

Investigation of Autoimmune Disease with Eosinophilic Esophagitis

A Nationwide Longitudinal Study

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Introduction

- Eosinophilic Esophagitis (EoE) is a chronic immune-mediated condition involving eosinophils that leads to esophageal dysfunction. Although EoE is found in up to 7% of patients undergoing endoscopy and is increasing in prevalence, its pathogenesis remains poorly understood.
- In this retrospective multicenter study, we investigated the incidence and risk factors for comorbid autoimmune diseases (AiD) using Cerner Health Facts, a national longitudinal database representing 519 million patient encounters.

Research Objectives

- We aim to investigate the incidence, characteristics, and risk factors for comorbid autoimmune diseases (AiD) in patients diagnosed with Eosinophilic Esophagitis (EoE) using Cerner Health Facts, a national longitudinal database representing 519 million patient encounters.

Methodology

- The Cerner HealthFacts database serves as our data source and is a deidentified, nationally representative sample of patient electronic health information (EHR). It includes information from 750 hospitals and covers over 69 million patients.
- All patients 18 years of age or older with EoE between January 1, 2010 and November 30, 2018 were included in our analysis. Patient characteristics were evaluated as potential risk factors for AiD comorbidity using multivariable regression built using all variables that had a p-value less or equal to 0.05.
- Patient sociodemographic factors, facility factors and medical issues including comorbidities and diagnoses suspected to be present at an initial patient encounter for a complaint of EoE were assessed as potential risk factors for the development of AiD.
- We compared variables of interest between the cohorts of patients with and without EoE using the χ^2 test for categorical variables, the Mann-Whitney U test for non-normally distributed continuous variables, and the t-test for normally distributed continuous variables. Statistical significance was defined as $p < 0.05$.
- Factors found to have $p \leq 0.05$ on univariable analysis were included in our multivariable regression model. Independent risk factors for the development of AiD were presented as adjusted odds ratios with 95% Confidence Intervals.

Results

- We identified 8,535 patients with EoE. The mean age was 44.16 ± 16.64 years and 42.44% (3,622) were female, and 6.22% (531) were obese.
- In terms of race, 85.24% (7,275) were white and 6.03% (515) were African American.
- Overall, 13.38% (1,142/8,535) of patients with EoE had at least one comorbid AiD.
- The most common AiD in those with EoE was autoimmune hypothyroidism (577 – 50.5%) followed by ulcerative colitis (199) and rheumatoid arthritis (89).
- On multivariable regression, the factors associated with a higher risk of AiD included female gender (OR 2.73), steroid use (OR 2.70), type2-diabetes (OR 1.88), long-term medication use (OR 1.87), digestive comorbidities (OR 1.59), anxiety (OR 1.47), nicotine use (OR 1.47), hyperlipidemia (OR 1.42), asthma (OR 1.36) and hypertension (OR 1.23).

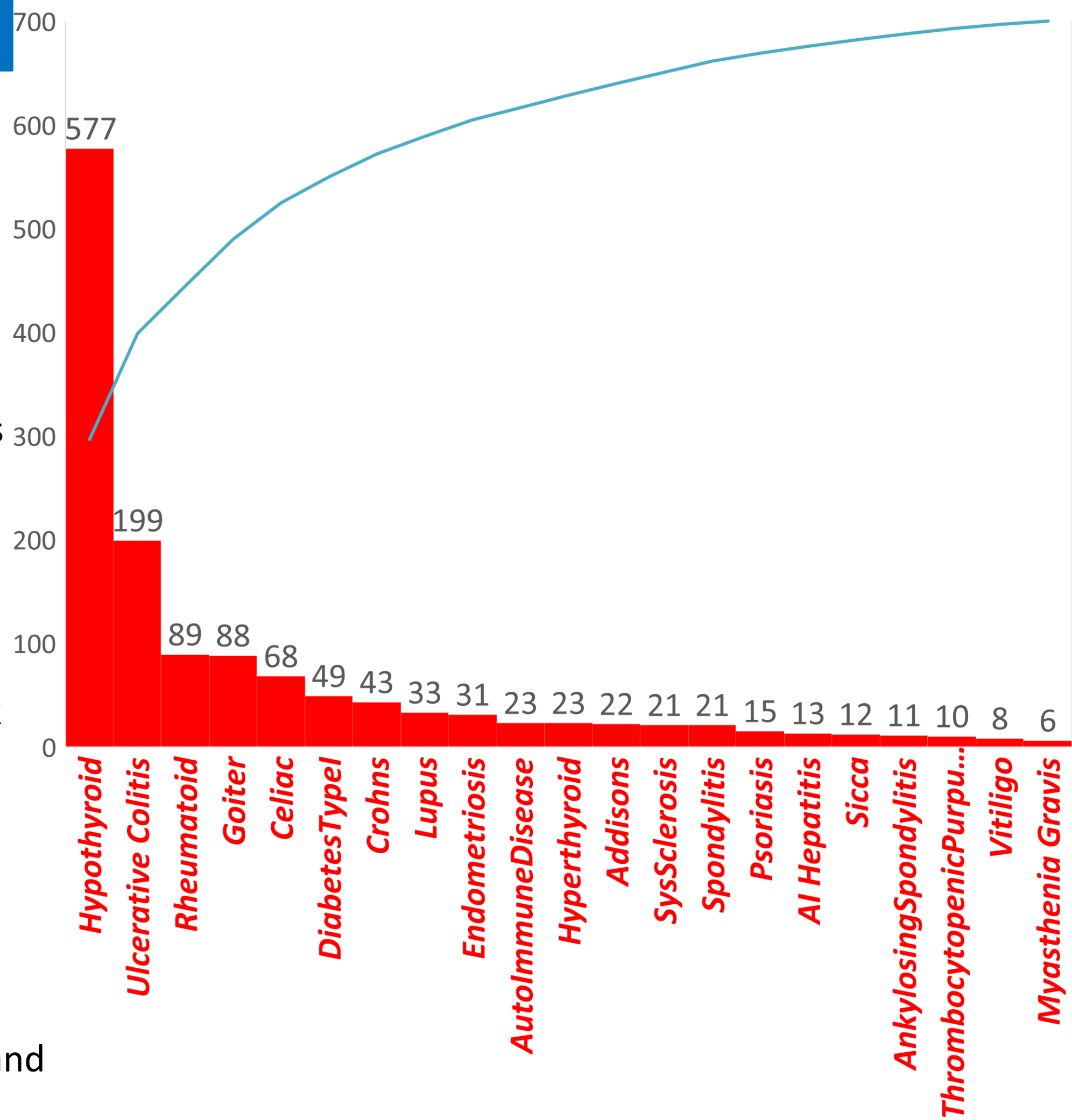


Fig 1: Autoimmune Disease Burden in Adults with Eosinophilic Esophagitis (EoE). *AutoImmuneDisease include Cholan, Uveitis, Biliary Cirrhosis, AutoimmunePolyendocrineSyndrome, AntiphospholipidSyndrome, Dermatomyositis and Autoimmune Hemolytic Anemias*

Table 1 Univariable Analysis and Multivariable Regression Model Results
** White race used as referent group*

Variable	Univariable Odds Ratio	95% Confidence Interval	Multivariable Odds Ratio	95% Confidence Interval
Diabetes Type 2	3.62	2.97-4.42	1.88	1.49-2.38
Age in Years	1.02	1.02-1.024	1.01	1.005-1.014
Hypertension	2.50	2.17-2.88	1.23	1.02-1.48
Female Gender**	3.40	3.00-3.85	2.73	2.38-3.14
Digestive Disorder	2.06	1.81-2.33	1.59	1.39-1.82
Nicotine Use Disorder	2.17	1.82-2.59	1.47	1.21-1.79
Hyperlipidemia	2.69	2.29-3.17	1.42	1.16-1.74
Anxiety	2.69	2.21-3.27	1.47	1.17-1.86
Obesity	2.19	1.78-2.70	1.14	0.90-1.45
Depression	2.91	2.35-3.61	1.26	1.00-1.63
Long Term Medications	2.69	2.05-3.51	1.87	1.39-2.51
Thromboemboli c Disorders	2.35	1.75-3.16	1.00	0.68-1.34
Steroid Use	5.45	3.16-9.40	2.70	1.44-5.04
Asthma	1.81	1.50-2.18	1.36	1.11-1.67
Bed Size > 200	0.84	0.74-0.95	1.14	1.00-1.31

Table 2 Univariable Analysis **P value<0.05; **P value < 0.01;***P value<0.001*

	Autoimmune Disease in Adult Patients with Eosinophilic Esophagitis (EoE)		Overall n=8535	p
	No N=7393	Yes n=1142		
Facility Factors, n (%)				
Presentation to Teaching Facility	3938 (53.27%)	582 (50.96%)	4520 (52.96%)	0.15
Facility Location				0.81
Rural	1119 (15.14%)	176 (15.41%)	1295 (15.17%)	
Urban	6274 (84.86%)	966 (84.59%)	7240 (84.83%)	
Bed Size > 200 Beds	4630 (62.63%)	668 (58.49%)	5298 (62.07%)	0.007**
Presentation to an Acute Care Facility	6800 (91.98%)	1050 (91.94%)	7850 (91.97%)	0.97
Patient Sociodemographic Factors				
Age in Years, Mean±SD	43.36 (16.46)	49.37 (16.87)	44.16 (16.64)	<0.001* **
Median (IQR)	42.0 (31.0 – 54.0)	50.0 (37.0 – 62.0)	43.0 (31.0 – 55.0)	
Married, n (%)	3913 (52.93%)	586 (51.31%)	4499 (52.71%)	0.31
Race, n (%)				0.64
White	6303 (85.26%)	972 (85.11%)	7275 (85.24%)	
African American	440 (5.95%)	75 (6.57%)	515 (6.03%)	
Other	650 (8.79%)	95 (8.32%)	745 (8.73%)	
Comorbidities, n (%)				
Type 2 Diabetes	327 (4.42%)	164 (14.36%)	491 (5.75%)	<0.001* **
Nicotine Use Disorder	622 (8.41%)	190 (16.64%)	812 (9.51%)	<0.001* **
Obesity	403 (5.45%)	128 (11.21%)	531 (6.22%)	<0.001* **
Hypertension	1084 (14.66%)	343 (30.04%)	1427 (16.72%)	<0.001* **
Hyperlipidemia	684 (9.25%)	246 (21.54%)	930 (10.90%)	<0.001* **
Asthma	603 (8.16%)	158 (13.84%)	761 (8.92%)	<0.001* **
Anxiety	416 (5.63%)	158 (13.84%)	574 (6.73%)	<0.001* **
Depression	310 (4.19%)	129 (11.30%)	439 (5.14%)	<0.001* **
Digestive Disorder	2981 (40.32%)	664 (58.14%)	3645 (42.71%)	<0.001* **
Long Term Medications	199 (2.69%)	79 (6.92%)	278 (3.26%)	<0.001* **
Atopic Diseases	43 (0.58%)	11 (0.96%)	0054 (0.63%)	<0.001* **
Allergic Rhinitis	315 (4.26%)	57 (4.99%)	372 (4.36%)	0.26
Atopic Dermatitis	13 (0.18%)	2 (0.18%)	15 (0.18%)	1.00
Thromboembolic Disorder	179 (2.42%)	63 (5.52%)	242 (2.84%)	<0.001* **
Food Allergy	150 (2.03%)	24 (2.10%)	174 (2.04%)	0.87
Steroid Use	29 (0.39%)	24 (2.10%)	53 (0.62%)	<0.001* **

Summary/Conclusion

- We utilized a national database of patients with diagnosed EoE to identify the incidence and risk factors for comorbid AiD. Autoimmune thyroid disease and ulcerative colitis were the most common AiDs comorbid with EoE.
- The largest risk factor for comorbid AiDs was female gender. The high prevalence of AiD in patients with EoE suggests potential overlap in immune dysregulation and warrants broader consideration and evaluation of AiD in patients with EoE.
- We are sensitive to the possibility of coding errors and are constrained to the variables in the database. These limitations are likely overshadowed by the benefits of the statistical power inherent to the HealthFacts database which contains data from 750 facilities across the United States, with diversity in terms of bed size and geographic distribution.
- We are unable to identify EoE-related interactions happening at non-Cerner institutions that may have resulted in misclassification errors since our analysis is restricted to facilities that participated in the HealthFacts database. However, this effect would be unidirectional and with a low rate of comorbid AiD, it would likely be a very small percentage of the overall population.