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Epidemiology of Irritable Bowel Syndrome in Saudi Arabia

Saleh Hadi Alharbi

Faculty of Medicine, Al Imam Mohammad Ibn Saud Islamic University, Riyadh, Kingdom of Saudi Arabia (KSA)

Abstract The irritable bowel syndrome (IBS), is a clinical syndrome characterized by chronic abdominal dis-comfort, is the most mutual complaint met by gastroenterologists. IBS associated with symptoms in bowel habits, which can't be clarified by any biochemical or organic disorders. The most common symptoms include, the existence of current or recurrent abdominal pain or discomfort accompanying with bloating and altered bowel habits. These symptoms could intensely change the quality of life. Several reports confirms the existence of dysfunction of the intrinsic enteric nervous system (ENS). Several reports have revealed that inflammation and immune dysregulation disturb the sensitivity of nerve fibers. A relatively high prevalence of IBS was reported in several Saudi studies with variable study population settings. This review is mainly focused on the current status of IBS in the Kingdom Saudi Arabia (KSA) in light of the existent literature. The prevalence of IBS in Saudi Arabia among the available literature was slightly higher but relatively comparable to some worldwide reports.

Keywords Irritable bowel syndrome, IBS, Saudi Arabia

1. Introduction

Irritable bowel syndrome (IBS) is the most common functional gastrointestinal disorder considered by abdominal discomfort and pain, which usually due to altered bowel habit. The prevalence and clinical features of IBS greatly vary throughout the world [1, 2]. IBS is chronic disorder that continue considerably to deteriorate work productivity and life quality. Although IBS upsetting as many as 7% to 21% of the overall population, a shortage of understanding of pathogenesis and assessment approaches results in diagnostic vagueness, and in turn frustration of both the clinician and the patients [3-5]. IBS can present as, diarrhea predominant IBS (DIBS) subtype, constipation predominant IBS (CIBS) subtype or mixed diarrhea and constipation subtype.

The pathophysiology and underlying pathogenesis of IBS stay mysterious. It is conventionally thought that IBS is a consequence of various factors comprising hypersensitivity of the bowel, changed bowel motility, inflammation and stress [6]. Environmental factors probably play an essential part in the pathogenesis and clinical indexes of IBS. Numerous latest studies propose a genetic basis for IBS, either in etiology or predicting response to treatment [7]. However, molecular biological knowledge continue to progress quickly and genetic testing offer much promise in the overall management of IBS [6].

The diagnosis of IBS depend on the identification of characteristic symptoms and the exclusion of other organic disorders. Diagnosis of IBS necessitates a careful personalized methodology, an inclusive clinical history, limited but related investigations, and sustained follow up. Abdominal pain that may or may not be relieved by defecation is the cardinal symptom of IBS; distension and bloating are other common symptoms [8].

There are many reports from Saudi Arabia regarding the assessment of IBS in different population settings. The studies showed a diverse prevalence rates within the different parts of the country as well as, suggestion of multifactorial etiological elements. Therefore, the aim of the present review was to highlight the epidemiology of IBS in Saudi Arabia in light of the available literature.

2. Pathophysiology of IBS

Although the pathophysiology of IBS is not completely recognized, but there have been several factors proposed to contribute to its etiology. It has been presented that environmental social factors, diet, intestinal microbiota, intestinal low-grade inflammation, abnormal gastrointestinal endocrine cells and genetic factors, play a chief role. Moreover, the decreased number of endocrine cells is responsible for the visceral hypersensitivity, disturbed gastrointestinal motility, and abnormal gut secretion realized in IBS patients [9].

More than 60 gene candidates have been suggested to represent a role in the genetic tendency to IBS [10]. The

* Corresponding author:
slamhot@hotmail.com (Saleh Hadi Alharbi)
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difference in the control of candidate genes involved in neurotransmitter synthesis, reuptake or receptor functions, ion channel function, and inflammatory diseases vulnerability loci may impact inconsistencies in prevalence of the symptom phenotype of abdominal pain in IBS. The candidate genes comprise SLC6A4, CNR1, and TNFSF15 imitating serotonin reuptake, cannabinoid receptors and inflammatory barrier functions [11]. A number of studies have concentrated on the HTTLPR genotype, which controls the expression of the SLC6A4 (serotonin transporter protein); but, the reported linked to IBS is unclear [12-14]. The IBS risk genes suggested so far are non-confirmed hits rather than true predisposing factors, and the studies done have been fundamentally too less supported to capture true connection signals [10].

Before selecting treatment options for patients suspected of IBS, the physician should carefully make a full history and physical examination to exclude other diagnoses with symptoms similar to those of IBS [15].

A 2009 position statement issued by the American College of Gastroenterology (ACG) states that no symptom-based criteria have ideal accuracy for diagnosing IBS. Trials propose psyllium fiber, certain antispasmodics, anti-diarrheal, 5HT 3 antagonists, 5HT 4 agonists, some probiotics, and peppermint oil are effective in IBS patients. Tricyclic antidepressants and selective serotonin reuptake inhibitors have been shown to be effective in IBS patients of all subtypes. Non absorbable antibiotics are effective particularly in IBS-D and selective C-2 chloride channel activators may be effective in IBS-C. Psychological therapies may also offer advantage to IBS patients. Patients with IBS often seek out Complementary and Alternative Medicine (CAM) therapies, including cognitive-behavioral therapy, herbal therapies, probiotics, mind-body therapies, acupuncture, dietary changes, and exercise. Although most CAM therapies appear to afford some advantage in relieving IBS, it is obvious that the duration, dosages, and particulars of the intervention significantly influence the consequences. A wide variety of novel agents targeting various mechanisms of IBS are now in various stages of drug development [16].

3. Global Prevalence of IBS

Epidemiological studies have revealed a larger variation in the prevalence rates of IBS in different epidemiological studies settings with a greater increase among first degree relatives [17]. It was reported that occurring in ranges from 10% to 23% in the general population worldwide [18-21]. The prevalence rates of IBS varies amongst countries, as well as, measures employed to state its existence. Women are at considerably greater risk for IBS than men. Several cross-sectional surveys have described the prevalence of IBS, but there have been no latest systematic review of data from all studies to conclude its global prevalence. Of the 390 citations assessed, 81 stated the prevalence of IBS in 80 discrete study subjects covering 260,960 subjects. Pooled prevalence in all studies was 11.2% (95% CI, 9.8%-12.8%). The prevalence wide-ranging depending on the country (from 1.1% to 45.0%) and criteria used to describe IBS. The highest prevalence values were designed when ≥3 Manning criteria were performed (14%; 95% CI, 10.0%-17.0%); by adopting the Rome I and Rome II criteria, prevalence values were 8.8% (95% CI, 6.8%-11.2%) and 9.4% (95% CI, 7.8%-11.1%), correspondingly. The prevalence was greater for women than men (OR, 1.67; 95% CI, 1.53-1.82) and lesser for persons older than 50 years, compared with those younger than 50 (OR, 0.75; 95% CI, 0.62-0.92). Socioeconomic status showed no influence, except for only 4 studies reported such data [22].

4. Prevalence of IBS in Saudi Arabia

Several studies have assessed the prevalence rates of IBS in different cross sectional survey with diverse settings in the KSA. A cross sectional study was conducted in AlJouf area, Northern KSA, involving a self-administered questionnaire based on Manning and Rome II criteria for diagnosis of IBS. The study included 2025 secondary school males' students. The prevalence of IBS was 8.9% and 9.2% according to Manning and Rome II criteria for diagnosis of IBS respectively in the patients with mean age of 17.5 +/- 3 years and range of 15-23 years [23]. In a systematic review and a meta-analysis of published literature to estimate the prevalence of IBS among Asian children including Saudi Arabia, the prevalence of IBS ranges from 2.8% to 25.7%, with a pooled prevalence of 12.41% (95% confidence interval 9.87-14.95). Prevalence risk ratio of girl: boy is 1.39. Prevalence of subtypes is diverse and varies between studies [24].

Another study was conducted in King Abdulaziz University, Jeddah, KSA, involving a self-administered questionnaire based on Rome III criteria for diagnosis of IBS. The study included 597 medical students. The prevalence of IBS was 31.8% [25]. In a systemic review involved 16 studies, the prevalence of IBS among medical students ranged from 9.3% to 35.5%. The relatively high prevalence among medical students may be attributed to their special stressful learning atmosphere [26].

Another study was conducted in King Abdulaziz University Hospital, Jeddah, KSA, involving a self-administered questionnaire based on Rome III criteria for diagnosis of IBS. The study included 229 nurses. The prevalence of IBS among nurses was 14.4%, and IBS-Mixed type was the commonest variety (54.5%) [27].

A cross sectional study was conducted in Qassim region, KSA, involving a self-administered questionnaire based on Rome III criteria for diagnosis of IBS. The study included 300 school teachers. The prevalence of IBS symptoms among teachers in Qassim region of KSA is 40.7% with no significant gender predilection [28].

A recent cross sectional study was conducted in King Saud bin Abdulaziz University for Health Sciences, KSA,

has used two self-administered, pre-validated questionnaires: Depression Anxiety Stress Scales-21 (DASS-21) and Rome III criteria for diagnosis of IBS. The study included 270 medical students. The overall prevalence of IBS was 21% (n=57), with a higher prevalence among females (26%, n=23) than males (19%, n=34). IBS was most and least prevalent among first-year students (14%, n=5) and fifth-year students (29%, n=21) respectively. Anxiety levels were normal, mild, moderate, and severe or extremely severe in 39% (n=105), 7% (n=19), 26% (n=70), and 27%. A significant association was found between gender & IBS and anxiety levels & IBS [29]. In a cross sectional study to assess the bowel patterns (function/habits) and its associated variables in an adult Saudi population, approximately 40% of both genders have bowel movements at least once a day [30].

5. Etiology of IBS

IBS has been hypothesized as a gastrointestinal disorder associated with abdominal discomfort or pain and gastrointestinal motor troubles resulting in diarrhea or constipation [31, 32]. It was suggested that these abnormalities are secondary to psychological disturbances rather than being of primary relevance. There is growing evidence that organic disease of the gastrointestinal tract can be recognized in subdivisions of patients who realize the Rome criteria for IBS.

There is growing data regarding the role of immune activation in the etiology of IBS [33]. Studies have revealed that 3%-36% of enteric infections result in persistent new IBS symptoms. Risk factors for evolving IBS post to infection comprise, in order of significance, extended duration of primary disease, toxicity of infecting bacterial species, smoking, mucosal markers of inflammation, female gender, depression, hypochondriasis, and adverse life events. The pathogenesis behind IBS post to infection is indefinite but it may be attributed to residual inflammation or persistent alterations in mucosal immunocytes, enterochromaffin and mast cells, enteric nerves, and the gastrointestinal microbiota [34]. Additionally, psychological stress has been described to be one of the factors that encourage immune activation. However, it still mysterious whether immune activation in IBS patients is mostly reliant on infectious gastroenteritis and/or psychological stress [35].

Serotonin dysregulation has been linked to IBS. Serotonin (5-HT), acting mainly via the 5-HT_3 and 5-HT_4 receptors, plays an important part in the regulation of gastrointestinal motility, sensation, and secretion [36, 37]. As a consequence there has been substantial interest in these receptors as promising therapeutic targets for IBS, with agonists at the 5-HT_4 receptor predicted to improve gastrointestinal propulsion [38, 39] and antagonists at the 5-HT_3 receptor to slow gastrointestinal transit and decrease visceral sensation [40, 41].

Some studies show that small intestinal bacterial overgrowth (SIBO) is prevalent in IBS. The association between SIBO and IBS is extremely unpredictable among some reports. Several competent IBS therapies do not target SIBO at all, so far have a more favorable than antibiotics. IBS doesn't act similar to regular infectious diseases, proposing that microbes may not chiefly be a reason the syndrome. Other factors may misperceive the association between SIBO and IBS, comprising proton pump inhibitors. While the brain-gut hypothesis is evolutionarily applied, the bacterial assumption is harder to support from an evolutionary outlook. Thus it can be assumed that bacteria may contribute to some IBS symptoms, but the bacteria can't be the only clarification, and a causative linkage between SIBO and IBS is not confident [42].

Psychosocial factors appear to be important in IBS, although whether these factors directly change gastrointestinal function leftovers unclear. It is also likely that gastrointestinal dysfunction modulates central routes also [43]. The central nervous system modulates different functions such as secretion, motility, and blood flow [44]. Signals from the gut, in turn, are intricate in regulating reflexes. Opinion of actions in the gut includes activation of various pathways, with information being modulated at diverse levels, peripheral as well as central [45].

The field of genetics disclosing the underlying potential IBS genes is fast progressing. However, huge gaps in the consideration of this multifaceted illness persist, which need more studies. Many studies have tried to connect single-nucleotide polymorphisms (SNPs) to IBS but there is slight indication that these SNPs are functional [6]. Familial aggregation studies and twin studies propose a modest influence of genetics to the progress of IBS. Pharmacogenomics and association reports offer solider, although far from definite, evidence for genetic variants that affect expression of IBS. Together, these studies suggest that a multidisciplinary approach with clinical and psychological tools, epidemiologic methods, and genetic methods might help clarify the molecular mechanisms leading to the common symptoms of IBS and result in improved treatments for patients with IBS [7].

Multiple IBS etiological factors have been reported in serval studies from KSA. Morbid anxiety, living in school dormitory, emotional stress, and higher educational level (grade) were found to be the predictors of IBS in a cross-sectional survey included 597 medical students in KSA [46]. Another study from KSA found that educational status, occupation (teacher and unemployed), diet habits, and chronic diseases are significantly associated with their bowel disorders [30, 47]. Positive family history of IBS, working in outpatient clinics, having day shift, poor sleep quality, and high anxiety and depression scale scores were significantly associated with IBS. This was reported in study included 229 nurses working at King Abdul-Aziz University Hospital, Jeddah, KSA [27]. The most common symptom compatible with IBS reported from Northern KSA were abdominal pain or discomfort in 37.9%, and feeling of incomplete rectal evacuation after defecation in 32.2% [23]. Another study from KSA reported high prevalence of IBS among medical students, which was attributed to their special stressful

learning environment. Some studies found that female gender, family history of IBS, psychiatric stress, anxiety, depression, infections, dietary factors, and sleep disorders were associated with IBS in KSA [26, 29].

6. Sex

Several epidemiological reports indicated that, twice as many women as men are affected by IBS in western countries, signifying a role for sex hormones in IBS pathophysiology. In spite of rising evidence about the effects of sex hormones in IBS symptom modulation, data on mechanisms by which they influence disease progress are scarce. Actually, IBS is largely diagnosed in women, with a female to male sex ratio ranging from 2:1 (questionnaire-based diagnostics) to 4:1 (practice-based diagnostics) [49]. It is also notable that several if not all the comorbid diseases related to IBS also share this female prevalence. To name the most common, fibromyalgia [50], migraine [51], other functional GI disorders such as functional dyspepsia [52], chronic pelvic pain [53], chronic fatigue syndrome [54], and depression [55] all have sex ratio skewed towards female gender [56].

Based on the female predominance as well as the relationship between IBS symptoms and hormonal status, several models have been proposed to study the role of sex hormones in gastrointestinal (GI) function including differences in GI symptoms expression in distinct phases of the menstrual cycle, in pre- and post-menopausal women, during pregnancy, hormonal treatment or after oophorectomy. Sex hormones may influence peripheral and central regulatory mechanisms of the brain-gut axis involved in the pathophysiology of IBS contributing to the alterations in visceral sensitivity, motility, intestinal barrier function, and immune activation of intestinal mucosa. Sex differences in stress response of the hypothalamic-pituitary-adrenal axis and autonomic nervous system, neuroimmune interactions triggered by stress, as well as estrogen interactions with serotonin and corticotropin-releasing factor signaling systems are being increasingly recognized [57].

With regard to Saudi Arabia almost all of the studies conducted in association with IBS, have reported female's patients predominance.

7. Age

Although IBS affects people across the age spectrum, IBS patients with medical comorbidities varies with age, with higher levels of anxiety and depression among younger adults than their older counterparts. Medical comorbidity may have a more selective impact on psychological distress as compared to IBS symptom severity and quality of life for younger adults with IBS [58].

However, studies from KSA have reported a diverse range of age associated IBS with relatively higher among younger adults [30].

8. Socioeconomic Status

The data regarding the influence of socioeconomic status on prevalence of IBS were limited. There was no statistical significance in prevalence between developing and developed countries (P = 0.319). Moreover, prevalence of IBS failed to witness a downtrend in worldwide over the past two decades. Interestingly, the ratio of female/male prevalence was correlated with national HDI according to linear regression analysis (r = 0.395), and the ratio in the developing was significant lower than that in the developed (P = 0.0394). Lastly, except methods of data collection (P < 0.000), it shows no difference between developing and developed countries in diagnostic criteria, IBS subtypes, and age distribution (P = 0.119, 0.327, and 0.845 respectively) [59]. In study assess the influence of the childhood environment on adult IBS, childhood social class was significantly associated with IBS according to Manning Criteria (p = 0.05) and Rome II Criteria (p = 0.05). The prevailing trend was identical for both measures of IBS in the sex-adjusted models: this trend can be characterized as a general, and near-linear decrease in the odds of IBS across decreasing levels of social class. Contrasts with the reference group were significant on all comparisons for Manning Criteria IBS (high vs upper middle, p = 0.04; lower middle, p = 0.04; low, p = 0.01), and on comparisons involving the two lower social class groups for Rome II Criteria IBS (high vs lower middle, p = 0.03; low, p = 0.03). The associations were attenuated, but not eliminated by further adjustment for adult social class [60]. However, no data in association between socioeconomic and IBS reported from Saudi Arabia.

9. Family History

IBS clusters in families, although previous studies documented family history only from patients. IBS aggregates strongly in families. The strength of the association does vary somewhat by relationship to proband, but the lack of association in spouses supports either a possible genetic etiology or a shared household environmental exposure as an underlying cause of IBS [61]. Twin studies of IBS and abdominal symptoms support the concept that IBS has both genetic and environmental contributors [62-66].

However, some studies have reported the association between positive family history and IBS. The study of IBS among nurses working at King Abdulaziz University Hospital, Jeddah, KSA, has reported positive family history of IBS (aOR=3.38; 95% CI: 1.12-13.23) [27, 26].

However, the prevalence of IBS in Saudi Arabia is seemed to be relatively higher compared to many other countries. This might be attributed to the fact that most of studies from Saudi Arabia in this context were conducted among people with conditions enhance the occurrence of IBS. Most of these studies devoted to students who are always at high pressure particularly during examination and nurses who are always at tension particularly during night shift.

10. Conclusions

The prevalence of IBS in Saudi Arabia among the available literature was slightly higher but relatively comparable to some worldwide reports. Most reports regarding IBS from Saudi Arabia involving students (medical or none medical) and nurses. This necessitate the need for further community base studies. High anxiety, depression and emotional stress were the most reported risk factors among Saudi. This study affords much prerequisite information to fill the gaps in the available evidences regarding IBS status in KSA.

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