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ORIGINAL PAPER

Systemic autoimmune diseases are associated with an increased risk of obsessive–compulsive disorder: a nationwide population-based cohort study

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Abstract

Purpose Studies suggested autoimmunity plays a role in the etiology of obsessive–compulsive disorder (OCD). The purpose of this study was to determine if a history of systemic autoimmune diseases (SADs) is associated with an increased risk of subsequent onset of OCD.

Methods Patients with or without SADs were identified in the Taiwan National Health Insurance Program. The SADs cohort consisted of 63,165, while the comparison cohort consisted of 315,825 patients. The incidence rates of OCD with a maximum follow-up period of 10 years between patients with and without SADs were compared using a Cox proportional hazard model to estimate the hazard ratio (HR) and 95% confidence interval (95% CI).

Results The major finding was the discovery of a higher incidence of subsequent OCD among patients with SADs (HR: 1.85; 95% CI 1.41–2.43) after adjusted for other demographic characteristics. Specifically, the risk of OCD was observed to be significant increase in systemic lupus erythematosus (1.65, 1.07–2.54) dermatomyositis (3.25, 1.04–10.17), and Sjögren's syndrome (2.38, 1.53–3.72). Also, this study revealed some potential risk factors for developing OCD, including younger age (less than or equal to 50-year-old) and some comorbidities (alcohol use disorder, liver cirrhosis, and malignancies). Conversely, this study found that steroid use was a potential protective factor for the development of OCD.

Conclusions This study confirms that SADs are associated with higher incidence of OCD, suggesting that abnormal autoimmune process is associated with increased expression of psychiatric disturbances.

Keywords Obsessive–compulsive disorder (OCD) · Systemic autoimmune diseases (SADs) · Cohort

Introduction

Obsessive–compulsive disorder (OCD) is a common, chronic and long-lasting disorder in which the patients have uncontrollable, reoccurring thoughts (obsessions) and behaviors (compulsions) that they feel the urge to repeat over and over [1]. Symptoms may come and go, ease over time, or worsen. Usually, these symptoms are associated with reduced quality of life and cause significant functional impairments [1]. In Taiwan, the estimated mean annual incidence was 0.028% and the 1-year prevalence was 0.065% [2]. Incidence and prevalence increased with age, peaking at age 18–24 years in males and at 35–44 years in females [2].

The cause of OCD is not exactly clear. Several family and twin studies have provided evidence for heritability of OCD [3, 4]. In the past years, a multitude of genetic association studies in OCD have been performed, but few consistent findings have been achieved [4–6]. Neuroimaging

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studies have demonstrated that OCD is associated with the structural and functional aberrations in the corticostriatal thalamocortical (CSTC) circuit [7, 8]. As with other complex neuropsychiatric disorders, OCD susceptibility seems to be determined by the sum of a large number of genes with modest effect, and most of them are related with abnormal modulation of neurotransmitter systems in CSTC circuit [9].

In addition to genetic factors, autoimmunity might play a role in the etiology of OCD [10–12]. Some children may develop a sudden onset or worsening of OCD symptoms after a group A streptococcal (GAS) infection. This post-infectious autoimmune syndrome is called pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections (PANDAS) [13]. Although the exact mechanism remains to be elucidated, molecular mimicry in which antibodies initially develop to respond to GAS infection and cross-react with neural epitopes has been suggested as a possible developing path [14, 15]. In line with this theoretical link, patients with other systemic autoimmune diseases (SADs), such as systemic lupus erythematosus (SLE), has also been suggested to present higher rates of OCD [16]. Although the results to date are difficult to interpret as no discrete immune profile has emerged, there are unequivocal immune changes in at least some OCD patients.

Following the theoretical link, we hypothesized that a history of SADs increases the risk of the subsequent onset of OCD. To test our hypothesis, we designed a nationwide population-based study to investigate the incidence of OCD among patients with SADs. Knowing whether SADs are more frequently associated with OCD may lead to a better understanding of the role that the immune system plays in this disorder, and help guiding gene–environment interaction studies.

Methods

Data source

In 1995, the national health insurance program (NHIP) was implemented in Taiwan. In 2011, 22.6 million individuals from a total population of 23.0 million were enrolled in this insurance program. Currently, 99.6% of residents are covered by NHIP. The National Health Insurance Research Database (NHIRD) consisted almost every medical record reimbursed by the NHIP. The NHIRD scrambled patient and hospital's identification numbers. It also contained demographic information, such as dates of birth, gender, clinical diagnoses, department of clinical visit, ambulatory and inpatient care claims. The diagnosis codes were based on International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM). Two subsets of NHRID: Longitudinal Health Insurance Database 2000 (LHID2000) and Registry for Catastrophic Illness Database (RCID) were used for this study.

LHID2000 was representative of all NHIRD. It contained all the original claim data of 1,000,000 individuals (about 4% of the Taiwanese population) randomly selected from the NHIRD in 2000. There were no statistically significant differences in age, gender, and medical costs between LHID2000 patients and the original NHIRD.

The Taiwan NHIP has defined several categories of serious illnesses or injuries as "catastrophic illness." Patients had to undergo a rigorous regulatory review before obtaining a Catastrophic Illness Certificate (CIC). Patients with CIC received free medical care for the duration of the certificate's validity. Patients with CIC accounted for 7–8% of the insured Taiwanese population and were classified as RCID in the NHIRD.

Definition of SADs

SADs is one of the 30 categories of serious illnesses or injuries. Patients who have been diagnosed with such serious illnesses and undergo a rigorous regulatory review would be issued with a CIC. SADs are consisted of SLE (ICD-9-CM: 710.0), rheumatoid arthritis (714.0), polyarticular juvenile rheumatoid arthritis (714.30-714.33), systemic sclerosis (710.1), polymyositis (710.4), dermatomyositis (710.3), autoimmune vasculitis [polyarteritis nodosa (446.0), hypersensitivity angiitis (446.2), Wegener's granulomatosis (446.4), giant cell arteritis (446.5), thromboangiitis obliterans (443.1), Takayasu's disease (446.7), acute febrile mucocutaneous lymph node syndrome (446.1), Behçet's syndrome (136.1)], pemphigus (694.4), Sjögren's syndrome (710.2), Crohn's disease (555) and ulcerative colitis (556.0–556.6, 556.8–556.9) .

Study participants

We identified the SADs cohort from the RCID. The index date was defined as the first diagnosis date of any SADs. The compared cohort (control group) was free from any of the SADs sampled from LHID2000. We excluded those patients with missing data for birthday or gender information, those diagnosed with OCD (ICD-9-CM: 300.3) prior to index date, and those hospitalized with any other mental disorder (ICD-9-CM: 290–319) before the index date. We then selected 5 control patients for each SADs patient matching by index year. We then collected demographic characteristics of both cohorts including gender, age (less than 25, 25–50, and over 50 year-old), and follow-up duration. Diagram summarizing the enrollment process was present in Fig. 1.

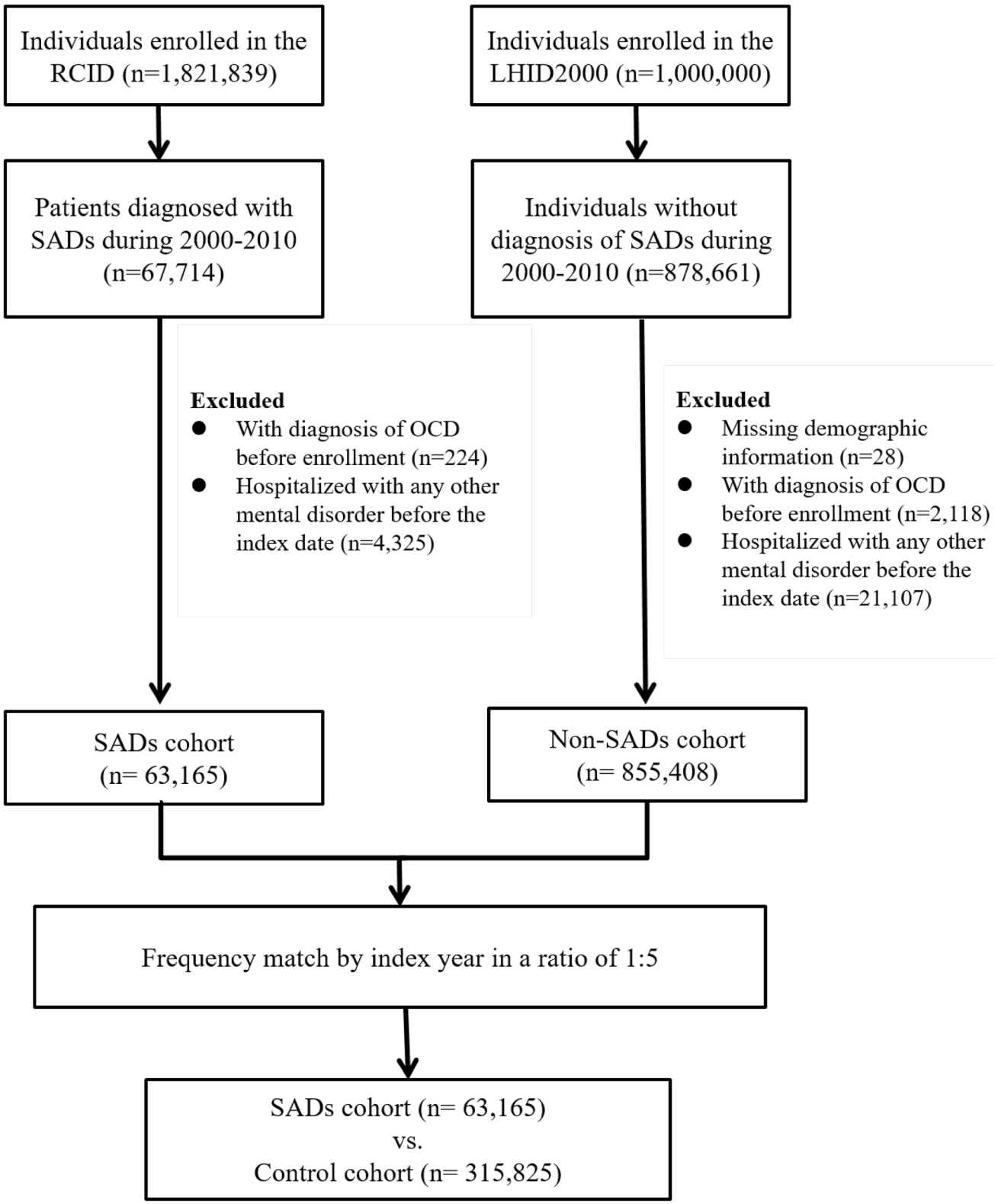

Fig. 1 Summary diagram of the enrollment process. *LHID2000* Longitudinal Health Insurance Database 2000, *RCID* Registry for Catastrophic Illness Database, *OCD* obsessive–compulsive disorder, *SADs* systemic autoimmune diseases

Covariates

We also investigated any potential risk factors in this study including the baseline comorbidities and the frequency of steroid use. The baseline comorbidities comprised of hypertension (ICD-9-CM: 401–405), hyperlipidemia (272), chronic obstructive pulmonary disease (491–492, 494 and 496), diabetes mellitus (250), asthma (493), chronic kidney disease (585), cerebrovascular disease (430–438), alcohol use disorder (303), liver cirrhosis (571), malignancies (140–239) and coronary artery disease (414). The frequency of steroid use was categorized as no use, infrequent user (the duration of steroid use was less than the median duration of steroid use in this dataset), and frequent user (the duration of steroid use was equal to or longer than the median duration).

Incidence of OCD

All study patients were followed up until newly diagnosed OCD, withdrawn from the NHIP or December 31, 2011 (whichever came first). A newly OCD had to meet following criteria: At least 2 clinical visits of OCD diagnoses (ICD-9-CM: 300.3) given by a clinical psychiatrist after the index date.

Statistical analysis

We compared baseline characteristic between patients with and without SADs using χ^2-tests (gender, age, baseline comorbidities and the frequency of steroid use) and Wilcoxon's rank-sum test (follow-up duration). Incidence rates (per 10,000 person-years) of OCD between patients with and without SADs were compared using a Cox proportional hazard model to estimate the hazard ratio (HR) and 95% confidence interval (95% CI). Next, a stratification analysis was conducted to examine whether HR differed between different age and gender groups, and the interaction between stratification variables was also examined. The cumulative incidence of OCD was estimated using the Kaplan–Meier method, and differences between cohorts were evaluated using the log-rank test. SAS 9.4 (SAS Institute Inc., Cary, NC, USA) was used for statistical analysis. A p value < 0.05 was considered as statistical significant.

Ethics statement

This study was approved by the Institutional Review Board of China Medical University (CMUH104-REC2-115).

Results

Patient characteristics

A total of 63,165 SADs patients and 315,825 control patients were included in our analysis. Table 1 showed baseline characteristics of both cohorts. In general, the distribution of gender and age were significantly different between the two cohorts. Compared to the control cohort, the SADs cohort displayed a higher prevalence of female (74.97% vs. 25.03%) which was consistent with the current understanding of SADs population. The mean age in SADs and control cohorts was around 46 and 36, respectively. The mean follow-up years were 5.46 and 6.35 for SADs and control cohorts, respectively. The majority of comorbidities listed and the frequency of steroid use showed statistically different between the two groups.

Incidence of OCD

As shown in Table 2, there were totally 452 incident OCD patients during the follow-up period (97 and 355 incident OCD patients in the SADs and control cohorts, respectively). The SADs cohort had almost 1.5-fold incidence rate than the control cohort (2.7 vs. 1.8 per 10,000 person-years). The adjusted HR (aHR) is 1.85 after adjusted for other demographic characteristics. Kaplan–Meier analysis demonstrated that the cumulative incidence curves of OCD was significantly higher in SADs cohort than in the control cohort (log-rank test, $p < 0.0001$) (Fig. 2).

In addition, females and males had similar incidence rate of OCD. Subjects less than or equal to 50 year-old had higher OCD incidence rate than subjects over 50 year-old (aHR: 3.41 for patients aged less than 25 year-old and 2.29 for patients aged between 25 and 50 year-old). As to other comorbidities, alcohol use disorder (7.24), liver cirrhosis (1.65), and malignancies (1.77) might be the potential risk factors for incident OCD. Furthermore, higher frequency of steroid use might have the protective association with incident OCD (aHR: 0.57 and 0.58 for infrequent and frequent user, respectively).

Table 3 showed the stratification analysis by gender and age. The two gender groups with SADs showed the same risky association with OCD, with the significant difference in female (aHR: 2.15) and the marginal difference (1.43) in the male. Otherwise, each age group with SADs had the same risky association with OCD, with a significant difference in patients aged 25–50 years (2.58) and a marginal difference in those under 25 years (1.41) and over 50 years (1.37).

Table 1 Demographic characteristics of patients with and without SADs

Variable	SADs patients				*p* value
	No *n* = 315,825 (83.33%)		Yes *n* = 63,165 (16.67%)		
	n	%	*n*	%	
Gender[a]					< 0.01
Female	155,552	49.25	47,353	74.97	
Male	160,273	50.75	15,812	25.03	
Age at baseline, years[a]					< 0.01
< 25	102,215	32.36	9078	14.37	
25–50	135,473	42.89	24,569	38.9	
> 50	78,137	24.74	29,518	46.73	
Mean (SD)	36.44 (19.65)		46.46 (19.11)		< 0.01
Comorbidities[a]					
Hypertension	46,599	14.75	16,853	26.68	< 0.01
Dyslipidemia	32,919	10.42	10,263	16.25	< 0.01
COPD	17,491	5.54	7966	12.61	< 0.01
Diabetes mellitus	21,480	6.8	7414	11.74	< 0.01
Asthma	19,650	6.22	5896	9.33	< 0.01
Chronic kidney disease	2250	0.71	1416	2.24	< 0.01
Cerebrovascular disease	13,750	4.35	5031	7.96	< 0.01
Alcohol use disorder	196	0.06	60	0.09	< 0.01
Liver cirrhosis	27,972	8.86	13,646	21.6	< 0.01
Malignancies	44,893	14.21	19,121	30.27	< 0.01
Coronary artery disease	14,526	4.6	6225	9.86	< 0.01
Frequency of steroid use[a]					< 0.01
No use	166,945	52.86	8320	13.17	
Infrequent user	81,229	25.72	4055	6.42	
Frequent user	67,651	21.42	50,790	80.41	
Follow-up period, years, median[b]	6.35		5.46		< 0.01

SADs systemic autoimmune diseases, *SD* standard deviation, *COPD* chronic obstructive pulmonary disease

[a]Chi-square test

[b]Wilcoxon's rank-sum test

Table 4 revealed that SLE (aHR: 1.65), dermatomyositis (3.25), and Sjögren's syndrome (2.38) had a higher risk of developing subsequent OCD among the studied SADs.

Discussion

This population-based cohort study systematically examined whether SADs were associated with an increased risk of the subsequent onset of OCD using an age-matched cohort and a maximal follow-up period of 10 years. The major finding of our study was the discovery of a higher incidence of subsequent OCD among patients with SADs. Specifically, the risk of OCD was observed to be significant increase in SLE, dermatomyositis and Sjögren's syndrome. Furthermore, our study revealed some potential risk factors for developing OCD include younger age (less than or equal to 50-year-old) and some comorbidities (alcohol use disorder, liver cirrhosis and malignancies). Finally, our study revealed that use of steroid was a potential protective factor for developing OCD.

Possible explanations for SADs increasing the risk of subsequent OCD

This study revealed that patients with SADs were at a higher risk of subsequent OCD. The following possible hypotheses are worth considering. First, SADs cause an organic form of OCD due to the pathophysiologic sequelae of brain involvement. For example, peripheral cytokines activated by SADs reach the brain through a variety of mechanisms, including a leaky brain barrier, active transport, endothelial cell activation, and cytokine receptor binding [17]. Cytokines created by autoimmune processes play a vital role in mediating crosstalk between the immune system and the brain and are therefore potential contributors to the development of OCD [18]. Second,

Table 2 Cox model with hazard ratios and 95% confidence intervals for OCD associated with and without SADs

Variable	OCD no. ($n=452$)	Person-years	IR[a]	Crude[b]			Adjusted[c]		
				HR	(95% CI)	*p* value	HR	(95% CI)	*p* value
SADs									
No	355	2,013,950	1.8	1	Reference		1	Reference	
Yes	97	360,161	2.7	1.53	(1.22–1.92)	<0.01	1.85	(1.41–2.43)	<0.01
Gender									
Female	263	1,272,090	2.1	1.21	(1–1.45)	0.05	1.15	(0.94–1.39)	0.17
Male	189	1,102,021	1.7	1	Reference		1	Reference	
Age at baseline, years									
<25	180	777,503	2.3	1.92	(1.46–2.53)	<0.01	3.41	(2.4–4.86)	<0.01
25–50	201	1,007,062	2.0	1.66	(1.26–2.17)	<0.01	2.29	(1.66–3.16)	<0.01
>50	71	589,546	1.2	1	Reference		1	Reference	
Comorbidities									
Hypertension	59	342,256	1.7	0.89	(0.68–1.18)	0.42	1.17	(0.82–1.67)	0.40
Dyslipidemia	46	229,483	2.0	1.06	(0.78–1.44)	0.69	1.16	(0.8–1.68)	0.44
COPD	27	131,634	2.1	1.09	(0.74–1.6)	0.68	1.26	(0.82–1.93)	0.30
Diabetes mellitus	29	151,825	1.9	1.01	(0.69–1.47)	0.97	1.09	(0.7–1.69)	0.71
Asthma	25	137,727	1.8	0.95	(0.64–1.43)	0.82	0.9	(0.59–1.37)	0.62
Chronic kidney disease	2	16,232	1.2	0.65	(0.16–2.61)	0.55	0.61	(0.15–2.47)	0.49
Cerebrovascular disease	22	96,817	2.3	1.21	(0.79–1.86)	0.39	1.5	(0.93–2.41)	0.10
Alcohol use disorder	2	1228	16.3	8.64	(2.15–34.64)	<0.01	7.24	(1.78–29.39)	<0.01
Liver cirrhosis	65	223,415	2.9	1.62	(1.25–2.11)	<0.01	1.65	(1.23–2.22)	<0.01
Malignancies	100	337,863	3.0	1.72	(1.38–2.15)	<0.01	1.77	(1.39–2.26)	<0.01
Coronary artery disease	18	104,096	1.7	0.91	(0.57–1.46)	0.69	0.96	(0.56–1.63)	0.88
Frequency of steroid use									
No use	222	951,873	2.3	1	Reference		1	Reference	
Infrequent user	85	598,838	1.4	0.6	(0.47–0.78)	<0.01	0.57	(0.44–0.73)	<0.01
Frequent user	145	823,400	1.8	0.75	(0.61–0.92)	<0.01	0.58	(0.45–0.74)	<0.01

OCD obsessive–compulsive disorder, *SADs* systemic autoimmune diseases, *HR* hazard ratio, *CI* confidence interval, *COPD* chronic obstructive pulmonary disease

[a]IR: incidence rates, per 10,000 person-years

[a]Crude HR represented relative hazard ratio

[c]Adjusted HR represented adjusted hazard ratio for SADs, gender, age, baseline comorbidities and the frequency of steroid use in Cox proportional hazard regression

SADs exacerbate the OCD syndrome in the presence of subclinical OCD vulnerability. The mechanisms could be direct (acting on the biological substrate of OCD) or indirect (acting on vulnerability to depression or other anxiety disorder that might then exacerbate OCD) [19]. Third, SADs and OCD have a shared etiology. The possibility of a common genetic etiology for SADs and OCD was supported by some SADs and OCD co-aggregate in families [20–22]. SADs may activate the presentation of OCD in vulnerable patients through shared genetic or epigenetic mechanisms. Future studies are needed to reveal the underlying mechanisms.

SLE, dermatomyositis and Sjögren's syndrome may increase the risk of subsequent OCD

Previous epidemiological study has documented a direct link between SLE and the subsequent OCD [16]. Except for SLE, our analysis further revealed that dermatomyositis and Sjögren's syndrome also had a higher risk of developing subsequent OCD.

Dermatomyositis is one of the idiopathic inflammatory myopathies characterized by progressive symmetrical proximal muscle weakness and a characteristic rash [23]. Although the process primarily attacks the skin and the muscles, it is a systemic disease with frequent manifestations in the gastrointestinal tract and pulmonary system [23].

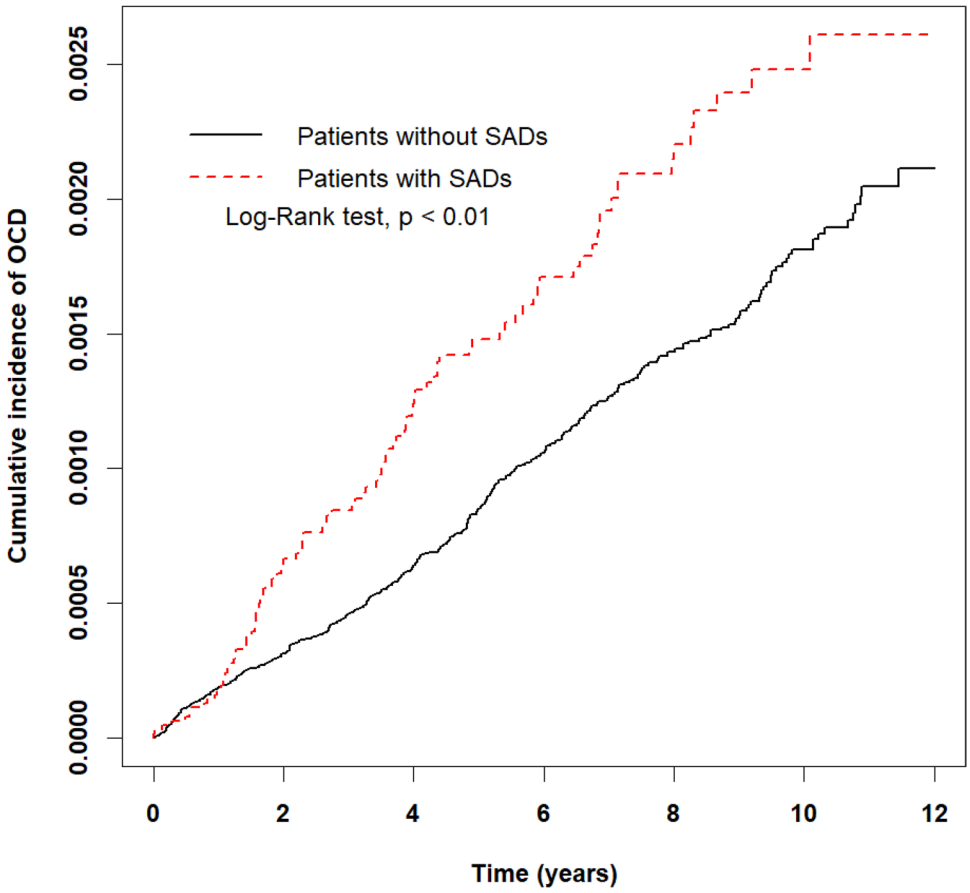

Fig. 2 Cumulative incidence of OCD for patients with SADs and without SADs. Kaplan–Meier analysis demonstrated that the cumulative incidence curves of OCD was significantly higher in patients with SADs than in patients without SADs (log-rank test, $p < 0.0001$). *OCD* obsessive–compulsive disorder, *SADs* systemic autoimmune diseases

Table 3 Cox model with hazard ratios and 95% confidence intervals for OCD associated with and without SADs stratified by gender and age group

Variable	SADs						Crude HR[b]	Adjusted HR[c]	*p* for interaction
	Non-SADs			SADs					
	Event	Person-years	IR[a]	Event	Person-years	IR[a]			
Gender									0.13
Female	182	996,287	0.18	81	275,803	0.29	1.61 (1.24–2.09)*	2.15 (1.57–2.95)*	
Male	173	1,017,663	0.17	16	84,358	0.19	1.12 (0.67–1.88)	1.43 (0.82–2.47)	
Age group, year									0.68
< 25	165	719,380	0.23	15	58,123.6	0.26	1.14 (0.67–1.93)	1.41 (0.8–2.48)	
25–50	138	859,068	0.16	63	147,994	0.43	2.64 (1.96–3.56)*	2.58 (1.79–3.72)*	
> 50	52	435,503	0.12	19	154,043	0.12	1.03 (0.61–1.74)	1.37 (0.75–2.5)	

OCD obsessive–compulsive disorder, *SADs* systemic autoimmune diseases, *HR* hazard ratio, *CI* confidence interval

*< 0.05

[a]IR: incidence rates, per 10,000 person-years

[b]Crude HR represented relative hazard ratio

[c]Adjusted HR represented adjusted hazard ratio for SADs, gender, age, baseline comorbidities and the frequency of steroid use in Cox proportional hazard regression

Dermatomyositis is rarely associated with brain involvement. There was only one report describing the psychiatric comorbidity of dermatomyositis including depression and anxiety [24]. Our study provided the initial evidence there might be some relationships between dermatomyositis and OCD.

Table 4 Incidence of OCD in patients with different SADs

SADs	*n*	No. of OCD	Person-years	IR[a]	Crude HR[b] (95% CI)	Adjusted HR[c] (95% CI)
Systemic lupus erythematosus	11,865	23	72,260	3.2	1.81 (1.19–2.75)*	1.65 (1.07–2.54)*
Rheumatoid arthritis	28,501	34	172,649	2.0	1.12 (0.79–1.59)	1.25 (0.86–1.81)
Systemic sclerosis	1476	3	8154	3.7	2.1 (0.67–6.54)	2.19 (0.7–6.87)
Polymyositis	673	2	3410	5.9	3.37 (0.84–13.48)	3.13 (0.78–12.64)
Dermatomyositis	948	3	4929	6.1	3.46 (1.11–10.78)*	3.25 (1.04–10.17)*
Vasculitis	6803	11	37,363	2.9	1.68 (0.92–3.06)	1.32 (0.72–2.43)
Pemphigus	895	2	4616	4.3	2.48 (0.62–9.96)	2.78 (0.69–11.19)
Sicca syndrome	11,339	24	57,655	4.2	2.39 (1.58–3.62)*	2.38 (1.53–3.72)*
Crohn's disease	480	1	2539	3.9	2.26 (0.32–16.07)	1.97 (0.28–14.08)
Ulcerative colitis	1229	1	4525	2.2	1.32 (0.19–9.43)	1.33 (0.19–9.5)

OCD obsessive–compulsive disorder, *SADs* systemic autoimmune diseases, *HR* hazard ratio, *CI* confidence interval

*<0.05

[a]IR: incidence rates per 10,000 person-years

[b]Crude HR represented relative hazard ratio

[c]Adjusted HR represented adjusted hazard ratio for SADs, gender, age, baseline comorbidities and the frequency of steroid use in Cox proportional hazard regression

Sjögren's syndrome is characterized by chronic inflammation and lymphocytic infiltration of exocrine lacrimal and saliva glands, causing dry mouth and dry eye [25]. Other than affecting glandular organs, Sjögren's syndrome can also have brain manifestations, including focal neurological deficits, diffuse cerebral involvement, and psychiatric disorders [26]. There was only one study revealing that patients with Sjögren's syndrome had higher anxiety disorder comorbidity including OCD than patients without Sjögren's syndrome [27]. Our study provided further evidence supporting the relationship between Sjögren's syndrome and OCD.

Potential risk and protective factors for developing subsequent OCD

In Taiwan, the incidence of OCD increased with age in adolescent and early adult patients of both gender, peaking at the age of 18–24 years in males and 35–44 years in females [2]. The male/female ratio of incidence of OCD was slightly higher in the 18–24 age group and slightly lower in the 35–64 age group [2]. For those above age 65, the incidence of clinically-recognized OCD markedly decreased in both genders [2]. These findings might explain why a higher incidence of subsequent OCD was found in patients with SADs aged less than 50 years.

Our analysis revealed that alcohol use disorder, liver cirrhosis, and malignancies were potential risk factors associated with subsequent OCD in patients with SADs. Alcohol use disorder and OCD share certain symptom characteristics. The craving for alcohol seen in alcohol use disorder resembles obsessive thought patterns and these alcohol abusers often have a compulsion to use alcohol [28, 29]. The similar symptom characteristics might contribute for the higher comorbidity of alcohol use disorder and OCD in patients with SADs [28, 29]. In addition, evidence has shown that chronic inflammatory processes of liver cirrhosis and malignancies, such as the pathophysiology of SADs, involve cytokine interactions, and these combined chronic inflammatory effects could further increase the risk of developing OCD [30–32].

Our study revealed that use of steroid was a potential protective factor for developing OCD. In our SAD cohort, OCD might be a consequence of autoimmune reactions affecting the brain and use of steroid might decrease the inflammation resulting in lower OCD incidence.

Limitations

Our study aims to examine SADs as a risk factor for the development of OCD. A large age-matched population-based cohort with many potential risk factors adjusted constitute the strengths of our study. However, several limitations that are inherent in the use of claims databases should be considered. First, not all forms of SADs were studied because some SADs were not included in catastrophic diseases defined by the Taiwanese NHIP, such as autoimmune hepatitis and autoimmune thyroiditis. Second, for a reliable diagnosis, only patients with SADs CIC were included, which might limit the generalizability of our results. Third, the current study is an observational design rather than an experimental design. Since both OCD and SADs are progressive diseases, it is hard to distinguish which disease began to grow first before the clinical symptoms appears. For example, some patients with first onset OCD may have

had obsessive–compulsive symptoms in childhood that they cannot remember or are not identified as OCD. Finally, information was unavailable on several demographic variables such as smoking, education level, life style and family history, which might have provided useful information regarding factors that are potentially associated with SADs and OCD.

Conclusion

This study revealed that SADs were associated with an increased risk of OCD development, suggesting that the abnormal autoimmune process was associated with increased expression of psychiatric disturbances. Further prospective clinical studies on the relationship between SADs and OCD are warranted.

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Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

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