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A Meta-analysis of Risk Factors for Irritable Bowel Syndrome in China

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Abstract: *In order to systematically evaluate the risk factors for irritable bowel syndrome, We searched CNKI, Wanfang, Weipu and PubMed databases for risk factors for irritable bowel syndrome in China, Newcastle-Ottawa Scale (NOS) used the most comprehensive data collection based on relevant case-control trials, combined with inclusion and exclusion criteria to evaluate the quality of the extracted literature, included the literature with a score of ≥7, and finally meta-analyzed using RevMan 5.4. In the end, 15 articles met the inclusion criteria, with a cumulative number of 5171 cases and 3088 controls, respectively. It was concluded that history of alcoholism, spicy food, seafood, irregular diet, gastrointestinal infection, drug history, anxiety (long-term tension), sleep disorder (insomnia), personality sensitivity (introversion), family history of IBS, smoking, psychiatric (psycho-depressive factors), and family and marital events were independent risk factors for IBS, and controlling the above factors could effectively reduce the risk of IBS patients.*

Keywords: *Irritable bowel syndrome; IBS; risk factors; Case-control studies*

1. Introduction

Irritable Bowel Syndrome (IBS) is an organic disease in which abdominal pain, bloating, or abdominal discomfort is the main symptom, associated with or accompanied by changes in bowel habits such as frequency and/or stool characteristics, and organic diseases that can explain these symptoms have not been detected through routine clinical examination [1]. It is currently believed that the onset of IBS may be related to the interaction of various factors such as intestinal motility abnormalities, visceral paresthesia, inflammation, infection, neuro-endocrine, genetics, and diet [2]. IBS is endemic worldwide, but its prevalence varies between countries or regions and populations, and the overall prevalence of IBS in Chinese groups is 6.5% [3]. Although there are many reports on the risk factors of IBS at home and abroad, the relevant systematic analysis in recent years is still incomplete. This study conducted a meta-analysis of the DOR research literature published from January 2000 to November 2022, aiming to screen for TOR-related risk factors and confirm the strength of the association between each factor, so as to provide theoretical support for the reduction of DOR prevalence.

2. Information and methodology

2.1. Literature search strategies

Beginning with "Irritable bowel syndrome" or "Irritable Bowel Syndromes" or "Syndrome, Irritable Bowel" or "Syndromes, Irritable Bowel" or "Colon, Irritable" or "Irritable Colon" or "Colitis, Mucous" or " Colitides, "Mucous" or "Mucous Colitides" or "Mucous Colitis" and "dangerous factor" or "risk factors" or "influence factors" or "association factors" or "related factors" were searched in English. Chinese searches were conducted by combining the subject words "irritable bowel syndrome" and "risk factors" with free words (irritable bowel syndrome, irritable bowel syndrome, irritable bowel syndrome, irritable colon syndrome, irritable bowel syndrome, influencing factors, etiology, related factors, risk factors, clinical trials, case-control studies, clinical trials).

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2.2. Inclusion and exclusion criteria

2.2.1. Inclusion Criteria

(1) The design type is a case-control study; (2) IBS patients confirmed in various medical institutions, the control group is 5 years old with an age difference of ≤ from the case, living in the same area. Or patients receiving treatment in the same hospital during the same period with a large similarity with the case in the above conditions were included; (3) Data in the study results that can be converted to 95% CI, OR value, and standard error (SE).

2.2.2. Exclusion criteria

(1) Literatures with incomplete research data, no control group and excessive follow-ups were excluded; (2) Republished literatures were excluded; (3) review literatures were excluded; (4) non-Chinese or English literatures were excluded; (5) Literatures from the same region and year were excluded.

2.3. Literature screening, data extraction and quality evaluation

Exclude irrelevant literature and duplicate published clinical research results, read the full text, and identify the literature that meets the inclusion criteria. Studies meeting the inclusion criteria were then assessed by two reviewers with reference to the NOS scale [4].

2.4. Data Processing

Review Manager 5.4 was used for meta-analysis. Heterogeneity between studies was analysed using Cochrane Q and the size of heterogeneity was assessed using I^2. If the P>0.1 and I^2<50%, it means that there is no statistical heterogeneity among studies, so a fixed-effect model (FE) is used; Conversely, a random effects model (RE) was used; The odds ratio (OR) was selected for dichotomous data as a pooled statistic, and each effect size was expressed as a 95% confidence interval (CI). Publication bias detection used funnel plots and Egger's methods to detect and assess publication bias. The sensitivity analysis was performed by changing the data model to test the stability of the research results.

3. Results

3.1. Literature search results

A preliminary search was carried out in the database, 408 articles were obtained, 361 documents were initially screened out after the duplicate literature was eliminated, 316 documents were eliminated after reading the title and abstract, 45 articles were included in the second screening, 30 articles were eliminated after reading the full text, and finally a total of 15 documents that met the conditions were included.

3.2. Basic characteristics and quality evaluation of literature inclusion

Among the 18 included literatures, all were case-control studies, published from 2001 to 2022, with a cumulative total of 5171 cases in the case group and 3088 cases in the control group. See Table 1.

Table 1: General characteristics of the studies included in the meta-analysis

NO.	First author	Year of publication	Study area	Case group	Control group	Research factors	NOS score
1	ChenZongxian [5]	2014	Sanya	85	120	(1)(2)(5)(6)(7)(8)(9)	9
2	Cui Lihong [6]	2014	Beijing	3242	1520	(4)(11)	7
3	Guo Hong [7]	2011	urumchi	100	100	(10)(12)	7
4	Wei Xiaojing [8]	2014	Ningbo	72	72	(4)(7)	7
5	Zhao Wenju [9]	2021	Wannan	300	150	(4)(7)(8)(12)	8
6	Zheng Jie [10]	2016	Baotou	105	96	(11)	7
7	Wang Siling [11]	2017	Weifang	118	100	(2)	7
8	Qi Lingzhi [12]	2016	Changchun	50	50	(7)(11)(12)	8

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9	Yao Lujing [13]	2012	Luoyang	150	150	(2)(13)	7
10	Lv Hongjie [14]	2014	Wenzhou	90	90	(1)(2)(5)(6)(7)(8)(9)	8
11	Jin Jianjun [15]	2003	Luoyang	132	132	(1)(2)(7)(8)(13)	9
12	Lin Hong [16]	2016	Xiamen	101	101	(5)(8)	7
13	Liu Chang [17]	2017	Shihezi	139	139	(1)(2)(7)(8)(12)	8
14	Luo Xu [18]	2015	Baotou	85	170	(10)	7
15	Xu Xiaoxing [19]	2005	Shanghai	402	98	(1)(5)(10)(12)(13)	8

Note: (1) Having a history of alcoholism; (2) Liking spicy food; (3) Liking to eat seafood; (4) Having irregular diet; (5) Having a history of gastrointestinal infection; (6) Having drug history; (7) Having anxiety (long-term stress); (8) Having sleep disorders (insomnia); (9) Having sensitive personality (introverted); (10) Having family history; (11) Having a history of smoking; (12) Having psychiatric (psycho-depressive) factors; (13) Having family, marriage events

3.3. The results of the meta-analysis of risk factors for irritable bowel syndrome

There was no heterogeneity in the risk factors of irritable bowel syndrome, such as preference for spicy food, history of gastrointestinal infection, history of long-term medication, anxiety (long-term stress), family history of IBS, smoking, mental-psychological factors, family-marital events, irregular diet, and preference for seafood (P>0.1, I^2<50%), while a fixed-effect model was used, while a history of alcoholism, sleep disorders (insomnia), and introversion (sensitivity) were the opposite, and a random-effects model was used.

3.3.1. Relationship between history of alcohol abuse and irritable bowel syndrome

A total of 8 studies were included, and after heterogeneity analysis, P=<0.00001, I^2=86%, using a random-effects model, by plotting forest plots, see Figure 1.

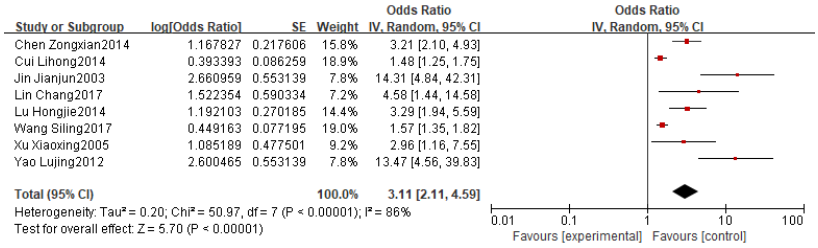

Figure 1: Forest map of the history of alcoholism

3.3.2. The relationship between spicy food and IBS

A total of 3 studies were included, P=0.26, I^2=25% after heterogeneity test analysis, using a fixed effect model, and the forest map was plotted, as shown in Figure 2.

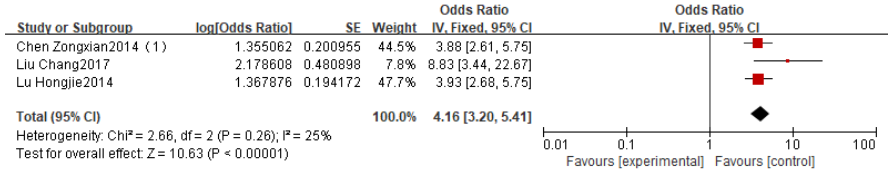

Figure 2: Diagram of a forest that likes spicy food

3.3.3. The relationship between seafood preference and IBS

3 studies were included in the study, which were analyzed by heterogeneity test. P=0.46, I^2=0%, using a fixed-effect model, by plotting the forest map, see Figure 3.

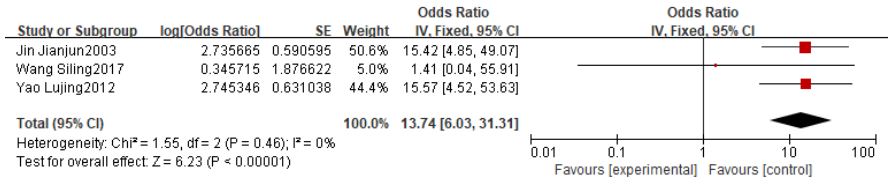

Figure 3: Diagram of seafood-loving forests

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3.3.4. Association between dietary irregularity and IBS

4 studies were included, which were analyzed by heterogeneity test. P=0.05, I^2=62%, using a fixed-effect model, by plotting the forest map, see Figure 4.

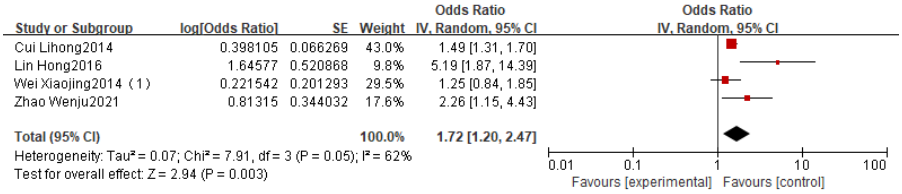

Figure 4: Illustration of a forest with an irregular diet

3.3.5. Relationship between history of gastrointestinal infection and IBS

4 studies were included, analyzed by heterogeneity test, P=1.00, I^2=0%, using a fixed-effect model, by plotting the forest, see Figure 5.

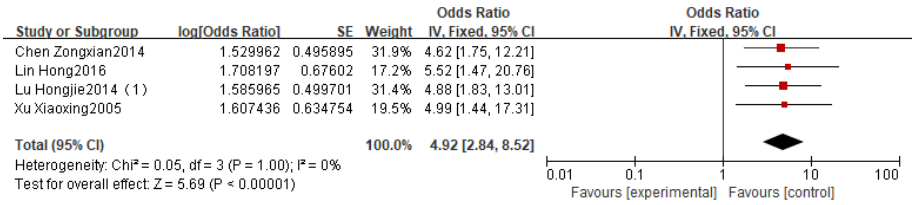

Figure 5: Forest diagram of gastrointestinal infection history

3.3.6. Relationship between long-term drug history and IBS

A total of 3 studies were included, and after heterogeneity test analysis, P=0.17, I^2=44%, using a fixed-effect model, by plotting forest maps, see Figure 6.

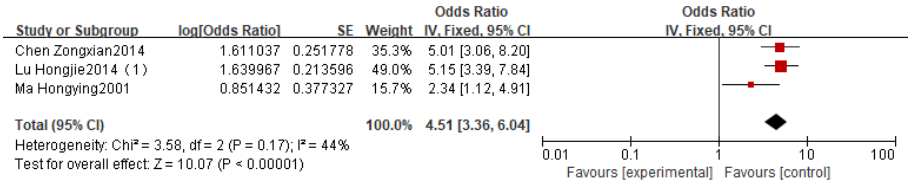

Figure 6: Forest diagram of long-term drug history

3.3.7. Association between anxiety (chronic stress) and IBS

8 studies were included, analysed by heterogeneity test, P=0.19, I^2=30%, using a fixed-effect model, by plotting the forest map, see Figure 7.

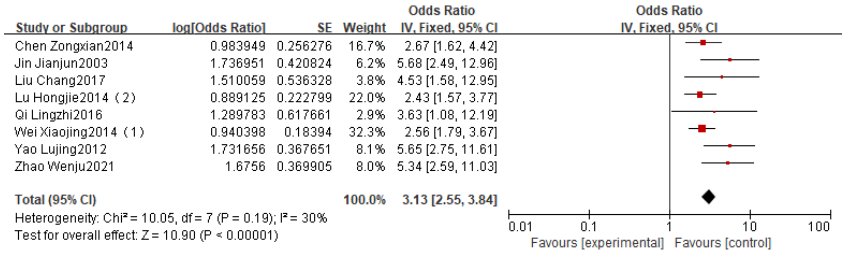

Figure 7: Forest diagram of anxiety (chronic stress)

3.3.8. Association between sleep disorders (insomnia) and IBS

9 studies were included, analysed by heterogeneity test, P<0.00001, I^2=95%, using a random-effects model, by plotting the forest, see Figure 8.

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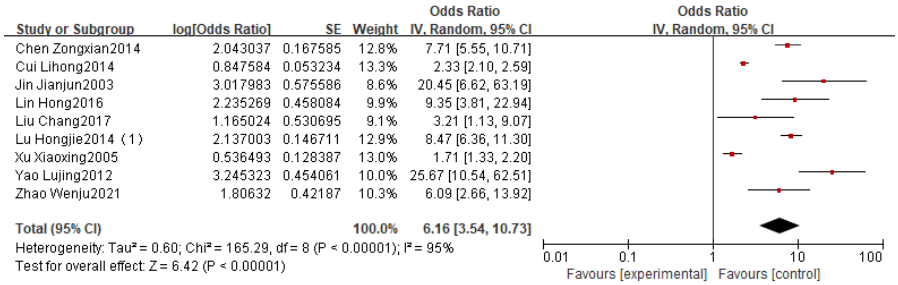

Figure 8: Forest diagram of sleep disorders (insomnia)

3.3.9. Relationship between personality sensitivity (introversion) and IBS

4 studies were included, analyzed by heterogeneity test, P<0.00001, I²=94%, using a random-effects model, by plotting the forest, see Figure 9.

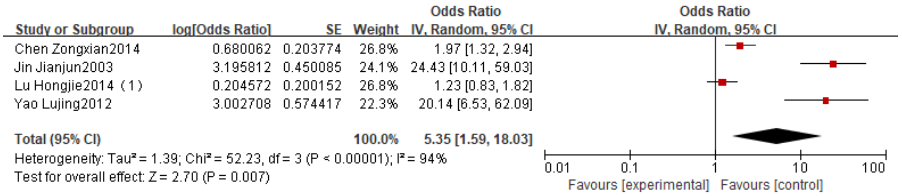

Figure 9: Forest diagram of sensitive (introverted) personalities IBS

3.3.10. Relationship between family history and IBS

3 studies were included, which were analyzed by heterogeneity test, P=0.49, I²=0%, using a fixed-effect model, by plotting the forest map, see Figure 10.

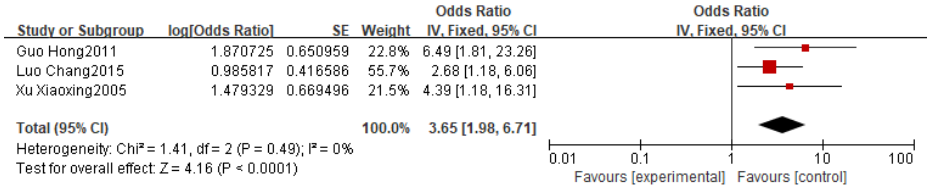

Figure 10: IBS Forest diagram of family history

3.3.11. Association between smoking and IBS

3 studies were included, tested for heterogeneity, P=0.29, I²=18%, using a fixed-effect model, by plotting the forest, see Figure 11.

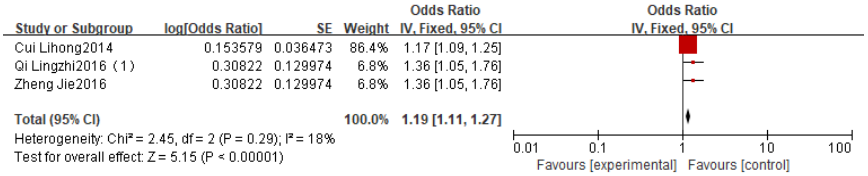

Figure 11: Diagram of a smoking forest

3.3.12. Relationship between psychiatry (psycho-depression) and IBS

5 studies were included, analysed by heterogeneity test, P=0.09, I²=50%, using a fixed-effect model, by plotting the forest, see Figure 12.

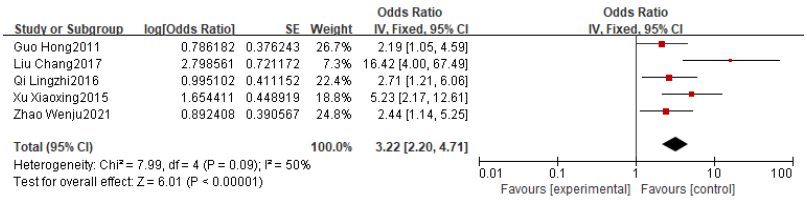

Figure 12: Forest diagram of psychiatric (psycho-depressive) factors

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3.3.13. Relationship between family, marital events and IBS

3 studies were included, and the heterogeneity test was analyzed. P=0.99, I^2=0%, using a fixed-effect model, by plotting the forest map, see Figure 13.

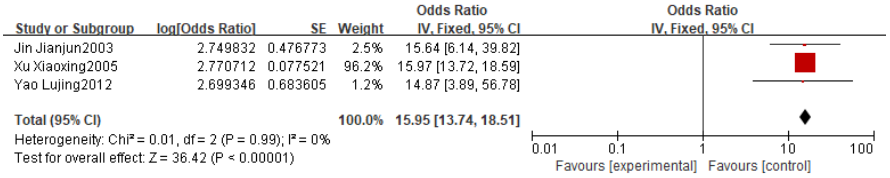

Figure 13: Forest diagram of family, marital events

3.3.14. Sensitivity analysis

The fixed and random-effects models were used to pool the OR values and 95% CIs, and the results were highly similar, reflecting the general reliability of the pooled results obtained in this study. See Table 2 for details.

Table 2: Sensitivity analysis

Risk factors	Fixed-effect model		Random-effects model	
	Merge OR values	95%CI	Merge OR values	95%CI
History of alcoholism	1.75	1.57-1.94	3.11	2.11-4.59
Likes spicy food	4.16	3.20-5.41	4.26	3.09-5.87
Likes seafood	13.74	6.03-31.31	13.74	6.03-31.31
Irregular diet	1.51	1.34-1.70	1.72	1.20-2.47
History of gastrointestinal infection	4.92	2.84-8.52	4.92	2.84-8.52
History of long-term medication	4.51	3.36-6.04	4.30	2.85-6.47
Anxiety (chronic stress)	3.13	2.55-3.85	3.35	2.57-4.36
Sleep disturbances	2.91	2.67-3.18	6.16	3.54-10.73
Personality Sensitive (Introverted)	2.26	1.74-2.92	5.35	1.59-18.03
Family history of IBS	3.65	1.98-6.17	3.65	1.98-6.17
Smoking	1.19	1.11-1.27	1.21	1.10-1.34
Mental factors	3.22	2.20-4.71	3.51	2.20-6.11
Family, matrimonial events	15.59	13.74-18.51	15.59	13.74-18.51

3.4. Analysis of publication bias

The results of the symmetry test for 13 factors included in Eeggr's test using Stata 17.0 software showed a p<0.05 for the symmetry test of alcohol history, preference for spicy food, anxiety (chronic stress), and mental-psychological factors, suggesting possible publication bias. The funnel plots of other risk factors generally maintained a symmetrical relationship, reflecting the good stability of the meta-analysis results. Funnel plots were plotted and symmetry tests were performed for sleep disorder (insomnia), a risk factor indicator with more studies, and p0.05>0.05 was performed, indicating that publication bias was basically well controlled, as shown in Figure 14.

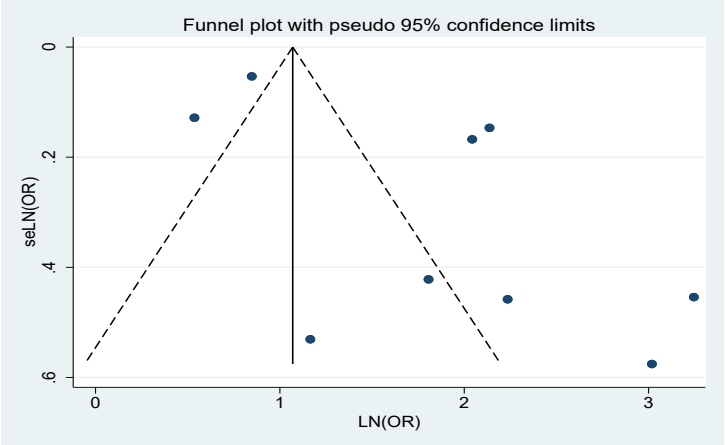

Figure 14: Funnel chart for sleep disorder (insomnia) analysis

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4. Discussions

The pathogenesis of IBS is closely related to the interaction of multiple factors. This study collected the latest epidemiological literature of IBS population at home and abroad in the past 20 years, and comprehensively summarized the risk factors for the incidence of IBS in the Chinese population in recent years.

4.1. Family, matrimonial events

Xiong Lishou et al. [20] used univariate analysis to investigate patients with irritable bowel syndrome in Guangdong and found that their onset was related to marital status such as divorce, mental and psychological disorders, and negative coping styles, which shows that family and marital harmony are crucial to the physical and mental health of the Chinese population.

4.2. Alcoholism, smoking and other bad habits

The nicotine in tobacco can excite the sympathetic nervous system, thereby inhibiting the movement of the gastrointestinal tract of smokers, affecting the normal secretory function of the digestive glands, and leading to gastrointestinal dysfunction. Alcohol is lipophilic and lipolytic, which can cause damage to intestinal epithelial cells and intramucosal bleeding, edema, destruction of the intestinal mucosal barrier. In the small intestine, alcohol reduces impedance wave movement (the muscles that preserve food for further digestion) but does not affect propulsion wave movement (the movement that pushes food through the intestines), which can lead to diarrhea in long-term drinkers [21]. In addition, alcohol is also believed to cause damage to the intestinal mucosa of animals, and studies have shown that smoking reduces blood flow, adversely affects the mucous membranes, and releases free radicals that slow down cell proliferation, which can lead to gastrointestinal diseases [22].

4.3. Personal eating habits such as spicy food, seafood and irregular diet

Frequent consumption of spicy food may be induced onset of food allergies or food intolerances, followed by IBS symptoms; Seafood contains a lot of protein and cholesterol, which can easily stimulate the immune system of the intestinal mucosa to produce an immune response [23]. Liu Chunbin etal [24] conducted a face-to-face survey using random, cluster, and stratified sampling methods, and found that factors such as preference for preserved seafood, raw and cold food, fruits, dairy products, dietary factors, and frequent poor mood were the main influencing factors for IBS in the community area of Nanning City, Guangxi.

4.4. Emotional factors such as anxiety, sleep disorders, personality sensitivities, and mental-psychological factors

Chen Feixue [25] identified the involvement of anxiety-induced BDNF-CRF brain-gut interaction in the pathogenesis of visceral hypersensitivity of IBS from the brain-gut axis (central and peripheral) levels, which further indicated that the brain-gut peptide BDNF regulates brain-gut interaction. By regulating the brain-gut interaction of BDNF-CRF on the brain-gut axis, it is expected to balance the abnormal brain-gut interaction in IBS patients and improve the symptoms of anxiety and visceral hypersensitivity, indicating that there is a two-way correlation between anxiety and IBS. Massimo Bellini et al [26] used questionnaires to demonstrate a strong positive correlation between IBS symptom severity and sleep disturbances. Chang Yuanyuan and others [27] found that patients with irritable bowel syndrome are more likely to have certain psychological abnormalities than people without irritable bowel syndrome, and patients with irritable bowel syndrome generally have abnormal psychology such as anxiety, depression, fear, obsessive-compulsive thoughts, and interpersonal sensitivity, among which anxiety and depression are the most prominent.

4.5. History of gastrointestinal infection, long-term drug use and family history of IBS

The infection state can damage the intestinal mucosal epithelial cells, significantly affect and destroy the intestinal mucosal barrier function [28]. Studies have shown that 33% of patients have a family history of IBS [29]. From the perspective of preventing IBS, it is necessary to maintain a happy mood, avoid smoking and alcohol, and eat modestly, so as to reduce the prevalence of IBS.

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Limitations of this study: (1) risk factors such as spicy food, seafood, family history, and smoking were included in the literature in a small number of literatures, which could only affect the conclusions of the meta-analysis; (2) The study area included in the literature was 15 urban areas in China, and the research scale was small. (3) The included literature was case-controlled, and it was difficult to comprehensively analyze the risk factors of irritable bowel syndrome; (4) Among the published literature, some of the literature does not have available data, or the research results are incomplete, so they cannot be applied to the analysis, resulting in the loss of information, or the inclusion of the literature has a large time span, and it is inevitable to face various biases, such as alcoholism history, preference for spicy food, anxiety (long-term stress), psycho-psychological factors and other risk factors.

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