Genetic Variants Associated With Alzheimer Disease in the 22 Arab Countries: A Systematic Review

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Supplementary Table 1: Genetic variants that are associated with AD among Arabs and their clinical phenotypes, associated diseases and other ethnic groups.

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| Nucleotide change | Protein change | SNP ID | Gene | Chromosomal location | Gene function | Country | Cases (n) | Controls (n) | # Patients withvariant | Clinical phenotype & Patients characteristics | Associated disease (s) with Alzheimer disease | Ref | Other ethnic group | Clinical phenotype | Ref |
| C.388T>C | p.Cys130Arg | rs429358 | *ApoE* | Chr. 19q | ApoE is involved in lipid metabolism (Rasmussen, 2016)regulates inflammation(Gonzalez, Abud, Abud, Poon, & Gylys, 2017), mediate CNS response to injury and oxidative stress(Handattu et al., 2013; Verghese, Castellano, & Holtzman, 2011b). ApoE have 3 variants, which are 𝜀2, 𝜀3 and 𝜀4, (Schächter et al., 1994) where ApoE 𝜀4 allele play a role in the pathogenesis of AD (Limon-Sztencel et al., 2016) (C.-C. Liu, Kanekiyo, Xu, & Bu, 2013). | Egypt | 53 | 100 | 28.3% had 𝜀4 allele | Age of control group was 65.9 ± 5.0 years, and clinically diagnosed AD patients were 70.5 ± 7.5 years, which means that it is associated with older age.AD patients were less educated than control group. Lower cognitive scoreApoE 𝜀4 is associated with longer duration of AD. | Cardiovascular disorders (Roses et al., 1994) | (Ramadan et al., 2019) | Chinese | Associated with older age;prolonged disease duration. | (M. Liu, Bian, Zhang, & Wen, 2014) |
| C.388T>C | p.Cys130Arg | rs429358 | *ApoE* | Chr. 19q | ApoE is involved in lipid metabolism (Rasmussen, 2016) regulates inflammation (Gonzalez et al., 2017), mediate CNS response to injury and oxidative stress (Handattu et al., 2013; Verghese, Castellano, & Holtzman, 2011a) ApoE have 3 variants, which are 𝜀2, 𝜀3 and 𝜀4, (Schächter et al., 1994) where ApoE 𝜀4 allele play a role in the pathogenesis of AD(Limon-Sztencel et al., 2016);(C.-C. Liu et al., 2013) . | Jordan | 102 | 101 | 4.5% had 𝜀4 allele | Older adults group (>85 yrs, mean age 91.4 yrs, n = 102: 67 male and 35 female) Young group (20–50 yrs, mean age 31.8 yrs, n = 101: 64 male 37 female) | Head trauma (Olivecrona & Koskinen, 2017)ischemic stroke (Chauhan & Debette, 2016)Coronary artery disease (Çiftdoğan, Coskun, Ulman, & Tıkız, 2012)Parkinson’s disease (Li et al., 2004; López et al., 2007) and diabetic neuropathy (Ng et al., 2006) | (Khabour & Abdelhalim, 2018); (Shafagoj et al., 2018) | \_ | \_ | \_ |
| C.388T>C | p.Cys130Arg | rs429358 | *ApoE* | Chr. 19q | ApoE is involved in lipid metabolism (Rasmussen, 2016)regulates inflammation(Gonzalez et al., 2017), mediate CNS response to injury and oxidative stress(Handattu et al., 2013; Verghese et al., 2011b). ApoE have 3 variants, which are 𝜀2, 𝜀3 and 𝜀4, (Schächter et al., 1994) where ApoE 𝜀4 allele play a role in the pathogenesis of AD (Limon-Sztencel et al., 2016) (C.-C. Liu et al., 2013). | Jordan | 38 | 33 | 15.8% had 𝜀4 allele | Mean age of AD cases: 74.2±5.4 yearsMean age of control: 72.4±6.3 years | hypercholesterolemia (Rockwood et al., 2002) | (Shafagoj et al., 2018) | Iranians , Turks, Greeks , Sardinians | Turkey: coronary artery disease | (Atis et al., 2016; Gozalpour et al., 2010), (Corbo, Scacchi, Mureddu, Mulas, & Alfano, 1995; Stakias, Liakos, Tsiapali, Goutou, & Koukoulis, 2006) |
| C.388T>C | p.Cys130Arg | rs429358 | *ApoE* | Chr. 19q | ApoE is involved in lipid metabolism (Rasmussen, 2016)regulates inflammation(Gonzalez et al., 2017), mediate CNS response to injury and oxidative stress(Handattu et al., 2013; Verghese et al., 2011b). ApoE have 3 variants, which are 𝜀2, 𝜀3 and 𝜀4, (Schächter et al., 1994) where ApoE 𝜀4 allele play a role in the pathogenesis of AD (Limon-Sztencel et al., 2016) (C.-C. Liu et al., 2013). | Tunisia | 48 | 48 | 25% had 𝜀4 allele | Mean age of AD cases: 75.45± 7.14Mean age of Control: 72.43± 6.64 (check these two please) 12.5% were diabetic, 16.6% were hypertensive, and 12.5% had history of stroke. | Stroke (Honig et al., 2003) | (Najiba Fekih-Mrissa et al., 2014) | Caucasian & Asian | ApoE 𝜀4 allele is found also to be associtaed with AD in the countries. | (Farrer et al., 1997; Łuczywek et al., 2002) |
| C.388T>C | p.Cys130Arg | rs429358 | *ApoE* | Chr. 19q | ApoE is involved in lipid metabolism (Rasmussen, 2016)regulates inflammation(Gonzalez et al., 2017), mediate CNS response to injury and oxidative stress(Handattu et al., 2013; Verghese et al., 2011b). ApoE have 3 variants, which are 𝜀2, 𝜀3 and 𝜀4, (Schächter et al., 1994) where ApoE 𝜀4 allele play a role in the pathogenesis of AD (Limon-Sztencel et al., 2016) (C.-C. Liu et al., 2013). | Tunisia | 58 | 71 | 13.3% had 𝜀4 allele | Mean age of AD cases: 73 ± 9.09Mean age of Control: 69± 15.1845% of AD cases had history of hypertension, and 30% with diabetes. | \_ | (Rassas et al., 2012) | Turkish , French, Canada, Iranian, Greek , Japanese , Spanish, Italy , Korea China | Showed higher levels of 𝜀4 allele among ADA patients, as in this study; Canada: dementia, cerebrovascular disease | (Malle et al., 1996) (Bétard et al., 1994; Chartier-Hariln et al., 1994) (Cariolou et al., 1995; Raygani, Rahimi, Kharazi, Tavilani, & Pourmotabbed, 2006) (Takei et al., 2009; Valveny, Esteban, Kandil, & Moral, 1997) (Bosco et al., 2005; Kim et al., 1999) (Mak et al., 1996) |
| C.388T>C | p.Cys130Arg | rs429358 | *ApoE* | Chr. 19q | ApoE is involved in lipid metabolism (Rasmussen, 2016)regulates inflammation(Gonzalez et al., 2017), mediate CNS response to injury and oxidative stress(Handattu et al., 2013; Verghese et al., 2011b). ApoE have 3 variants, which are 𝜀2, 𝜀3 and 𝜀4, (Schächter et al., 1994) where ApoE 𝜀4 allele play a role in the pathogenesis of AD (Limon-Sztencel et al., 2016) (C.-C. Liu et al., 2013). | Lebanon | 78 | 56 | mutation: 21% of AD patients 20% frequency of E4 allele in AD | Mean age of AD cases: 80±7.4Mean age of control: 75.06 ± 8Mean age of general population: 40.58 ± 14.2 | Cardiovascular diseases (Roses et al., 1994)Hypercholesterolemia (Rockwood et al., 2002) | (Shamieh, Costanian, Kassir, Visvkis-Siest, & Bissar-Tadmouri, 2019) | India, Bangladesh, Pakistan, Hai Chinese of Beijing, Japan , Europeans | Asia: genotype distribution similar to Lebanon; Europe: association between E4 allele and higher plasma concentrations of total and LDL-C in the general population | (Shamieh et al., 2019) (Petkeviciene et al., 2012) |
| -491A>T | \_ | rs449647 | *ApoE* | Chr. 19q | ApoE is involved in lipid metabolism (Rasmussen, 2016)regulates inflammation(Gonzalez et al., 2017), mediate CNS response to injury and oxidative stress(Handattu et al., 2013; Verghese et al., 2011b). ApoE have 3 variants, which are 𝜀2, 𝜀3 and 𝜀4, (Schächter et al., 1994) where ApoE 𝜀4 allele play a role in the pathogenesis of AD (Limon-Sztencel et al., 2016) (C.-C. Liu et al., 2013). | Tunisia | 85 | 90 | frequency of the T allele resulted higher in AD than in controls (45.30 vs. 32.78 %) | Mean age of AD cases: 72 years.96% of AD were illiterate45% of AD with hypertention and 30% with diabetes. | (Achouri-Rassas et al., 2014) | \_ | \_ | \_ |
| c.677C>T | \_ | rs1801133 | *MTHFR* | Chr 1p36.3 | Methylenetetrahydrofolate reductase plays a central role in folate and homocysteine metabolism by catalyzing the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, the primary circulatory form of folate which is utilized in homocysteine remethylation to methionine(Rosenblatt, 1995) | Egypt | 43 | 32 | 40% of AD had C/T. 18.6% of AD had 677T/T genotype. T allele was significantly overrepresented in the AD group when compared with the control group (38% versus 22%). | Male:female (control): 1:2.2male:female (AD): 1:2.1677C>T was significantly asscoiated with the severity of AD.19% of AD patients were illiterate,.95.3% were sporadic AD, with 58% with late age of onset. Mean level of total homocysteine in plasma was significantly higher in AD cases (18.4 ± 6.3 𝜇mol/L) than in controls (13.0 ± 3.8 𝜇mol/L) | cardiovascular disease (Varga, Sturm, Misita, & Moll, 2005)congenital abnormalities (Van Beynum, Den Heijer, Blom, & Kapusta, 2007)cancer (Chen et al., 2005)and psychiatric disorders (Bjelland, Tell, Vollset, Refsum, & Ueland, 2003)Plasma homocysteine was significantly higher in AD cases with 677T/T genotype, while Vitamin B12 was significantly lower. | (Elhawary et al., 2013) | East Asians | \_ | (M.-Y. Zhang, Miao, Li, & Hu, 2010) |
| 287-bp Alu ins/del in intron 16 | \_ | rs4646994;rs1799752 | *ACE* | Chr 17q23 | ACE (Angiotensin converting enzyme) gene is responsible for ACE enzyme, which play a role in in renin-angiotensin system pathway. The product of ACE, which is Ang 2, play a role in hypertension, and it has role in the pathogenesis of AD. (Sayed-Tabatabaei, Oostra, Isaacs, van Duijn, & Witteman, 2006)  | Egypt | 84 | 86 | The I allele distribution in AD cases and controls was 74% vs. 15%, and the I/I genotype frequency was 60% vs. 5%, respectively. | mean age of AD cases: 65 ± 7 years.mean age of control: 63 ± 6 yearsAD patients with dementia | Cardiovascular diseases renal disease (J. Yang et al., 2013) | (Hassanin, Moustafa, & El Masry, 2014) | Japanese | \_ | (Hu et al., 1999) |
| 287-bp Alu ins/del in intron 16 | \_ | rs4646994;rs1799752 | *ACE* | Chr 17q23 | ACE (Angiotensin converting enzyme) gene is resposible for ACE enzyme, which play a role in in renin-angiotensin system pathway. The product of ACE, which is Ang 2, play a role in hypertension, and it has role in the pathogenesis of AD. (Sayed-Tabatabaei, Oostra, Isaacs, van Duijn, & Witteman, 2006)  | Lebanon | 83 | 80 | ACE II genotype was significantly higher in AD patients (17%) compared to controls (1%) | mean age of AD cases: 80.5 ± 7.2 mean age of control: 78.6 ± 5.7 | ObesityHypertesionDiabetes (El Shamieh, Saleh, Masri, Fakhoury, & Fakhoury, 2018) | (El Shamieh et al., 2018) | Han Chinese , Japanese, and German | \_ | (J. D. Yang et al., 2000) (Hu et al., 1999; Kölsch et al., 2005) |
| 287-bp Alu ins/del | \_ | rs4646994;rs1799752 | *ACE* | Chr 17q23 | ACE (Angiotensin converting enzyme) gene is responsible for ACE enzyme, which play a role in in renin-angiotensin system pathway. The product of ACE, which is Ang 2, play a role in hypertension, and it has role in the pathogenesis of AD. (Sayed-Tabatabaei, Oostra, Isaacs, van Duijn, & Witteman, 2006)  | Tunisia | 85 | 90 | The D/D genotype was overrepresented in the AD group as compared to the controls (61.2 vs. 38.9 %). The frequency of D allele was higher in the patients group (77.1%) | Patients have amnesia, circumscribed language disorder and perceptuospatial or frontal dysfunction. | \_ | (Achouri-Rassas et al., 2016) | Indian, Chinese, Taiwanese | \_ | (Nirmal, Tripathi, Shastri, Sagar, & S, 2011) (Wang et al., 2006; Z. Zhang et al., 2012) |
| c.1133\_1134insG | p.G378fs | \_ | *PSEN1* | Chr 14q24.2 | PSEN1 codes for presenilin 1 protein, which is considered as the proteolytic subunit of γ-secretase. And this functions in cleaving APP into smaller peptides.  (https://ghr.nlm.nih.gov/gene/PSEN1) | Morocco | 25 | \_ | 1 out of 8 familial early- onset AD cases | in a 68-year-old female with an onset age of 63 and a positive family history of EOAD. Neuropsychological examination at the age of 68 showed severe cognitive impairment. The early progressive impairment of episodic memory was noticed 5 years ago. The patient presented memory and language impairments, aphasia, visio spatial disorientation, decreased autonomy, executive dysfunction and praxis deficits, all leading causes of severe dementia. | (Nadia El Kadmiri et al., 2014) | \_ | \_ |
| c.248T>C | P.I83T | \_ | *PSEN1* | Chr 14q24.2 | PSEN1 codes for presenilin 1 protein, which is considered as the proteolytic subunit of γ-secretase. And this functions in cleaving APP into smaller peptides.  (https://ghr.nlm.nih.gov/gene/PSEN1) | Tunisia | 2 | \_ | Both members have T>C missense mutation | 63 years old male with AD onset at age of 55 years.69 years old female with onset at 64 years. | (Achouri-Rassas et al., 2015) | \_ | \_ |
| c.1130G>C | p.Arg377Thr | \_ | *PSEN1* | Chr 14q24.2 | PSEN1 codes for presenilin 1 protein, which is considered as the proteolytic subunit of γ-secretase. And this functions in cleaving APP into smaller peptides.  (https://ghr.nlm.nih.gov/gene/PSEN1) | Saudi Arabia | 11 | 11 | 1 had the mutation | 60 years old female, with slowly progressive memory loss, and impaired decision making. Head CT scan shows mild generalized atrophy. | (Al-Khedhairy et al., 2005) | \_ | \_ |
| c.584 A>G | p.Tyr195Cys | rs200065583 | *PSEN1* | Chr 14q24.2 | PSEN1 codes for presenilin 1 protein, which is considered as the proteolytic subunit of γ-secretase. And this functions in cleaving APP into smaller peptides.  (https://ghr.nlm.nih.gov/gene/PSEN1) | Saudi Arabia | 117 | \_ | not specified | 74 AD cases were sporadic, while 43 were familial AD cases. The mean age for the Familial AD cases was 58.9 and for sporadic was 71.2.54 AD cases were females and 63 were males.Typical amnestic behavioral and neurological presentation of the disease. Worsening of cognition.Impairment of learning.Brain atrophy. Found in transmembrane 4 domain of PSEN1 where conformational changes and altered production of Abeta42 | (El Bitar et al., 2019) |  | \_ | \_ |
| c.815 T>A | p.Val272Asp | \_ | *PSEN1* | Chr 14q24.2 | PSEN1 codes for presenilin 1 protein, which is considered as the proteolytic subunit of γ-secretase. And this functions in cleaving APP into smaller peptides.  (https://ghr.nlm.nih.gov/gene/PSEN1) | Iraq | 1 | \_ | n= 1 | Speech impairment and memory decline at age 46 years.MRI showed frontotemporal atrophy.Increased AB42 production. | (Mengel et al., 2020) | Caucasian, Spanish and Portuguese. | Mean age was 52.9All the patients included in the study were confirmed to have AD. | (Guerreiro et al., 2010) |
| c.378\_379insA | p.E126fs | \_ | *PSEN2* | Chr 1 | PSEN2 encodes for presenilin 2 protein, which helps in transmitting signals across cell membrane to the nucleus, and there it activates genes required for cell growth and maturation. (https://ghr.nlm.nih.gov/gene/PSEN2) | Morocco | 25 | \_ | 1 out of 8 familial early- onset AD cases | identified in a 62-year-old male. The patient’s initial symptom was observed at the age of 60, which was memory loss; the patient showed a difficulty in remembering recently learned facts and the inability to acquire new information, while retaining old memories. Followed in our clinic 2years later, the memory deficit gradually progressed to involve primary progressive aphasia. Neuroimaging revealed hippocampal and parahippocampal atrophy | (Nadia El Kadmiri et al., 2014) | \_ | \_ |
| c.917delA | p.K306fs | \_ | *PSEN2* | Chr 1 | PSEN2 encodes for presenilin 2 protein, which helps in transmitting signals across cell membrane to the nucleus, and there it activates genes required for cell growth and maturation. (https://ghr.nlm.nih.gov/gene/PSEN2) | Morocco | 25 | \_ | 1 out of 8 familial early- onset AD cases |  | (Nadia El Kadmiri et al., 2014) | \_ | \_ |
| c.415G>A | p.Val139Met | rs202178897 | *PSEN2* | Chr 1 | PSEN2 encodes for presenilin 2 protein, which helps in transmitting signals across cell membrane to the nucleus, and there it activates genes required for cell growth and maturation. (https://ghr.nlm.nih.gov/gene/PSEN2) | Saudi Arabia | 117 | \_ | not specified | 74 AD cases were sporadic, while 43 were familial AD cases. The mean age for the Familial AD cases was 58.9 and for sporadic was 71.2.54 AD cases were females and 63 were males.Typical amnestic behavioral and neurological presentation of the disease. Worsening of cognition.Impairment of learning.Brain atrophy. | (El Bitar et al., 2019) | Chinese and Italian | This variant was associated with language and memory defects in both of the other groups, while it was reported to be associated with early onset AD among Chinse and late onset among italian. | (Jiang et al., 2019) |
| c.1767\_1768insC | \_ | \_ | *APP* | Chr 21q21.3 | APP gene encodes for Amyloid Precursor Protein. It is an integral membrane protein and it is concentrated in the synapses of the neurons. | Morocco | 25 | \_ | 3 familial cases | 3 females with age at disease onset ranging from 60 to 64 years. With positive family history, memory loss as an initial symptom, illiterate and brain atrophy. | \_ | (N. El Kadmiri et al., 2014) | \_ | \_ |
| c.1764\_1765insC | \_ | \_ | *APP* | Chr 21q21.3 | APP gene encodes for Amyloid Precursor Protein. It is an integral membrane protein and it is concentrated in the synapses of the neurons. | Morocco | 25 | \_ | 1 familial case | Male with positive family history, and disease onset at age of 63 years. The patient experienced progressive demetia 2 years before AD diagnosis, along with cognitive and memory impairment. | \_ | (N. El Kadmiri et al., 2014) | \_ | \_ | \_ |
| c.1886\_1887insC | \_ | \_ | *APP* | Chr 21q21.3 | APP gene encodes for Amyloid Precursor Protein. It is an integral membrane protein and it is concentrated in the synapses of the neurons. | Morocco | 25 | \_ | 1 familial case | Male patient with family history of AD, and disease onset at 49 years. The patient had brain atrophy, memory impairment, aphasia, and praxis. | \_ | (N. El Kadmiri et al., 2014) | \_ | \_ |
| c.1968delT | \_ | \_ | *APP* | Chr 21q21.3 | APP gene encodes for Amyloid Precursor Protein. It is an integral membrane protein and it is concentrated in the synapses of the neurons. | Morocco | 25 | \_ | 1 familial case | \_ | (N. El Kadmiri et al., 2014) | \_ | \_ |
| c.1881\_1882insG | \_ | \_ | *APP* | Chr 21q21.3 | APP gene encodes for Amyloid Precursor Protein. It is an integral membrane protein and it is concentrated in the synapses of the neurons. | Morocco | 25 | \_ | 1 familial case | 62 years old male, with initial sysptoms of memory deficts at age of 60 years. | \_ | (N. El Kadmiri et al., 2014) | \_ | \_ |
| c.1886\_1887insC | \_ | \_ | *APP* | Chr 21q21.3 | APP gene encodes for Amyloid Precursor Protein. It is an integral membrane protein and it is concentrated in the synapses of the neurons. | Morocco | 25 | \_ | 1 sporadic case | male patients with sporadic AD, and disease onset at age of 56 years. the patients experienced memory and praxis deficits with brain atrophy and no family history. | \_ | (N. El Kadmiri et al., 2014) | \_ | \_ |
| c.1138 G>A | p.Glu380Lys | \_ | *APP* | Chr 21q21.3 | APP gene encodes for Amyloid Precursor Protein. It is an integral membrane protein and it is concentrated in the synapses of the neurons. | Saudi Arabia | 117 | \_ | NR | 74 AD cases were sporadic, while 43 were familial AD cases. The mean age for the Familial AD cases was 58.9 and for sporadic was 71.2.54 AD cases were females and 63 were males.Typical amnestic behavioral and neurological presentation of the disease. Worsening of cognition.Impairment of learning.Brain atrophy. | \_ | (N. El Kadmiri et al., 2014) |  | \_ | \_ |
| c.889 G>A | p.Val297Met | \_ | *SORL1* | Chr 11q21.1 | SORL1 gene encodes for vacuolar protein sorting 10 domain containing receptor family, and the low density lipoprotein receptor family. Mutation in this gene maybe associated with Alzheimer's disease. https://www.ncbi.nlm.nih.gov/gene/6653 | Saudi Arabia | 117 | \_ | NR | 74 AD cases were sporadic, while 43 were familial AD cases. The mean age for the Familial AD cases was 58.9 and for sporadic was 71.2.54 AD cases were females and 63 were males.Typical amnestic behavioral and neurological presentation of the disease. Worsening of cognition.Impairment of learning.Brain atrophy. | (El Bitar et al., 2019) |  | \_ | \_ |
| c.3250 C>T | p.Arg1084Cys | \_ | *SORL1* | Chr 11q21.1 | SORL1 gene encodes for vacuolar protein sorting 10 domain containing receptor family, and the low density lipoprotein receptor family. Mutation in this gene maybe associated with Alzheimer's disease. https://www.ncbi.nlm.nih.gov/gene/6653 | Saudi Arabia | 117 | \_ | NR | 74 AD cases were sporadic, while 43 were familial AD cases. The mean age for the Familial AD cases was 58.9 and for sporadic was 71.2.54 AD cases were females and 63 were males.Typical amnestic behavioral and neurological presentation of the disease. Worsening of cognition.Impairment of learning.Brain atrophy. | (El Bitar et al., 2019) |  | \_ | \_ |
| c.3637 C>T | p.Pro1213Ser | \_ | *SORL1* | Chr 11q21.1 | SORL1 gene encodes for vacuolar protein sorting 10 domain containing receptor family, and the low density lipoprotein receptor family. Mutation in this gene maybe associated with Alzheimer's disease. https://www.ncbi.nlm.nih.gov/gene/6653 | Saudi Arabia | 117 | \_ | NR | 74 AD cases were sporadic, while 43 were familial AD cases. The mean age for the Familial AD cases was 58.9 and for sporadic was 71.2.54 AD cases were females and 63 were males.Typical amnestic behavioral and neurological presentation of the disease. Worsening of cognition.Impairment of learning.Brain atrophy. | (El Bitar et al., 2019) |  | \_ | \_ |
| c.3298 G>A | p.Asp1100Asn | \_ | *SORL1* | Chr 11q21.1 | SORL1 gene encodes for vacuolar protein sorting 10 domain containing receptor family, and the low density lipoprotein receptor family. Mutation in this gene maybe associated with Alzheimer's disease. https://www.ncbi.nlm.nih.gov/gene/6653 | Saudi Arabia | 117 | \_ | NR | 74 AD cases were sporadic, while 43 were familial AD cases. The mean age for the Familial AD cases was 58.9 and for sporadic was 71.2.54 AD cases were females and 63 were males.Typical amnestic behavioral and neurological presentation of the disease. Worsening of cognition.Impairment of learning.Brain atrophy. | (El Bitar et al., 2019) |  | \_ | \_ |
| c.808 G>A | p.Glu270Lys | rs117260922 | *SORL1* | Chr 11q21.1 | SORL1 gene encodes for vacuolar protein sorting 10 domain containing receptor family, and the low density lipoprotein receptor family. Mutation in this gene maybe associated with Alzheimer's disease. https://www.ncbi.nlm.nih.gov/gene/6653 | Saudi Arabia | 117 | \_ | NR | 74 AD cases were sporadic, while 43 were familial AD cases. The mean age for the Familial AD cases was 58.9 and for sporadic was 71.2.54 AD cases were females and 63 were males.Typical amnestic behavioral and neurological presentation of the disease. Worsening of cognition.Impairment of learning.Brain atrophy. | (El Bitar et al., 2019) | Carribbean Hispanics and Northern Europe | Mean age among Carribbean Hispanics was 77.0, and 73 among Europeans. Reported to be asscoiated with late onset of the disease along with mild cognitive impairment. | (B. N. Vardarajan, D. J. Schaid, et al., 2015; B. N. Vardarajan, Y. Zhang, et al., 2015) |
| c.1582G>A | p.Ala528Thr | \_ | *SORL1* | Chr 11q21.1 | SORL1 gene encodes for vacuolar protein sorting 10 domain containing receptor family, and the low density lipoprotein receptor family. Mutation in this gene maybe associated with Alzheimer's disease. https://www.ncbi.nlm.nih.gov/gene/6653 | Saudi Arabia | 117 | \_ | NR | 74 AD cases were sporadic, while 43 were familial AD cases. The mean age for the Familial AD cases was 58.9 and for sporadic was 71.2.54 AD cases were females and 63 were males.Typical amnestic behavioral and neurological presentation of the disease. Worsening of cognition.Impairment of learning.Brain atrophy. | (El Bitar et al., 2019) | Caribbean Hispanics and Northern Europe | Mean age among Caribbean Hispanics was 77.0, and 73 among Europeans. Reported to be associated with late onset of the disease along with mild cognitive impairment. | (Badri N. Vardarajan et al., 2015) |
| c.3561T>G | p.Ser1187Ser | \_ | *SORL1* | Chr 11q21.1 | SORL1 gene encodes for vacuolar protein sorting 10 domain containing receptor family, and the low density lipoprotein receptor family. Mutation in this gene maybe associated with Alzheimer's disease. https://www.ncbi.nlm.nih.gov/gene/6653 | Saudi Arabia | 117 | \_ | NR | 74 AD cases were sporadic, while 43 were familial AD cases. The mean age for the Familial AD cases was 58.9 and for sporadic was 71.2.54 AD cases were females and 63 were males.Typical amnestic behavioral and neurological presentation of the disease. Worsening of cognition.Impairment of learning.Brain atrophy. | (El Bitar et al., 2019) | BelgiumSpainPortugalItalySwedenGermany | \_ | (Verheijen et al., 2016) |
| -675 4G/5G | \_ | rs1799889 | *SERPINE1* | Chr 7q22.1 | SERPINE1 gene provides instructions for maing plasminogen activator inhibitor 1 protein (PAI-1), which is invloved in blood clotting. (https://ghr.nlm.nih.gov/gene/SERPINE1#location) | Tunisia | 60 | 120 | 50 AD cases had 4G allel. | Mean age of AD cases: 75.18 Mean age of controls: 72.94AD cases: male = 40, females = 20controls: males = 74, females = 46 | \_ | (N. Fekih-Mrissa et al., 2017) | Korean, (Oh, Lee, Song, Park, & Kim, 2014) | \_ | (Oh et al., 2014) |

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