

Alzheimer Disease Occurs More Frequently in Patients With Celiac Disease: A Nationwide Population-Based Cohort Study



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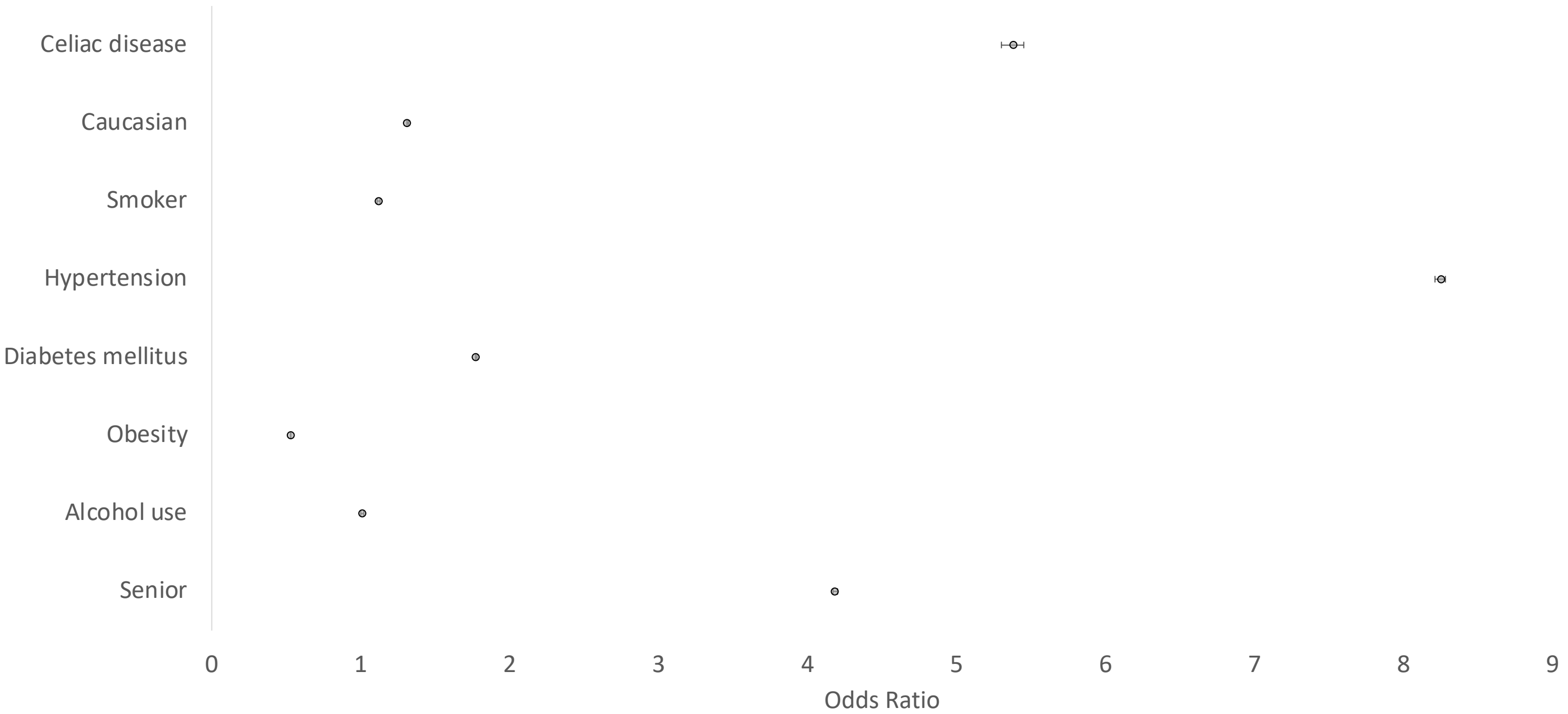
Introduction

Alzheimer disease (AD) affects greater than 5 million Americans and is increasingly prevalent among an aging population. Cognitive decline in general has been linked to chronic inflammation and altered intestinal microbiome. Celiac disease (CD) is an autoimmune enteropathy characterized by immune-mediated damage caused by exposure to gluten. This study was designed to describe the epidemiology and risk association of Alzheimer disease in patients with CD.

Methods

- Surveyed a multi-institutional database (Explorys Inc., Cleveland, OH)
 - An aggregate of electronic health record data from 26 major US health systems.
- Cohorts of patients with AD and CD were generated using Systemized Nomenclature of Medicine – Clinical Terms (SNOMED-CT).
 - AD was defined as SNOMED terms for “Alzheimer’s disease” or “Alzheimer’s dementia” with prescribed Alzheimer’s treatment (donepezil, memantine, galantamine, or rivastigmine).
 - CD was defined as SNOMED terms for “celiac disease” or ”celiac sprue”
- Patients with vascular dementia or Parkinson’s disease were excluded.
- Univariate and multivariate analyses were performed on the data, and associations were reported as adjusted odds ratios (aORs) with 95% confidence intervals (CIs) using IBM SPSS Statistics version 25.

Forest Plot for Associated Risk Factors



Demographic and Risk Factor Data

Celiac Disease	With Alzheimer’s Disease (n [%])	Without Alzheimer’s Disease (n [%])	Multivariate Analysis (aOR [95% CI])
Total	970	87800	5.38 (5.30-5.45)
Risk factor			
Alcohol use	40 (4.1)	2900 (3.3)	1.01 (1.00-1.02)
Obesity	180 (18.6)	30510 (34.7)	0.53 (0.53-0.53)
Diabetes mellitus	390 (40.2)	29430 (33.5)	1.77 (1.77-1.78)
Hypertension	810 (83.5)	38880 (44.3)	8.25 (8.21-8.28)
Smoker	290 (29.9)	10460 (11.9)	1.12 (1.11-1.13)
Caucasian	890 (91.7)	71120 (81.0)	1.31 (1.31-1.32)
Senior (Age >65)	890 (91.7)	33050 (37.6)	4.18 (4.17-4.20)

Results

- Of 25,298,080 individuals in the database (2017-2022):
 - 88,770 were diagnosed with celiac disease (0.35%)
- Among CD patients:
 - 970 (1.1%) carried an AD diagnosis compared to 194,030 (0.8%) of the non-CD patients (p <0.0001).
- After multivariate analysis:
 - CD was associated with increased odds of Alzheimer’s disease (aOR = 5.38, 95% CI = 5.30-5.45, p <0.0001) (Figure 1).
 - Diabetes mellitus, tobacco use, Caucasian race, senior age, and hypertension were also significantly associated with increased AD risk (p<0.0001).

Discussion

- This large population-based cohort study demonstrated a significantly higher odds of Alzheimer disease among celiac disease patients compared to those without celiac disease.
- Ability to define Alzheimer disease by combined diagnosis codes and prescriptions strengthens these data
- Conclusions limited by inability to discern patients adhering to gluten free diet
- Larger prospective work would be beneficial to identify possible mechanisms. Further work may examine possible interventions to minimize the odds of developing AD in this population and to assess the effect of gluten-free diet adherence on its development.

Contact

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