Association Between Herpes Simplex Virus Type 1 and the Risk of Alzheimer's Disease

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Introduction

- There is a significant unmet need of novel therapeutics for Alzheimer's disease (AD) and AD-related dementia (ADRD)[1]
- A growing body of evidence suggests a role for herpesviruses in the development of AD/ADRD and reduced risk of AD/ADRD among patients receiving antiviral[2-6]
- We investigated the association between *herpes simplex virus type 1* (HSV-1) and AD/ADRD, and the effect of antiviral medications using real-world data

Objectives

Primary:

- To describe the demographic and clinical characteristics of patients with AD/ADRD
- To assess the association between HSV-1 infection and AD/ADRD

Secondary:

- To assess if antiviral use reduces risk of AD/ADRD in patients with HSV-1 infection

Methods

- A matched case-control study design was used; patients with AD aged ≥50 y diagnosed between 2006 and 2021 were identified from the IQVIA® PharMetrics® Plus (Durham, NC) claims database using International Classification of Disease (ICD) codes (ICD-9 331.0; ICD-10 G30.x)
- Controls without any history of neurologic disorders were matched in a 1:1 ratio with patients with AD on age, sex, region, database entry year, and healthcare visit numbers
- HSV-1 diagnoses were identified using relevant ICD codes
- Multivariate conditional logistic regression was used to evaluate the association between HSV-1 and AD
- The association between antiviral use and AD was assessed by multivariate Cox proportional hazards model in patients with HSV-1 diagnosis
- A parallel analysis was conducted including all patients with ADRD and matched controls

Results

Study Flow: Attrition and Matching

Patient Demographic Characteristics

Patient Clinical Characteristics

Characteristics	AD Case n=344,628	Control n=344,628	p-Value
Database entry year, n (%)			1.00
2006–10	285,085 (82.7)	285,085 (82.7)	
2011–15	45,850 (13.3)	45,850 (13.3)	
2016–21	13,693 (4.0)	13,693 (4.0)	
Outpatient visit #			1.00
Mean (SD)	13.32 (10.10)	13.32 (10.10)	
Median (Q1, Q3)	11 (6, 18)	11 (6, 18)	
Inpatient visit #			1.00
Mean (SD)	3.36 (4.88)	3.36 (4.88)	
Median (Q1, Q3)	2 (1, 4)	2 (1, 4)	
Comorbidities, n (%)			<0.001
None	101,458 (29.4)	119,351 (34.6)	
1	69,603 (20.2)	69,552 (20.2)	
≥2	173,567 (50.4)	155,725 (45.2)	
CCI (Charlson)			<0.001
Mean (SD)	2.61 (2.89)	2.41 (2.93)	
Median (Q1, Q3)	2 (0, 4)	1 (0, 4)	
Follow-up time, mo			<0.001
Mean (SD)	47.86 (46.24)	53.98 (39.97)	
Median (Q1, Q3)	33 (9, 74)	48 (24, 72)	
HSV-1, n (%)	**1507 (0.4)**	**823 (0.2)**	**<0.001**

CCI, Charlson Comorbidity Index; Q, quartiles; SD, standard deviation.

Association Between HSV-1 and AD
Overall and Stratified by Age

CI, confidence interval; OR, adjusted odds ratio.

Effects of Antiviral Medications in Patients With HSV-1 Diagnosis

HR, adjusted hazard ratio.

Limitations

- Real-world data could be missing or incomplete, the extent of which could not be ascertained
- Commercial claims data don't capture patients insured solely by Medicare; therefore, patients aged ≥65 y were underrepresented in this study
- Asymptomatic HSV-1 infection may not be captured by claims data

Conclusions

- Findings from this large real-world data study are consistent with emerging literature on the association between HSV-1 and risk of AD/ADRD and the possible protective role of antiviral drugs

References: 1. 2021 Alzheimer's disease facts and figures. Alzheimers Dement 2021;17:327-406; 2. James C, et al. Bull World Health Organ 2020;98:315-29; 3. Linard M, et al. Alzheimers Res Ther 2022;14:3; 4. Lopatko Lindman K, et al. Alzheimers Dement 2021;7:e12119; 5. Tzeng NS, et al. Neurotherapeutics 2018;15:417-29; 6. Young-Xu Y, et al. Neurotherapeutics 2021;18:2458. Acknowledgments: We extend our thanks to the patients and their families. This study was funded by Gilead Sciences, Inc. Editing and production assistance were provided by BioScience Communications, New York, New York, USA, funded by Gilead. Disclosures: L. Liu, N. Jarousse, S.P. Fletcher, and S. Iqbal: Gilead; C. Johnston: Gilead, AbbVie, GSK.