Original Article

Higher Risk for Papilledema in Inflammatory Bowel Disease: A Nationwide Population-Based Study Cohort Study in Taiwan

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Key Words
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Retrospective cohort study

Purpose. Inflammatory bowel disease (IBD) is a multifactorial disease with many ocular complications, including papilledema. Using the National Health Insurance Research Database (NHIRD), this study aimed to evaluate whether patients with IBD are exposed to the potential risk of papilledema.
Methods. Data were collected from the NHIRD over a 14-year period. Variables were analyzed with the Pearson chi-square test and Fisher's exact test. The risk factors for disease development were examined by the adjusted hazard ratio (aHR). Kaplan-Meier analysis was performed to compare the survival of papilledema.
Results. A total of 4498 patients with IBD were enrolled in the study cohort, and there were 17992 patients without IBD in the control cohort. The papilledema incidence rate was higher in the study cohort than in the control cohort (aHR = 4.330, p = 0.012). Papilledema occurred equally in both genders. The overall incidence of papilledema was 12.67 per 100,000 person-years in the study cohort and 3.44 per 100,000 person-years in the control cohort. For IBD patients, male, young age onset, sleep apnea, hypertension, medicine use (tetracycline, minocycline, doxycycline), spring are the predisposing factors of developing papilledema.
Conclusions. Patients with IBD were associated with an increased risk of papilledema. Patients with IBD should stay alert for any potential visual impairment disorder. Further prospective studies examining the relationship between IBD and papilledema may provide more information.
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Inflammatory bowel disease (IBD) comprises two intestinal disorders, including ulcerative colitis (UC) and Crohn's disease (CD). It is a chronic, multifactorial disease associated with mucosal immune re-

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action stimulated by the gut microbiota.[1] The incidence in Asia is much lower than in Western countries but has increased in recent decades. There are multiple extraintestinal manifestations, including the skin, joints, liver and eye.[2,3] However, ocular involvement is infrequent, accounting for less than 10% of cases.[4] There are some theories as to the pathogenesis of ocular inflammation in IBD, one is immune complex type hypersensitivity reaction to a colonic antigen,[5] another is cytotoxic antibodies or delayed-type hypersensitivity reactions.[4] Steroids remain one of the most important IBD treatments.[6] The ocular structures affected by IBD include the orbital tissue, uvea, lens, trabecular meshwork, optic nerve, cranial nerve and retina.[7-9]

The optic nerve complications in IBD include neuroretinitis,[10] optic neuritis,[11] ischemic optic neuropathy[12] and papilledema. The pathogenesis of papilledema is unclear. It may be related to long term use of steroids and subsequent sudden withdrawal of the steroid, followed by intracranial hypertension.[6,7]

The aim of our retrospective study was to conduct a nationwide review of the medical records of patients receiving a diagnosis of IBD between January 2000 and December 2013, to evaluate the risk of the complications of papilledema related to IBDs compared to non-IBD patients in Taiwan.

Methods

Data source

This study was approved by the Institutional Review Board of the Tri-Service General Hospital (TSGH IRB No. 2-105-05-082; Taipei, Taiwan). Medical data were extracted from the National Health Insurance Research Database (NHIRD) for the years 2000 to 2013. The National Health Insurance (NHI) is a social health insurance system comprising almost all Taiwanese citizens. Approximately 23 million people are registered in the NHI system.[6,8] The NHIRD contains comprehensive information including age, sex, index year, clinical visits, and diagnostic codes. The International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) was used to define the diagnostic codes.

Sample participants

As shown in Fig. 1, we identified the patients aged 20 years or older with newly diagnosed IBD (ICD-9-CM codes 555, 556) for the period from 2000 to 2013. The definition of IBD included ulcerative colitis and Crohn's disease. Those with a documented IBD before January 1, 2000 or with incomplete medical information were excluded to ensure the first diagnosis of IBD. We also excluded people with a history of papilledema (ICD-9-CM code: 377.00, 377.01). For each identified patient with IBD, four comparison patients were randomly identified and frequency-matched according to the age (each 5-year span), sex, and year of index date for the non-IBD cohort.

Outcome

The outcome of interest was incident papilledema. (ICD-9-CM code: 377.00, 377.01). Papilledema related to brain tumor (ICD-9-CM codes:239.6, 191.x) was excluded. The length of follow-up for people who developed incident papilledema was the period from the index date to the date of the first diagnosis of papilledema in inpatient or outpatient records. We also used ICD-9-CM codes to identify, differentiate, and

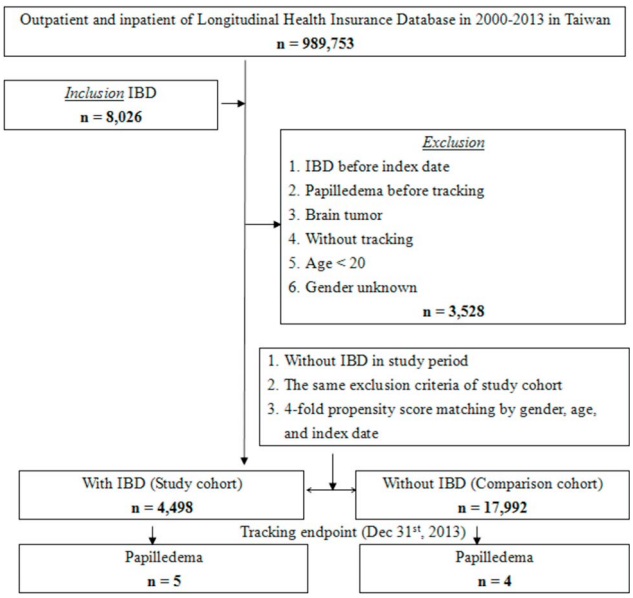

Fig. 1. The flowchart of study sample selection. IBD, inflammatory bowel disease.

analyze comorbidities in papilledema patients, including sleep apnea (ICD-9-CM codes 780.51, 780.53, 780.57), hypertension (HTN) (ICD-9-CM codes 401.xx through 405.xx). Based on the findings of previous studies, there offered some evidence that cycline antibiotics may increase the risk of papilledema,[13,14] so we also analyzed the medication use of tetracycline (drug code: AC04963100, AC049631G0, AC12059100, AC12639100, AC15791100, AC157911G0, AC22572100, AC225721G0), minocycline (drug code: A032761100, A033214100, A035969100, A036813100, A043111100, AB40644100, AC33471100, AC35868100, AC36266100, AC36281100, AC36667100, AC36815100, AC36940100, AC38761100, AC39074100, AC39600100) and doxycycline (drug code: A009397100, AC07233100, AC12782100, AC16227100, AC19254100, AC192541G0, AC23648100, AC236481G0, AC24085100, AC31219100, AC34900100, AC35692100, AC356921G0). We replaced the Charlson comorbidity index (CCI) with the (CCI_R) (CCI excluding sleep apnea, hypertension [HTN], medication use including tetracycline, minocycline and doxycycline because the removed diseases were also variables in this study.

Statistical analysis

The Pearson chi-square test and Fisher's exact test were used to evaluate differences in categorical variables, such as gender, age group, and insurance premium, and statistical significance was defined as $p < 0.05$. After adjusting the variables, univariate and multivariate Cox regression analyses were employed to evaluate the adjusted hazard ratio (aHR) for the influence of IBD on developing papilledema. Kaplan-Meier analysis was performed to estimate papilledema survival in these two cohorts. All statistical analyses were performed using SPSS software (Version 22.0; SPSS Inc., Chicago, IL, USA).

Results

Table 1 shows the demographic characteristics of both cohorts. The mean age was 55.37 ± 17.44 years in the study cohort and 55.14 ± 17.43 years in the control cohort. The difference was not significant ($p = 0.420$). In addition, there was no significant difference in gender or age group for both groups. Regarding insurance premiums New Taiwan dollar (NT$) in both cohorts, almost all of the enrolled patients were in the < 18,000 group (98.44%), followed by the 18,000 to 34,999 group (1.19%) and the > 35,000 group (0.37%). There was no significant difference in the insurance premium (NT$) in both groups ($p = 0.308$). In terms of the comorbidity comparison, patients with IBD had higher rates of sleep apnea, HTN, medication use including tetracycline, minocycline and doxycycline. The CCI_R value was 1.25 ± 1.38 in the study cohort and 1.01 ± 1.17 in the control cohort ($p < 0.001$). In addition, more individuals in the study cohort than in the control cohort lived in southern, eastern Taiwan and lower urbanized areas and received therapy in local hospitals ($p < 0.001$).

The papilledema survival rate was calculated by the Kaplan-Meier method (Fig. 2). The results showed the study cohort had a significantly lower papilledema survival rate than the control cohort (log-rank test $p = 0.035$). The papilledema survival rate increased steadily annually to 0.37% (90/24 426 individuals) at the endpoint in the study cohort and to 0.29% (72/24 426 individuals) in the control cohort. Further, the difference between both groups was significant during each year of follow-up ($p < 0.050$ during each year).

Table 2 shows the Cox regression analysis of the risk factors for papilledema. After adjusting for IBD, gender, age groups (20-59 years and ≥ 60 years), insurance premium and preexisting comorbidities including sleep apnea, HTN, medication use including tetracycline, minocycline and doxycycline, only IBD (aHR = 4.330, 95% confidence interval [CI] = 1.130-16.590, $p = 0.012$) and age groups (20-29 years old) (aHR = 15.024, $p = 0.017$) patients showed an increased risk of papilledema diagnosis.

In addition, patients with HTN had an increased risk of developing papilledema than those without HTN (aHR = 2.998, $p < 0.001$). Patients with other comorbidities, such as age groups and insurance premium as well as other chronic diseases were not significantly associated with papilledema diagnosis ac-

Table 1. Characteristics of study in the baseline

IBD	Total		With IBD		Without IBD		*p*
Variables	n	%	n	%	n	%	
Total	22,490		4,498	20.00	17,992	80.00	
Gender							0.999
Male	12,130	53.94	2,426	53.94	9,704	53.94	
Female	10,360	46.06	2,072	46.06	8,288	46.06	
Age (years)	55.18 ± 17.43		55.37 ± 17.44		55.14 ± 17.43		0.420
Age groups (years)							0.999
20-29	2,230	9.92	446	9.92	1,784	9.92	
30-39	3,265	14.52	653	14.52	2,612	14.52	
40-49	3,370	14.98	674	14.98	2,696	14.98	
50-59	3,195	14.21	639	14.21	2,556	14.21	
≥ 60	10,430	46.38	2,086	46.38	8,344	46.38	
Insured premium (NT$)							0.308
< 18,000	22,139	98.44	4,438	98.67	17,701	98.38	
18,000-34,999	268	1.19	48	1.07	220	1.22	
≥ 35,000	83	0.37	12	0.27	71	0.39	
Comorbidity							
Sleep apnea	751	3.34	373	8.29	378	2.10	< 0.001
HTN	1,467	6.52	489	10.87	978	5.44	< 0.001
Medication							
Tetracycline	2,798	12.44	785	17.45	2,013	11.19	< 0.001
Minocycline	2,602	11.57	718	15.96	1,884	10.47	< 0.001
Doxycycline	2,648	11.77	737	16.39	1,911	10.62	< 0.001
CCI_R	1.06 ± 1.22		1.25 ± 1.38		1.01 ± 1.17		< 0.001
Season							0.999
Spring (Mar-May)	6,605	29.37	1,321	29.37	5,284	29.37	
Summer (Jun-Aug)	4,955	22.03	991	22.03	3,964	22.03	
Autumn (Sep-Nov)	4,325	19.23	865	19.23	3,460	19.23	
Winter (Dec-Feb)	6,605	29.37	1,321	29.37	5,284	29.37	
Location							< 0.001
Northern Taiwan	8,787	39.07	1,570	34.90	7,217	40.11	
Middle Taiwan	6,156	27.37	1,185	26.35	4,971	27.63	
Southern Taiwan	5,934	26.39	1,327	29.50	4,607	25.61	
Eastern Taiwan	1,520	6.76	393	8.74	1,127	6.26	
Outlets islands	93	0.41	23	0.51	70	0.39	
Urbanization level							< 0.001
1 (The highest)	7,459	33.17	1,259	27.99	6,200	34.46	
2	9,230	41.04	1,644	36.55	7,586	42.16	
3	1,863	8.28	441	9.80	1,422	7.90	
4 (The lowest)	3,938	17.51	1,154	25.66	2,784	15.47	
Level of care							< 0.001
Hospital center	6,389	28.41	864	19.21	5,525	30.71	
Regional hospital	6,631	29.48	1,114	24.77	5,517	30.66	
Local hospital	9,470	42.11	2,520	56.02	6,950	38.63	

Note. CCI_R, Charlson comorbidity index removed sleep apnea; HTN, medication use of tetracycline, minocycline and doxycycline; HTN, hypertension.
p: Chi-square/Fisher exact test on category variables and t-test on continue variables.

cording to the hazard ratios (all $p > 0.05$).

In the subgroup analysis comparing patients with and without IBD (Table 3), the overall incidence of papilledema was 12.67 per 100,000 person-years in the study cohort and 3.44 per 100,000 person-years in the control cohort. Male IBD patients showed an increased risk of developing papilledema (aHR = 5.340, $p < 0.001$). In the age group analysis, IBD patients in 20-29 and ≥ 60 years age groups were independently associated with an increased risk following papilledema

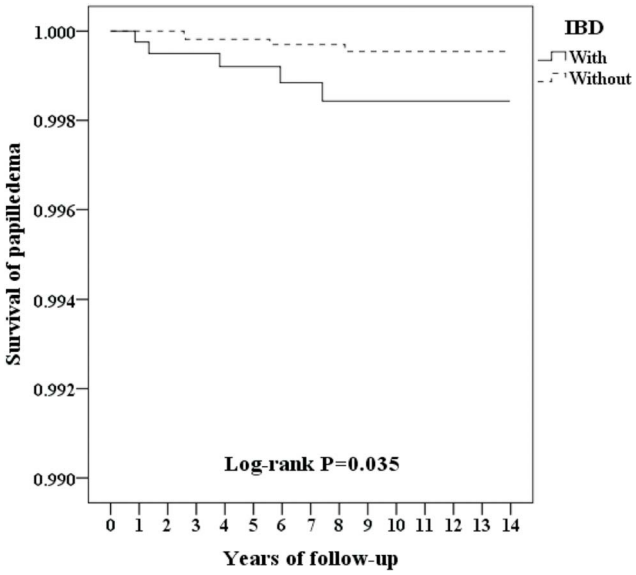

Fig. 2. Kaplan-Meier for survival of papilledema among aged 20 and over stratified by IBD with log-rank test. IBD, inflammatory bowel disease.

diagnosis than patients without IBD (aHR = 10.484 in the age group 20-29 years and 5.177 in the age group of ≥ 60 years, $p < 0.001$). In the insured premium group analysis, IBD patients in the < 18,000 group showed an increased risk of developing papilledema (aHR = 4.330, $p = 0.012$). In the preexisting group analysis, IBD patients with sleep apnea, HTN, medication use including tetracycline, minocycline and doxycycline displayed an increased risk of developing papilledema (aHR = 3.955, $p = 0.018$ in sleep apnea; aHR = 10.407, $p < 0.001$ in HTN; aHR = 6.672, $p < 0.001$ in tetracycline use; aHR = 5.120, $p < 0.001$ in minocycline use; aHR = 6.746, $p < 0.001$ in doxycycline use). In the season group analysis, IBD patients in the spring group showed an increased risk of developing papilledema (aHR = 7.071, $p < 0.001$). In the level of care group analysis, IBD patients in the hospital center group displayed an increased risk of developing papilledema (aHR = 8.208, $p < 0.001$).

Discussion

This population-based study enrolled 4498 patients in the study cohort and 17992 patients in the control cohort. We found the rate of papilledema development was significantly higher in the study cohort (IBD patients) than in the control cohort. Kaplan-Meier analysis also indicated the survival rate of papilledema development significantly decreased in the study cohort in each year. To our knowledge, there is no large population-based study evaluating the relationship between these two diseases. Only two case reports stated the relationship between these two diseases.[12,15]

The precise mechanism of papilledema following IBD is poorly understood. The term "papilledema" is defined as optic disc edema secondary to intracranial hypertension (IH). There are three hypothesesas to the reason for IH occurrence. First, it has been suggested IH may be related to cerebral vein and sinus thrombosis in patients with defective coagulation mechanisms and hyperviscosity rather than steroid use. It is suggested there are some abnormalities in the blood clotting system of IBD patients, which may predispose them to vascular incidents.[16] Second, according to some case reports, sudden withdrawn of steroidsis associated with IH in some IBD patients through an unknown mechanism. IH related to drugs rarely occurs and has been reported with the use of oral contraceptives, nalidixic acid[17] and corticosteroids. IH usually occurs at the onset of withdrawal from steroids following long-term use, in diseases such as asthma,[18,19] nephrotic syndrome,[20,21] psoriatic arthritis, polyarthritis, the adrenogenital syndrome, and topical treatment for eczema and psoriasis.[22,23] Third, IH was found in IBD patients treated with drugs other than steroids, including mesalamine, sulfasalazine or mesalazine.[24-26]

Regarding the demographic findings, papilledema developed from any cause of IH may occur at any age, gender or racial group.[27] However, it is more common in women from the ages of 15 to 40 years.[7] In addition, cases of IH related to steroid treatment were reported to occur more in younger children.[13] Our study revealed no gender predominance (aHR = 1.132, $p = 0.855$) among papilledema patients. The age group analysis revealed significantly higher risk of papilledema development in younger patients (20-29 years, aHR = 15.024, $p = 0.017$).

This study has several limitations. First, we supposed the correlation between IBD and papilledema is

Table 2. Factors of papilledema by using Cox regression

Variables	Crude HR	95% CI	95% CI	*p*	Adjusted HR	95% CI	95% CI	*p*
IBD								
Without	Reference				Reference			
With	4.121	1.076	14.421	0.035	4.330	1.130	16.590	0.012
Gender								
Male	1.865	0.488	4.673	0.712	1.132	0.301	4.262	0.855
Female	Reference				Reference			
Age groups (yrs)								
20-29	19.985	2.235	188.452	0.003	15.024	1.639	137.718	0.017
30-39	0.000	-	-	0.989	0.000	-	-	0.991
40-49	0.842	0.121	6.624	0.713	0.736	0.090	6.034	0.775
50-59	0.000	-	-	0.989	0.000	-	-	0.996
≥ 60	Reference				Reference			
Insured premium (NT$)								
< 18,000	Reference				Reference			
18,000-34,999	0.000	-	-	0.986	0.000	-	-	0.989
≥ 35,000	0.000	-	-	0.994	0.000	-	-	0.997
Sleep apnea								
Without	Reference				Reference			
With	1.896	1.001	2.897	0.049	1.752	0.842	2.776	0.158
HTN								
Without	Reference				Reference			
With	3.102	1.289	5.898	< 0.001	2.998	1.184	5.230	< 0.001
Tetracycline								
Without	Reference				Reference			
With	1.562	0.613	2.876	0.252	1.601	0.756	2.897	0.297
Minocycline								
Without	Reference				Reference			
With	1.423	0.745	2.775	0.284	1.382	0.642	2.684	0.301
Doxycycline								
Without	Reference				Reference			
With	1.876	0.568	2.318	0.225	1.227	0.443	2.201	0.286
CCI_R	1.245	1.103	1.338	< 0.001	1.212	1.099	1.318	< 0.001
Season								
Spring	Reference				Reference			
Summer	0.468	0.124	2.801	0.345	0.362	0.070	1.878	0.227
Autumn	0.298	0.113	2.373	0.255	0.166	0.019	1.427	0.102
Winter	0.286	0.101	2.584	0.297	0.193	0.023	1.655	0.134
Location								
Northern Taiwan	Reference				Multicollinearity with urbanization level			
Middle Taiwan	0.740	0.112	4.892	0.755	Multicollinearity with urbanization level			
Southern Taiwan	1.223	0.228	6.554	0.814	Multicollinearity with urbanization level			
Eastern Taiwan	1.252	0.107	12.364	0.907	Multicollinearity with urbanization level			
Outlets islands	0.000	-	-	0.996	Multicollinearity with urbanization level			
Urbanization level								
1 (The highest)	0.301	0.028	3.334	0.273	0.203	0.012	3.322	0.264
2	0.998	0.133	6.285	0.981	1.001	0.148	6.786	0.976
3	0.000	-	-	0.980	0.000	-	-	0.983
4 (The lowest)	Reference				Reference			
Level of care								
Hospital center	2.672	0.488	19.024	0.403	2.596	0.363	18.494	0.342
Regional hospital	1.132	0.254	6.786	0.992	1.000	0.158	6.369	0.985
Local hospital	Reference				Reference			

HR, hazard ratio; CI, confidence interval; HTN, hypertension; IBD, inflammatory bowel disease; Adjusted HR, adjusted variables are listed.

p: Chi-square/Fisher exact test on category variables and t-test on continue variables.

Table 3. Factors of papilledema stratified by variables listed in the table by using Cox regression

	With IBD			Without IBD			Ratio	With vs. Without (Reference)			
	Events	PYs	Rate	Events	PYs	Rate		Adjusted HR	95% CI	95% CI	*p*
Total	5	39,458.90	12.67	4	116,148.37	3.44	3.679	4.330	1.130	16.590	0.012
Gender											
Male	3	20,459.64	14.66	2	61,890.13	3.23	4.537	5.340	1.394	20.459	< 0.001
Female	2	18,999.26	10.53	2	54,258.24	3.69	2.856	3.361	0.877	12.876	0.067
Age groups (yrs)											
20-29	2	274.93	727.47	1	1,224.67	81.65	8.909	10.484	2.736	40.170	< 0.001
30-39	0	2,678.89	0.00	0	7,952.56	0.00	-	-	-	-	0.975
40-49	0	5,676.01	0.00	1	12,984.02	7.70	0.000	0.000	-	-	0.913
50-59	0	6,119.22	0.00	0	16,911.55	0.00	-	-	-	-	0.989
≥ 60	3	39,183.97	7.66	2	114,923.69	1.74	4.399	5.177	1.351	19.836	< 0.001
Insured premium (NT$)											
< 18,000	5	38,866.37	12.86	4	114,058.98	3.51	3.668	4.330	1.130	16.590	0.012
18,000-34,999	0	470.93	0.00	0	1,674.79	0.00	-	-	-	-	-
≥ 35,000	0	121.60	0.00	0	414.60	0.00	-	-	-	-	-
Sleep apnea											
Without	2	36,523.39	5.48	3	112,859.77	2.66	2.060	2.424	0.633	9.288	0.521
With	3	2,935.51	102.20	1	3,288.60	30.41	3.361	3.955	1.032	15.154	0.018
HTN											
Without	1	35,610.47	2.81	3	107,639.77	2.79	1.008	1.186	0.309	4.543	0.295
With	4	3,848.43	103.94	1	8,508.60	11.75	8.844	10.407	2.716	39.875	< 0.001
Tetracycline											
Without	3	33,280.95	9.01	3	98,635.27	3.04	2.964	3.488	0.910	13.363	0.062
With	2	6,177.95	32.37	1	17,513.10	5.71	5.670	6.672	1.741	25.563	< 0.001
Minocycline											
Without	2	33,808.24	5.92	2	99,757.57	2.00	2.951	3.472	0.906	13.304	0.060
With	3	5,650.66	53.09	2	16,390.80	12.20	4.351	5.120	1.336	19.618	< 0.001
Doxycycline											
Without	3	33,658.71	8.91	3	99,522.67	3.01	2.957	3.480	0.908	13.332	0.068
With	2	5,800.19	34.48	1	16,625.70	6.01	5.733	6.746	1.761	25.849	< 0.001
Season											
Spring	2	8,929.35	22.40	1	26,828.13	3.73	6.009	7.071	1.845	27.094	< 0.001
Summer	1	9,757.80	10.25	1	29,500.98	3.39	3.023	3.558	0.929	13.632	0.297
Autumn	1	11,420.63	8.76	1	31,529.55	3.17	2.761	3.249	0.848	12.448	0.345
Winter	1	9,351.12	10.69	1	28,289.70	3.53	3.025	3.560	0.929	13.641	0.265
Urbanization level											
1 (The highest)	1	10,611.91	9.42	0	33,896.66	0.00	8	8	-	-	0.989
2	3	16,057.77	18.68	3	51,597.01	5.81	3.213	3.781	0.987	14.488	0.297
3	0	3,515.22	0.00	0	9,343.24	0.00	-	-	-	-	-
4 (The lowest)	1	9,273.99	10.78	1	21,311.45	4.69	2.298	2.704	0.706	10.361	0.384
Level of care											
Hospital center	2	10,490.04	19.07	1	36,583.31	2.73	6.975	8.208	2.142	31.449	< 0.001
Regional hospital	2	17,489.22	11.44	2	52,642.79	3.80	3.010	3.542	0.924	13.572	0.086
Local hospital	1	11,479.64	8.71	1	26,922.26	3.71	2.345	2.760	0.720	10.574	0.255

PYs, person-years; Rate, per 10^5 PYs; Adjusted HR, adjusted hazard ratio: adjusted for the variables listed in Table 2; CI, confidence interval; HTN, hypertension; IBD, inflammatory bowel disease.

through the mechanism of papilledema being induced by benign intracranial hypertension following sudden withdrawal of steroids, which is one of the main treatments for IBD. Thus steroid use is a confounding factor but we didn't adjust this factor in our analysis. Second it was a retrospective study. Third, database research studies lack imaging examination tools, such as optical coherence tomography and fundus photograph findings, to confirm an accurate diagnosis of papilledema. Fourth, the main population in Taiwan is

Han Chinese, and the study results may not be applicable to other races. Fifth, the cohort enrollment was limited to patients with IBD and the control cohort in this study, which could have led to selection bias. However, this study has several strengths. The NHI system was introduced in Taiwan in 1995, so we were able to conduct a longitudinal data analysis over a long term study period to compare the survival of papilledema between the study cohort and control cohort; compared to cross-sectional research, this study design is more effective. Further, it is mandatory for all citizens in Taiwan to enroll in NHI, and almost all citizens were covered (approximately 99%);[6] thus, the data collected in this study were from a nationwide, population-based database containing medical information of insured people in Taiwan.

In conclusion, our study suggests patients with IBD have an increased risk of papilledema. Further prospective studies including clinical diagnosis, lumbar puncture, and serologic test would be helpful to elucidate the underlying mechanism between IBD and papilledema. Patients with IBD should be aware of the potential risk of papilledema development.

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原　著

發炎性腸道疾病增加視乳頭水腫的風險性：台灣全國人口之世代研究

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目的　發炎性腸炎是一個多發性疾病，並且可能對身上各部位器官造成影響，本計畫使用世代研究法 (cohort study)，以台灣健保資料庫針對發炎性腸炎患者進行全面且長期的追蹤研究，比較是否會增加罹患視乳頭水腫的風險性。

方法　利用台灣全民健康保險資料庫之承保抽樣百萬歸人檔，研究期間為 2000 年到 2013 年，總共 14 年的數據，並利用 SPSS 進行資料處理及統計分析，分析方法包括卡方檢定法及費雪精確檢定。使用校正風險比值 (aHR)，用 Kaplan-Meier 曲線分析比較發炎性腸炎患者的視乳頭水腫的發生率。

結果　自資料庫中截取 2000-2013 年共 989,753 人，依照相關因子進行 1:4 配對，抽出發炎性腸炎有 4,498 位個案，及對照組為 17,992 位個案。在病例組裡罹患視乳頭水腫的比例 (12.67%)，比再對照組的比例 (3.44%) 高，且校正控制變相後 aHR 為 4.330 (95% CI = 1.130-16.590, p = 0.012)。結果分析顯示，在發炎性腸炎患者中，男性、年輕人發作、睡眠中止症、高血壓，合併有相關藥物使用者 (四環黴素，美諾四環素，去氧羥四環素)，以及春季是發生乳頭水腫的風險因子。

結論　在本研究中主要為罹患發炎性腸炎患者，會有顯著的高風險罹患視乳頭水腫病變。由本研究結果，站在預防醫學的觀點，應該針對有發炎性腸炎診斷之個案，針對同時具有相關風險因子病患，應該加強衛教及視神經檢查以降低視乳頭水腫的發生風險。

關鍵詞　發炎性腸道疾病、視乳頭水腫、台灣全民健康保險資料庫、世代研究法。