Family History of Alzheimer's Disease Increases the Risk of COVID-19 Positivity: A SUMS Employees Cohort-based Study

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ABSTRACT

Background: Substantial data indicate that genetic and environmental factors play a key role in determining the risk of Alzheimer's disease (AD). Moreover, it is known that having relatives with AD increases the risk of developing this disease.

Objective: This study is aimed at investigating whether having a family history of AD, may increase the risk of COVID-19 in a cohort-based study.

Material and Methods: Participants of this retrospective cohort study were previously enrolled in the SUMS Employees Cohort (SUMSEC). All participants including those whose SARS-CoV-2 infection was confirmed by positive PCR test and chest CT scan were requested to respond to interviewer-administered questionnaires. Moreover, AD was diagnosed via memory and thinking impairment, concentration problems, confusion with location, and problems in finishing daily tasks.

Results: The total numbers of female and male participants with a family history of AD were 463 and 222 individuals, respectively. When all types of family history of AD were considered, a 51.3% increase was found in the relative frequency of the participants with both family history of AD and confirmed COVID-19 compared with those only with a family history of AD.

Conclusion: Despite the limitations of our study, and from a broader perspective, our findings can further support the concept that AD risk haplotypes including APOE are linked to the same morbidities from cardiovascular disease and obesity that increase vulnerability to COVID-19. Given this consideration, millions of APOE ε4 carriers around the globe should be advised to take additional precautions to prevent life-threatening diseases such as COVID-19.

Keywords

Alzheimer's Disease; APOe4 Gene; SARS-CoV-2; COVID-19

Introduction

The COVID-19 pandemic is overwhelming the health care system in many developed and developing countries [1] and causing substantial life loss [2]. As of Dec 31, 2020, Iran has reported a total of 1.21 million COVID-19 cases, which includes 54,946 deaths. The worldwide cases and deaths reach 82.7 million and 1.8 million, respectively. Besides a tragic health crisis, COVID-19 has also drastically

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affected the world economy [3].

The SARS-CoV-2 virus generates COVID-19 infection by attaching to ACE2 and neuropilin. These two type receptors are involved in COVID-19 complications. In general, ACE superfamily including ACE2 and ACE are associated with the renin–angiotensin system (RAS). Furthermore, ACE activity leads to inflammation, and vasoconstriction. However, ACE2 activates the anti-inflammation and vasodilation. Notably, susceptibility to COVID-19 can be caused via the imbalance of these regulatory pathways. Moreover, the RAS-equilibrium disturbance leads to Alzheimer's disease (AD). Both genetic and environmental factors are believed to be involved in the risk of AD [4-11]. Substantial data now indicates that having relatives with AD increases the risk of developing Alzheimer's disease [12]. Moreover, compared to the general population, having at least 2 siblings with late-onset AD increase the risk of Alzheimer's disease by 3-fold [13-15].

Some studies also show that the APOE e4 genotype is linked to dementia and delirium [16]. APOE e4 genotype increases AD risk 14 times compared to the common e3e3 genotype, (4). Recently, researcher showed that ACE2, is highly expressed in type II lungs' alveolar cells, where there is co-expression of APOE genes [17].

These documents demonstrate that the variability in incidence and manifestations of COVID-19 in different populations could be traced in the human genome differences. Therefore, the goal of this study was to answer the key question whether having a family history of AD, in particular a parental history, may increases the risk of COVID-19 in a cohort-based study.

Material and Methods

This retrospective cohort study was a part of the Shiraz University of Medical Sciences' Employee's Cohort (SUMSEC) that is in turn, a part of the large-scale Persian Cohort. Participants of this study were previously enrolled in SUMSEC. All participants including those, whose SARS-CoV-2 infection was confirmed by positive PCR test and chest CT scan, were requested to respond to interviewer-administered questionnaires. Socio-demographic characteristics, life style data, travel history, contact history, symptoms and their duration and severity were collected for all participants. Moreover, an expert neurologist diagnosed Alzheimer patients via memory and thinking impairment, concentration problem, confusion with location and problem in finishing daily tasks.

Results

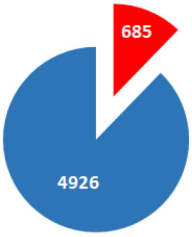
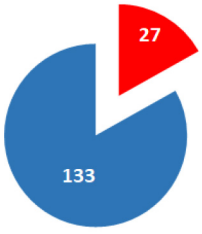
The findings obtained in our study are summarized in Table 1. The mean ± SD (range) age of the participants with AD Family History (ADFH) and those with both ADFH and confirmed COVID-19 (CCOVID19) were 41.96 ± 6.94 (21-62) years and 41.52 ± 8.71 (28-58), respectively. The total numbers of female and male participants with the family history of Alzheimer's disease were 463 and 222 individuals, respectively. Among COIVID-19 infected participants with the family history of Alzheimer's disease, 18 were female and 9 were male.

Regarding paternal history of AD, while the relative frequency of the participants with both ADFH and CCOVID19 was about 45% less than that of the participants only with ADFH, for maternal history of AD, it was 33.55 higher. Moreover, regarding the history of AD in Grandparents, the relative frequency of the participants with both ADFH and CCOVID19 was 16.6% higher than that of the participants with only ADFH. When all types of family history of AD were considered, a 51.3% increase was found in the relative frequency of the participants with both ADFH and CCOVID19 compared with those only with ADFH.

Discussion

From a broader perspective, our findings

Table 1: The relative frequencies of the participants with both family history of Alzheimer's Disease (ADFH) and confirmed COVID-19 (+COVID19) compared to those with only ADFH.

Family History of Alzheimer's Disease (Whole Cohort N=4926)	Only ADFH (Only AD Family History) N=685	ADFH #+CCOVID19 (COVID+ & AD Family History) N=27	Difference (Change %)
Age (y) Mean ± SD	41.96 ±6.94	41.52 ±8.71	
Range	(21-62)	(28-58)	
Percentiles			-
25	31	34	
50	41	42	
75	47	49	
Male, Female, Ratio (M/F)	222, 463 (0.48)	9, 18 (0.50)	
Paternal History of AD (%)	16.50%	7.41%	↓44.91
Maternal History of AD (%)	11.09%	14.81%	↑33.54
History of AD in Grandparents (%)	54.01%	62.96%	↑16.57
Other Blood Relatives	18.40%	14.82	↓24.16
Total	100%	100%	
	13.93%	21.05%	
All Types of Family History of AD (%)			↑51.33

ADFH: Family History of Alzheimer's Disease (AD)

#+CCOVID19: Confirmed COVID-19

may generally support the reports that indicated AD risk haplotypes including APOE are linked to the same morbidities from cardiovascular disease (CVD) and obesity [18, 19] that increase vulnerability to COVID-19 [20]. The findings obtained in our study are also in line with those reported by Kuo et al. who showed a strong association between severe COVID-19 and APOE ε4ε4 genotype, independent of the known comorbidities. Given this consideration, it is reported that through regulating pro-inflammatory pathways, APOE modulates the severity of COVID-19. Altogether, it can be concluded that millions of APOE ε4 carriers around the globe should be advised to take additional precautions to prevent life-threatening diseases such as COVID-19 [21]. Due to limitations of our study, in particular the small sample size, and being genome wide, further studies are warranted to discover different aspects of this issue.

Conclusion

Despite a few limitations of our study, looking at the issue from a broader perspective, our findings can further support the concept that AD risk haplotypes including ApoE are linked to the same morbidities from cardiovascular disease and obesity that increase vulnerability to COVID-19. Considering the association between having a family history of AD and the risk of COVID-19, millions of APOE ε4 carriers around the word should be advised to take additional precautions to prevent COVID-19.

Conflict of Interest

None

References

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