



Measuring Community Awareness about Factors Influencing the Development of Alzheimer's Disease in Saudi Arabia

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ABSTRACT

AD is a progressive condition in which symptoms gradually develop and ultimately become more severe and lead to irreversible damage to multiple brain functions. Studies have shown that AD pathology and progression might be affected by several factors including age, diet, and mental and physical exercise. Additionally, studies have demonstrated the existence of some diseases such as diabetes mellitus and Down syndrome may enhance the development of AD. On the other hand, several evidence suggests that a healthy lifestyle can help decrease the risk of developing AD. This study aimed to measure the awareness of the Saudi community regarding the factors that might contribute to the development of AD. A questionnaire was distributed amongst the public through campaigns that took place in shopping centers and schools. Additionally, the questionnaire was distributed through emails and WhatsApp messages to ensure the coverage of different areas of the kingdom. Results demonstrated overall good awareness in the community however, more awareness programs and campaigns are highly recommended.

Key Words: Alzheimer's disease, Age, Genetic factors, Diabetes mellitus, Down syndrome

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INTRODUCTION

Neurodegeneration is a broad range of conditions that mainly leads to the damage of neurons in the human brain as a result of toxic, aggregation-prone proteins. Neurodegenerative disorders such as Parkinson's disease (PD), motor neuron disease (MND), and Alzheimer's disease (AD) share a common feature, which is the aggregation and deposition of abnormal proteins. AD is the most common cause of dementia [1]. Dementia itself is not a disease but it is a term that describes the gradual loss of brain functions such as the loss of cognitive function including memory, learning, attention, and judgment. It has been thought that dementia appears only in the elderly. However, studies showed that there is a number of individuals who develop dementia relatively early in life. Most of these early dementias are caused by AD [2]. AD was first discovered in 1906 by Dr. Alois Alzheimer who noticed changes in the brain tissue of a woman who had

died of an unusual mental illness. Her symptoms included memory loss, language problems, and unpredictable behavior. After she died, he examined her brain and found many abnormal clumps and tangles, which were then called amyloid plaques and neurofibrillary tangles, respectively [3]. Currently, there are around 50 million people with AD worldwide, and approximately 10 million new cases are discovered every year. Statistics show that approximately more than 33.9 million people worldwide and 130,000 people in Saudi Arabia have AD. Also, studies expect that in 2050 the number of AD patients will be doubled. AD is a progressive condition in which symptoms gradually develop and ultimately become more severe and lead to irreversible damage to multiple brain functions. Unfortunately, there is no cure for AD but the symptoms of dementia can be reduced temporarily [4]. The human brain contains billions of neurons. These neurons produce electrical signals, which allow them to

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communicate with different parts of the brain, as well as the other organs in the body. AD affects this communication among neurons, resulting in loss of cellular function followed by cell death. This neurodegeneration is derived from non-functional, modified proteins that form the foundation of the pathological cascade [5]. Several hypotheses on the etiology of AD have been developed over time. Studies showed that the main proteins involved in AD pathology are amyloid-beta and tau, which accumulate and aggregate progressively outside and inside neuronal cells, leading to the formation of amyloid-beta plaques and neurofibrillary tangles, respectively [6]. In the neuronal cell membrane, there are molecules called

Amyloid Precursor Protein (APP), which are essential in neuronal growth and repair. After performing the required function, APP normally gets chopped up by some enzymes called alpha-secretases and gamma-secretases resulting in the formation of a soluble peptide that will be removed. If other enzymes called beta-secretases get involved in the break-down process with these gamma-secretases, it results in the formation of insoluble monomers called amyloid-beta ($A\beta$) (**Figure 1**). These sticky monomers bond outside neurons forming beta amyloid plaques. The presence of these clumps in synapses blocks the neuron-to-neuron communication leading to neuronal degeneration [7, 8] (**Figure 1**).

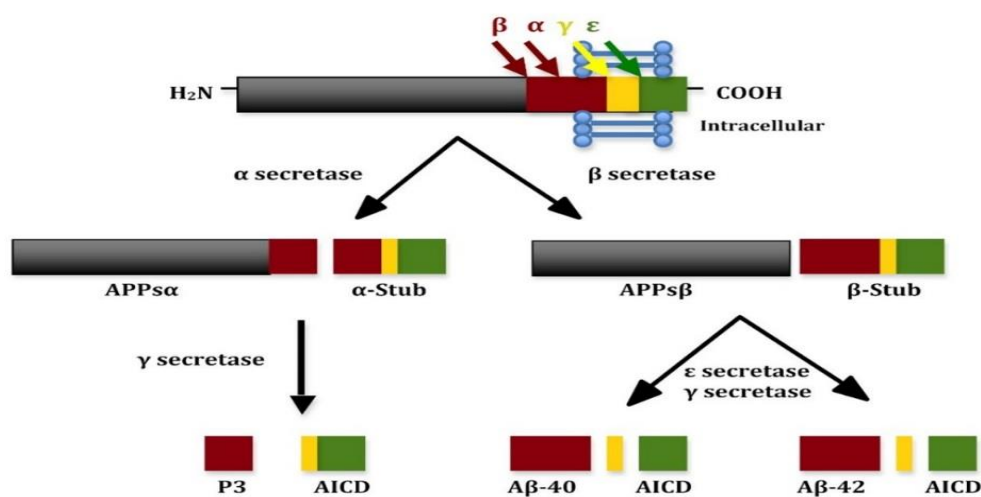


Figure 1. The formation of beta amyloids through the processing of APP by beta-secretases [9]

Tau is a microtubule-associated protein (MAP) present in both the central and peripheral nervous systems. It is involved in microtubule assembly and stabilization. This protein with a set of other MAPs (e.g. MAP1a, b, and MAP2), plays a basic role in axoplasmic transport. In AD, the hyperphosphorylation of tau occurs by a number of protein kinases that prevent tau from binding to microtubules and from promoting microtubule assembly, and therefore, the microtubule structures collapse. These free tau molecules then combine together to form neurofibrillary tangles, which are insoluble twisted fibers found inside the neuron. Neurofibrillary tangles

aggregation triggers immune cells such as microglia and astrocytes to initiate an inflammatory reaction causing neuronal degeneration (**Figure 2**). It has been shown that AD is not a disorder of specific brain regions or specific neurotransmitter systems. The neuronal damage begins in the hippocampus, which is responsible for memory and learning functions, then eventually expands throughout the brain affecting the parts of the brain that control basic bodily functions such as swallowing, moving, and speaking. Patients in the last stages are bed-bound and require care all-time [6, 10].

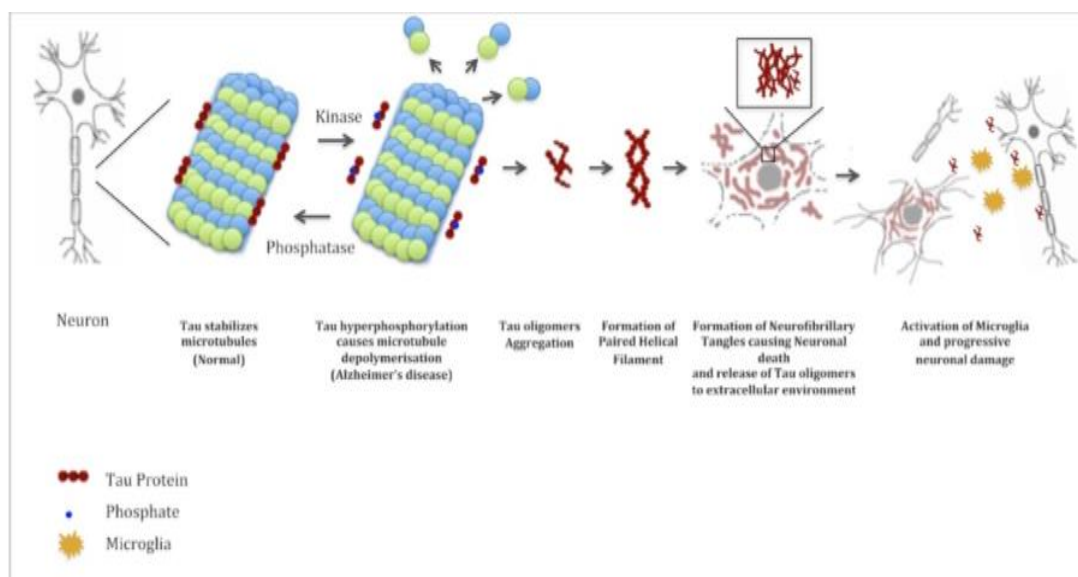


Figure 2. The formation of neurofibrillary tangles through tau hyperphosphorylation [9]

Understanding the factors that might increase or reduce the risk of AD development aids in the prevention and confers the chance to slow the progression of the disease. The comprehension of these factors is not limited to community health but also for economic purposes. Various factors have been identified to influence AD although some of them are still under debate [11-14].

Aging is the most related risk factor to AD. Individuals over the age of 65 have high susceptibility to develop AD, which duplicates every five years after this age. The risk of developing AD extends to approximately 50% above 85 years old [15]. In 1995, a study was conducted on 32,000 people at and above the age of 65 in East Boston, Massachusetts. The results showed that 10% of people aged over 65, and 47% of those over 85 have AD. AD cases with no familial association usually develop AD after the age of 60, which is known as late-onset AD (LOAD) or sporadic AD [16]. However, AD cases related to genetic mutation, such as Presenilin-1 (PSEN1), Presenilin-2 (PSEN2), and Amyloid Precursor Protein (APP) mutations, usually develop AD as early as 30 to 40 years old and is known as early-onset AD (EOAD). Age is an uncontrolled risk factor however several evidence suggests that a healthy lifestyle can help decrease the risk of developing AD [17].

The genetic factor is highly associated with age at onset. Gene mutations are classified according to the age at onset of AD into EOAD and LOAD [18]. Three main genes have been demonstrated to be involved in EOAD including PSEN1 on chromosome 14q, PSEN2 on chromosome 1q, and APP on chromosome 21q. Recently, more than 270 mutations have been identified in these three genes. Mutations in APP enhance AD pathogenesis by increasing the production of A β , hence the formation of A β plaques [19]. Currently, approximately 50 mutations in the APP gene have been identified and each mutation has a different

impact on the amyloidogenic pathway. PSEN1 gene, which is the core component of the γ -secretase complex, leads to the production of A β fragments. Although 215 genetic mutations in the PSEN1 gene have been discovered, only 50% of them are believed to cause EOAD [20, 21]. Mutations of the PSEN1 gene lead to the rise in A β 42/40 ratio. Studies have demonstrated that A β 42 has a higher ability to clump in the brain than A β 40, hence playing a key role in amyloidosis and neuronal damage [21]. PSEN2 gene is similar to PSEN1 in the structure and function however, PSEN2 mutations are very rare and lesser involved in the production of amyloid peptide [22]. As mentioned earlier, LOAD represents the sporadic form of AD. It has been thought that the APOE ϵ 4 allele is the only risk factor for LOAD pathogenesis. Recent studies discovered a number of other genes that could increase the risk of LOAD. However, the APOE gene is the major genetic risk factor for LOAD. APOE gene plays a key role in inflammation control, transport of lipid, cholesterol metabolism, neurogenesis, and synaptic function [23, 24]. APOE gene has three common alleles ϵ 2, ϵ 3, and ϵ 4. It has been demonstrated that ϵ 4 enhances LOAD development while ϵ 2 and ϵ 3 have an antagonizing effect. Studies performed on humans and transgenic mice show that APOE3 and APOE2 are more efficient to contribute to A β clearance than APOE4 [25]. Moreover, studies have shown that the homozygotes pattern of APOE ϵ 4 increases the levels of phosphorylated tau and total tau in AD patients [24].

AD and diabetes mellitus type 2 (DMT2) are aging disorders, but the actual link between them is not clear yet. It has been thought that the relationship between AD and DMT2 is coincidental rather than being comorbid [26]. However, recent studies suggest that due to common pathologic mechanisms including inflammation, insulin resistance, and mitochondrial dysfunction, patients with

DMT2 are significantly at high risk to develop AD [27]. Another major component that links AD and DMT2 is glycogen synthase kinase-3 β (GSK-3 β), which leads to insulin resistance in DMT2 and tau hyperphosphorylation in AD [28]. Moreover, studies performed on 524 AD patients showed that 74 of these patients had diabetes. Furthermore, studies suggest that high glucose levels are considered a risk factor for developing dementia even in non-diabetic individuals and that diabetic patients have a chance to develop dementia twice more than normal people [29].

Trisomy 21 is the main genetic feature that links Down syndrome (DS) with AD. Since the APP gene is located on chromosome 21, the additional copy of that gene leads to the overproduction of A β proteins, which eventually forms A β plaques. All individuals with DS above the age of 40 have shown A β plaques and tau tangles development. Currently, studies show that more than 30% and 50% of DS patients over the age of 50 and 60 respectively are affected by AD [30, 31].

Various statistical studies were performed to indicate the relationship between head traumas and AD. Results suggested that head traumas may significantly increase the risk of developing dementia and AD as a result of A β aggregation. Furthermore, studies found that males have a higher risk of AD development than females as a side effect of head trauma [32-34].

Age, gene mutations, and apolipoprotein E represent the non-modifiable risk factors of AD, while recent studies suggest that nutrients, food and beverages, and physical and mental exercise could be significant modifiable factors of AD [35]. Studies suggested that nutrients such as vitamins, antioxidants, and polyunsaturated fatty acids decrease the risk of developing AD. Furthermore, studies showed that the consumption of some food and beverage including fish, fruits, vegetables, and coffee decreases the risk of AD development [36]. Also, it has been demonstrated that nutrients including carbohydrates, fat, vitamins, and antioxidants are modifiable factors of AD [37]. As mentioned earlier, the risk of AD increases in people with DMT2 [38]. Additionally, studies suggested that the excess exposure of neurons to glucose enhances protein glycation leading eventually to the development of AD [39].

The effect of main fat types on cognitive aging varies. It has been demonstrated that a high intake of monounsaturated fatty acids reduces cognitive decline [40, 41]. Also, studies showed that a high intake of omega-3 polyunsaturated fatty acids slows Down cognitive decline in the elderly with no signs of dementia [42, 43]. It has been demonstrated that DHA, which is one of the main forms of omega-3 polyunsaturated fatty acids, decreases A β production in AD animal paradigms [44-46]. On the other hand, a different study showed that DHA does not

enhance cognitive and functional decline [47, 48]. Studies proved that excess intake of saturated fatty acids could lead to deterioration of cognitive functions [49]. Moreover, a study of 1,449 individuals showed that mild intake of saturated fatty acids is linked with an elevated risk of AD and dementia [50]. It has been demonstrated that this elevated risk results from trans fatty acid accumulation, which leads to an increase in A β production by enhancing the amyloidogenic and reducing the non-amyloidogenic processing of APP [51]. However, some studies denied that there exists a relationship between high trans fatty acid intake and cognitive decline [41].

It has been demonstrated that vitamin A along with β -carotene could be the master molecules to prevent and/or treat AD. Studies showed that these two molecules have the potency to discourage the composition of both A β oligomers and fibrils [52]. In AD patients, decreased concentrations of vitamin A and β -carotene in the serum and plasma have been observed [53, 54]. However, no study has demonstrated the role of vitamin A alone in AD patients yet. Both in vivo and in vitro studies demonstrated the role of vitamin C in reducing the composition of the A β oligomer [55, 56]. In addition, many studies have indicated that utilization of vitamin C together with vitamin E for a 3-year period or more contributes to reducing the prevalence of AD [57]. Moreover, studies proved that vitamin A, β -Carotene, and vitamin C are classified as antioxidants and that they could prevent AD by reducing oxidative stress [58]. It has been shown that high homocysteine concentrations could increase the risk of developing AD [59, 60]. Vitamins B including folic acid, vitamin B6, and vitamin B12 are believed to decrease homocysteine concentration [61].

It has been demonstrated that the ingestion of fruits, vegetables, fish, and coffee could decrease AD incidence [62-64]. However, it has been shown that tea and milk consumption might influence cognition, but their effect on AD is unclear [37].

It has been demonstrated that exercise enhances neuroplasticity and maintains mental health. Many studies have been performed to evaluate the effect of exercise on AD patients [65]. Moreover, several studies have been carried out on two groups of patients, physically exercising and non-exercising. Results showed that physical exercise could reduce brain atrophy, improve intellectual activity and decrease neuropsychiatric symptoms. In addition, the intensity level of the exercise may be an important factor in mental improvement [66]. Another study has randomly divided AD patients into two groups, the first group undertaken computer rehabilitation programs three times a week for three months while the other group was subjected to a control intervention. Cognitive functions were tested in three different time periods, pre-training, post-training, and at the six-month follow-up. After that, memory,

executive function, attention, and language skills improved significantly in those patients who used the rehabilitation program [65]. On the other hand, numerous studies failed to prove the existence of any positive effect of exercise to reduce the risk of dementia or to improve the mental ability of the elderly [67].

A study containing 60 AD patients was carried out to define the effect of various activities such as music, exercise, and drawing on cognitive health and social skills. Results showed that the group who undertaken musical treatment were more alert and pleased and had a good retrospect of last memories. Also, multiple studies suggest that music is a simple and enjoyable way to use as a therapy for AD patients [68].

MATERIALS AND METHODS

This study focuses on the awareness of Saudi society about the factors that may affect the development of AD. Data were collected through a solid questionnaire, which consists of 11 questions including the participant's age and education, and whether he/she thinks that there exists a relationship between several factors on the development and/or progression of AD. The answers were based on a four-point scale (strongly agree, agree, disagree, and strongly disagree). The questionnaire was published through awareness campaigns at shopping centers and schools as well as emails and WhatsApp messages. 1,513 participants successfully filled in the questionnaire, 42.4% of them aged 20-30 years, 19.4% aged 30-40 years, 15.3% aged 10-20 years, 11.8% aged 40-50 years and 11.2% were older than 50 years. 4.8% of the participants were holding a doctorate degree, 62.9 were holding a bachelor's degree, 29.2% were intermediate or high school students, and 3.1% were illiterates.

RESULTS AND DISCUSSION

AD is an irreversible, progressive, and incurable disease. The global economic cost of the disease is massive and was estimated to be 604 billion US dollars in 2010 [69]. AD has become the fourth most common cause of death in developed countries with no effective treatment [70]. Fortunately, studies approve that multiple factors may inhibit and/or enhance the risk of developing AD. Due to the elevated incidence of this disease in Saudi Arabia, this study was conducted to assess public awareness about these factors.

Community awareness about the relationship between AD and age

The first question that was conducted in the survey was whether the participant thinks that there is a relationship between AD and age. The data shows that the majority of

the participants, approximately 62.4% (943 individuals), believe that AD is an age-related disorder. However, a high percentage of the participants, approximately 37.6% (491 individuals), do not believe that there exists a relationship between AD and age. Moreover, 5.2% of this group (79 individuals) strongly disagree with that statement (**Figure 3**).

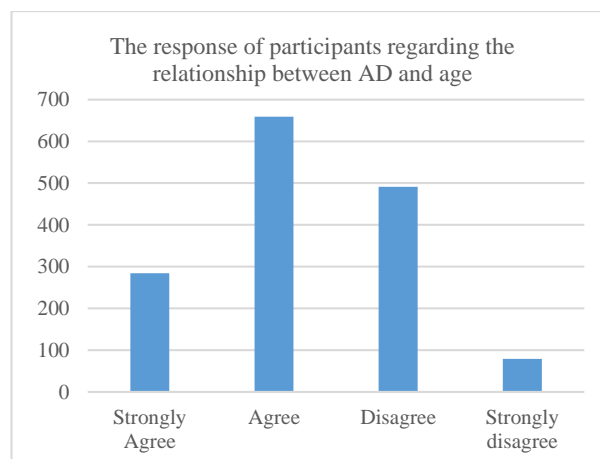


Figure 3. The response of participants regarding the relationship between AD and age

Community awareness about the relationship between Alzheimer's disease and genetic factors

The second question in the questionnaire assesses the number of people who think that AD is a hereditary disorder. The results of this question showed that 10.2% (155 individuals) coincide that AD is a genetic disorder. Moreover, 38.3% of this group (579 individuals) believe there is a link between genetic factors and AD. On the other hand, 43.5% (658 individuals) do not think that AD is a genetic disorder. Furthermore, there is a proportion of 8% (121 individuals) who strongly disagree with this idea (**Figure 2**).

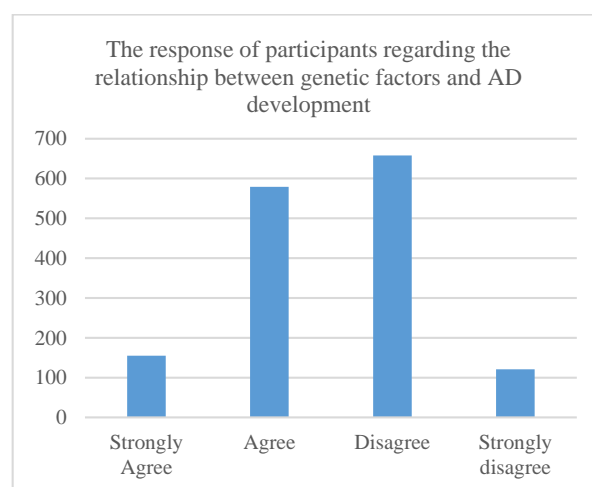


Figure 4. The response of participants regarding the relationship between genetic factors and AD development

Community awareness about the relationship between Alzheimer's disease and diabetes mellitus

The next question in the questionnaire emphasizes the awareness of the relationship between AD and diabetes mellitus. According to the data, a significant percentage of the participants, approximately 57.1% (864 individuals), believe that there is no relationship between Alzheimer's disease and diabetes mellitus. Also, 8.4% (127 individuals) strongly disagree with that hypothesis. On the other hand, 30.9% (467 individuals) think that there might exist a relationship between the two disorders. Lastly, 3.6% (57 individuals) strongly believe in this relationship, representing the lowest percentage (**Figure 5**).

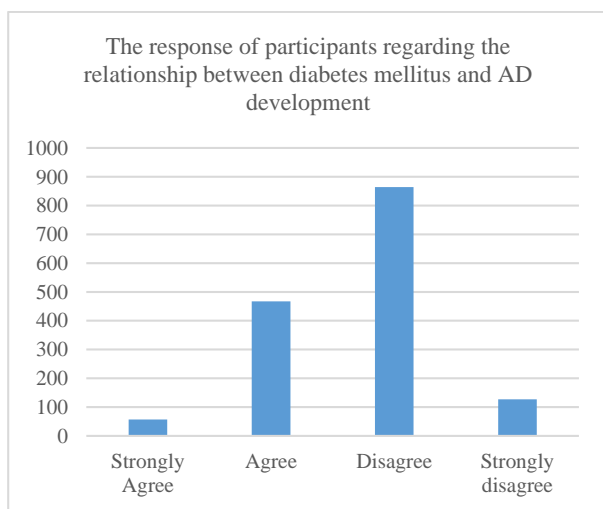


Figure 5. The response of participants regarding the relationship between diabetes mellitus and AD development

Community awareness about the relationship between Alzheimer's disease and Down syndrome

The following question in the questionnaire weights the awareness about the relationship between AD and Down syndrome. As shown in the graph below, most individuals do not think that there is a link between AD and Down syndrome, which represents 67% (1025 individuals) of the total group. Moreover, 15.9% (241 individuals) strongly disagree with that relationship. There was still a group that weighs approximately 14.1% (214 individuals), who believe in the existence of this link and a minority, 2.2% (33 individuals), who strongly consider that relationship (**Figure 6**).

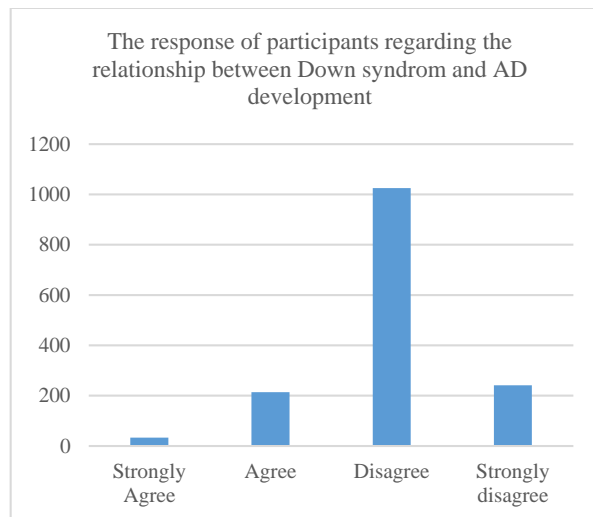


Figure 6. The response of participants regarding the relationship between Down syndrome and AD development

Community awareness about the relationship between Alzheimer's disease and head trauma

The next question stresses the relationship between AD and head traumas. Results show that 50.6% (766 individuals) believe that head trauma may cause AD. Moreover, 16.8% (254 individuals) strongly agree with that hypothesis. However, 29.3% and 3.2% of the participants (a total of 493 individuals) do not believe that head trauma may lead to AD (**Figure 7**).

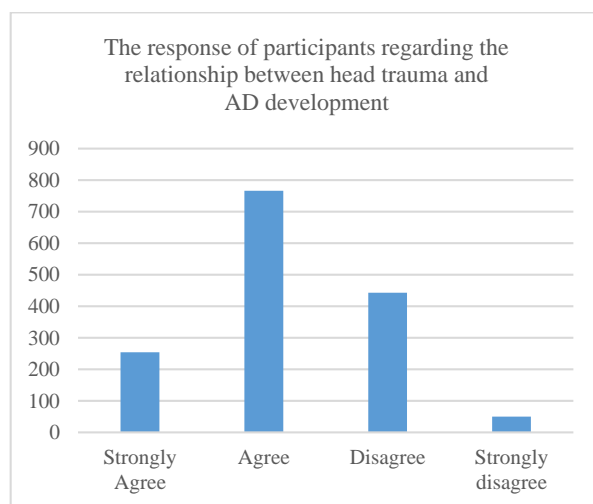


Figure 7. The response of participants regarding the relationship between head trauma and AD development

Community awareness about the relationship between Alzheimer's disease and diet

The subsequent question highlights the relationship between AD and diet. The graph shows that a large number believe that the type of diet may be linked to AD, which represents 46.2% (699 individuals). Also, 18.3% (277 individuals) strongly agree with this idea. On the other

hand, 30.4% (460 individuals) do not believe in the existence of a link between diet and AD. Moreover, 5.1% (77 individuals) strongly disagree with that (**Figure 8**).

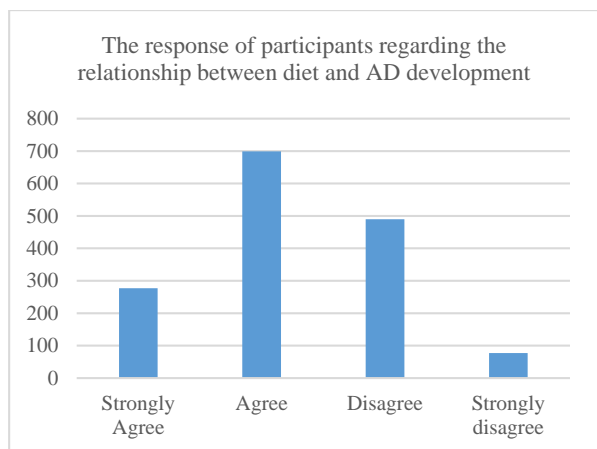


Figure 8. The response of participants regarding the relationship between diet and AD development

Community awareness about the relationship between Alzheimer's disease and physical exercise

The latter question focuses on the relationship between AD and physical exercise. As shown in the figure below, there is a huge proportion, 53.4% (808 individuals), who think that there is a link between physical exercise and AD. Additionally, 35.4% (536 individuals) strongly believe in this linkage. Nevertheless, 9.7% (147 individuals) do not think that there is a link between AD and physical exercise. Also, 1.5% (22 individuals) strongly disagree with that statement (**Figure 9**).

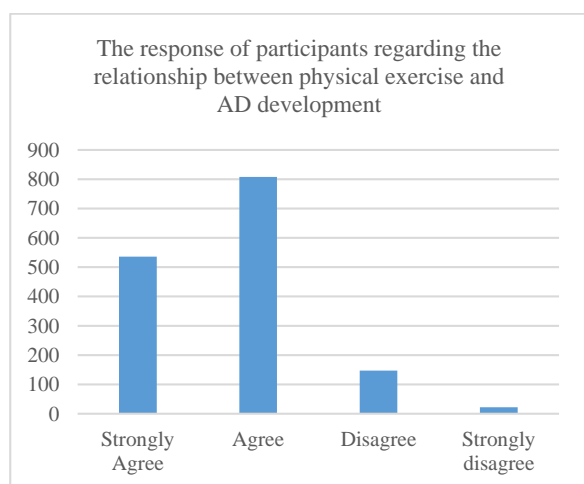


Figure 9. The response of participants regarding the relationship between physical exercise and AD development

Community awareness about the relationship between Alzheimer's disease and mental exercise

The following question concentrates on the relationship between AD and mental exercise. According to the data

below, about 48.4% and 44.9% (a total of 1,411 individuals) believe that mental exercise may reduce the chances of developing AD. On the opposite side, a very small percentage, 5.9% (89 individuals), do not believe that mental exercises can minimize AD development. Also, the minority, about 0.9% (13 individuals), totally refuse the connection between AD and mental exercises (**Figure 10**).

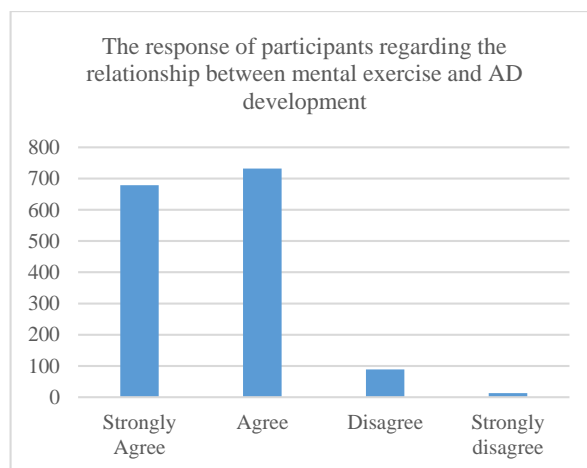


Figure 10. The response of participants regarding the relationship between mental exercise and AD development

Community awareness about the relationship between Alzheimer's disease and music

The last question focuses on the relationship between AD and music. As shown in the following graph, half the participants, 50.2% (760 individuals), do not think that music is a factor that can help Alzheimer's sufferers. Also, 19.9% (301 individuals) believe that there is no effect of music on Alzheimer's sufferers [71-75]. On the other side, 24.7% (374 individuals) think that music might help AD patients. Finally, 5.2% (78 individuals) strongly believe that music would aid AD patients (**Figure 11**).

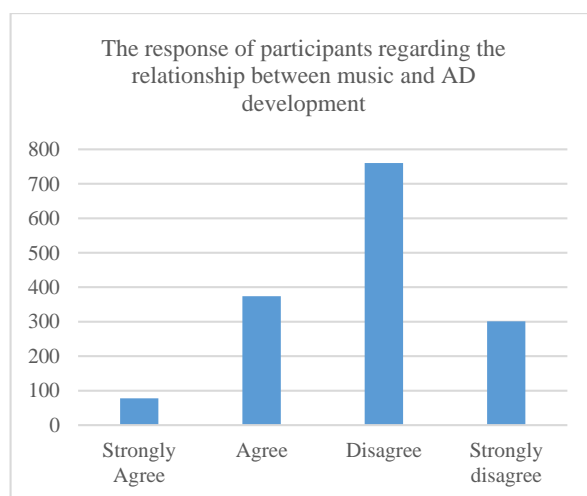


Figure 11. The response of participants regarding the relationship between music and AD development

Over the past century, the aging of our population (the proportion of people aged ≥ 65 years) in industrialized countries has exceeded that of the population as a whole. It is predicted that in future generations, the proportion of the elderly population will double, and so the proportion will suffer from neurodegenerative disorders [76]. The diagnosis of AD requires significant and costly health care. In addition, it causes the shortens of human life span [77]. This study aimed to measure peoples' knowledge about the relationship between AD and lifestyle and other medical conditions. Additionally, the study aimed to perform an awareness campaign to educate the public about AD prevention methods in order to reduce the incidence of the disease.

According to our data, about 62.4% believe that age is strongly related to AD, which reflects good awareness about this factor among the Saudi community. On the other hand, only 15.7% believe that age is a major risk factor for AD in an awareness statistical study that was performed in Tianjin, China [78]. As explained earlier, AD incidence increases with age and older people have a higher chance to develop AD. LOAD cases have a higher prevalence than EOAD, which shows the important role of age in AD development [79].

Our results show that 51.5% of the Saudi society has no knowledge about the relationship between genetic factors and AD development. In contrast, 51.3% of the U.S population aware that genetics is an important factor for the development of AD [80]. This demonstrates that there is a gap of knowledge about this risk factor and further educational campaigns are required. It has been demonstrated that EOAD is enhanced by genetic factors rather than age. Studies identified genetics as a key perceived risk factor in AD development [81].

According to our data, the awareness of Saudi society about the effect of diabetes mellitus on AD development is generally poor, where 65.5% had no idea about the linkage. A similar study among community residents in Tianjin, China reported that only 12.9% thought that diabetes mellitus is an important factor for the development of AD, which shows that there exists a lack of knowledge about AD risk factors. A study was conducted in the United States on 824 older people over the course of 9 years, 127 of whom had diabetes mellitus. Within five years of observation, 151 people were diagnosed with AD. Individuals with diabetes mellitus had a 65% higher risk of AD than non-diabetic patients [82]. While diabetes Mellitus's role in the development of AD has been reported, some studies have noticed no association between the two conditions.

Only 16.4% thought that there is a relationship between Down syndrome and AD, indicating weak public knowledge in the Saudi community. Down syndrome autopsy studies observed that during the age of 40, most of

the patients develop specific hallmarks of AD including β -amyloid plaques and neurofibrillary tangles. This indicates that Down syndrome patients have a higher risk to develop AD [4].

Amongst the Saudi community, 67.4% aware that head trauma is one of the most common risk factors to the development of AD. On the other hand, only 33.6% of the Korean society believe that head trauma is a risk factor for AD development [83]. However, head traumas should not cause panic in the community as not all brain injuries lead to AD, but it is another risk factor that cannot be applied to all AD cases.

In Saudi society, 64.5% believe that diet has a linkage to AD development, which is a fairly good proportion. However, the population of the U.S has greater awareness, where 87.8% of the population believe that diet has a good effect on AD. Increased awareness could be due to recent studies that state that there is a strong relationship between diet and AD development [37]. One study has proved that a higher Mediterranean diet is closely linked to reducing the risk of AD [84, 85]. Other studies have also reported that those individuals who take cholesterol-lowering drugs have a lower risk of AD development when compared to those who do not [86]. On the other hand, there are several studies that show no association between AD and nutrients. For example, an exploratory study stated that there is no association between food that increases blood glucose and the risk of AD development [87]. Another study was conducted on 980 individuals, who had been taking vitamin C and vitamin E for four years, to determine the effect of both vitamins on the incidence of AD. The results showed that the rate of incidence of the disease did not change [88].

The influence of mental exercises on AD is a well-known fact in the Saudi community. A very high percentage of individuals, 93.3%, believe that mental exercises may reduce the risk of the development of AD, while 88.8% believe that physical exercises have also a positive impact on AD. Similarly, statistical studies applied to the US population about the positive impact of mental and physical activity on AD patients show that 61.4% and 40.6%, respectively, believe that this relationship exists. This awareness could be due to the high number of studies that confirm the role of physical and mental exercises in reducing cognitive decline and AD development [67, 89]. However, a review stated that these studies are not sufficient as they lack some information such as duration and number of sessions, which are important criteria for evaluation [90].

Our study demonstrated that 50.2% of the Saudi community are aware of the positive effect of music on AD patients. This might be a result of various studies that show that music is effective in improving cognitive function in AD patients. No study has targeted public awareness of the

role of Down syndrome and music in AD. It is worth noting that our study is the first in Saudi Arabia to deal with people's awareness about certain factors such as Down syndrome and music. Results obtained from this study support a call for more public awareness campaigns about AD risk and preventive factors. Moreover, the study encourages Saudi society to start a healthy lifestyle and work to improve the modifiable risk factors of AD. Therefore, we advise health institutions to perform campaigns to educate the public about AD prevention methods in order to reduce the incidence of the disease and encourage people to undergo early AD screening tests in order to be able to reduce the symptoms of the disease by changing daily life habits.

CONCLUSION

Outcomes of our study showed the importance of spreading awareness among the Saudi society and how small daily life habits may increase or decrease the chance to develop AD. Therefore, we anticipate positive feedback from society, hospitals, and organizations by launching awareness campaigns in schools, shopping, and medical centers, about AD prevention methods and risk factors. Hopefully, this study encourages the public to start a healthy lifestyle and work to improve the modifiable risk factors of AD and help to reduce the incidence and/or the symptoms of AD.

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REFERENCES

- [1] Katsuno M, Sahashi K, Iguchi Y, Hashizume A. Preclinical progression of neurodegenerative diseases. Nagoya J Med Sci. 2018;80(3):289-98.
- [2] Skovronsky DM, Lee VM, Trojanowski JQ. Neurodegenerative diseases: new concepts of pathogenesis and their therapeutic implications. Annu Rev Pathol. 2006;1:151-70.
- [3] Alzheimer's Association. 2015 Alzheimer's disease facts and figures. Alzheimers Dement. 2015;11(3):332-84.
- [4] Hardy J, Allsop D. Amyloid deposition as the central event in the aetiology of Alzheimer's disease. Trends Pharmacol Sci. 1991;12(10):383-8.
- [5] Kocahan S, Doğan Z. Mechanisms of Alzheimer's Disease Pathogenesis and Prevention: The Brain, Neural Pathology, N-methyl-D-aspartate Receptors, Tau Protein and Other Risk Factors. Clin Psychopharmacol Neurosci. 2017;15(1):1-8.
- [6] Swerdlow RH. Pathogenesis of Alzheimer's disease. Clin Interv Aging. 2007;2(3):347-59.
- [7] Hardy J, Selkoe DJ. The amyloid hypothesis of Alzheimer's disease: progress and problems on the road to therapeutics. Science. 2002;297(5580):353-6.
- [8] Mawuenyega KG, Sigurdson W, Ovod V, Munsell L, Kasten T, Morris JC, et al. Decreased clearance of CNS amyloid-beta in Alzheimer's disease. Science. 2010;330(6012):1774.
- [9] Mokhtar SH, Bakhuraysah MM, Cram DS, Petratos S. The Amyloid-beta protein of Alzheimer's disease: communication breakdown by modifying the neuronal cytoskeleton. Int J Alzheimers Dis. 2013;2013:910502.
- [10] Maccioni RB, Farías G, Morales I, Navarrete L. The revitalized tau hypothesis on Alzheimer's disease. Arch Med Res. 2010;41(3):226-31.
- [11] Lindsay J, Laurin D, Verreault R, Hébert R, Helliwell B, Hill GB, et al. Risk factors for Alzheimer's disease: a prospective analysis from the Canadian Study of Health and Aging. Am J Epidemiol. 2002;156(5):445-53.
- [12] Crous-Bou M, Minguillón C, Gramunt N, Molinuevo JL. Alzheimer's disease prevention: from risk factors to early intervention. Alzheimers Res Ther. 2017;9(1):71.
- [13] Tsvetkova D, Obreshkova D. Modern Approaches and Strategies for Prevention and Therapeutic Influence of Alzheimer's Disease. Int J Pharm Res Allied Sci. 2019;8(1):1-16.
- [14] Alafnan A. Biochemical Interaction Analysis of Natural SGLT2 Inhibitors with Alzheimer Targets: A Computational Approach. Arch Pharma Pract. 2020;11(4):73-84.
- [15] Dolan D, Troncoso J, Resnick SM, Crain BJ, Zonderman AB, O'Brien RJ. Age, Alzheimer's disease and dementia in the Baltimore Longitudinal Study of Ageing. Brain. 2010;133(Pt 8):2225-31.
- [16] Qiu C, Kivipelto M, von Strauss E. Epidemiology of Alzheimer's disease: occurrence, determinants, and strategies toward intervention. Dialogues Clin Neurosci. 2009;11(2):111-28.
- [17] Guerreiro R, Bras J. The age factor in Alzheimer's disease. Genome Med. 2015;7(1):106.
- [18] Giri M, Zhang M, Lü Y. Genes associated with Alzheimer's disease: an overview and current status. Clin. Interv. Aging. 2016;11:665-81.
- [19] Gatz M, Reynolds CA, Fratiglioni L, Johansson B, Mortimer JA, Berg S, et al. Role of genes and environments for explaining Alzheimer disease. Arch Gen Psychiatry. 2006;63(2):168-74.

- [20]Cruts M, Theuns J, Van Broeckhoven C. Locus-specific mutation databases for neurodegenerative brain diseases. *Hum Mutat.* 2012;33(9):1340-4.
- [21]Esler WP, Wolfe MS. A portrait of Alzheimer secretases--new features and familiar faces. *Science.* 2001;293(5534):1449-54.
- [22]Bentahir M, Nyabi O, Verhamme J, Tolia A, Horré K, Wiltfang J, et al. Presenilin clinical mutations can affect gamma-secretase activity by different mechanisms. *J Neurochem.* 2006;96(3):732-42.
- [23]Huang Y. Roles of apolipoprotein E4 (ApoE4) in the pathogenesis of Alzheimer's disease: lessons from ApoE mouse models. *Biochem Soc Trans.* 2011;39(4):924-32.
- [24]Liu CC, Kanekiyo T, Xu H, Bu G. Apolipoprotein E and Alzheimer disease: risk, mechanisms and therapy. *Nat Rev Neurol.* 2013;9(2):106-18.
- [25]Bekris LM, Yu CE, Bird TD, Tsuang DW. Genetics of Alzheimer disease. *J Geriatr Psychiatry Neurol.* 2010;23(4):213-27.
- [26]Akter K, Lanza EA, Martin SA, Myronyuk N, Rua M, Raffa RB. Diabetes mellitus and Alzheimer's disease: shared pathology and treatment? *Br J Clin Pharmacol.* 2011;71(3):365-76.
- [27]De Felice FG, Ferreira ST. Inflammation, defective insulin signaling, and mitochondrial dysfunction as common molecular denominators connecting type 2 diabetes to Alzheimer disease. *Diabetes.* 2014;63(7):2262-72.
- [28]Zhang Y, Huang NQ, Yan F, Jin H, Zhou SY, Shi JS, et al. Diabetes mellitus and Alzheimer's disease: GSK-3 β as a potential link. *Behav Brain Res.* 2018;339:57-65.
- [29]Crane PK, Walker R, Larson EB. Glucose levels and risk of dementia. *N Engl J Med.* 2013;369(19):1863-4.
- [30]Head E, Powell D, Gold BT, Schmitt FA. Alzheimer's Disease in Down Syndrome. *Eur J Neurodegener Dis.* 2012;1(3):353-64.
- [31]Choong XY, Tosh JL, Pulford LJ, Fisher EM. Dissecting Alzheimer disease in Down syndrome using mouse models. *Front Behav Neurosci.* 2015;9:268.
- [32]Graves AB, White E, Koepsell TD, Reifler BV, van Belle G, Larson EB, et al. The association between head trauma and Alzheimer's disease. *Am J Epidemiol.* 1990;131(3):491-501.
- [33]Graham DI, Gentleman SM, Nicoll JA, Royston MC, McKenzie JE, Roberts GW, et al. Altered beta-APP metabolism after head injury and its relationship to the aetiology of Alzheimer's disease. *Acta Neurochir Suppl.* 1996;66:96-102.
- [34]Li Y, Li X, Zhang S, Zhao J, Zhu X, Tian G. Head Injury as a Risk Factor for Dementia and Alzheimer's Disease: A Systematic Review and Meta-Analysis of 32 Observational Studies. *PLoS One.* 2017;12(1):e0169650.
- [35]Jiang T, Yu JT, Tan L. Novel disease-modifying therapies for Alzheimer's disease. *J Alzheimers Dis.* 2012;31(3):475-92.
- [36]Ramassamy C, Belkacémi A. Nutrition and Alzheimer's disease: is there any connection? *Curr Alzheimer Res.* 2011;8(5):443-4.
- [37]Hu N, Yu JT, Tan L, Wang YL, Sun L. Nutrition and the risk of Alzheimer's disease. *Biomed Res Int.* 2013;2013:524820.
- [38]Williams JW, Plassman BL, Burke J, Benjamin S. Preventing Alzheimer's disease and cognitive decline. *Evid Rep Technol Assess (Full Rep).* 2010(193):1-727.
- [39]Kikuchi S, Shinpo K, Takeuchi M, Yamagishi S, Makita Z, Sasaki N, et al. Glycation--a sweet tempter for neuronal death. *Brain Res Brain Res Rev.* 2003;41(2-3):306-23.
- [40]Okereke OI, Rosner BA, Kim DH, Kang JH, Cook NR, Manson JE, et al. Dietary fat types and 4-year cognitive change in community-dwelling older women. *Ann Neurol.* 2012;72(1):124-34.
- [41]Naqvi AZ, Harty B, Mukamal KJ, Stoddard AM, Vitolins M, Dunn JE. Monounsaturated, trans, and saturated Fatty acids and cognitive decline in women. *J Am Geriatr Soc.* 2011;59(5):837-43.
- [42]Boudrault C, Bazinet RP, Ma DW. Experimental models and mechanisms underlying the protective effects of n-3 polyunsaturated fatty acids in Alzheimer's disease. *J Nutr Biochem.* 2009;20(1):1-10.
- [43]Canhada S, Castro K, Perry IS, Luft VC. Omega-3 fatty acids' supplementation in Alzheimer's disease: A systematic review. *Nutr Neurosci.* 2018;21(8):529-38.
- [44]Tou JC, Altman SN, Gigliotti JC, Benedito VA, Cordonier EL. Different sources of omega-3 polyunsaturated fatty acids affects apparent digestibility, tissue deposition, and tissue oxidative stability in growing female rats. *Lipids Health Dis.* 2011;10(1):179.
- [45]Calon F, Lim GP, Yang F, Morihara T, Teter B, Ubeda O, et al. Docosahexaenoic acid protects from dendritic pathology in an Alzheimer's disease mouse model. *Neuron.* 2004;43(5):633-45.
- [46]Perez SE, Berg BM, Moore KA, He B, Counts SE, Fritz JJ, et al. DHA diet reduces AD pathology in young APPswe/PS1 Delta E9 transgenic mice: possible gender effects. *J Neurosci Res.* 2010;88(5):1026-40.
- [47]Quinn JF, Raman R, Thomas RG, Yurko-Mauro K, Nelson EB, Van Dyck C, et al. Docosahexaenoic acid supplementation and cognitive decline in Alzheimer

- disease: a randomized trial. *JAMA*. 2010;304(17):1903-11.
- [48] van de Rest O, Geleijnse JM, Kok FJ, van Staveren WA, Hoefnagels WH, Beekman AT, et al. Effect of fish-oil supplementation on mental well-being in older subjects: a randomized, double-blind, placebo-controlled trial. *Am J Clin Nutr*. 2008;88(3):706-13.
- [49] Solfrizzi V, Frisardi V, Capurso C, D'Introno A, Colacicco AM, Vendemiale G, et al. Dietary fatty acids in dementia and predementia syndromes: epidemiological evidence and possible underlying mechanisms. *Ageing Res Rev*. 2010;9(2):184-99.
- [50] Laitinen MH, Ngandu T, Rovio S, Helkala EL, Uusitalo U, Viitanen M, et al. Fat intake at midlife and risk of dementia and Alzheimer's disease: a population-based study. *Dement Geriatr Cogn Disord*. 2006;22(1):99-107.
- [51] Grimm MO, Rothhaar TL, Grösgen S, Burg VK, Hundsdörfer B, Haupenthal VJ, et al. Trans fatty acids enhance amyloidogenic processing of the Alzheimer amyloid precursor protein (APP). *J Nutr Biochem*. 2012;23(10):1214-23.
- [52] Ono K, Yamada M. Vitamin A and Alzheimer's disease. *Geriatr Gerontol Int*. 2012;12(2):180-8.
- [53] Bourdel-Marchasson I, Delmas-Beauvieux MC, Peuchant E, Richard-Harston S, Decamps A, Reignier B, et al. Antioxidant defences and oxidative stress markers in erythrocytes and plasma from normally nourished elderly Alzheimer patients. *Age Ageing*. 2001;30(3):235-41.
- [54] Jiménez-Jiménez FJ, Molina JA, de Bustos F, Ortí-Pareja M, Benito-León J, Tallón-Barranco A, et al. Serum levels of beta-carotene, alpha-carotene and vitamin A in patients with Alzheimer's disease. *Eur J Neurol*. 1999;6(4):495-7.
- [55] Montilla-López P, Muñoz-Agueda MC, Feijóo López M, Muñoz-Castañeda JR, Bujalance-Arenas I, Túnez-Fiñana I. Comparison of melatonin versus vitamin C on oxidative stress and antioxidant enzyme activity in Alzheimer's disease induced by okadaic acid in neuroblastoma cells. *Eur J Pharmacol*. 2002;451(3):237-43.
- [56] Murakami K, Murata N, Ozawa Y, Kinoshita N, Irie K, Shirasawa T, et al. Vitamin C restores behavioral deficits and amyloid- β oligomerization without affecting plaque formation in a mouse model of Alzheimer's disease. *J Alzheimers Dis*. 2011;26(1):7-18.
- [57] Zandi PP, Anthony JC, Khachaturian AS, Stone SV, Gustafson D, Tschanz JT, et al. Reduced risk of Alzheimer disease in users of antioxidant vitamin supplements: the Cache County Study. *Arch Neurol*. 2004;61(1):82-8.
- [58] Viña J, Lloret A, Giraldo E, Badia MC, Alonso MD. Antioxidant pathways in Alzheimer's disease: possibilities of intervention. *Curr Pharm Des*. 2011;17(35):3861-4.
- [59] Cito A, Porcelli B, Coppola MG, Mangiavacchi P, Cortelazzo A, Terzuoli L. WITHDRAWN: Analysis of serum levels of homocysteine and oxidative stress markers in patients with Alzheimer disease. *Biomed Pharmacother*. 2010.
- [60] Van Dam F, Van Gool WA. Hyperhomocysteinemia and Alzheimer's disease: A systematic review. *Arch Gerontol Geriatr*. 2009;48(3):425-30.
- [61] Aisen PS, Schneider LS, Sano M, Diaz-Arrastia R, van Dyck CH, Weiner MF, et al. High-dose B vitamin supplementation and cognitive decline in Alzheimer disease: a randomized controlled trial. *JAMA*. 2008;300(15):1774-83.
- [62] Barberger-Gateau P, Raffaitin C, Letenneur L, Berr C, Tzourio C, Dartigues JF, et al. Dietary patterns and risk of dementia: the Three-City cohort study. *Neurology*. 2007;69(20):1921-30.
- [63] Eskelinen MH, Kivipelto M. Caffeine as a protective factor in dementia and Alzheimer's disease. *J Alzheimers Dis*. 2010;20 Suppl 1:S167-74.
- [64] Anstey KJ, Mack HA, Cherbuin N. Alcohol consumption as a risk factor for dementia and cognitive decline: meta-analysis of prospective studies. *Am J Geriatr Psychiatry*. 2009;17(7):542-55.
- [65] Shen Y, Li R. What do we know from clinical trials on exercise and Alzheimer's disease? *J Sport Health Sci*. 2016;5(4):397-9.
- [66] Dougherty RJ, Ellingson LD, Schultz SA, Boots EA, Meyer JD, Lindheimer JB, et al. Meeting physical activity recommendations may be protective against temporal lobe atrophy in older adults at risk for Alzheimer's disease. *Alzheimers Dement (Amst)*. 2016;4(1):14-7.
- [67] Machado S, Filho ASS, Wilbert M, Barbieri G, Almeida V, Gurgel A, et al. Physical Exercise As Stabilizer For Alzheimer'S Disease Cognitive Decline: Current Status. *Clin Pract Epidemiol Ment Health*. 2017;13(1):181-4.
- [68] Lord TR, Garner JE. Effects of music on Alzheimer patients. *Percept Mot Skills*. 1993;76(2):451-5.
- [69] Wimo A, Jönsson L, Bond J, Prince M, Winblad B, International AD. The worldwide economic impact of dementia 2010. *Alzheimers Dement*. 2013;9(1):1-11.e3.
- [70] Aguzzi A, O'Connor T. Protein aggregation diseases: pathogenicity and therapeutic perspectives. *Nat Rev Drug Discov*. 2010;9(3):237-48.
- [71] Khouja HA, Alshehri RA, Alhalal HM, Alabisi HD, Alajmi SM, Al Radi ZM, et al. Calcitonin-gene-related peptide (CGRP) monoclonal antibodies in

- migraine prevention; literature review. *World J Environ Biosci.* 2021;10(1):48-51. doi:10.51847/ogC7ozOJpH
- [72] Kurkuman GA, Alsululi HAA, Alshehri OAM, Alsuaayri MAM, Alqahtani SHS, Altalhiyyah KSS, et al. An overview on ischemic colitis diagnostic & management approach. *World J Environ Biosci.* 2021;10(1):52-6. doi:10.51847/ueTWoTfKw9
- [73] Albarakati MH, Almhmadi AH, Baamer MK, Alqarni BMH, Alsuwaidan MF, Mulla ZMA, et al. An overview on monteggia fracture diagnostic and management approach. *World J Environ Biosci.* 2021;10(1):57-60. doi:10.51847/fb4EksSbxI
- [74] Sheth TR, Gokhe AA, Kumar PN, Chitnis KS. Recycling flower and kitchen waste to make biodegradable paper. *World J Environ Biosci.* 2021;10(1):35-8. doi:10.51847/tkMmywD2fA
- [75] Alghamdi S, Alhazmi K. Appendectomy impact on inflammatory bowel diseases: a meta-analysis. *World J Environ Biosci.* 2021;10(1):13-8. doi:10.51847/Dz8IEE5R1x
- [76] Przedborski S, Vila M, Jackson-Lewis V. Neurodegeneration: what is it and where are we? *J Clin Invest.* 2003;111(1):3-10.
- [77] van Gelder BM, Tijhuis MA, Kalmijn S, Giampaoli S, Kromhout D. Decline in cognitive functioning is associated with a higher mortality risk. *Neuroepidemiology.* 2007;28(2):93-100.
- [78] Yang HF, Cong JY, Zang XY, Jiang N, Zhao Y. A study on knowledge, attitudes and health behaviours regarding Alzheimer's disease among community residents in Tianjin, China. *J Psychiatr Ment Health Nurs.* 2015;22(9):706-14.
- [79] Wattmo C, Wallin Å. Early- versus late-onset Alzheimer's disease in clinical practice: cognitive and global outcomes over 3 years. *Alzheimers Res Ther* 2017;9(1):70.
- [80] Roberts JS, McLaughlin SJ, Connell CM. Public beliefs and knowledge about risk and protective factors for Alzheimer's disease. *Alzheimers Dement.* 2014;10(5 Suppl):S381-9.
- [81] Ganguli M, Rodriguez E. Age, Alzheimer's disease, and the big picture. *Int Psychogeriatr.* 2011;23(10):1531-4.
- [82] Arvanitakis Z, Wilson RS, Bienias JL, Evans DA, Bennett DA. Diabetes mellitus and risk of Alzheimer disease and decline in cognitive function. *Arch Neurol.* 2004;61(5):661-6.
- [83] Park MH, Jo SA, Jo I, Kim E, Woo EK, Kim SS, et al. Awareness of putative risk factors for Alzheimer's disease among elderly Koreans. *Acta Neuropsychiatr.* 2008;20(1):20-4.
- [84] Otaegui-Arrazola A, Amiano P, Elbusto A, Urdaneta E, Martínez-Lage P. Diet, cognition, and Alzheimer's disease: food for thought. *Eur J Nutr.* 2014;53(1):1-23.
- [85] Scarmeas N, Stern Y, Mayeux R, Luchsinger JA. Mediterranean diet, Alzheimer disease, and vascular mediation. *Arch Neurol.* 2006;63(12):1709-17.
- [86] Haag MD, Hofman A, Koudstaal PJ, Stricker BH, Breteler MM. Statins are associated with a reduced risk of Alzheimer disease regardless of lipophilicity. The Rotterdam Study. *J Neurol Neurosurg Psychiatry.* 2009;80(1):13-7.
- [87] Luchsinger JA, Tang MX, Mayeux R. Glycemic load and risk of Alzheimer's disease. *J Nutr Health Aging.* 2007;11(3):238-41.
- [88] Luchsinger JA, Tang MX, Shea S, Mayeux R. Antioxidant vitamin intake and risk of Alzheimer disease. *Arch Neurol.* 2003;60(2):203-8.
- [89] Gatz M. Educating the brain to avoid dementia: can mental exercise prevent Alzheimer disease? *PLoS Med.* 2005;2(1):e7.
- [90] Heyn P, Abreu BC, Ottenbacher KJ. The effects of exercise training on elderly persons with cognitive impairment and dementia: a meta-analysis. *Arch Phys Med Rehabil.* 2004;85(10):1694-704.