspects of diseases. However, in this study we do not attempt to cover this proposal. Since there are no established studies aimed at explaining comorbidity based on shared mechanisms, we believe that understanding the co-morbid mechanisms between complex diseases can be dealt with systems biology approaches like integrative modeling [8].

A role of innate immunity and inflammation in AD etiology is independently supported by a large body of functional evidence. Among the risk genes from the immune pathways, TREM2 stands out with its high effect-size of AD risk. TREM2 stands for triggering receptor expressed on myeloid cells 2, a single-transmembrane protein expressed by monocytic myeloid cells. Both ApoE and Clusterin (encoded by CLU) are extracellular chaperons that prevent protein aggregation[8]. In addition, both bind to the microglial receptor TREM2 and thus may promote uptake of Aβ by microglia. Studies on animal and human brains indicated that the TREM2 risk variant p.R47H impairs TREM2 detection of lipid ligands leading to microglia dysfunction. Observational studies have suggested that diabetes, mid-life obesity, mid-life hypertension, high cholesterol, and smoking are modifiable risk factors for AD [9]. In terms of modifiable protective factors, education has been robustly shown to reduce AD risk. However, for many modifiable factors, no consistent pattern was found across studies. A recent comprehensive meta-analysis of 93 modifiable risk factors was conducted from 323 retrospective case/control and prospective cohort studies, which were selected after a systematic review of 16,906 publications. This study analyzed associations between AD risk and medical, dietary and occupational exposures as well as serum biochemistry, preexisting diseases, lifestyle, and psychological factors [10].

CONCLUSION:

It is concluded that there are no clear and perfect medication for AD. The current diseased approach for AD consists of optimizing modifiable risk factors to reduce and delay symptom onset as well as symptomatic treatment after disease onset.

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