REVIEW ARTICLE

Potential influential factors on incidence and prevalence of inflammatory bowel disease in mainland China

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Abstract

The incidence of inflammatory bowel disease (IBD) has increased annually in newly industrialized countries. In mainland China, there is also a trend of increasing incidence and prevalence of IBD. Epidemiological studies have shown that the incidence of IBD in mainland China is higher in the south and lower in the north. However, the existing research results are affected by the factor of floating population. Some socioeconomic factors also seem to play a role in the rising trend of IBD incidence and prevalence. These underlying factors provide opportunities and challenges for our IBD epidemiological studies over the next decade.

Introduction

In recent years, there have been increasing cases of inflammatory bowel disease (IBD) in Chinese hospitals. Traditionally, IBD is a Western disease, commonly seen in areas of Western countries, such as North America and Northern Europe. Compared to Western countries, the incidence and prevalence of IBD are still low in mainland China, but the growing trend has attracted increasing attention from scholars.[1,2] However, in mainland China, a systemic national IBD epidemiological study is still lacking. The great number of migrant workers may influence the incidence and prevalence of IBD. Economic development is variable in different areas. Some cities are very developed and industrialized, and other cities are less developed. No single study of one city or one province can represent the true situation in all of mainland China. In this review, we will provide some potential factors that may influence the incidence and prevalence of IBD.

Incidence and prevalence of IBD in mainland China

Incidence data were collected in five cities and one province, and crude prevalence data were collected only from Yunnan Province.[1] In 2015, Miao from Kunming Medical University described the epidemiology of IBD in Yunnan Province in his or her doctoral thesis.[3] This research included all newly diagnosed IBD cases in Yunnan Province, which is located in Southwest China, from 1 January 1998 to 31 December 2013. This is the only whole provincial study completed in mainland China. It seems to be the epidemiological study of IBD with the longest time span in mainland China. Both Ng et al. and Cui et al. provided incidence data of five cities in their review.[1,4] These cities were Zhongshan[1]* (Guangdong Province),[5,6] Wuhan (Hubei Province),[7] Daqing (Heilongjiang Province),[8] Chengdu (Sichuan Province),[5] and Xi'an (Shaanxi Province).[5] They represented South China, Central China, Northwest China, Southwest China, and Northeast China, respectively. Data from all five cities were collected between 2010 and 2013. There is a lack of data from North China and East China, including two large cities, Beijing and Shanghai.

The highest incidence of IBD in mainland China was in Zhongshan. The crude incidence of IBD was 3.44 per 100 000 persons.[1,4–6] The incidence of Crohn's disease (CD) was 1.22 per 100 000 persons and that of ulcerative colitis (UC) was 2.22 per 100 000 persons. The lowest incidence of IBD in mainland China was in Xi'an. The crude incidence of IBD was 0.54 per 100 000 persons.[1,4,5] The incidence of CD was 0.07 per 100 000

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* Incidence data of Guangzhou were collected in Zhongshan as mentioned by Ng et al. in the appendix of Ref. 5.

persons and that of UC was 0.42 per 100 000 persons. The age-standardized incidence of IBD was six times higher in Zhongshan than in Xi'an.[5] Ng *et al.* also reported a 50% missed incidence rate in Xi'an. An incidence of 1.0 per 100 000 was shown in the sensitivity analysis, but it was still much lower than the incidence in Zhongshan.[5]

Percentage of mobile residents, a factor that cannot be neglected

It is not difficult to see that the incidence in South China was higher than in Northeast and Northwest China in the same period. Is this the real difference in IBD incidence in mainland China? It is hard to say. Although we know the IBD incidences of different areas, we cannot neglect another important factor, the migration of people, that affects the results. When a migrant patient works in a large city, he may likely be diagnosed in the large city. If the patient is counted in the study of the large city, there can be a potential overestimation of the incidence. On the other hand, the incidence in the original city from which the patient migrated may be underestimated. The first situation could be prevented by using registered household population as the background population, but the second situation is hard to prevent. Most of time, migrant workers are counted as inhabitants of their registered cities, not their working cities. This is called people's separation between registered household and actual residence (PSBHA), and this population is called the floating population. PSBHA is not rarely seen in mainland China. There are also many newly registered immigrants from other provinces, and they are counted as registered inhabitants. Qi *et al.* provided the provincial distribution of the net migrant scale of the floating population during 2000–2015.[9] Although we know Shaanxi, Sichuan, and Heilongjiang were out-migration population provinces, we did not find any population data for 2010–2013 for Xi'an, Chengdu, and Daqing. A report from the Hubei Provincial Bureau of Statistics showed that, in 2010, there were 3.84 million mobile residents in Wuhan, and the entire population of Wuhan was 9.79 million.[10] The percentage of the floating population in Wuhan was approximately 39.2%. Guangdong Province was listed as the top in-migration population province.[9] In Zhongshan, a city located 70 km south of Guangzhou in Guangdong Province, one report showed that it had 3.17 million inhabitants, with only 1.54 million registered household residents at the end of 2013.[11,12] The percentage of the floating population was 51.45%. In the study performed in Zhongshan, only registered household residents who actually resided in Zhongshan were included in the background population.[6] All PSBHAs (the floating population) were excluded from the background population, both in-migration and out-migration. Although the out-migration population is small,[6] the in-migration population is large.[11,12] In fact, we do not know where these mobile residents come from and how they influence the incidence and prevalence in other areas. In Hong Kong, a special administrative region of China, the percentage of the floating population was much smaller than in Zhongshan. The report released by the Hong Kong government showed that there were 6.97 million registered residents and 0.21 million mobile residents in mid-2013.[13] The percentage of mobile residents was only approximately 2.9%. Therefore, in mainland China, we require more understanding of how

population migration influences regional IBD incidence and prevalence. A nationwide epidemiological study is needed, and it would be better to pay more attention to mobile residents.

The influence of economic, population density, and urbanization

Doctors believe that the trend of IBD incidence in mainland China has increased in recent years, but it is not easy to find a study that directly demonstrates this trend. The study in Yunnan is the only provincial study and provides data of the trend.[3] Yunnan is a province with a small floating population. In the Sixth National Population Census, the entire population in Yunnan Province was 45.97 million, and the floating population was 6.05 million.[14] The percentage of the floating population was 13.2%. It was higher than that of Hong Kong but much lower than that of cities in Guangdong Province. In 1998, the crude incidence of IBD in Yunnan was 0.068 per 100 000 persons. The incidence of CD was 0 per 100 000 persons and that of UC was 0.068 per 100 000 persons.[3] In 2013, the crude incidence of IBD in Yunnan was 1.152 per 100 000 persons. The incidence of CD was 0.077 per 100 000 persons and that of UC was 1.075 per 100 000 persons.[3] Miao provided the incidence trend from 1998 to 2013 in a figure,[3] which was reproduced by Cui *et al.* in their review.[1] The figure shows a large and continuous increase in incidences of both CD and UC. Prevalence showed the same increasing trend. In 1998, the crude prevalence of IBD in Yunnan was 0.246 per 100 000 persons. The prevalence of CD was 0.005 per 100 000 persons and that of UC was 0.241 per 100 000 persons.[3] In 2013, the crude prevalence of IBD in Yunnan was 7.453 per 100 000 persons. The prevalence of CD was 0.418 per 100 000 persons and that of UC was 7.035 per 100 000 persons.[3]

Scholars believe that the increasing IBD incidence is associated with industrialization.[1,2,4] The data showed that developed areas had a higher IBD incidence and prevalence than developing areas.[1,2,4] In addition, the incidence of IBD increased in Western countries during industrialization in the 20th century.[2] Yunnan Province is a developing province in mainland China. In 2013, the gross regional domestic product (GRDP) per capita of Yunnan was 25 083 Chinese Yuan (CNY), equivalent to 4110.35 United States Dollars (USD).[15] The development was still imbalanced. The highest GRDP per capita was 52 094 CNY (8536.64 USD) in Kunming, and the lowest GRDP per capita was 11 933 CNY (1955.46 USD) in Zhaotong.[15] Miao provided the IBD prevalence rates of 16 different areas of Yunnan Province in his or her doctoral thesis.[3] The Yunnan Provincial Bureau of Statistics provided all the economic and population data of these 16 areas on its website.[15] We reviewed and listed these data in Table 1, and we performed a brief analysis of these data. As not all the parameters fit a Gaussian distribution, we chose Spearman correlation to assess the relationship between the prevalence and other data. Spearman R_s represents the correlation coefficient, and $P < 0.05$ represents statistical significance. The results show that population density and urbanization rate are factors moderately and positively correlated with IBD prevalence in Yunnan Province (Table 2). GRDP per capita has a moderate correlation with IBD prevalence, but the P values are marginal, ranging from 0.057 to 0.080.

Table 1 Economic, population, and IBD prevalence data of Yunnan Province in the year 2013

Region	Composition of each economic sector (%)			Contribution of each economic sector for per capita GRDP (CNY/person)				Population					Crude IBD prevalence[b]		
	Primary industry	Secondary industry	Tertiary industry	Primary industry	Secondary industry	Tertiary industry	Per capita GRDP (CNY/person)	Total population (10 000 persons)	Urban (10 000 persons)	Rural (10 000 persons)	Population density (person/sq. km)	Urbanization rate (%)	IBD (per 100 000 persons)	UC (per 100 000 persons)	CD (per 100 000 persons)
Kunming	5.0	45.0	50.0	2604.7	23 442.3	26 047.0	52 094	657.9	447.7	210.2	304.8	68.0	11.932	11.157	0.775
Qujing	18.0	48.0	34.0	4781.5	12 773.8	9043.7	26 599	597.4	248.5	348.9	200.1	41.6	7.419	6.917	0.502
Yuxi	10.1	60.3	29.6	4768.7	28 470.6	13 975.6	47 215	234.0	103.2	130.8	153.1	44.1	14.086	13.367	0.719
Baoshan	28.1	34.5	37.4	4961.9	6092.0	6604.1	17 658	255.4	74.1	181.3	130.1	29.0	4.729	4.338	0.391
Zhaotong	19.9	50.3	29.8	2374.7	6002.3	3556.0	11 933	534.2	140.0	394.2	232.0	26.2	3.34	3.21	0.131
Lijiang	16.1	45.3	38.6	3165.4	8906.4	7589.1	19 661	126.9	41.4	85.5	59.8	32.6	2.408	2.097	0.311
Pu'er	30.0	38.2	31.8	4947.3	6299.6	5244.1	16 491	258.4	92.8	165.6	56.9	35.9	1.627	1.395	0.232
Lincang	30.7	42.2	27.1	5169.6	7106.1	4563.4	16 839	247.9	84.0	163.9	101.3	33.9	4.896	4.531	0.364
Chuxiong	21.7	41.6	36.7	5043.3	9668.3	8529.4	23 241	272.4	102.0	170.4	62.9	37.4	8.934	8.568	0.366
Honghe	17.6	52.5	29.9	3949.8	11 782.1	6710.2	22 442	459.1	183.5	275.6	139.4	40.0	14.006	13.505	0.501
Wenshan	23.8	39.2	37.0	3694.5	6085.0	5743.5	15 523	357.8	122.4	235.4	111.0	34.2	3.229	3.034	0.195
Xishuangbanna	28.4	29.6	42.0	6722.3	7006.3	9941.4	23 670	115.2	46.6	68.6	58.5	40.5	4.25	3.99	0.26
Dali	20.7	42.0	37.3	4497.5	9125.3	8104.2	21 727	351.0	137.6	213.4	119.2	39.2	8.071	7.758	0.314
Dehong	28.5	32.4	39.1	5314.8	6052.4	7295.8	18 663	124.5	48.2	76.3	108.0	38.7	5.313	4.844	0.469
Nujiang	15.2	33.9	50.9	2422.3	5402.3	8111.4	15 936	53.9	13.6	40.3	36.7	25.2	5.937	5.566	0.371
Diqing	7.3	41.4	51.3	2363.7	13 405.3	16 610.9	32 380	40.6	11.4	29.2	17.0	28.1	0.725	0.745	0

[a]Data from Ref. 15.
[b]Data from Ref. 3.
CD, Crohn's disease; CNY, Chinese Yuan; GRDP, gross regional domestic product; IBD, inflammatory bowel disease; UC, ulcerative colitis.

Table 2 Spearman correlation between IBD prevalence and factors of economic and population data of Yunnan Province

	Composition of each economic sector (%)			Contribution of each economic sector for per capita GRDP (CNY/person)			Per capita gross regional domestic product (CNY/person)	Total population (10 000 persons)	Population density (person/sq.km)	Urbanization rate (%)
	Primary industry	Secondary industry	Tertiary industry	Primary industry	Secondary industry	Tertiary industry				
IBD (per 100 000 persons)	$R_s = -0.300$	$R_s = 0.421$	$R_s = -0.244$	$R_s = 0.156$	$R_s = 0.450$	$R_s = 0.362$	$R_s = 0.465$	$R_s = 0.365$	$R_s = 0.559*$	$R_s = 0.638**$
UC (per 100 000 persons)	$R_s = -0.291$	$R_s = 0.418$	$R_s = -0.238$	$R_s = 0.150$	$R_s = 0.438$	$R_s = 0.338$	$R_s = 0.450$	$R_s = 0.385$	$R_s = 0.556*$	$R_s = 0.629**$
CD (per 100 000 persons)	$R_s = -0.271$	$R_s = 0.294$	$R_s = -0.091$	$R_s = 0.229$	$R_s = 0.409$	$R_s = 0.374$	$R_s = 0.485$	$R_s = 0.276$	$R_s = 0.541*$	$R_s = 0.624**$

$*P < 0.05.$
$**P < 0.01.$
CD, Crohn's disease; CNY, Chinese Yuan; GRDP, gross regional domestic product; IBD, inflammatory bowel disease; Rs, Spearman rank correlation coefficient; UC, ulcerative colitis.

The definition of the urbanization rate is the percentage of urban population in an area. The urban definition was the definition used in the Sixth National Population Census of mainland China.[16] Ng et al. mentioned that the variation in IBD incidence was associated with population density and urbanization in mainland China.[2] Gong et al. described the influence of urbanization on health and health care in China.[17] Our analysis suggests that population density and urbanization may play a role in the regional variation of the prevalence of IBD. Although we cannot confirm the direct influence of the economy on IBD incidence and prevalence, we still need to pay attention to the role of economic sectors. The proportion of the three sectors can reflect some aspects of working style and lifestyle.

Opportunities and challenges

In the next decade, China will have more opportunities to conduct IBD epidemiological studies. China is the country with the highest population in the world. Most of the Chinese population lives in mainland China. According to statistics, at the end of 2018, the population of mainland China was 1.395 billion.[18] Among the population of mainland China, the Han population accounts for approximately 91.5%.[18] The genetic factor is important in the pathogenesis of IBD. A single ethnic group can reduce the difference in the incidence of IBD due to genetic variation. Unlike many developed countries, China's economic development is still varied, with developed and underdeveloped regions. In mainland China, we can see the incidence and prevalence of diseases in different economic development states of the same ethnic group at the same time. Epidemiological studies across the country or between different provinces and cities can more intuitively show the impact of economic development on the incidence and prevalence of IBD.

Mainland China has a large floating population and new immigrant groups. The floating population is both an opportunity and a challenge for epidemiological research. If the household registered population is considered to be a permanent resident population, the definition of the floating population is relatively vague. The statistical department usually refers to the household registered population and the floating population that has lived in an area for more than 6 months as the resident population, while the floating population living there for less than 6 months is not included.[19] Six months is unacceptable for statistically reporting the incidence of IBD. Some IBD patients have already developed symptoms before becoming residents but were diagnosed shortly after becoming residents. On the other hand, the policy of applying for household registration varies from city to city. Both in-migration and out-migration patients will affect the authenticity of the incidence of IBD. From another perspective, the difference in the incidence of IBD between migrants and permanent residents is also worth studying. China's huge floating population is dominated by young and middle-aged people. This age group is also the age with the highest incidence of IBD. Due to the stable composition of the household registered population, the incidence of IBD in this population is more valuable than that of the resident population, especially in the comparison of the interannual incidence rate.

Although many Chinese hospitals have adopted electronic medical records, the integration of national or regional electronic medical record management systems is still not perfect. There is a comprehensive reporting system for cancer and infectious diseases in mainland China, but there is no corresponding reporting system

for noninfectious diseases with a low incidence, such as IBD. Due to the low incidence of IBD, methods such as the epidemiological investigation of obesity or irritable bowel syndrome are not feasible. However, it is still common for IBD patients to seek medical treatment across provinces and cities. These patients may be missed or repeated during statistical analyses. As a chronic disease that is costly and requires long-term follow-up, it is still necessary to establish a regional or national IBD reporting system similar to those for infectious diseases and cancer. Current electronic medical record systems offer the possibility of creating such a system.

It is not difficult to foresee that, with further development of the economy, the incidence and prevalence of IBD in mainland China will further increase. We should be prepared to meet the challenge.

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