



Review Article

Mysteries of Irritable Bowel Syndrome: Post Infections and Psychophysiological Reactions

Hlaing HH^{1*}, Ahmad U¹ and Tsai H²

¹Registrar, Gastroenterology Department, Hull and East Yorkshire Hospitals, NHS Trust, UK

²Consultant, Gastroenterology Department, Hull and East Yorkshire Hospitals, NHS Trust, UK

Abstract

The relationship between gastrointestinal infections and ongoing symptoms after the infections is well established in many studies across many regions of the world. The duration of symptoms are related to the types of infections and sensitivities of the patients. Many psychosomatic symptom associations have been established after post infection according to studies. Many treatment modalities have been tried for minimal ongoing inflammation, microbiota compositions and dietary modifications. However, there is no proper established consensus treatment for post infectious IBS and needs more ongoing works to establish a consensus guideline for these symptom associations.

Introduction

Functional bowel disorders are significant fractions of the clinic consultations in everyday practice. There are many proposed hypotheses and ongoing studies about the culprits of the functional gastrointestinal symptoms and management of these disorders are still challenging. Among many studies and reviews, the possible relationship

***Corresponding author:** Hlaing HH, Registrar, Gastroenterology Department, Hull and East Yorkshire Hospitals, NHS Trust, England, UK, Tel: +44 07492724192; Email: hhtar@gmail.com; htartar.hlaing@hey.nhs.uk

Citation: Hlaing HH, Ahmad U, Tsai H (2018) Mysteries of Irritable Bowel Syndrome: Post Infections and Psychophysiological Reactions. J Gastroenterol Hepatology Res 3: 021.

Received: July 03, 2018; **Accepted:** August 09, 2018; **Published:** August 27, 2018

Copyright: © 2018 Hlaing HH, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

between the infection of the gastrointestinal tract and Irritable bowel syndrome seems well established based on clinical, epidemiological data and animal models.

Sir Arthur Hurst (1943) introduced a term “Post-dysenteric colonic irritability” and it mentioned the persistent irritability of the bowel following an acute attack of bacillary or amoebic dysentery [1]. The later symptoms which persisted after the infection died out were assumed as functional irritability of the colon [1]. Stewart described 2 types of post dysenteric colitis and type 1 which accounts for 55% and associated mostly with diarrhoea which is intermittent, seldom severe and sometimes morning symptoms with no organic changes in colon [2]. In some cases psychological factors noted with symptoms. These cases were self-limiting and less severe with slow natural improvement without much treatment [2]. However, type 2 post dysenteric colitis is associated with more inflammatory response and more severe outcome with the requirement for extensive treatment [2]. It is documented that 3% to 36% of gastrointestinal infections are associated with new onset IBS symptoms and bacterial, protozoal and helminthic infections are associated with more prolonged symptoms [3]. In 1962, Chaudhury and Truelove carried out observational study in 130 patients with irritable colon syndrome and noted that the syndrome has strongly linked to previous history of dysentery and post dysenteric group has more favorable outcome than others [4].

Risk Factors and Associations

There are many risk factors which are identified to be associated with post infectious irritable bowel syndrome. It includes prolonged duration of initial illness, toxicity of infecting bacterial strain, smoking, mucosal markers of inflammation, female gender, depression, hypochondriasis and adverse life events in the preceding 3 months [3]. A systematic review and meta-analysis revealed that the odds developing irritable bowel syndrome increased six fold after bowel infections and young age, prolonged fever, anxiety and depression are associated risk factors [5]. Host factors; female gender (relative risk-2.9) and advancing age seem to have modest degree of protection [6]. Interestingly, patients who presented with vomiting were less likely to develop persistent bowel symptoms and may even be protective due to reduce infecting dose [6]. The more severe the attack of infection and inflammation, the longer the symptoms and reaction with persistently increasing concentration of inflammatory cytokines like interleukin 1[6].

Epidemiology of Post Infectious Irritable Bowel Syndrome

Post infectious IBS is associated with more virulent organisms like *Campylobacter jejuni* and *E. Coli* O157:H7 which are associated with mucosal ulceration [7]. The highest incidence of PI-IBS was seen in the cases after the dual infection with *C. Jejuni* and *E. coli* O157: H7 and which was 36% after 24 months of post infection [3]. In 1993, a study was done in 38 patients following infection with salmonella food poisoning and it was found out that 31% are associated with PI-IBS symptoms fulfilling ROME 3 criteria with female predominance [7]. A prospective cohort study was done in the subjects after

infection with *Salmonella enteritidis* and questionnaires were asked in 481 cases and 547 controls and it was found out that cumulative incidence of IBS in 12 months after infection was 11.6% in cases and 1.5% in controls with significant relative risk of 7.8 [8]. A large cohort study (Walkerton Health Study) was done in 2002 which was 2 years after outbreak of acute *E. coli* O157: H7 and *Campylobacter Jejuni* infection following contamination of municipal water supply [9]. Among 2069 participants, ROME I criteria were met in 71 of 701 controls (10.1%) and 249 of 904 subjects (27.5%) in self-reported gastroenteritis and 168 of 464 subjects (36.2%) with clinically suspected gastroenteritis ($p < 0.001$) [9].

The prevalence of the symptoms of post infectious IBS after norovirus infection was carried out in the Canada and it was found out that 21 of 89 (23.6%) had symptoms of post infectious IBS (ROME 1 criteria) at 3 months after infection compared to 3.4% of those who were well during outbreak but the prevalence among cases and controls was not significantly different in 6, 12 and 24 months post infection [10]. It is concluded that the IBS symptoms are more transient after viral infections [10]. There was a large prospective cohort study in 1252 subjects following 6 years after lab-confirmed *Giardia* infection and it was found out that 39.4% of cases were met ROME III criteria for IBS which was significantly elevated compared to controls. It was concluded that intestinal protozoan infections are associated with long term and slow self-limiting complications [11]. The risks of IBS have been found to increase in patients following enteric infections in Western countries and travelers' diarrhea coming back from developing countries [12].

Clinical Features of Post Infectious IBS

ROME III criteria for IBS mentioned that recurrent abdominal pain or discomfort at least 3 days/month in the last 3 months associated with two or more of the followings: Improvement with defecation, Onset associated with a change in frequency of stool, Onset associated with a change in form (appearance) of stool. The diagnosis of post infectious IBS was considered in the patients who have no previous history of IBS in the studies. Most of the studies were done 3 months to 6 years post infection in previously asymptomatic individuals.

Post infectious IBS was found to have more diarrheal symptoms compared to non-infectious IBS. A six year follow up study after post infectious IBS was done by Neal et al., and comparing 14 PI-IBS with 20 new IBS, it was found out that PI-IBS had significantly more days with loose stools ($p < 0.005$) but a similar number of days with pain, urgency and bloating though large number needed to confirm that [13].

Pathophysiology of Post Infectious IBS

There are several factors which can contribute to the pathophysiology of post infectious IBS. A study which was done in 2000 by Spiller et al., revealed that the number of enteroendocrine cells and T lymphocytes in rectal biopsies increased along with increasing gut permeability in acute infection following *Campylobacter enteritis* and it can persist for more than one year which contributes to post dysenteric IBS [14]. The gut motility and secretion are related to serotonin (5-HT) which releases from enterochromaffin cells and both UC and IBS are associated with similar molecular changes in serotonergic signaling mechanisms [15]. A study which was done in PI-IBS and IBS-C patients matched with controls to monitor post prandial

5 HT level revealed that PI-IBS patients have significantly higher peak post prandial 5 HT values than patients with IBS-C and controls [16].

In 1993, a study of changes in anorectal function was done in patients who had chronic persistent symptoms 2 years after *Salmonella* infection revealed that all patients had increased rectal sensitivity and decreased rectal compliance [17]. A study done by Kanazawa et al., in 2014 which is a comparative study between PI-IBS and Non PI-IBS mentioned that PI-IBS has greater colonic hypercontractility than non PI-IBS and speculated that mild mucosal inflammation may cause that problem [18].

There is a study regarding the possibility of genetic predisposition in post infectious IBS done by Alexandra-Chloe' Villani et al., in 2001 and it mentioned that four genetic variants were likely to be associated with PI-IBS though it is not significant after correction for number of single nucleotide polymorphism. Two of them are located in TLR9 which are pattern recognition receptors and one in CDH-1 encodes tight junction protein and the other in IL-6, cytokines. It was concluded that genes which are responsible for encoding proteins for epithelial cell barrier function and innate immune response are associated with post infectious IBS [19]. Regarding the concept of microbiota in post infectious IBS, current data with limited number of patients could not define any entire phylogenetic for PI-IBS though it supports the idea that the alterations in commensal proportion which can in turn affect the overall microbiological picture [20]. However, psychological factors found out to have as a precipitation to the PI-IBS as stress can increase intestinal permeability and depression can lower the threshold to inflammatory response [21,22].

Infectious gastroenteritis can result in Post-Infectious Malabsorption Syndrome (PI-MAS) known as tropical sprue and in turn PI-MAS can link to Small Intestinal Bacterial Overgrowth (SIBO). There are also some suggestions that SIBO can link to diarrhoea predominant IBS as in PI-IBS [23]. However, a systematic review and meta analysis showed the role of testing in SIBO in IBS patients remains unclear [24].

Treatment of Post Infectious IBS

There are many treatment modalities which had been tried in PI-IBS like steroids, mesalazine, probiotics and dietary modifications. A study was done in 29 patients with PI-IBS regarding the response to oral Prednisolone 30 mg/day for 3 weeks and it did not improve the symptoms and intestinal enterochromaffin cells were not reduced though T-lymphocytes counts decreased [25,26]. There was a study based on both post infectious IBS and non infective IBS regarding Mesalazine therapy which has anti-inflammatory effects. It included 61 patients who met ROME III criteria for IBS with diarrhea predominant features and 18 and 43 for PI-IBS and non infective IBS respectively. They were given Mesalazine 800 mg 3 times/day for 30 days and it was found out that both groups had significant reduction in total symptom score, stool frequency, consistency, abdominal pain and discomfort and all were statistically significant with $P < 0.0001$. There were no differences in response between these two groups [27].

There were some studies which were done in dietary implications like FODMAP in IBS and found out to have symptom improvements but these are not limited to post infectious IBS and mostly generalized IBS. As general IBS patients, individual sensitivity of diet plays a

role in post-infectious IBS patients and tailored dietary advice with low FODMAP diets and probiotics can change the microbiota composition and regulates the gastrointestinal endocrine cells [28,29]. Based on the hypothesis that the IBS is associated with Small Intestinal Bacterial Overgrowth [SIBO], the symptoms improvement was assessed after treatment of SIBO and it showed significant reduction [30]. In 2006, a study which was based on non-absorbable oral antibiotic Rifaximin 400 mg three times daily for 10 days given to IBS patients and global improvement scale was measured for 10 weeks after discontinuation. Symptom improvement was seen up to 10 weeks after discontinuation of treatment though the study has limitations of modest sample size, short duration and patients were from one centre [31]. As the post infectious IBS can follow traveler's diarrhea and has impaction on long term morbidity, there were two studies which use Rifaximin to prevent traveler's diarrhea. Both were randomized double-blinded, placebo controlled trials and they showed that Rifaximin was effective and well tolerated with minimal alteration of faecal flora [32,33]. However, the possibility of preventing PI-IBS in long term needs more evaluation [12]. In diarrhea predominant IBS, 5 HT3 receptor antagonist, alosetron, was recently approved only for female diarrhea predominant IBS in US but only for limited prescriptions due to side effects of severe constipation, ischaemic colitis and bowel perforation. It is based on serotonin pathway causing enhancement in small intestinal absorption, slow colonic transit and reduces visceral pain [34]. There is a study which reviewed the records of 70 patients with *Clostridium difficile* infection who had faecal microbiota transplantation and it showed that faecal microbiota transplantation through colonoscopy seems an effective treatment option for recurrent and virulent *C. Diff* infection with post-infectious bowel symptoms [35]. The use of central neuromodulators in functional bowel disorders based on the hypothesis of brain-gut interaction was published recently as ROME foundation working team report though it is under the process of further refinement [36].

Conclusion

Post infectious IBS is a long term debilitating condition with not very promising treatment options at the moment. It is likely preventable if the infection can be prevented and the researches regarding this condition might need to explore further bearing in mind about emergence of antimicrobial resistance all over the world. It is also an area that still needs addressing in depth relating pathophysiological mechanisms and treatment modalities. Moreover, multidisciplinary involvement in developing consensus guideline is important. As there can be different microbiota composition with variant strains of infection in different population, the new concept of ROME IV which based on multicultural focus hope to get more solutions for such subtypes of IBS.

References

1. Powell SJ, Wilmot AJ (1966) Ulcerative Post-dysenteric Colitis. Gut 7: 438-443.
2. Stewart GT (1950) Post-dysenteric Colitis. Br Med J 1: 405-409.
3. Spiller R, Garsed K (2009) Postinfectious Irritable Bowel Syndrome. Gastroenterology 136: 1979-1988.
4. Chaudhary Na, Truelove Sc (1962) The Irritable Colon Syndrome. A Study Of The Clinical Features, Predisposing Causes, And Prognosis In 130 Cases. Q J Med 31: 307-322.
5. Thabane M, Kottachchi DT, Marshall JK (2007) Systematic review and meta-analysis: The incidence and prognosis of post-infectious irritable bowel syndrome. Aliment Pharmacol Ther 26: 535-544.
6. Neal KR, Hebden J, Spiller R (1997) Prevalence of gastrointestinal symptoms six months after bacterial gastroenteritis and risk factors for development of the irritable bowel syndrome: postal survey of patients. BMJ 314: 779-782.
7. McKendrick MW, Read NW (1994) Irritable bowel syndrome--post salmonella infection. J Infect 29: 1-3.
8. Mearin F, Perez-Oliveras M, Perello A, Vinyet J, Ibañez A, et al. (2005) Dyspepsia and irritable bowel syndrome after a Salmonella gastroenteritis outbreak: one-year follow-up cohort study. Gastroenterology 129: 98-104.
9. Marshall JK, Thabane M, Garg AX, Clark WF, Salvadori M, et al. (2006) Incidence and epidemiology of irritable bowel syndrome after a large waterborne outbreak of bacterial dysentery. Gastroenterology 131: 445-450.
10. Marshall JK, Thabane M, Borgaonkar MR, James C. Postinfectious irritable bowel syndrome after a food-borne outbreak of acute gastroenteritis attributed to a viral pathogen. Clin Gastroenterol Hepatol 5: 457-460.
11. Hanevik K, Wensaas KA, Rortveit G, Eide GE, Mørch K, et al. (2014) Irritable bowel syndrome and chronic fatigue 6 years after giardia infection: a controlled prospective cohort study. Clin Infect Dis 59: 1394-1400.
12. Ericsson CD, Hatz C, DuPont AW (2008) Postinfectious Irritable Bowel Syndrome. Clinical Infectious Diseases 46: 594-599.
13. Neal KR, Barker L, Spiller RC (2002) Irritable bowel syndrome and the enteric nervous system, Prognosis in post-infective irritable bowel syndrome: a six year follow up study. Gut 51: 410-413.
14. Spiller RC, Jenkins D, Thornley JP, Hebden JM, Wright T, et al. (2000) Increased rectal mucosal enteroendocrine cells, T lymphocytes, and increased gut permeability following acute Campylobacter enteritis and in post-dysenteric irritable bowel syndrome. Gut 47: 804-811.
15. Coates MD, Mahoney CR, Linden DR, Sampson JE, Chen J, et al. (2004) Molecular defects in mucosal serotonin content and decreased serotonin reuptake transporter in ulcerative colitis and irritable bowel syndrome. Gastroenterology 126: 1657-1664.
16. Dunlop SP, Coleman NS, Blackshaw E, Perkins AC, Singh G, et al. (2005) Abnormalities of 5-hydroxytryptamine metabolism in irritable bowel syndrome. Clin Gastroenterol Hepatol 3: 349-357.
17. Bergin AJ, Donnelly TC, McKendrick MW, Nicholas WR (1993) Changes in anorectal function in persistent bowel disturbance following salmonella gastroenteritis. European Journal of Gastroenterology & Hepatology 5: 617-620.
18. Kanazawa M, Palsson OS, van Tilburg MA, Gangarosa LM, Fukudo S, et al. (2014) Motility response to colonic distention is increased in postinfectious irritable bowel syndrome (PI-IBS). 26: 696-704.
19. Villani AC, Lemire M, Thabane M, Belisle A, Geneau G, et al. (2010) Genetic risk factors for post-infectious irritable bowel syndrome following a waterborne outbreak of gastroenteritis. Gastroenterology 138:1502-1513.
20. Salonen A, de Vos WM, Palva A (2010) Gastrointestinal microbiota in irritable bowel syndrome: present state and perspectives. Microbiology 156: 3205-3215.
21. Söderholm JD, Perdue MH (2001) Stress and gastrointestinal tract. II. Stress and intestinal barrier function. Am J Physiol Gastrointest Liver Physiol 280: 7-13.
22. Ghia JE, Blennerhassett P, Collins SM (2008) Impaired parasympathetic function increases susceptibility to inflammatory bowel disease in a mouse model of depression. J Clin Invest 118: 2209-2218.

23. Ghoshal UC, Gwee KA (2017) Post-infectious IBS, tropical sprue and small intestinal bacterial overgrowth: the missing link. *Nat Rev Gastroenterol Hepatol* 14: 435-441.
24. Ford AC, Spiegel BM, Talley NJ, Moayyedi P (2009) Small intestinal bacterial overgrowth in irritable bowel syndrome: systematic review and meta-analysis. *Clin Gastroenterol Hepatol* 7: 1279-1286.
25. Dunlop SP, Jenkins D, Neal KR, Naesdal J, Borgaonker M, et al. (2003) Randomized, double-blind, placebo-controlled trial of prednisolone in post-infectious irritable bowel syndrome. *Aliment Pharmacol Ther* 18: 77-84.
26. Collins SM, Chang C, Mearin F (2012) Postinfectious Chronic Gut Dysfunction: From Bench to Bedside. *Am J Gastroenterol Suppl* 1: 2-8.
27. Bafutto M, Almeida JR, Leite NV, Oliveira EC, Gabriel-Neto S, et al. (2011) Treatment of postinfectious irritable bowel syndrome and noninfective irritable bowel syndrome with mesalazine. *Arq Gastroenterol* 48: 36-40.
28. El-Salhy M, Gundersen D (2015) Diet in irritable bowel syndrome. *Nutrition Journal* 14: 36.
29. Iacob T, Țăulescu DF, Dumitrașcu DL (2017) Therapy of the postinfectious irritable bowel syndrome: an update. *Clujul Med* 90: 133-138.
30. Pimentel M, Chow EJ, Lin HC (2000) Eradication of small intestinal bacterial overgrowth reduces symptoms of irritable bowel syndrome. *Am J Gastroenterol* 95: 3503-3506.
31. Pimentel M, Park S, Mirocha J, Kane SV, Kong Y (2006) The effect of a nonabsorbed oral antibiotic (rifaximin) on the symptoms of the irritable bowel syndrome: a randomized trial. *Ann Intern Med* 145: 557-563.
32. DuPont HL, Jiang ZD, Okhuysen PC, Ericsson CD, de la Cabada FJ, et al. (2005) A randomized, double-blind, placebo-controlled trial of rifaximin to prevent travelers' diarrhea. *Ann Intern Med* 142: 805-812.
33. Taylor DN, McKenzie R, Durbin A, Carpenter C, Atzinger CB, et al. (2006) Rifaximin, a nonabsorbed oral antibiotic, prevents shigellosis after experimental challenge. *Clin Infect Dis* 42: 1283-1288.
34. De Ponti F, Tonini M (2001) Irritable bowel syndrome: new agents targeting serotonin receptor subtypes. *Drugs* 61: 317-332.
35. Mattila E, Uusitalo-Seppälä R, Wuorela M, Lehtola L, Nurmi H, et al. (2012) Fecal transplantation, through colonoscopy, is effective therapy for recurrent *Clostridium difficile* infection. *Gastroenterology* 142: 490-496.
36. Drossman DA, Tack J, Ford AC, Szegedy E, Törnblom H, et al. (2018) Neuromodulators for Functional Gastrointestinal Disorders (Disorders of Gut-Brain Interaction): A Rome Foundation Working Team Report. *Gastroenterology* 154: 1140-1171.



Addiction & Addictive Disorders
Advances in Industrial Biotechnology
Advances in Microbiology Research
Agronomy and Agricultural Science
AIDS Clinical Research & STDs
Alcoholism, Drug Abuse & Substance Dependence
Allergy Disorders and Therapy
Alternative, Complementary & Integrative Medicine
Alzheimer's & Neurodegenerative Diseases
Anesthesia & Clinical care
Angiology & Vascular Surgery
Animal Research and Veterinary Science
Aquaculture & Fisheries
Archives of Urology
Archives of Zoological Studies
Atmospheric & Earth Sciences
Biotech Research & Biochemistry
Brain & Neuroscience Research
Cancer Biology and Treatment
Cardiology and Neurocardiovascular Diseases
Cell Biology & Cell Metabolism
Clinical Dermatology and Therapy
Clinical Immunology & Immunotherapy
Clinical Studies and Medical Case Reports
Community Medicine & Public Health Care
Current Trends: Medical & Biological Engineering
Cytology & Tissue Biology
Dentistry: Oral Health & Cosmesis
Diabetes & Metabolic Syndrome Disorders
Emergency Medicine, Trauma and Surgical Care
Environmental Science: Current Research
Food Science & Nutrition
Forensic, Legal & Investigative Sciences
Gastroenterology & Hepatology Research
Genetics & Genomic Sciences
Gerontology & Geriatric Medicine
Hematology, Blood Transfusion & Disorders
Hospice & Palliative Medical Care
Human Endocrinology
Infectious & Non Infectious Diseases
Internal Medicine and Primary HealthCare
Laser Research & Applications
Medicine: Study & Research
Modern Chemical Sciences
Nanotechnology: Nanomedicine & Nanobiotechnology
Neonatology and Clinical Pediatrics
Nephrology & Renal Therapy
Non-invasive Vascular Investigations
Nuclear Medicine, Radiology & Radiation Therapy
Obesity & Weight Loss
Ophthalmology & Clinical Research
Orthopedic Research & Physiotherapy
Otolaryngology, Head and Neck Surgery
Pathology: Clinical & Medical Research
Pharmacology, Pharmaceuticals & Pharmacovigilance
Physical Medicine, Rehabilitation & Disabilities
Plant Science: Current Research
Practical and Professional Nursing
Protein Research & Bioinformatics
Psychiatry, Depression and Anxiety
Pulmonary Medicine & Respiratory Research
Reproductive Medicine, Gynaecology and Obstetrics
Stem Cells Research, Development & Therapy
Surgery: Current Trends & Innovations
Toxicology: Current Research
Translational Science and Research
Vaccines Research and Vaccination
Virology & Antivirals

Submit Your Manuscript: <http://www.heraldopenaccess.us/Online-Submission.php>