Received: 22 March 2023 | First decision: 18 April 2023 | Accepted: 16 May 2023

DOI: 10.1111/apt.17567

AP&T Alimentary Pharmacology & Therapeutics WILEY

A prospective comparison of UK and Malaysian patients with irritable bowel syndrome in secondary care

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Summary

Background: The prevalence of irritable bowel syndrome (IBS) is now known to be similar in various geographical regions, but there has been no study directly comparing characteristics of patients with IBS between populations.

Aims: To evaluate clinical and psychological differences between adults with IBS seen in secondary care in the United Kingdom (UK) and Malaysia.

Methods: Age- and sex-matched patients with IBS from a single centre in the UK (Leeds) and two centres in Malaysia (Kuala Lumpur and Kota Bharu), who fulfilled Rome III criteria, were recruited prospectively. Demographic characteristics and gastrointestinal and psychological symptoms were compared between both groups.

Results: A total of 266 (133 UK and 133 Malaysian) age- and sex-matched patients with Rome III IBS were recruited (mean age: 45.1 years Malaysia, vs. 46.5 years UK; 57.9% female). UK patients were more likely to consume alcohol than Malaysian patients (54.1% vs. 10.5%, $p < 0.001$). Compared with Malaysian patients, UK patients had more frequent abdominal pain, abdominal bloating, meal-related symptoms ($p < 0.001$ for all), higher symptom scores (mean 268.0 vs 166.0; $p < 0.001$), greater limitation of activities due to IBS ($p = 0.007$) and were more likely to report abnormal anxiety scores ($p < 0.001$). Higher perceived stress (mean 21.3 vs. 19.1, $p = 0.014$) and gastrointestinal symptom-specific anxiety scores (mean 50.8 vs. 43.0, $p < 0.001$) were also observed in UK patients. Finally, UK patients had higher somatoform symptom-reporting scores (mean 8.9 vs. 6.9, $p < 0.001$).

Conclusions: IBS is more severe and is associated with a higher level of psychological symptoms in the UK compared with Malaysian patients in secondary care.

The Handling Editor for this article was Professor Peter Gibson, and it was accepted for publication after full peer-review.

1 | INTRODUCTION

Irritable bowel syndrome (IBS) is amongst the most studied disorders of gut–brain interaction, previously known as functional gastrointestinal disorders. The condition is characterised by recurrent abdominal pain or discomfort, in association with a change in stool form or frequency.[1] IBS does not lead to increased mortality,[2] but it is well known to impair quality of life and lead to increased healthcare utilisation.[3–6] Although previous epidemiological studies have suggested a difference in IBS prevalence between geographical regions,[7] the recent Rome Foundation global internet survey demonstrated that prevalence using the Rome IV criteria ranged between 3% and 5% in most countries.[6]

The pathophysiology of IBS is complex and thought to result from the interaction of multiple biopsychosocial factors. Individuals with a family history of IBS are at least two times more likely to have IBS and a genome-wide association study identified six genetic susceptibility loci for IBS. Amongst them, four of the implicated genes were associated with mood and anxiety disorders, suggesting a shared pathogenic pathway.[8] On that note, the association of IBS with stress and psychological comorbidities is well recognised.[9] However, cultural factors and dietary practices may also be implicated in the development of IBS.[3,10]

Differences in characteristics of patients with IBS between populations from different geographical regions have been implied previously,[11] but there have been no direct comparisons between patients in different countries, to our knowledge. Studies comparing patients with IBS from both the West (Europe/North America) and the East (Asia) would enhance global understanding of the condition further, encourage international research collaboration, and facilitate localised clinical management strategies. The present study, therefore, aimed to compare demographic characteristics and gastrointestinal and psychological symptoms between matched patients with IBS seen in secondary care in both the UK and Malaysia.

2 | METHODS

2.1 | Participants and setting

We conducted a cross-sectional study of age- and sex-matched adults with IBS attending secondary care institutions in both the UK and Malaysia. The Malaysian patients were recruited from two centres, one in Kuala Lumpur (University Malaya Medical Centre) and the other in Kota Bharu (Hospital Universiti Sains Malaysia). The UK patients were taken from a study conducted in Leeds Teaching Hospitals Trust recruiting individuals with IBS who had seen a gastroenterologist with symptoms in secondary care, which has been described elsewhere.[12,13] There were no exclusion criteria, other than an inability to understand written Malay or English. Patients from Malaysia completed self-administered paper-based questionnaires in Malay, while those from the UK completed a self-administered web-based questionnaire in English, with their responses stored in a secure online database. Ethics approvals were obtained from the individual institutions (Malaysia: University Malaya Medical Centre Medical Research Ethics Committee in May 2020 and Human Research Ethics Committee of Universiti Sains Malaysia in May 2022; UK: University of Leeds research ethics committee in November 2017).

2.2 | Data collection and synthesis

2.2.1 | Demographic and symptom data

Demographic data from all participants in both countries and lower gastrointestinal symptom data were collected using English[14,15] and Malay[6,16] versions of the Rome III and Rome IV questionnaires, assigning the presence or absence of either Rome III or Rome IV-defined IBS amongst all individuals according to the proposed scoring algorithms.[1,17] IBS subtypes were categorised according to the criteria recommended in the questionnaire, subgrouping into IBS with constipation (IBS-C), diarrhoea (IBS-D), mixed bowel habits (IBS-M), or unclassified (IBS-U), where stool form or frequency cannot classify the individual accurately into one of the other three subtypes. We also assessed the frequency of lower gastrointestinal symptoms, such as abdominal pain, bloating, urgency, and faecal incontinence, as well as the degree to which IBS symptoms were impacting activities of daily living, using the Rome questionnaire.

We assessed the severity of IBS symptoms using the IBS severity scoring system (IBS-SSS).[18] This measures the presence, severity and frequency of abdominal pain, the presence and severity of abdominal distension, satisfaction with bowel habits, and degree to which IBS symptoms are affecting, or interfering with, the person's life. The maximum score is 500 points: <75 points indicates remission of symptoms, 75–174 points for mild symptoms, 175–299 points for moderate symptoms and 300–500 points for severe symptoms.

2.3 | Assessment of mood and extra-intestinal symptoms

Data on anxiety and depression were collected using both English and Malay language versions of the hospital anxiety and depression scale (HADS).[19,20] The total HADS score ranges from a minimum of 0 to a maximum of 21 for either anxiety or depression. We collected extra-intestinal symptom data using the patient health questionnaire-12 (PHQ-12),[21] derived from the validated PHQ-15.[22] The total PHQ-12 score ranges from a minimum of 0 to a maximum of 24. A Malay version of the questionnaire was developed using standard forward-back translation procedures.[23]

2.4 | Assessment of gastrointestinal symptom-specific anxiety and perceived stress

We used the 15-item visceral sensitivity index (VSI),[24] which measures gastrointestinal symptom-specific anxiety. Replies to each item

are provided on a 6-point scale from "strongly disagree" (scored as 0) to "strongly agree" (scored as 5). Again, a Malay version of the questionnaire was developed using standard forward-back translation procedures.[23] We utilised both the English and Malay 10-item versions of the Cohen perceived stress scale (CPSS) to assess perceived stress, which is derived from the original 14-item instrument.[25,26] It is considered to be psychometrically reliable and comparable with its predecessor,[27] and measures the degree to which the individual feels they have experienced stress in the previous month.

2.5 | Statistical analysis

Due to the more restrictive nature of the Rome IV criteria,[28] leading to a reduced prevalence of IBS and more severe symptoms and higher psychological burden with this definition,[12] we used the Rome III criteria in our primary analysis, but we also examined how many patients met both Rome III and Rome IV criteria for IBS in each population. We compared categorical variables between the Malaysian and UK patients, such as sex, symptom severity scores, IBS subtype, impact on activities of daily living, frequency of lower gastrointestinal symptoms and presence or absence of abnormal anxiety scores, abnormal depression scores and high somatoform-symptom reporting scores using a χ^2 test, and continuous data such as age, scores for IBS-SSS, HADS, PHQ-12, VSI and CPSS using an independent samples *t*-test. Due to multiple comparisons, we considered a two-tailed *p* value of <0.01 as statistically significant for these analyses, which we performed using SPSS for Windows (version 26.0 SPSS Inc.).

3 | RESULTS

In total, 266 patients (133 patients from each country) with Rome III IBS were recruited (mean age: 45.1 years in Malaysia vs. 46.5 years in the UK; 57.9% female in both Malaysia and the UK). In terms of demographic characteristics, there were no differences in smoking behaviour, level of education or marital status (Table 1). However, UK patients were more likely to consume alcohol than their Malaysian counterparts (54.1% vs. 10.5%, $p<0.001$).

3.1 | Comparison of gastrointestinal symptoms between UK and Malaysian patients

Amongst patients meeting Rome III criteria for IBS, 70.7% of UK and 48.9% of Malaysian patients also fulfilled Rome IV criteria ($p<0.001$). Although most patients from both countries had a mixed bowel habit (UK: 51.9%, Malaysia: 52.6%), other subtypes differed (IBS-D 42.9% UK vs. 21.1% Malaysia, IBS-C 4.5% UK vs. 12.8% Malaysia, and IBS-U 0.8% UK vs. 13.5% Malaysia, $p<0.001$). UK patients reported more severe IBS symptoms (moderate severity: 49.6%, severe severity: 36.1%, mean IBS-SSS score: 268.0 UK vs. moderate severity: 30.1%, severe severity 10.5%, mean IBS-SSS score: 166.0 Malaysia; $p<0.001$ for both). In addition, UK patients with IBS were significantly more likely to report weekly abdominal pain (71.4% vs. 49.6%, $p<0.001$), weekly abdominal bloating (80.5% vs. 61.1%, $p=0.001$), and meal-related IBS symptoms ≥50% of the time (69.9% vs. 47.0%, $p<0.001$) than patients with IBS from Malaysia ($p<0.001$). Compared with Malaysian patients, UK patients were also more likely to report limitation of activities due to IBS ≥50% of the time (60.2% vs. 43.6%, $p=0.007$). However, there were no significant differences in reporting urgency or faecal incontinence between the two populations.

3.2 | Comparison of psychological symptoms between UK and Malaysian patients

UK patients with IBS were more likely to have abnormal anxiety scores (48.9% vs. 24.1%, $p<0.001$), but significantly more Malaysian patients had abnormal depression scores (40.6% vs. 23.3%, $p=0.008$) (Table 2). Low levels of somatoform symptom reporting were significantly more frequent in Malaysian patients (29.5% vs. 9.8%, $p=0.001$). Back pain, palpitations, tiredness and insomnia were all reported significantly more frequently in UK patients (Table 3). VSI scores were significantly higher in UK patients (mean 50.8 vs. 43.0, $p<0.001$) and CPSS scores were also generally higher, although this difference was not statistically significant (mean 21.3 vs. 19.1, $p=0.014$).

4 | DISCUSSION

We have shown that significant differences exist between patients with IBS seen in secondary care in the UK and Malaysia, based on Rome III criteria, in an age- and sex-matched cohort. UK patients had more severe gastrointestinal symptoms, a larger negative impact on their daily activities and higher levels of psychological symptoms. Additionally, a greater number of UK, as opposed to Malaysian, patients fulfilled the Rome IV criteria for IBS. With respect to IBS subtypes, IBS-D was commoner in UK patients and IBS-C, or IBS-U were commoner in Malaysian patients. Although both groups of patients had substantial psychological comorbidity, UK patients with IBS had higher levels of anxiety, somatoform symptom-reporting, gastrointestinal symptom-specific anxiety and perceived stress, whereas Malaysian patients had higher levels of depression.

The pooled prevalence of IBS from the Rome Foundation global internet survey was 10.1% and 4.1%, based on the Rome III and the Rome IV criteria, respectively.[6] The Rome IV criteria requires abdominal 'pain', instead of 'discomfort', that is related to defaecation to diagnose IBS, a higher symptom frequency threshold of at least once per week, and has been reported to be associated with a more severe spectrum of IBS.[12,29] Given the UK patients with IBS in the current study had more severe symptoms, it is not surprising that a greater proportion of UK patients fulfilled Rome IV criteria for IBS, and this may explain our findings to some degree. However, there are several other possibilities

TABLE 1 Demographic characteristics and gastrointestinal symptoms in UK versus Malaysian patients with Rome III IBS.

	UK patients with Rome III IBS ($n = 133$)	Malaysian patients with Rome III IBS ($n = 133$)	p value*
Mean age (SD)	46.5 (16.9)	45.1 (18.0)	0.54
Female sex (%)	77 (57.9)	77 (57.9)	1.00
Smoker (%)	6 (4.5)	12 (9.0)	0.14
Alcohol use (%)	72 (54.1)	14 (10.5)	<0.001
Married or co-habiting (%)	77 (57.9)	75 (56.4)	0.80
University or postgraduate level of education (%)	72 (54.5)	65 (49.2)	0.39
Ethnicity (%)			
White	126 (94.7)	0 (0)	
South Asian	0	1 (0.8)	
Southeast Asian	1 (0.8)	131 (98.5)	
Middle Eastern	1 (0.8)	1 (0.8)	
Latin American	1 (0.8)	0 (0)	
Other	4 (3.0)	0 (0)	<0.001
Rome IV criteria for IBS met (%)	94 (70.7)	65 (48.9)	<0.001
IBS subtype (%)			
Constipation	6 (4.5)	17 (12.8)	
Diarrhoea	57 (42.9)	28 (21.1)	
Mixed stool pattern	69 (51.9)	70 (52.6)	
Unclassified	1 (0.8)	18 (13.5)	<0.001
IBS-SSS symptom severity (%)			
Remission	2 (1.5)	27 (20.3)	
Mild	17 (12.8)	52 (39.1)	
Moderate	66 (49.6)	40 (30.1)	
Severe	48 (36.1)	14 (10.5)	<0.001
Mean IBS-SSS score (SD)	268.0 (92.1)	166.0 (103.1)	<0.001
Abdominal pain severity (SD)	41.3 (29.5)	17.9 (27.1)	<0.001
Abdominal pain frequency (SD)	44.7 (34.4)	20.4 (30.5)	<0.001
Bloating severity (SD)	40.8 (32.5)	30.8 (28.4)	0.008
Dissatisfaction with bowel habit (SD)	68.5 (28.7)	51.4 (29.9)	<0.001
Interference with life (SD)	72.6 (25.0)	45.6 (30.4)	<0.001
Abdominal pain at least once per week (%)	95 (71.4)	66 (49.6)	<0.001
Abdominal bloating at least once per week (%)	107 (80.5)	80 (61.1)	0.001
Meal-related IBS symptoms ≥50% of the time (%)	93 (69.9)	62 (47.0)	<0.001
IBS limits activities ≥50% of the time (%)	80 (60.2)	58 (43.6)	0.007
Urgency at least most days (%)	40 (30.1)	28 (21.1)	0.092
Faecal incontinence at least once a week (%)	21 (15.8)	14 (10.5)	0.20

*p value for independent samples t-test for continuous data and Pearson χ^2 for comparison of categorical data.

for the observed differences in symptom severity between UK and Malaysian patients. Firstly, UK patients had higher levels of anxiety, gastrointestinal symptom-specific anxiety and perceived stress than patients from Malaysia. Several studies have demonstrated that anxiety, but not depression, is associated with more severe IBS, with a correlation between anxiety scores and IBS severity.[30,31] Furthermore, anxiety has been shown to be an independent predictor of dissatisfaction with medical care and higher healthcare utilisation among patients with IBS.[32] Somatoform symptom-reporting is a recognised psychological factor directly associated with IBS severity. In cross-sectional studies in both the UK and Canada, patients with IBS with higher levels of anxiety were reported to have higher levels of somatoform symptom reporting, which was associated with a greater frequency of abdominal bloating and abdominal pain.[33,34] Furthermore, lower overall quality of life among IBS patients has been shown to be influenced by both somatoform symptoms and anxiety.[35]

Another possible explanation for differences in symptom severity may relate to variations in cultural factors and dietary habits between the two countries. In this study, a higher proportion of UK, compared with Malaysian, patients with IBS consumed regular alcohol (54.1% vs. 10.5%). This is consistent with the higher total alcohol per capita consumption among European, compared with Asian, countries.[36] Furthermore, the population of Malaysia is predominantly Muslim, and alcohol is forbidden in the religion.[37] Alcohol affects gastrointestinal motility, absorption and permeability, which may contribute to more gastrointestinal symptoms.[38] In addition, the typical Western diet is high in fat and sodium.[39] Fatty food stimulates the gastrocolic reflex, which may explain the higher prevalence of diarrhoea and weekly abdominal pain among UK patients. Another dietary difference between Western and Asian foods is the fermentable oligo-, di-, mono-saccharide and polyol (FODMAP) content of the habitual diet. Based on studies conducted in subjects

TABLE 2 Psychological symptoms in UK versus Malaysian patients with Rome III IBS.

	UK patients with Rome III IBS ($n = 133$)	Malaysian patients with Rome III IBS ($n = 133$)	p value*
HADS-A categories (%)			
Normal	33 (24.8)	49 (36.8)	
Borderline abnormal	35 (26.3)	52 (39.1)	
Abnormal	65 (48.9)	32 (24.1)	<0.001
Mean HADS-A score (SD)	10.8 (4.9)	8.3 (3.7)	<0.001
HADS-D categories (%)			
Normal	71 (53.4)	51 (38.3)	
Borderline abnormal	31 (23.3)	28 (21.1)	
Abnormal	31 (23.3)	54 (40.6)	0.008
Mean HADS-D score (SD)	7.6 (4.7)	8.5 (5.3)	0.13
PHQ-12 severity (%)			
Low	13 (9.8)	39 (29.5)	
Mild	41 (30.8)	32 (24.2)	
Moderate	52 (39.1)	42 (31.8)	
Severe	27 (20.3)	19 (14.4)	0.001
Mean PHQ-12 score (SD)	8.9 (4.1)	6.9 (4.9)	<0.001
Mean VSI score (SD)	50.8 (15.6)	43.0 (17.5)	<0.001
Mean CPSS score (SD)	21.3 (8.3)	19.1 (6.1)	0.014

*p value for independent samples t-test for continuous data and Pearson χ^2 for comparison of categorical data.

TABLE 3 PHQ-12 Symptom Frequency in UK Versus Malaysian Patients with Rome III IBS.

	UK patients with Rome III IBS ($n = 133$)	Malaysian patients with Rome III IBS ($n = 133$)	p value*
Back pain (%)	103 (77.4)	78 (58.6)	0.001
Joint pain (%)	91 (68.4)	77 (57.9)	0.075
Period pain (%)	35 (26.3)	35 (26.3)	1.00
Headache (%)	89 (66.9)	76 (57.1)	0.10
Chest pain (%)	41 (30.8)	52 (39.1)	0.16
Dizzy (%)	69 (51.9)	66 (49.6)	0.71
Faint (%)	15 (11.3)	9 (6.8)	0.20
Palpitations (%)	72 (54.1)	46 (34.6)	0.001
Short of breath (%)	55 (41.4)	45 (34.1)	0.22
Dyspareunia (%)	32 (24.1)	21 (15.8)	0.091
Tired (%)	130 (97.7)	97 (72.9)	<0.001
Insomnia (%)	112 (84.2)	80 (60.2)	<0.001

*p value for Pearson χ^2.

with IBS and healthy controls, the quantity of dietary FODMAPs is at least 17 g per day in the West,[40] compared with approximately 13 g per day in Asia.[41] FODMAPs are non-digestible, poorly absorbed, short-chain carbohydrates that commonly trigger gastrointestinal symptoms, including abdominal pain, bloating and diarrhoea. A low FODMAP diet has been shown to improve IBS symptoms[42,43] and is currently recommended in several management guidelines.[44,45] Hence, it is possible that a higher FODMAP intake may explain the significantly higher levels of these symptoms, as well as the higher frequency of meal-related symptoms, among UK patients.

Despite our best efforts, there were several limitations to this study. Differences in the referral pattern to secondary care in Malaysia and the UK might have led to a selection bias of more patients with severe IBS in the latter. However, consultation in secondary care in both countries requires a referral from primary care, although the threshold for this may vary. Several sociodemographic

factors, including socioeconomic status and body mass index (BMI), which may influence symptoms, were not collected in this study. An increased BMI has been associated with more severe IBS symptoms,[46] and Caucasians are recognised to have a higher BMI compared with Asians.[47] We used identical questionnaires in both countries but the method of administration differed slightly, which may have affected study findings,[48] although they were still self-completed. Overlap of disorders of gut–brain interaction is common in patients consulting with symptoms, which may drive symptom severity, an issue we did not study. We did not perform a formal sample size calculation but instead recruited sufficient numbers of patients in each country to be able to match them closely on age and sex. Finally, the IBS patients in all three institutions may not have been entirely representative of typical secondary care patients in the UK and Malaysia. However, a major strength to this study was that it was conducted prospectively and, therefore, utilised identical, detailed, questionnaires, which had either been developed or culturally validated within both populations.

In conclusion, UK patients with IBS in secondary care have more severe symptoms, which have a greater impact on daily activities, compared with Malaysian patients. Although higher levels of anxiety, somatoform symptom-reporting, gastrointestinal symptom-specific anxiety, and stress were observed in UK patients, differences in cultural practices and dietary habits may also be contributory. The findings from this study indicate that variations in the clinical characteristics of IBS exist among adult patients in different geographical regions, despite similarities in prevalence globally. Further studies, directly comparing IBS subjects between different regions, are required to confirm our findings.

AUTHOR CONTRIBUTIONS

Kee Huat Chuah: Data curation (equal); project administration (equal); writing – original draft (equal). **Christopher J. Black:** Conceptualization (equal); data curation (equal); project administration (equal). **Vincent Tee:** Data curation (equal); project administration (equal). **Sze Zee Lim:** Data curation (equal); project administration (equal). **Wen Xuan Hian:** Data curation (equal); project administration (equal). **Nur- Fazimah Sahran:** Data curation (equal); project administration (equal). **Yeong Yeh Lee:** Conceptualization (equal); writing – original draft (equal). **Sanjiv Mahadeva:** Conceptualization (equal); formal analysis (equal); writing – original draft (equal); writing – review and editing (equal). **Alexander C. Ford:** Conceptualization (equal); formal analysis (lead); writing – original draft (equal); writing – review and editing (lead).

ACKNOWLEDGEMENTS

We are grateful to the participants who gave their time to answer our questionnaire.

AUTHORSHIP

Guarantor of the article: ACF is a guarantor.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST STATEMENT

Kee-Huat Chuah: none. Christopher J. Black: none. Vincent Tee: none. Sze-Zee Lim: none. Wen-Xuan Hian: none. Nur-Fazimah Sahran: none. Yeong-Yeh Lee: none. Sanjiv Mahadeva: none. Alexander C. Ford: none.

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How to cite this article: Chuah K-H, Black CJ, Tee V, Lim S-Z, Hian W-X, Sahran N-F, et al. A prospective comparison of UK and Malaysian patients with irritable bowel syndrome in secondary care. Aliment Pharmacol Ther. 2023;58:168–174. https://doi.org/10.1111/apt.17567