Association of autoimmune diseases with chronic rhinosinusitis in general practices in Germany*

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Dear Editor:

Several population-based studies have reported increased prevalence of autoimmune diseases (AID) in patients with chronic rhinosinusitis (CRS). Large-scale datasets from Taiwan demonstrated associations between CRS and conditions such as rheumatoid arthritis, ankylosing spondylitis, polymyositis, psoriasis, Sjögren's syndrome, and systemic lupus erythematosus (SLE) [1,2]. However, sex-specific patterns have not been investigated.

We examined associations between CRS and 20 pre-existing AID using a nationally representative primary care database, with a focus on sex-specific differences. Data were drawn from the IQVIA Disease Analyzer (>1,300 general practices in Germany, including diagnoses and prescriptions). Adults with an initial diagnosis of CRS (ICD-10: J32) between 2010–2024 were matched 1:1 to controls without CRS or nasal polyps (J33), based on age, sex, observation time, and CRS-related comorbidities [3] (Figure S1, online supplement). Conditional logistic regression was used to calculate odds ratios (ORs) with 95% confidence intervals, stratified by sex. We also performed subgroup analyses by age, asthma, allergy, and nicotine dependence.

In total, 281,437 CRS patients and controls were analysed (Table S1, online supplement). Eleven AID were significantly associated with CRS: primary sclerosing cholangitis, idiopathic thrombocytopenic purpura, Sjögren's syndrome, vitiligo, alopecia areata, rheumatoid arthritis, psoriasis, ankylosing spondylitis, autoimmune thyroiditis, inflammatory bowel disease, and coeliac disease (ORs 1.12–1.60). Type 1 diabetes was negatively associated (OR: 0.71). No significant associations were found for SLE or multiple sclerosis (Table 1).

Sex-specific associations were observed for four conditions. Temporal arteritis, Sjögren's syndrome, and coeliac disease were significantly associated with CRS in women only. Polymyalgia rheumatica was associated in men only. The strongest associations overall were seen for temporal arteritis, primary sclerosing cholangitis, Sjögren's syndrome, and vitiligo. Notably, this is the first large-scale real-world study linking CRS with autoimmune thyroiditis, inflammatory bowel disease, and coeliac disease. Prior evidence for inflammatory bowel disease was limited to small studies [4], and a large study previously found no association with autoimmune thyroiditis [5]. To our knowledge, coeliac disease has not yet been analysed in real-world datasets, although genetic studies have linked it to CRS [6]. Mendelian randomisation showed a positive link between type 1 diabetes and CRS [6]; our inverse association may reflect the low case number (0.5%) or under-recording. Stratified analyses showed no major variation in the AID–CRS association (Table S2).

Several mechanisms may underlie these associations, including shared immune dysregulation—especially in CRSwNP [7], susceptibility to infection due to immunosuppressive therapy—primarily in CRSsNP [8], and direct sinonasal involvement of AID.

The sex-specific link for coeliac disease, which is not treated with immunosuppressants, may indicate a distinct female phenotype. In contrast, most AID showed no sex-specific differences despite female predominance, suggesting that immunosuppressive therapy may play a more prominent role than sex-linked genetics. For rare AID such as temporal arteritis and Sjögren's syndrome, female-specific associations may also reflect reduced statistical power in men.

Compared to specialist-based data from Taiwan [1,2], our ORs were lower, possibly due to less specific coding of CRS in primary care [9]. Nonetheless, the large sample size, robust matching, and use of real-world data strengthen the relevance of our findings.

This study has limitations. Diagnoses were based on ICD-10 codes without clinical validation. CRS subtypes (with/without nasal polyps) could not be distinguished, as nasal polyps are rarely coded in German general practice [9]. As an observational study, causality cannot be established. Strengths include large sample size, rigorous matching, and representative real-world data from primary care.

Table 1. Association between AID and CRS. AID, CRS, OR, CI = see abbreviations.

Variable	Proportion of patients among chronic sinusitis cases (%)	Proportion of patients among controls without chronic sinusitis (%)	OR (95% CI)	P value
All patients				
Inflammatory bowel diseases	1.06	0.94	1.12 (1.06-1.18)	<0.001
Rheumatoid arthritis	1.74	1.35	1.27 (1.22-1.33)	<0.001
Psoriasis	2.27	1.81	1.25 (1.20-1,29)	<0.001
Systemic lupus erythematosus	0.05	0.05	0.81 (0.64-1.02)	0.077
Autoimmune thyroiditis	3.18	2.69	1.19 (1.15-1.22)	<0.001
Multiple sclerosis	0.42	0.41	1.03 (0.95-1.12)	0.512
Celiac disease	0.22	0.20	1.12 (1.00-1.25)	0.056
Ankylosing spondylitis	0.39	0.30	1.25 (1.14-1.37)	<0.001
Type 1 Diabetes	0.22	0.31	0.71 (0.64–0.79)	<0.001
Graves' disease	0.55	0.52	1.03 (0.96-1.10)	0.468
Pernicious anemia	0.14	0.15	0.90 (0.78-1.04)	0.143
Vitiligo	0.14	0.11	1.31 (1.13-1.52)	<0.001
Alopecia areata	1.74	1.35	1.29 (1.23-1.34)	<0.001
Myasthenia gravis	0.02	0.02	0.89 (0.63-1.25)	0.489
Sjögren's syndrome	0.17	0.13	1.31 (1.14-1.51)	<0.001
Autoimmune hepatitis	0.04	0.03	1.14 (0.87-1.51)	0.345
Primary biliary cholangitis	0.03	0.03	0.95 (0.69-1.31)	.0.760
Primary sclerosing cholangitis	0.12	0.08	1.50 (1.26-1.78)	<0.001
Polymyalgia rheumatica	0.33	0.29	1.10 (0.99-1.21)	0.054
Temporal arteritis (Giant Cell Arteritis)	0.04	0.03	1.60 (1.19-2.15)	0.002
Idiopathic thrombocytopenic purpura	0.04	0.03	1.32 (1.00-1.72)	0.048
Women				
Inflammatory bowel diseases	1.08	0.97	1.10 (1.02-1.17)	0.009
Rheumatoid arthritis	2.16	1.70	1.24 (1.18-1.31)	<0.001
Psoriasis	2.21	1.71	1.27 (1.21-1.34)	<0.001
Systemic lupus erythematosus	0.07	0.08	0.83 (0.65-1.07)	0.151
Autoimmune thyroiditis	4.84	4.05	1.20 (1.15-1.24)	<0.001
Multiple sclerosis	0.55	0.52	1.06 (0.96-1.16)	0.267
Celiac disease	0.31	0.26	1.18 (1.04-1.34)	0.012
Ankylosing spondylitis	0.33	0.25	1.25 (1.10-1.42)	<0.001
Typ 1 Diabetes	0.18	0.25	0.71 (0.61–0.82)	<0.001
Graves' disease	0.81	0.74	1.05 (0.97-1.14)	0.231
Pernicious anemia	0.17	0.18	0.87 (0.74-1.02)	0.092
Vitiligo	0.14	0.10	1.36 81.10-1.63)	0.004
Alopecia areata	1.74	1.34	1.28 (1.21-1.36)	<0.001
Myasthenia gravis	0.03	0.03	0.90 (0.59-1.37)	0.612
Sjögren's syndrome	0.23	0.17	1.35 (1.15-1.57)	<0.001
Autoimmune hepatitis	0.05	0.04	1.13 (0.82-1.56)	0.443
Primary biliary cholangitis	0.04	0.04	1.01 (0.72-1.41)	0.978
Primary sclerosing cholangitis	0.13	0.09	1.45 (1.17-1.79)	0.001
Polymyalgia rheumatica	0.38	0.35	1.02 (0.91-1.14)	0.788
Temporal arteritis (Giant Cell Arteritis)	0.05	0.03	1.77 (1.23-2.54)	0.002
Idiopathic thrombocytopenic purpura	0.05	0.04	1.34 (0.97-1.86)	0.075

Table 1 *continued* . Association between AID and CRS. AID, CRS, OR, CI = see abbreviations.

Variable	Proportion of patients among chronic sinusitis cases (%)	Proportion of patients among controls without chronic sinusitis (%)	OR (95% CI)	P value
Men				
Inflammatory bowel diseases	1.03	0.88	1.16 (1.06-1.26)	<0.001
Rheumatoid arthritis	1.15	0.86	1.31 (1.20-1.42)	<0.001
Psoriasis	2.37	1.96	1.20 (1.13-1.27)	<0.001
Systemic lupus erythematosus	0.01	0.02	0.63 (0.30-1.31)	0.215
Autoimmune thyroiditis	0.89	0.80	1.11 (1.02-1.21)	0.021
Multiple sclerosis	0.24	0.25	0.94 (0.80-1.11)	0.473
Celiac disease	0.11	0.11	0.93 (0.73-1.19)	0.569
Ankylosing spondylitis	0.48	0.38	1.23 (1.09-1.40)	0.001
Typ 1 Diabetes	0.27	0.38	0.70 (0.61–0.81)	<0.001
Graves' disease	0.19	0.21	0.89 (0.75-1.07)	0.231
Pernicious anemia	0.09	0.10	0.95 (0.73-1.23)	0.679
Vitiligo	0.14	0.11	1.26 (1.00-1.60)	0.047
Alopecia areata	1.75	1.37	1.27 (1.19-1.36)	<0.001
Myasthenia gravis	0.02	0.02	0.89 (0.50-1.59)	0.689
Sjögren's syndrome	0.09	0.07	1.16 (0.87-1.55)	0.305
Autoimmune hepatitis	0.02	0.02	1.12 (0.65-1.95)	0.678
Primary biliary cholangitis	0.01	0.01	0.55 (0.21-1.43)	0.218
Primary sclerosing cholangitis	0.10	0.06	1.54 (1.15-2.06)	0.003
Polymyalgia rheumatica	0.26	0.20	1.26 (1.06-1.49)	0.009
Temporal arteritis (Giant Cell Arteritis)	0.03	0.02	1.28 (0.76-2.15)	0.352
Idiopathic thrombocytopenic purpura	0.03	0.02	1.24 (0.76-2.01)	0.394

Abbreviations: OR odds ratio; CI confidence interval.

Conclusion

CRS was associated with several autoimmune diseases, with sex-specific associations for coeliac disease, Sjögren's syndrome, temporal arteritis, and polymyalgia rheumatica. These findings highlight systemic immune mechanisms in CRS and support the need for further sex- and subtype-specific investigations.

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Abbreviations

AID, autoimmune diseases; CI, confidence interval; CRS, chronic rhinosinusitis; CRSwNP, chronic rhinosinusitis with nasal polyps; CRSsNP chronic rhinosinusitis without nasal polyps; IQR, interquartile range; OR, odds ratio; SLE, systemic lupus erythematosus; SD, standard deviation; SMD, standardised mean difference.

Authorship contribution

DUS: writing – original draft; SB: writing – review & editing; KK: conceptualisation, methodology, investigation, formal analysis, writing – review & editing

Compliance with ethical guidelines

German law allows the use of anonymized electronic medical data for research purposes under certain conditions. Under this law, this type of observational study without identifiable patient data does not require informed consent or ethics approval. The authors did not have access to identifiable patient data at any point in the study.

Conflict of interest

None.

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This manuscript contains online supplementary material

SUPPLEMENTARY MATERIAL

Table S1. Baseline characteristics after 1:5 matching. CRS, SMD, SD, IQR = see abbreviations.

Variable	CRS (n=281,437)	No CRS (n=281,437)	SMD
Age (in years)			
Mean (SD)	44.3 (16.3)	44.2 (16.4)	0.009
≤ 30	66,540 (23.6)	67,849 (24.1)	
31-40	60,041 (21.3)	59,855 (21.3)	
41-50	55,238 (19.6)	54,781 (19.5)	
51-60	51,815 (18.4)	51,491 (18.3)	
>60	47,803 (17.0)	47,461 (16.8)	
Sex			
Female	163,360 (58.0)	163,931 (58.3)	-0.002
Male	118,077 (42.0)	117,506 (41.7)	
Observation time prior to index date in years, mean (SD)	6.6 (5.0)	6.6 (5.0)	-0.024
Diagnoses documented prior to index date			
Allergic rhinitis	28,964 (10.3)	28,836 (10.3)	0.000
Asthma	31,120 (11.1)	30,842 (11.0)	-0.001
GERD	32,773 (11.6)	32,490 (11.5)	-0.001
COPD	17,841 (6.3)	16,085 (5.7)	-0.006
Nicotine dependence	15,445 (5.5)	14,390 (5.1)	-0.004
Acute upper respiratory tract infections, median (IQR)	1 (2)	1 (2)	0.002

Values are given as n (%) unless stated otherwise.

Table S2. Association between any AID and CRS. AID, CRS, OR, CI = see abbreviations.

Variable	OR (95% CI)	P value
All patients	1.19 (1.17–1.22)	<0.001
Women	1.21 (1.1–1.23)	<0.001
Men	1.16 (1.12–1.20)	<0.001
Age ≤ 30 years	1.20 (1.13–1.27)	<0.001
Age 31-40 years	1.17 (1.11–1.22)	<0.001
Age 41-50 years	1.14 (1.09–1.19)	<0.001
Age 51-60 years	1.21 (1.17–1.26)	<0.001
Age >60 years	1.21 (1.16–1.26)	<0.001
Patients with allergic rhinitis	1.13 (1.07–1.19)	<0.001
Patients with asthma	1.16 (1.10–1.22)	<0.001
Patient with nicotine addiction	1.14 (1.05–1.22)	<0.001

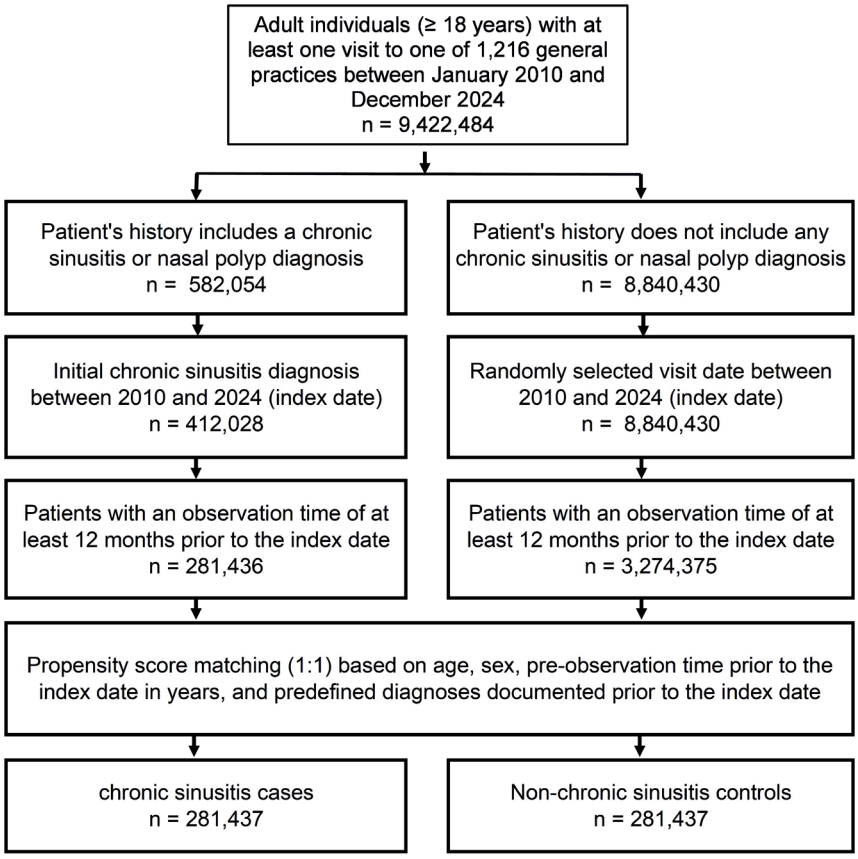

Figure S1. Selection of study patients.