"INCIDENCE AND RISK FACTORS ASSOCIATED WITH DEVELOPMENT OF POST INFECTION IRRITABLE BOWEL SYNDROME (PI-IBS)- A ONE YEAR PROSPECTIVE LONGITUDINAL STUDY"

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LIST OF ABBREVIATIONS

AGE	–	Acute Gastroenteritis
CCK	-	Cholecystokinin
EC	-	Enterochromaffin cells
ESR	-	Erythrocyte Sedimentation Rate
FGID	-	Functional gastrointestinal disorders
FODMAP	-	Fermentable Oligo-, Di-, Mono- saccharides and Polyols
HADS	-	Hospital Anxiety and Depression Scale
IBD	-	Inflammatory Bowel Disease
IBS	-	Irritable Bowel Syndrome
OR	-	Odds Ratio
PI-IBS	-	Post infection Irritable Bowel Syndrome
RBC	-	Red blood cell
RCT	-	Randomized Control Trials
RFWT	-	ROME foundation working team
TLR	-	Toll like receptors

ABSTRACT

Background and objectives: Post-infection Irritable Bowel syndrome (PI-IBS) is seen following an episode of Acute Gastroenteritis(AGE). There is paucity of literature in this field with respect to Indian population. This study aims to evaluate the incidence of PI-IBS and identify the risk factors associated with it.

Materials and Methods: This prospective study was carried out over a period of one year on AGE patients admitted in KLE Dr.Prabhakar Kore Hospital, Belgaum. Clinical and demographic characteristics were noted, risk factors evaluated and previous or current IBS was ruled out by means of an IBS questionnaire. The patients were followed up after 6 months to look for development of IBS (ROME IV criteria).

Results: Out of 100 hospitalised AGE patients, one-fourth i.e. 25 developed PI-IBS after 6 months. Out of these, 18 patients had IBS-D type and remaining 7 had IBS-C type. The factors significantly associated with PI-IBS were younger age, longer duration of AGE, depression, abdominal cramps.On multivariate logistic regression analysis, longer duration of acute gastroenteritis (>7 days) (p-value=0.0040) and presence of abdominal cramps (p-value=0.0130) were found to be significantly influencing the development of PI-IBS at 6 months.

Conclusion: One fourth of the patients in our study developed PI-IBS after 6 months of AGE episode. Younger age, depression, longer duration of diarrhoea and abdominal cramps were statistically significant risk factors for development of AGE. Physicians should keep a high suspicion for PI-IBS, in patients with predisposing risk factors. The possibly involved molecular mechanisms in the pathogenesis of PI-IBS should be investigated for better understanding of the disease, and to plan and strategize therapeutic options.

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INTRODUCTION

Irritable Bowel Syndrome (IBS) is a common condition diagnosed in the daily out-patient department. It is characterised by abdominal pain and altered bowel habits, with no detectable structural abnormalities and normal routine diagnostic tests.[1] IBS involves gut disturbances, predominantly intestinal motility and sensation. IBS is a form of brain-gut disorder as most intestinal functions are found to be regulated by the brain.

IBS affects approximately 8.8% of the population worldwide, causing significant morbidity.[2] Healthcare expenditure increases and quality of life decreases for the affected individuals. As the etiology of IBS is unclear, treatment mainly focusses on resolution of symptoms, and improving the quality of life. The pathophysiology mainly involves psychological factors and gastrointestinal dysfunction.[3]

The prevalence of IBS in India ranges from 4.2% to 7.5%.[4] IBS is reported to be more prevalent in rural areas rather than urban in Asian countries, with significant variations in socio-demographic and symptom profile.[4] The ROME criteria is used to diagnose IBS, currently in practice being ROME IV.

Post Infection IBS (PI-IBS) is development of de novo IBS symptoms (by Rome criteria) in an individual after he experiences an episode of acute infectious gastroenteritis (AGE) which includes two or more of the following: fever, vomiting, diarrhoea or a positive stool culture.[5,6] This includes persistent abdominal discomfort, diarrhoea, bloating despite clearance of the inciting pathogen. PI-IBS was first described, in 1962, by Chaudhary and Truelove in patients who were presumed to have bacterial or amoebic dysentery.[7] Since then, numerous studies have reported

association between AGE and development of IBS.[8] There are quite a few studies in Western countries on PI-IBS, its incidence, demographics, risk factors. However, very few studies in India have dealt with PI-IBS.

Long term follow up studies have reported that bacterial pathogen related PI-IBS may persist for up to 8-10 years after the episode of AGE and that the risk for development of PI-IBS increases six-fold after gastrointestinal infection.[9]Global studies have reported a higher prevalence of IBS in females but no significant sex-related differences were reported in South Asia.[10]

India has a high incidence of AGE, hence a lot of people have a chance of developing PI-IBS. The present study is being undertaken to learn about the incidence of PI-IBS in our local population, and to understand the risk factors associated with it. There is paucity of literature in this field with respect to Indian population, more so in this region of Karnataka. This study will help us identify the patients at risk of developing PI-IBS, giving us early interventional opportunities to ameliorate symptom development and to educate the patients with acute gastroenteritis about the possibility of development of IBS in future and how to deal with it.

OBJECTIVES

- To study the incidence of Post Infection- Irritable Bowel Syndrome (PI-IBS)
- To identify the risk factors associated with the development of PI-IBS

REVIEW OF LITERATURE

Irritable Bowel Syndrome(IBS) is one of the most prevalent functional gastrointestinal disorders(FGIDs) in the world, with an estimated worldwide prevalence to be around 12%.[11] IBS is defined by the ROME IV as "a functional bowel disorder in which recurrent abdominal pain is associated with defecation or a change in bowel habits." Bloating may or may not be present, but is not considered essential for diagnosis.[1]

HISTORY OF IBS

Irritable Bowel was first used as a term in 1950, in the Rocky Mountain Medical Journal. It was used for patients with diarrhoea, abdominal pain and constipation without a known infective cause. It was believed to be caused by psychosomatic or mental disorders.[12] Manning and his colleagues, in 1978, reported that patients who were found to have IBS had six symptoms more commonly. These were looser and more frequent stools at onset of pain, relief of pain with bowel movement, distension, passage of mucus and sensation of incomplete evacuation. Out of these, first four were significantly more common in IBS than in organic disease.[13] The Kruis scoring system was developed a few years later, and included symptom duration, normal physical examination, and laboratory tests, that gave it an overall modest diagnostic value.[14]

Based on the Manning and Kruis criteria, the Rome criteria were created to enhance diagnostic utility after a consensus process. This provided a standard for clinical research. The Rome I criteria had sensitivity and specificity of 71% and 85% respectively, making it useful for clinical practice.[15] Subsequently, Rome II, III, and

IV criteria were developed, each though being similar to Rome I had changes according to recent researches and outcomes.

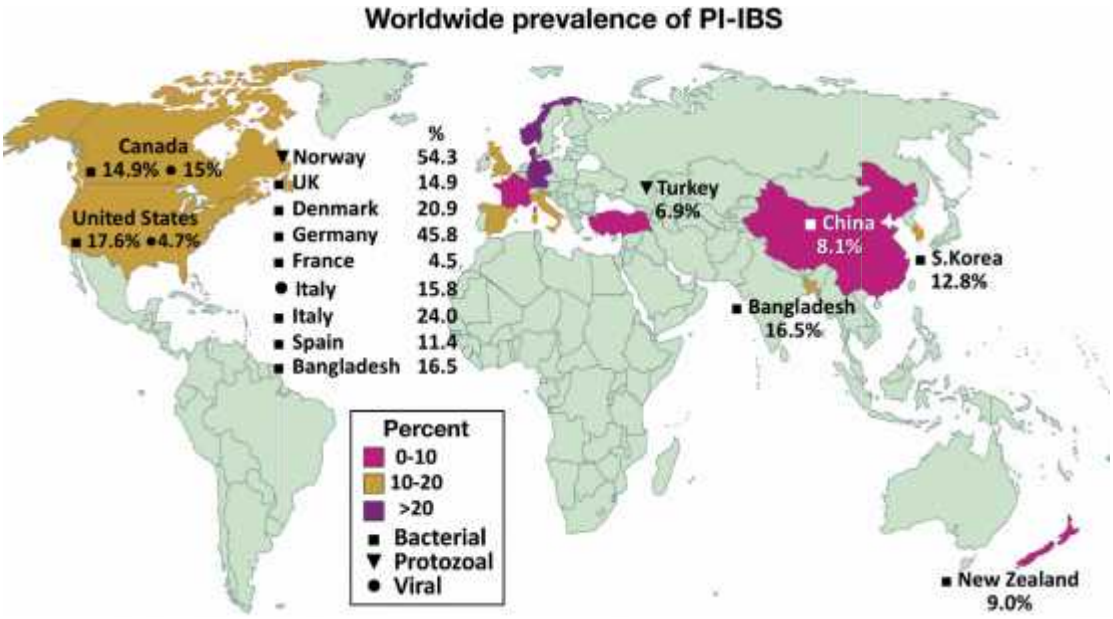
Development of IBS after an episode of infectious gastroenteritis has been reported for more than 60 years, with the earliest reports being those of IBS following bacillary and amoebic dysentery.[16–19] Older reports also supported development of bowel irritability after an episode of infectious diarrhoea.[20] There was a long gap in research on PI-IBS after these initial reports, until 1990s when more literature started cropping up. Post infection IBS is now a well acknowledged entity and Rome foundation has finally come up with a diagnostic criteria in 2019 separately for post infection IBS.

EPIDEMIOLOGY

Prevalence of IBS worldwide varies from 1% to 45%. It is substantially influenced by the definition applied. For example, in China, a cross sectional survey showed the prevalence of IBS as 12% when ROME III criteria were used. However it fell to 6% when ROME IV criteria were applied.[21] People under 50 years of age have a higher prevalence of IBS. However, population based studies suggest that IBS increases with increasing age. It is a known fact that organic diseases are more frequent in older individuals, which could explain some of the IBS-like symptoms. IBS in older adults might be underdiagnosed or misdiagnosed as another gastrointestinal illness. In the USA, women with IBS outnumber men, partly because of greater health seeking behaviour in women. This is exactly opposite to the situation in India. In a recent systematic analysis, 45 studies with roughly 21,000 enteritis patients were taken into consideration, where subjects were followed from 3 months

to 10 years after enteritis, and a pooled prevalence of 10.1% was found for IBS at 12 months after infectious enteritis.[22]

Ghoshal*et al,* in a prospective multi-centre study in India with more than 7000 subjects, reported the clinical and epidemiological profile of IBS. Most of the subjects were middle aged, and males outnumbered females amongst complainants. IBS was commoner in males in India, with most common complaints being incomplete evacuation and mucus in stools. 4.2% of the community subjects had IBS.[23]



Worldwide prevalence of PI-IBS based on inciting pathogen[3]

RISK FACTORS

The most widely recognised risk factor for development of IBS is bacterial gastroenteritis.[24–26] Multiple meta-analysis and global studies have reported significant association between an episode of gastroenteritis and development of IBS weeks to months later.

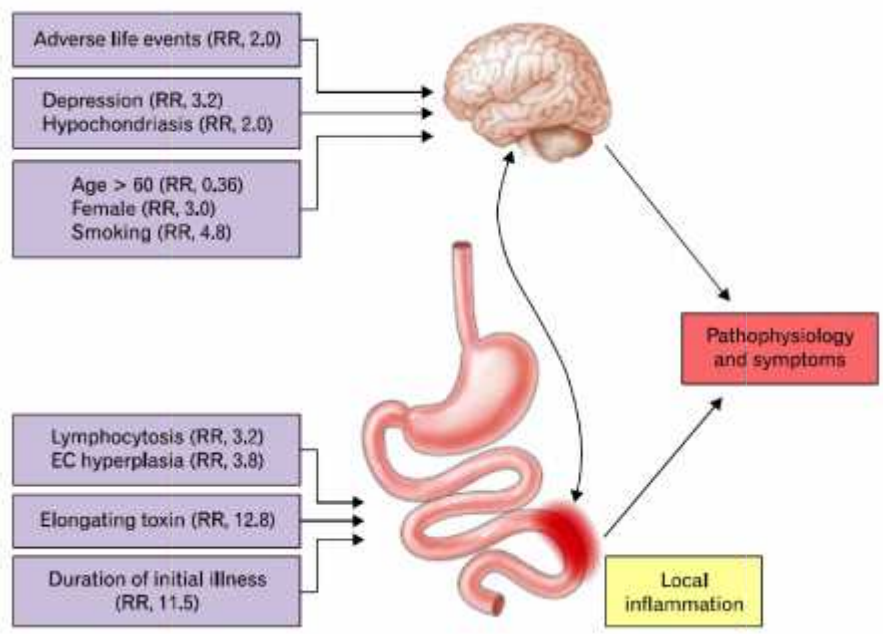
Multiple studies have also shown females having greater risk of developing Post Infection IBS.[6,27–29] However, there has been variability in this aspect as some other factors influence the results. Females might seek healthcare more often, or may have responded more than the other gender during follow-ups. Males have shown to seek healthcare only in case of severe symptoms.

Thabane et al. have reported younger age at the time of AGE episode to be a significant risk factor for development of PI-IBS.[30]

Multiple studies also evaluated anxiety and depression at the time of AGE episode as risk factors for development of PI-IBS.[26,28,29,31,32] Anxiety and depression scores have been found to be higher in individuals with PI-IBS as compared to controls who did not develop PI-IBS after recovering from AGE.[30,33]

In a considerable proportion of infected individuals, the symptoms became chronic according to longitudinal studies. More than 40% of those infected by a protozoan were reporting IBS symptoms even at 10 years, and about 15% of those infected by bacterium met the IBS criteria even at 8 years.[34,35]

Paula *et al,* in 2015 studied the use of antibiotics as a risk factor for development of functional gastrointestinal disorders, and found that development of IBS was independently associated with use of antibiotics to treat non-enteric infections.[36] Some other risk factors like contact with livestock, poor quality of life, affluent childhood environment, extra-intestinal somatic symptoms, family history of IBS have also been found to predispose an individual to developing IBS. Certain perinatal factors like caesarean section, low maternal age, and low birth weight have also been independently associated with IBS.



Risk factors for Post Infection-IBS. *EC*, enterochromaffin cell; *RR*, relative risk. (Spiller and Garsed)[8]

Several factors related to acute gastroenteritis episode have been associated with occurrence of PI-IBS. Severe enteritis episodes are more likely to cause PI-IBS. Duration of diarrhoea for more than 7 days is a risk factor.[6,19,37–39] Abdominal pain or more recently, abdominal cramping during the episode of AGE has been associated with increased incidence of PI-IBS.[5,40,41] Antibiotic use during the episode of AGE is a controversial risk factor, as three studies have shown no association,[29,42,43] whereas four others have shown a positive association for development of PI-IBS.[28,37,44,45] Fever was associated with PI-IBS development in Walkerton Cohort Study. During the episode of AGE, more extensive weight loss also was found to be a significant risk factor for development of PI-IBS.[5,6,37]Thabane Scoring has been widely validated to predict PI-IBS in patients of AGE. Singh et al, in 2018 have validated the same in Indian population, concluding that a PI-IBS risk score of 50 or more places the patient at high risk of developing PI-IBS after an episode of acute gastroenteritis.[46]

Risk factor	Categories	Points
Age	<60 years	6
	>60 years	0
Gender	Male	0
	Female	9
Duration of diarrhea	≤7 days	0
	>7 days	7
Maximum number of stools per day	≤6/day	0
	>6/day	8
Bloody stools	Absent	0
	Present	4
Abdominal cramps	Absent	0
	Present	32
Fever	Absent	0
	Present	5
Weight loss > 10 lbs	Absent	0
	Present	8
Anxiety and depression	None	0
	Pre morbid	1
	Post-infection	10
	Total points	90

PI-IBS Risk Score by Thabane et al.[30]

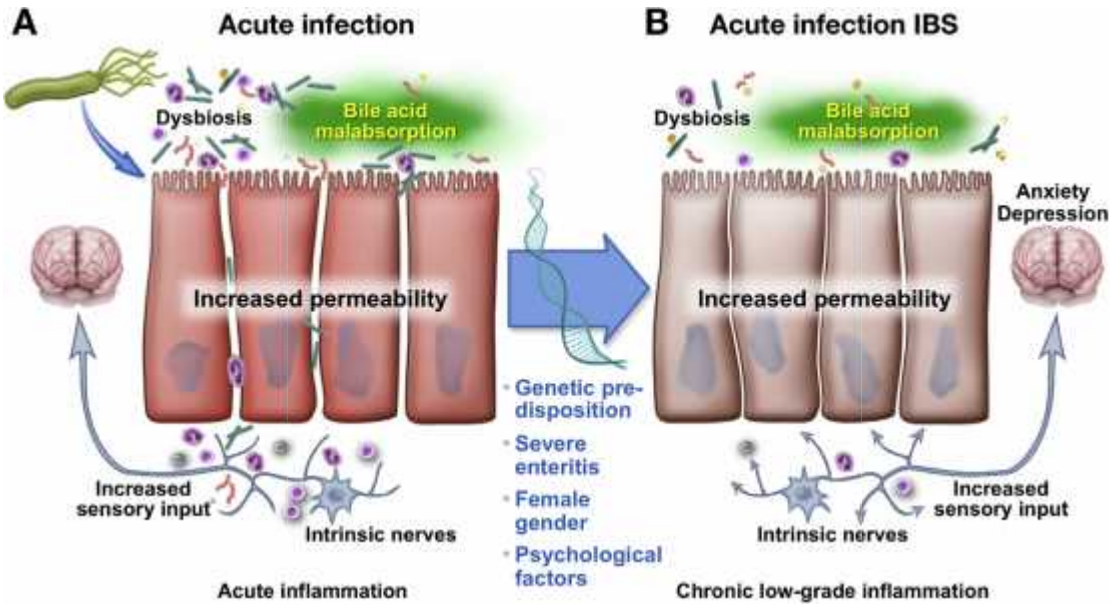
NATURAL HISTORY OF POST INFECTION IRRITABLE BOWEL SYNDROME

The symptoms of PI-IBS typically start in continuation with the symptoms of AGE as it resolves. They may persist for a time period from weeks to years and tend to affect the patient's quality of life noticeably. PI-IBS can persist up to even 16 years after infection.[47] However, the magnitude of risk and symptom severity more often than not, declines after 12 months of enteritis episode. Very little is known about PI-IBS evolution over time. The patients of PI-IBS can however expect a slow recovery that might be better than in case of IBS. More prospective studies are needed in this area.[48]

Incidence of PI-IBS post viral infection has been reported lesser than that after bacterial infection.[49]Noroviruses may lead to ileal microvilli damage and subsequent malabsorption, but obvious mucosal inflammation may not occur as in case of *Campylobacter jejuni.* This explains why PI-IBS after viral infections may be of more transient nature. It has been found that rotavirus increases intestinal permeability and more lymphocytes in intraepithelial space, but without ulceration and mucosal architecture returns to normal rapidly.[50]

PATHOPHYSIOLOGY

IBS traditionally has no known structural, anatomical or physiological abnormality. This concept however, may now be outdated as the functional nature of IBS is now being challenged. A number pathogenic mechanisms have now been implicated. The pathophysiology of PI-IBS in particular revolves mainly around the central and peripheral factors that include the microbiota, enteroendocrine, immunologic, epithelial and neuromotor mechanisms. Most of the understanding of gut and behavioural dysfunction comes from animal model experiments.



Schematic representation of pathophysiology underlying PI-IBS

Gut Dysmotility and Visceral hypersensitivity

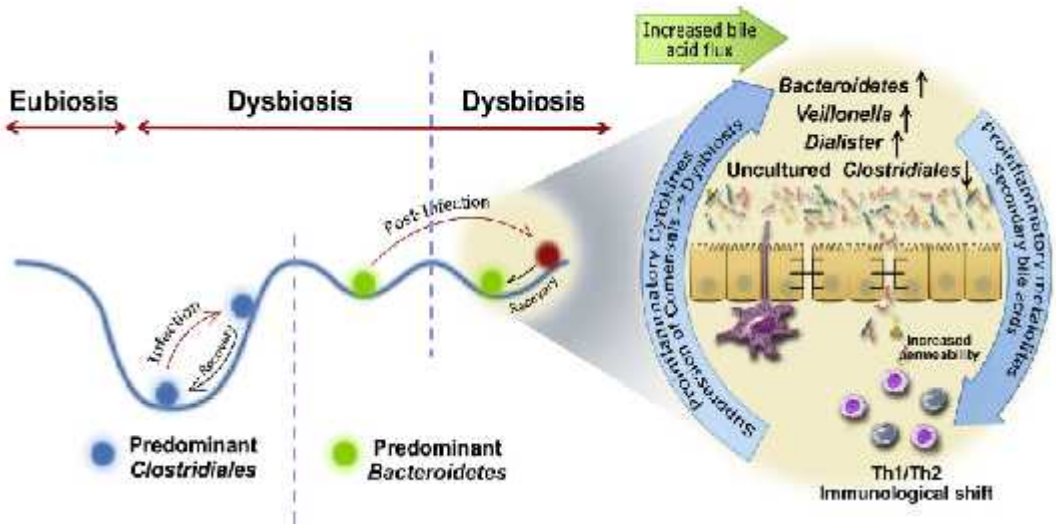
Bowel physiology has been described in very few studies in PI-IBS.[51]Gwee et al studied bowel motility after 3 months of an infection and reported persistent rectal hypersensitivity and hyperreactivity.[31] This was associated with the development of PI-IBS. Constipation may be secondary to increased segmental (non- propulsive) contractions, decreased high-amplitude propagated contractions, or reduced rectal sensation.

5-HT, neurokinins, and calcitonin gene- related peptide are putative neurotransmitters of relevance to visceral hypersensitivity. The transient receptor potential vanilloid-1 are likely to be increased in the rectosigmoid colon in IBS and may mediate abdominal pain. Stool serine proteases have been observed in increased quantity in diarrhoea predominant IBS patients. They might come from mast cells or colonic microbiota.[52]

Gut Microbiota

Gut microbiota is remarkably resistant to environmental disturbances and has the ability to preserve its function and structure. However those who develop PI-IBS may have primarily been unable “to restore microbial ecosystem or may have a secondary inability to restore gut microbiota”. Microbial signatures in PI-IBS are unlike those in IBS patients in general.[53] Increased levels of bacteria belonging to Bacteroidetes phylum were seen in poultry abattoir workers prone to infection. This phylum was also found abundantly in PI-IBS patients as compared to other IBS patients who have higher Firmicutes to Bacteroidetes ratio.

A host having Clostridiales predominant gut microbiota more often maintains eubiosis after infection. Those with Bacteroidetes predominant microbiota may predispose to long term dysbiosis after infection which further disturbs the cytokine and immune milieu. This changes the neuromuscular and epithelial function.



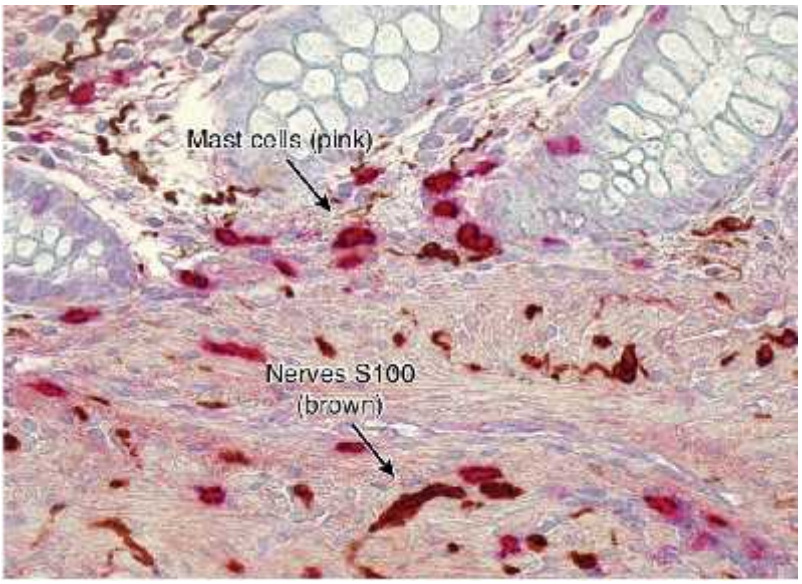
Gut microbiota affecting the host response to infection and predisposition to long term dysbiosis.

Intestinal permeability and immune dysregulation

Low grade immune activation causes raised intestinal permeability. This diminishes over time after bacterial enteritis in patients who develop PI-IBS. Macrophages and mast cells are altered in intestinal mucosa of PI-IBS patients. Increased no. of mast cells surrounding nerve fibres have been found in terminal ileum mucosa in PI-IBS patients as compared to healthy individuals.[39] This closely relates to abdominal bloating and pain.[54]

PI-IBS patients have been shown to have more lamina propria T lymphocytes, memory $CD45^{+}$ T cells and decreased B cells. Recent studies showed increased

plasma levels of anti-CdtB and anti-viniculin antibodies in patients with IBS-D[55] and a higher prevalence of antibodies to flagellin antigen in IBS patients with a previous history of gastroenteritis.[56] Increased interferon gamma levels in mucosa and reduced IL-10 levels were reported in PI-IBS patients that suggests role of Th1 and Th2 cells respectively.[57]



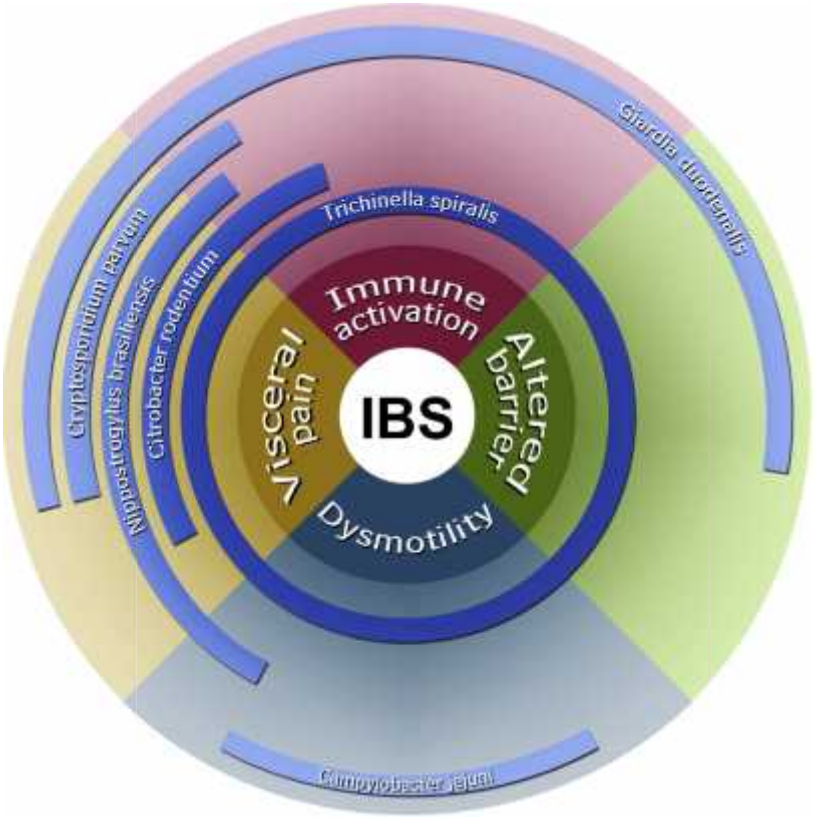
Rectal mucosal biopsy showing mast calls in proximity to nerve fibres[58]

Enteroendocrine pathways

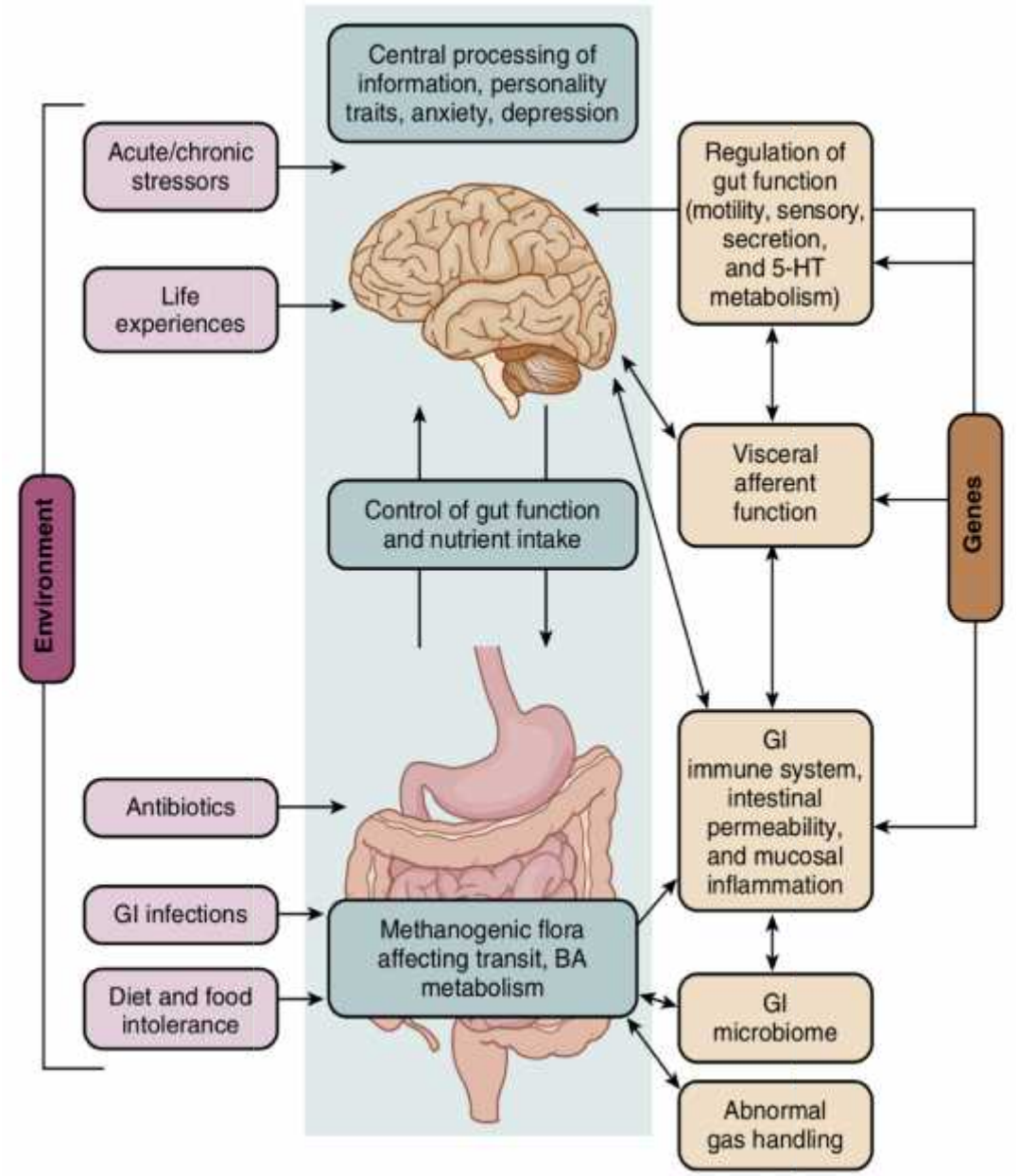
The synthesis of 5-HT, that is a key signalling molecule may be regulated by gut commensals including spore forming Clostridiales. In Shigella-associated PI-IBS, 5-HT containing EC cells were increased compared to healthy individuals, whereas in Giardia-associated PI-IBS, lower number of duodenal EC cells but increased number of CCK+ cells were found. Hence, gut hormones seem to play a controversial in pathophysiology behind development of PI-IBS.

Genetics

Four variant functional genes including TLR-9, IL-6 and CDH-1 have been found linked with PI-IBS independent of clinical risk factors. Some association between TNF-α SNP and Campylobacter jejuni PI-IBS was found, however it needs larger studies to be confirmed.[59]



Several animal models have already been studied to associate various pathogens with development of PI-IBS. Different observations have been noted with different pathogens causing enteritis that might contribute to understanding pathogenesis of PI-IBS.



Factors determining manifestation of IBS symptoms[60]

CLINICAL FEATURES

There is no validated definition for Post-infection Irritable Bowel Syndrome. It is characterised by "new onset ROME criteria-positive IBS after an episode of acute gastroenteritis in individuals who were previously not harbouring any such symptoms."

Commonly experienced symptoms are:

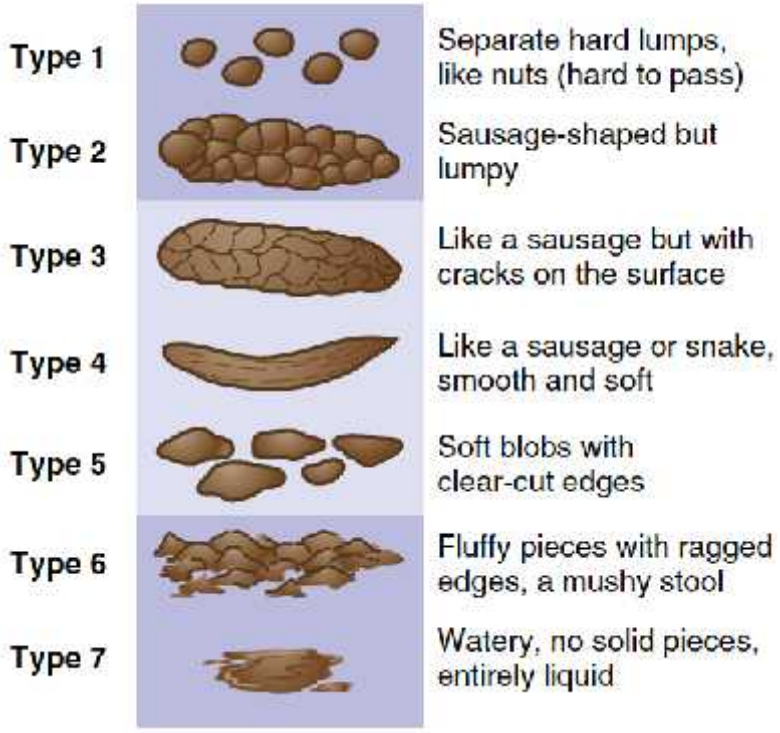
Abdominal pain

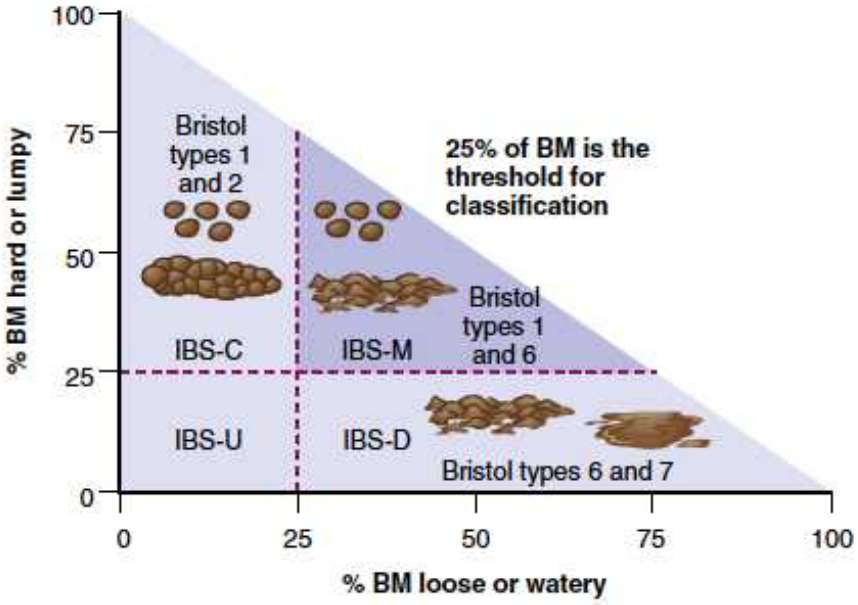
Abdominal pain is an essential symptom for diagnosis of IBS. It is usually related to defecation, and is associated with change in frequency of stools, or harder or looser stools. It is poorly localised, can be aggravated by eating and is more classically located in lower abdomen. Pain is exacerbated by difficult life situations and life events.

Diarrhoea and constipation

Patients with IBS may experience diarrhoea (stools>3 per day) or constipation(stools<3 per week) or a mixture of both. Hence IBS is classified based on the major symptom to ease the management: a) IBS-D (diarrhoea predominant), b) IBS-C (constipation predominant), c) IBS-M (Mixed stool pattern), d) IBS-U (undetermined).

Stool frequency is variable and patients can change patterns. Irregular consistency of stool is typical. It can be objectively measured by **Bristol Stool Chart**. However, constipation and diarrhoea in India are defined from the patient's point of view differently. Most patients who come with complaints of constipation or diarrhoea do not fit in the western definitions of the same. A newer criteria, more suited to the population might be needed in our country.



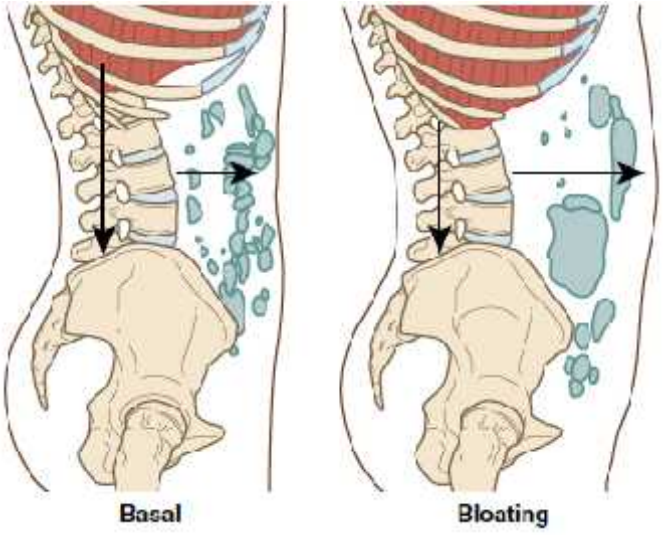


The Bristol Stool chart and classification of IBS subtypes[61]

Bloating and visible abdominal distension

More than 60% of the patients with IBS can have a feeling of bloating, poorly localised. It can be a bothersome experience in constipation predominant IBS patients. Visible distension of abdomen is a characteristic symptom of IBS but less common

than bloating. It is seen more in women and can be objectively measured. Distension may worsen in the later half of the day. Abnormal accommodation ofthe diaphragm, contraction of intercostal muscles, and relaxation ofthe abdominal wall musculature,appear to be involved as part of aninvoluntary reflex response.



Ultrasound confirms protrusion of anterior abdominal wall with descent of diaphragm and only minimal increase in intraabdominal gas while bloating in IBS patients.[62]

Non colonic symptoms

Patients with IBS have an 8-fold risk of having dyspepsia like symptoms over those without IBS. Such symptoms are not diagnostic themselves but aid in the diagnosis of IBS. Symptoms of GERD may also occur in patients with IBS. Other symptoms like headache, backache, jointpains, impaired sleep, chronic fatigue, dizziness,palpitations, anddyspareunia are commonly seen in patients with IBS. These may improve specificity of ROME criteria.

Chronicity

Symptoms of IBS should be usually present for minimum 6 months to have a confident diagnosis of IBS. It may accompany other chronic disorders like coeliac disease. Up to 40% of IBD patients may suffer from IBS symptoms.[63] This is

associated with increasedutilization of healthcare and hampered psychologic health. Several conditions may cause transient bowel symptoms in individuals with pre-existing IBS like pregnancy, dietary imprudence, food poisoning, travellers' diarrhoea, bed rest, weight loss, and acute stress (nervous diarrhoea); these should be differentiated from chronic or recurrent symptoms of IBS.

DIAGNOSIS

The diagnostic criteria for Post Infection Irritable Bowel Syndrome was proposed by ROME Foundation Working Team (RFWT) in 2019 based on the ROME IV criteria. Manning et al in 1978 and Kruis et al in 1984 were the first ones to propose symptom based diagnostic criteria for IBS. Manning's criteria lacks the consideration for duration of symptoms, but till date has fared well in diagnosing IBS.Manning's criteria requires usually atleast 3 of the following symptoms to diagnose IBS:

1. Abdominal pain relieved by defecation
2. More frequent stools with onset of pain
3. Looser stools with onset of pain
4. Mucus per rectum
5. Feeling of incomplete emptying
6. Patient-reported visible abdominal distension

An overall pooled sensitivity of 78% and specificity of 72% was reported for Manning's criteria.[64] The ROME I criteria was introduced in 1990, that needed symptoms to be present for 3 months on at least 25% of the days. With more literature emerging and testing the ROME I criteria, it was refined to be upgraded to ROME II in 1999 and ROME III in 2006. ROME III criteria needed a patient to have pain

abdomen or discomfort for 3 days in a month for the last three months associated with 2 or more of the following:

1. Improvement with defecation
2. Onset associated with change in frequency of stool
3. Onset associated with change in form of stool.

In the ROME IV criteria, certain changes were made. The term "discomfort" was removed due to ambiguity in various languages. The ROME IV criteria[61] is as follows:

"Recurrent abdominal pain, on an average at least 1 day per week in the last three months, associated with 2 or more of the following:

1. Related to defecation
2. Associated with change in frequency of stool
3. Associated with change in form (appearance) of stool.

Criteria fulfilled for the last three months with onset of symptom at least 6 months before diagnosis."

Some studies have also concluded that certain serum markers like C-reactive protein and faecal calprotectin may prove useful in excluding diseases like IBD and aid in diagnosing IBS better.[15,65]

Diagnostic criteria for PI-IBS according to RFWT[3] is as follows:

1. "Recurrent abdominal pain, on average, at least 1 day per week in the last 3 months, with symptom onset at least 6 months before diagnosis,associated with >= 2 of the following:

   a) defecation

   b) a change in frequency of stool

   c) a change in form (appearance) of stool

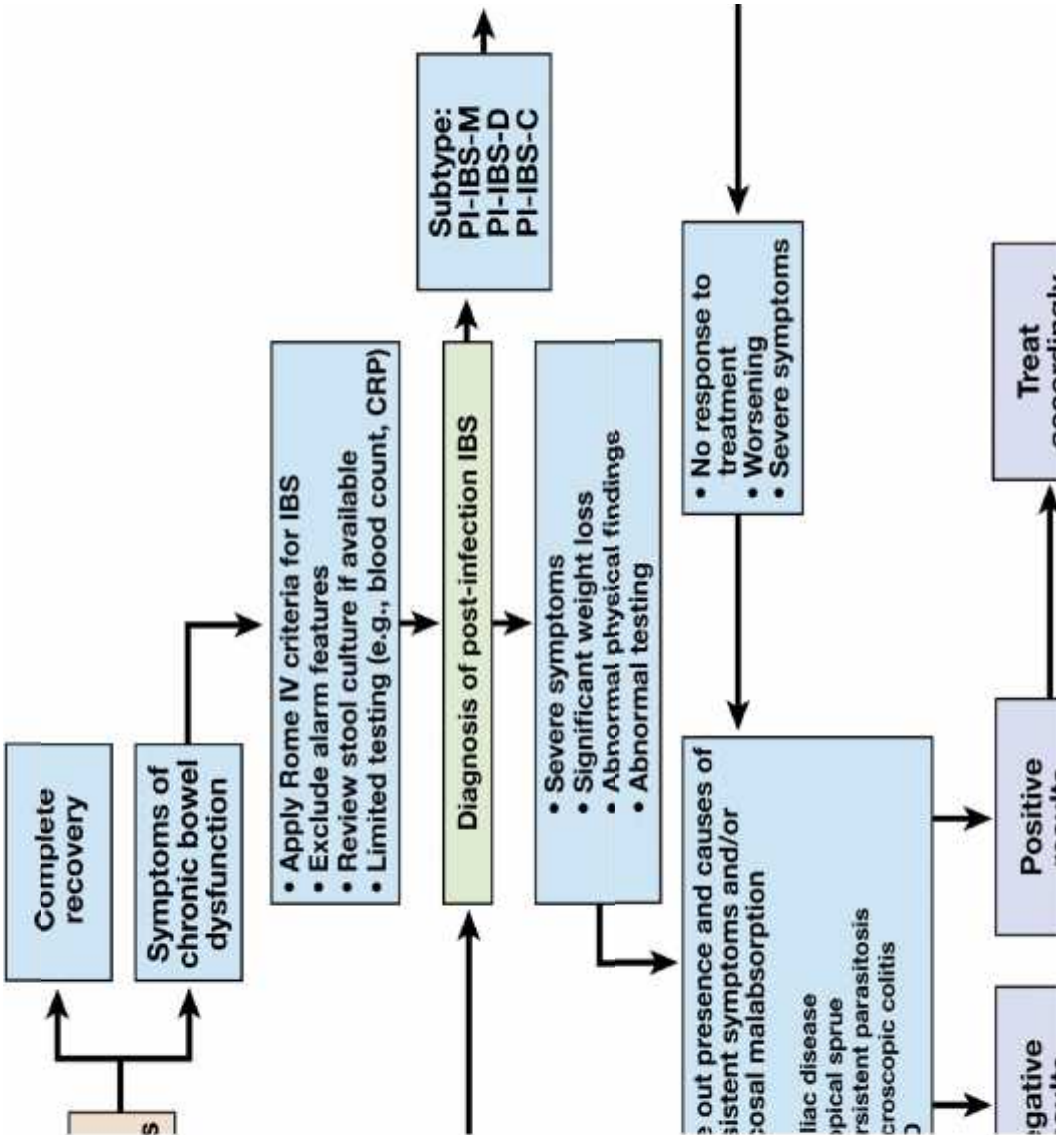
2. Symptom development immediately after resolution of acute infectious gastroenteritis
3. Infectious gastroenteritis is defined by positive stool culture in a symptomatic individual or presence of >=2 of the following acute symptoms:

   a) fever

   b) vomiting

   c) diarrhoea
4. Should not meet IBS criteria before onset of acute illness"

One should always look out for warning signs or "alarm features" in patients with IBS to hold high suspicion for organic diseases. These may be rectal bleed, weight loss, anaemia, night time symptoms and family history of diseases like colorectal malignancy, IBD or celiac sprue.[66]



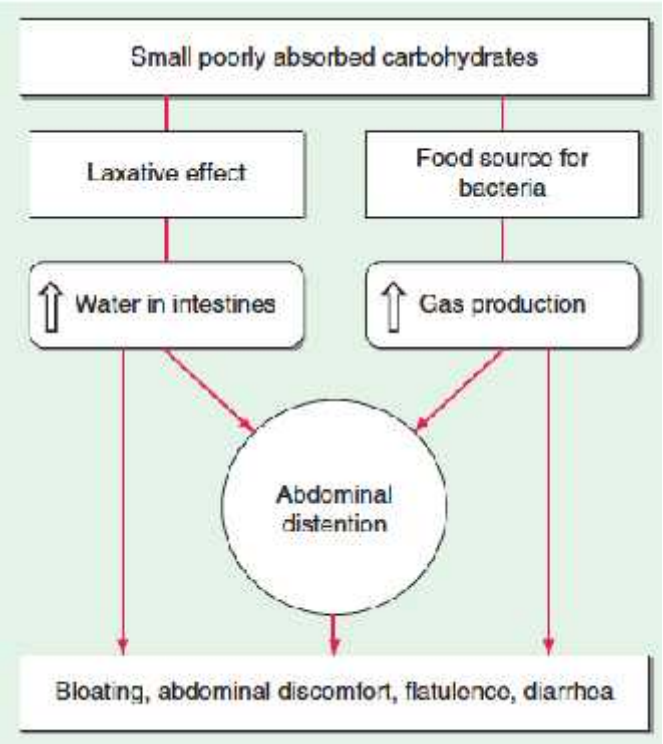
A diagnostic algorithm for PI-IBS

MANAGEMENT OF PI-IBS

IBS tends to last for a long time, however, PI-IBS recovery rates have been found to be faster as discussed earlier. No specific therapy has been so far designated as a cure for PI-IBS, but options similar to those used in other IBS patients have been proposed. These approaches are majorly nonspecificmeasures intended to relieve symptoms.

Patient education remains the initial step in management of PI-IBS. The patient needs to be educated about the link between infectious diarrhoea and chronicity of their bowel symptoms as there now exists substantial evidence to support the same. A good physician-patient relationship helps recognise psychiatric morbidity earlier and also reduces burden on healthcare services.

Diet and lifestyle modification is another way to effectively help alleviate patient's symptoms. High soluble fibre diet has proven to be of global benefit. Exclusion of certain substances from diet have benefited a lot of patients with IBS. A low FODMAP diet has proven to be of much help in reducing symptoms like bloating, pain abdomen as well as form of stool.[67] However the microbiome in the gut may suffer on continuing low FODMAP diet for a long time. Hence, these foods need to be reintroduced to diet carefully, assessing the effect of such an action on IBS symptoms. Pathogenesis of FODMAPs related symptoms has been demonstrated in the following figure.



Pharmacotherapy in PI-IBS

Antispasmodic agents like pinaverium, mebeverine, peppermint oil, dycyclomine have reduced the symptoms related to abdominal pain considerably.

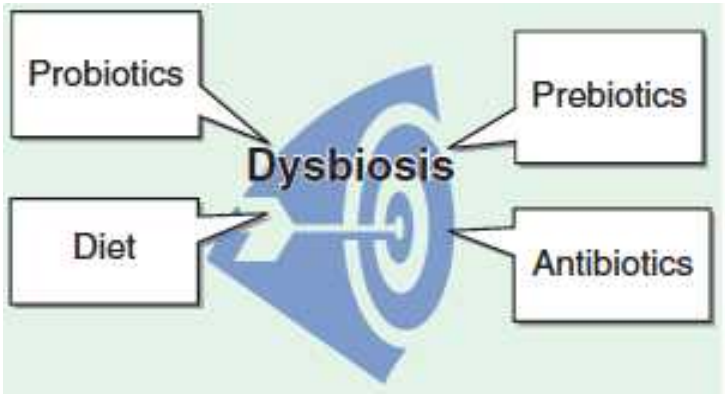
IBS-C type is most effectively treated by stimulant laxatives but they often induce abdominal cramping. Osmotic laxatives are also useful in increasing frequency of bowel movements. Other options include chloride channel activators like Lubiprostone, and guanylatecyclase agonists like linaclotide and plecanatide. SSRIs tend to increase intestinal transit and help in IBS-C.

IBS-D type also has a variety of treatment options. Opioid receptor agonist Loperamide is efficacious in reducing frequency of stool, but does not help abdominal pain or bloating. 5-HT_3 receptor antagonists like Alosetron, Ramosetron and Ondansetron are beneficial in improving stool frequency and consistency. Tricyclic antidepressants such as desipramine and nortriptyline have a constipating effect and benefit IBS-D patients.

Antibiotics like rifaximin are superior to placebo in non-constipated patients with IBS for both global symptoms and bloating. It has shown anti-inflammatory effects and it improves barrier function as well as visceral hypersensitivity.

Probiotics have shown to alter commensals naturally and thereby help in restoring the natural microbiota of the gut. Dysbiosis is a proposed mechanism in diarrhoea predominant IBS.[68] A meta-analysis of 10 studies with probiotics has shown that *Bifidobacteriumbreve, B longum,* and *Lactobacillus acidophilus* species are superior compared to placebo in relieving pain abdomen and bloating. However,

large-scale studies of well phenotyped IBS patients are needed to obtain more data on efficacy of probiotics in IBS.



Dysbiosis: A potential treatment target

About one-third of the patients with IBS-D show increased synthesis of bile acid or faecal excretion, causing diarrhoea. Cholestyramine is acceptable in treating bile acid bile acid malabsorption. However, it is not a very palatable drug and reduces compliance. Colesevelam alters hepatic synthesis of bile acid and reduces faecal excretion, resulting in less soft stools.[69]Colestipol also has been shown to have a high response rate in IBS-D patients.[70]

Emerging Drugs

Tenapanor is a drug that acts on the sodium-hydrogen exchanger. At a dose of 50 mg twice daily, it appeared to be beneficial in IBS-C patients.[71] It has finished phase-II trials. It improves pain abdomen and frequency of stools. Ibodutant, a neurokinin receptor-2 antagonist, which mayhave beneficial effects onmotility in IBS-D, has been tested inone phase 2 RCT.[72]Ebastine, a histamine-1 receptor antagonist had shown considerable relief in symptoms in one small trial.[73]

Psychologic treatments

Psychotherapy, hypnotherapy, yoga and cognitive behavioural therapy have been found to be useful treatments in IBS. They have helped in controlling pain and discomfort and are seen as ancillary to medical treatments.

Fecalmicrobiometransplant has also been proposed for treatment of IBS but it needs validation in large studies to be seen as a potential treatment.

PROGNOSIS

IBS till date has not been found to have increased mortality in any patient on long term follow ups. PI-IBS has been shown to have reduced prevalence after one year of the inciting AGE episode. In Asian studies, some have reported a 25% recovery rate after 3 years of infection.[74] Viral gastroenteritis preceding IBS development have showed very transient bowel disturbances and most patients had relief from IBS symptoms after 3 months of the enteritis episode. Patients with PI-IBS have shown better and faster recovery over other IBS patients.

METHODOLOGY

Study site

This study was conducted in the Department of General Medicine, KLE's Dr. Prabhakar Kore Hospital and MRC, Belgaum.

Study designand duration

The current study was a one year Prospective Longitudinal study.

Study period

The study was conductedfrom January 2019 to December 2019.

Study population

All cases of Acute Gastroenteritis (AGE) admitted in wards of general medicinedepartment at Dr.Prabhakar Kore hospital, were considered as the study population.

Sample size

The study included a total of 100 patients of Acute Gastroenteritis.

Sampling procedure

The sample size was calculated by the followingformula:

Sample size (n) = $4\ PQ/D^2$

P = Prevalence of the disease

Q= 100- P

D = Absolute error taken as 6%

(P = 10; Q = 90; D=6)

$n = 4 \times 10 \times 90 / 6^2$

$n = 100$

All eligible patients were recruited in this study consecutively by convenient sampling till the sample size was reached.

Selection criteria

Inclusion Criteria

- Age > 18 years
- Clinical features suggestive of acute gastroenteritis characterized by presence of ≥2 of the following: fever, vomiting, diarrhoea, or a positive stool culture
- Free from symptoms of IBS prior to this episode of acute gastroenteritis.

Exclusion criteria

- Any associated disease, which might cause chronic diarrhoea(based on history) such as:
    a. Inflammatory Bowel Disease
    b. Tuberculosis
    c. Colorectal Carcinoma
    d. Prior intestinal resection
    e. Radiation enterocolitis
    f. Hereditary polyposis syndromes
    g. Microscopic colitis
    h. Intestinal ischemia

Ethical clearance

The study was approved by the Institutional Ethics Committee, Jawaharlal Nehru Medical College, Belagavi prior to the commencement.(Annexure-I)

Informed consent

The patients fulfilling the selection criteria were briefed about the study and those who expressed their willingness to participate in the study were enrolled after obtaining a written informed consent (Annexure-II).

Data collection

The relevant patient data with history, and demographics were recorded in a structured study proforma that includes the IBS Questionnaire and the HADS proforma for psychiatric evaluation (Annexure-III).

Investigations

Patients were subjected to following investigations.

- Haemoglobin
- Stool culture
- Stool routine/microscopy
- Stool occult blood
- ESR
- Lactose intolerance test

Methodology

At the time of admission, patients of acute gastroenteritis satisfying the inclusion and exclusion criteria were enrolled into the study after taking a written informed consent. The selected patients were assessed for the various risk factors associated with development of Post infection IBS (PI-IBS) in a face-to-face interview. These included age, gender, duration of episode, peak stool frequency per day, abdominal cramping, bloody stools, fever, use of antibiotics, anaemia, direct contact with livestock and psychological factors (anxiety and depression). Stool samples were collected for microscopic study and culture.

Follow-up:

Follow-up survey at 6 months included the IBS questionnaire. Follow-up was done either face-to-face or telephonically. PI-IBS was diagnosed based on ROME IV criteria. PI-IBS patients were categorised into IBS-C and IBS-D based on stool frequency. Those who were passing more than 3 stools per day were classified as IBS-D and those with less than 3 stools per week were classified as IBS-C. Those who developed IBS at 6-months follow up were subjected to a lactose intolerance test to separate the entity.

The association of risk factors was studied in those who developed PI-IBS, and compared with those who had normal bowel habits at follow up.

Statistical methods

The data obtained was coded and entered into Microsoft excel spreadsheet and data was analyzed using SPSS version 20. The categorical data was expressed in terms of rates, ratio and percentage and the continuous data was expressed in terms of mean ± standard deviation. The association between risk factors and development of PI-IBS was tested using chi-square test. Odds ratio was calculated for each risk factor. Multiple logistic regression analysis was used to study the risk factors together and individually. Probability (p) value of ≤ 0.05 was considered as statistically significant.

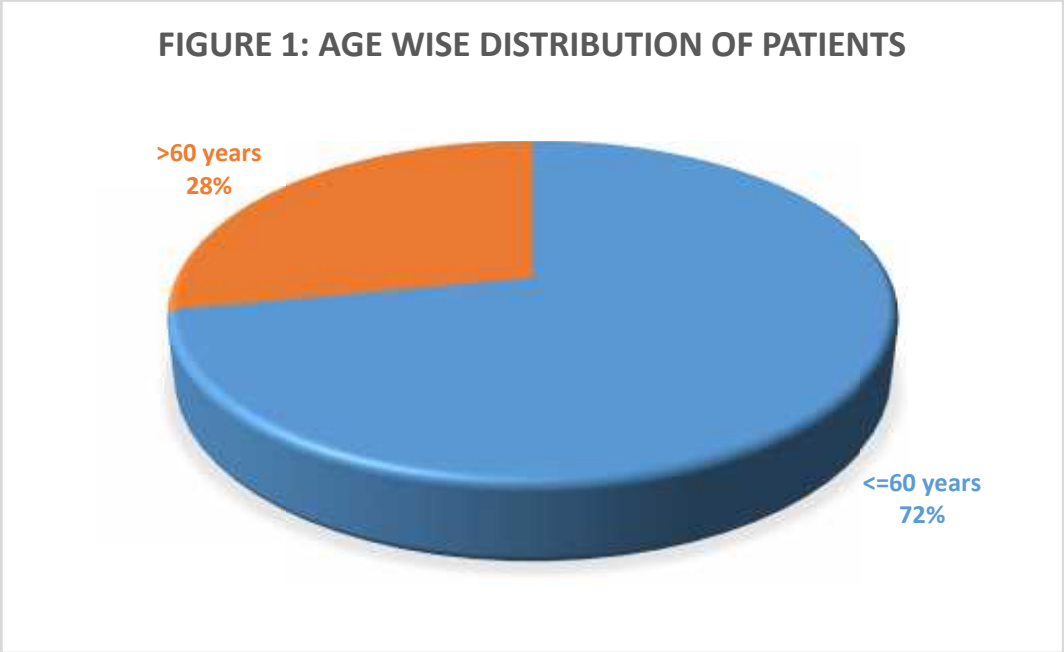
RESULTS

The present one-year longitudinal study was conducted on patients in the Department of General Medicine, KLES Dr. Prabhakar Kore Hospital and MRC.A total of 100 patients with acute gastroenteritis, who met the inclusion criteria were enrolled in the present study. They were followed up after 6 months of the acute gastroenteritis episode and with the help of the IBS Questionnaire, Post-infection Irritable Bowel Syndrome was diagnosed based on ROME IV criteria.

The data obtained was analyzed and the final results were tabulated and interpreted as follows:

Table 1: Age wise distribution of patients

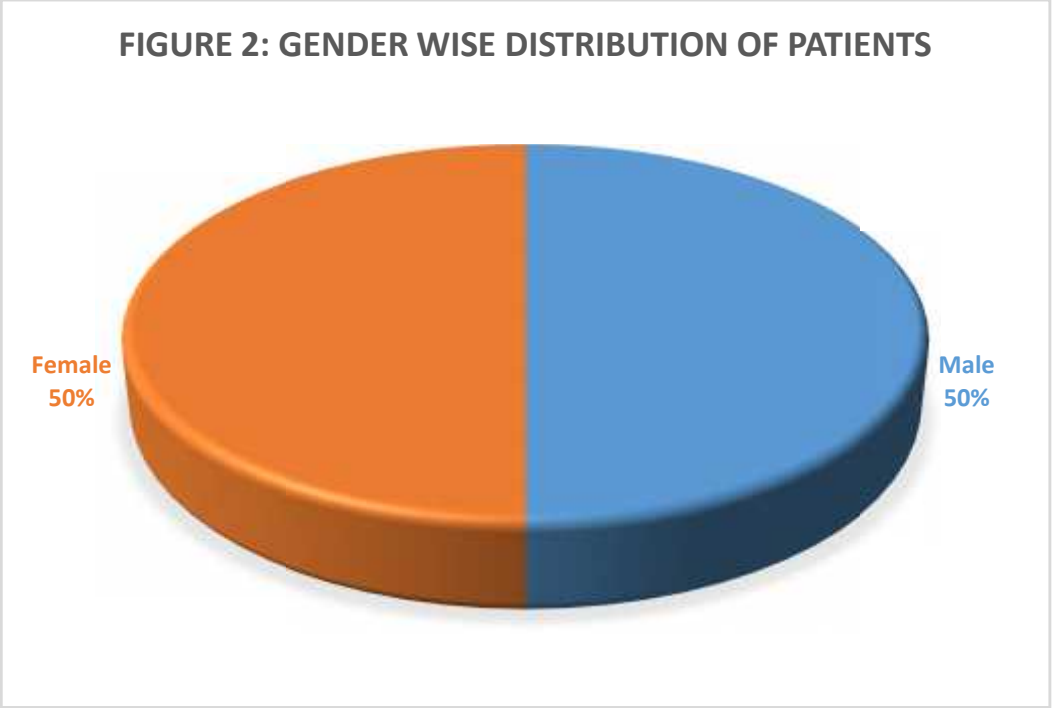
Age (years)	No of patients	% of patients
<=60yrs	72	72.00
>60yrs	28	28.00
Total	100	100.00



In this study, the age of patients ranged from 18 years to 86 years. 28% of the patients were of age more than 60 years and 72% of the patients were aged less than or equal to 60 years.

Table 2: Gender wise distribution of patients

Gender	No of patients	% of patients
Male	50	50.00
Female	50	50.00
Total	100	100.00

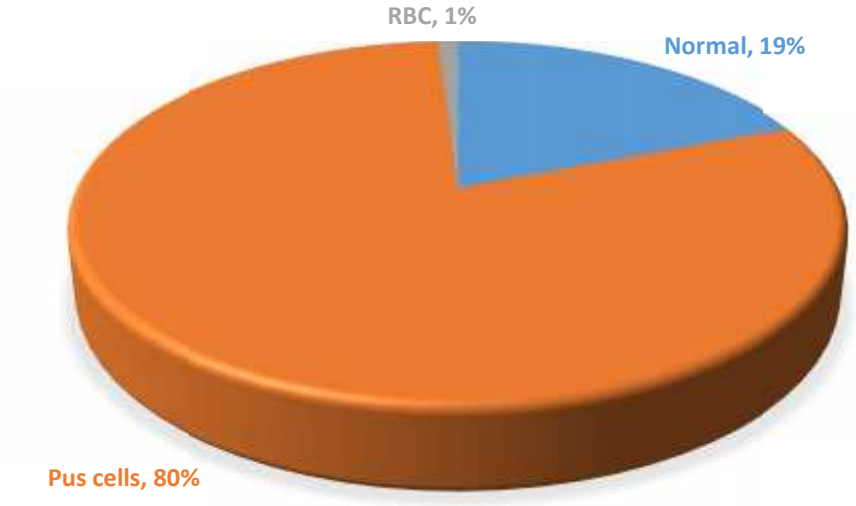


In the present study, 50% of the patients were females and 50% males. Male to female ratio was 1:1.

Table 3: Stool microscopy of patients

Stool routine	No of patients	% of patients
Normal	19	19.00
Pus cell+	80	80.00
RBC+	1	1.00
Total	100	100.00

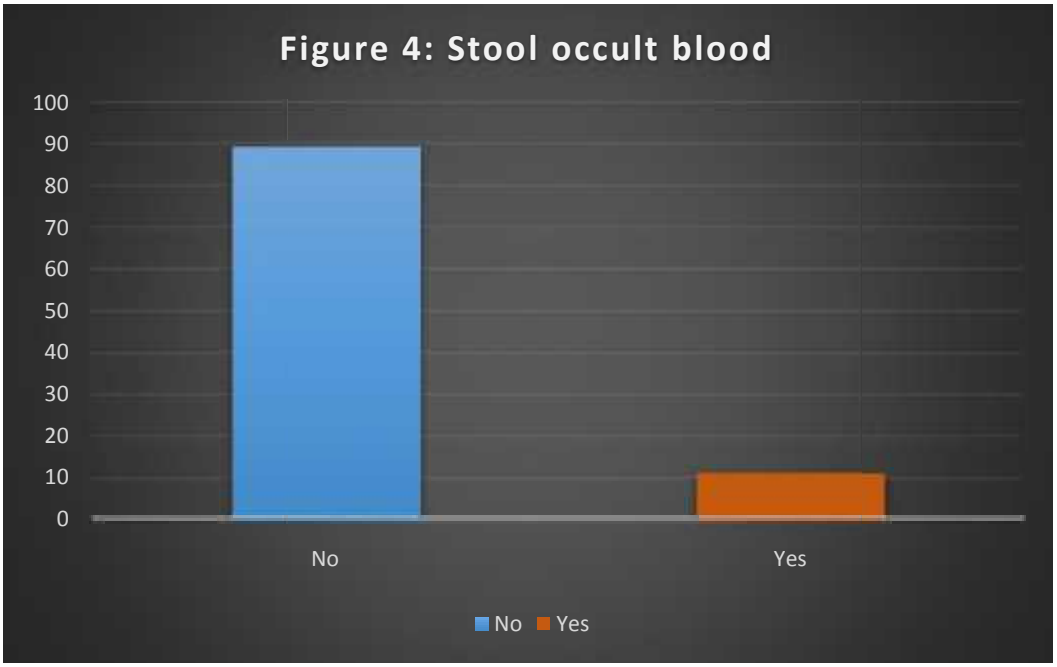
FIGURE 3: STOOL MICROSCOPY



19% of the patients had normal stool microscopic examination, 1 patient had RBCs in stool, and 80% patients had pus cells in their stool on admission.

Table 4: Presence of stool occult blood

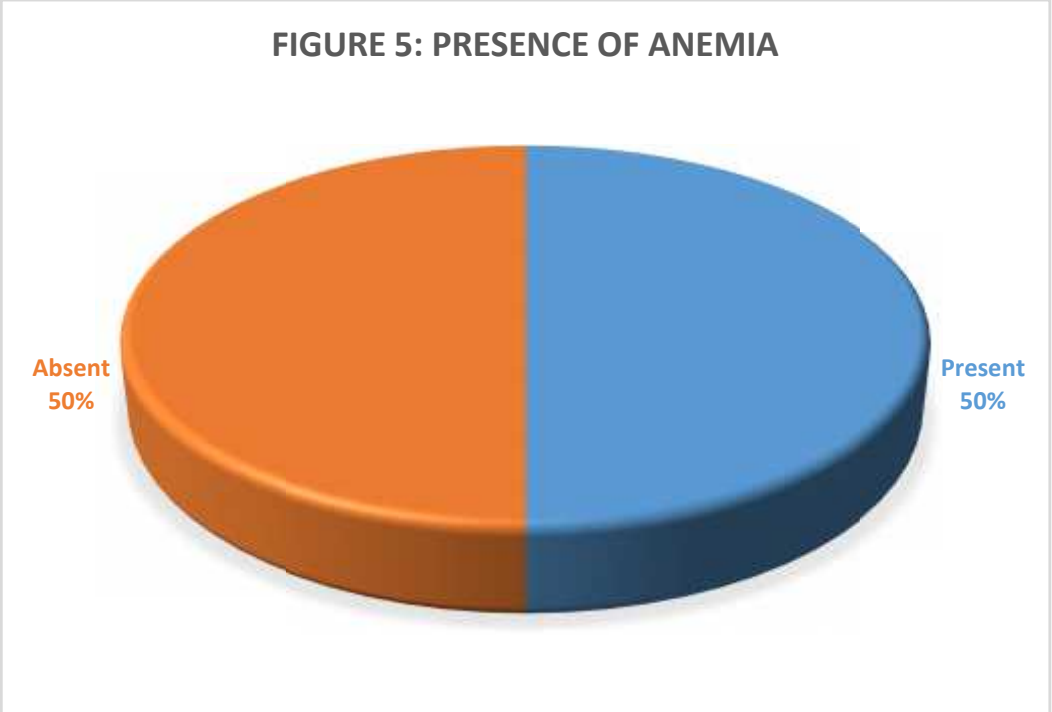
Stool occult blood	No of patients	% of patients
No	89	89.00
Yes	11	11.00
Total	100	100.00



11% of the patients had occult blood positive in stool examination. 89% of the patients did not have occult blood on stool examination.

Table 5: Anaemia in enrolled patients

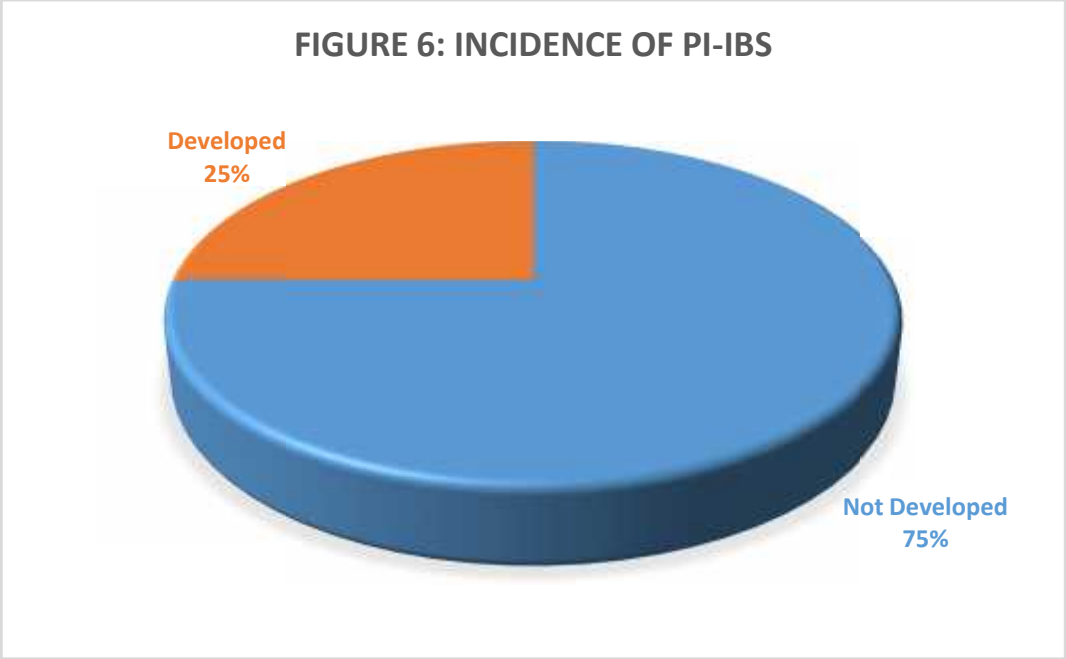
Anaemia	No of patients	% of patients
Anaemic	50	50.00
Healthy	50	50.00
Total	100	100.00



50% of the patients in our study were anaemic on admission, i.e. with Haemoglobin< 12g/dL. Remaining 50% of the patients were non-anaemic.

Table 6: Incidence of PI-IBS

Incidence of PI-IBS	No of patients	% of patients
Absent	75	75.00
Present	25	25.00
Total	100	100.00

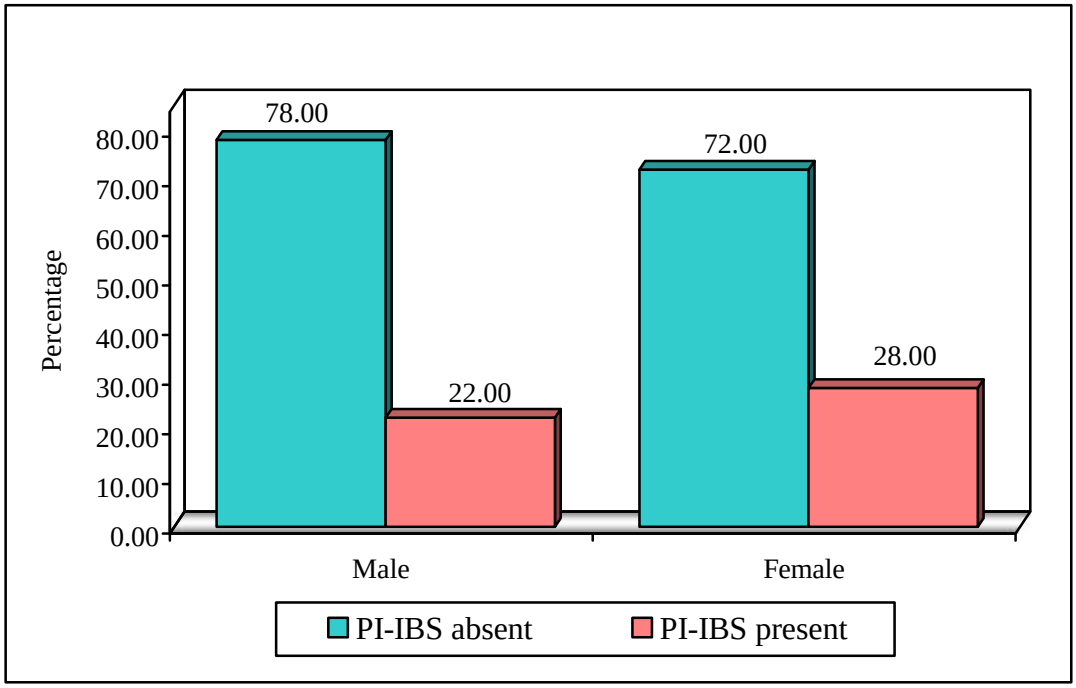


In this study, the incidence of Post Infection Irritable bowel syndrome was found to be 25% i.e. 25 out of the 100 patients with acute gastroenteritis had developed IBS at 6 month follow up.

Table 7: Incidence of PI-IBS by gender

Gender	PI-IBS absent	%	PI-IBS present	%	Total	%
Male	39	78.00	11	22.00	50	50.00
Female	36	72.00	14	28.00	50	50.00
Total	75	75.00	25	25.00	100	100.00
Chi-square=0.4800, p=0.4880, NS						

Figure 7: Incidence of PI-IBS by gender

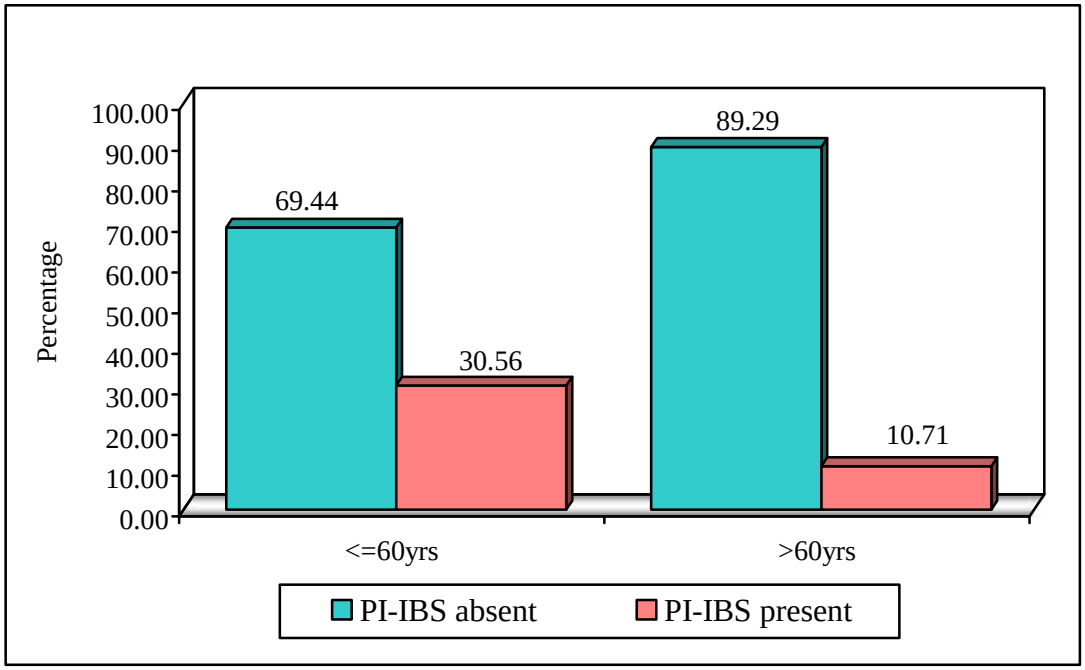


22% of the males and 28% of the females developed PI-IBS. Gender was not a statistically significant risk factor in our study, however more females than males developed PI-IBS.

Table 8: Incidence of PI-IBS by age groups

Age (years)	PI-IBS absent	%	PI-IBS present	%	Total	%
<=60yrs	50	69.44	22	30.56	72	72.00
>60yrs	25	89.29	3	10.71	28	28.00
Total	75	75.00	25	25.00	100	100.00
Chi-square=4.2330, p=0.0400, S						

Figure 8: Incidence of PI-IBS by age groups

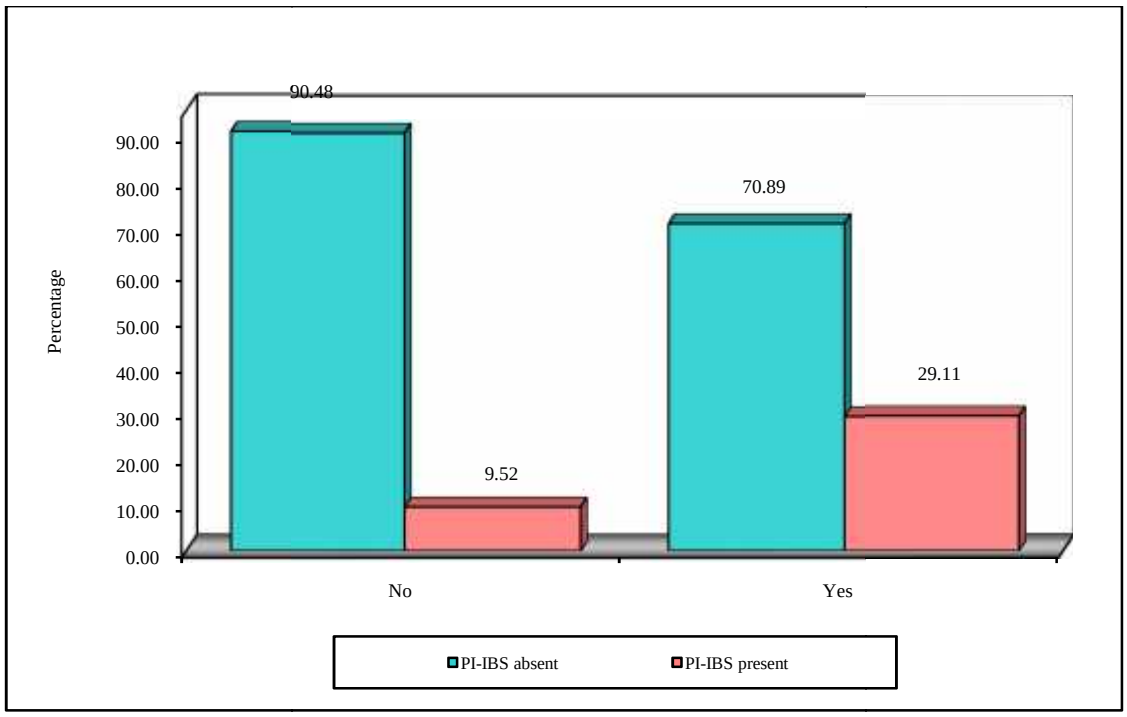


30.56% of the patients with age less than or equal to 60 years developed PI-IBS. However, only 10.71% of those above 60 years of age developed PI-IBS. Hence in our study, age less than or equal to 60 years is a statistically significant risk factor for development of PI-IBS. (p-value: 0.040)

Table 9: Incidence of PI-IBS by fever

Fever	PI-IBS absent	%	PI-IBS present	%	Total	%
No	19	90.48	2	9.52	21	21.00
Yes	56	70.89	23	29.11	79	79.00
Total	75	75.00	25	25.00	100	100.00
Chi-square=3.3960, p=0.0650, NS						

Figure9: Incidence of PI-IBS by fever

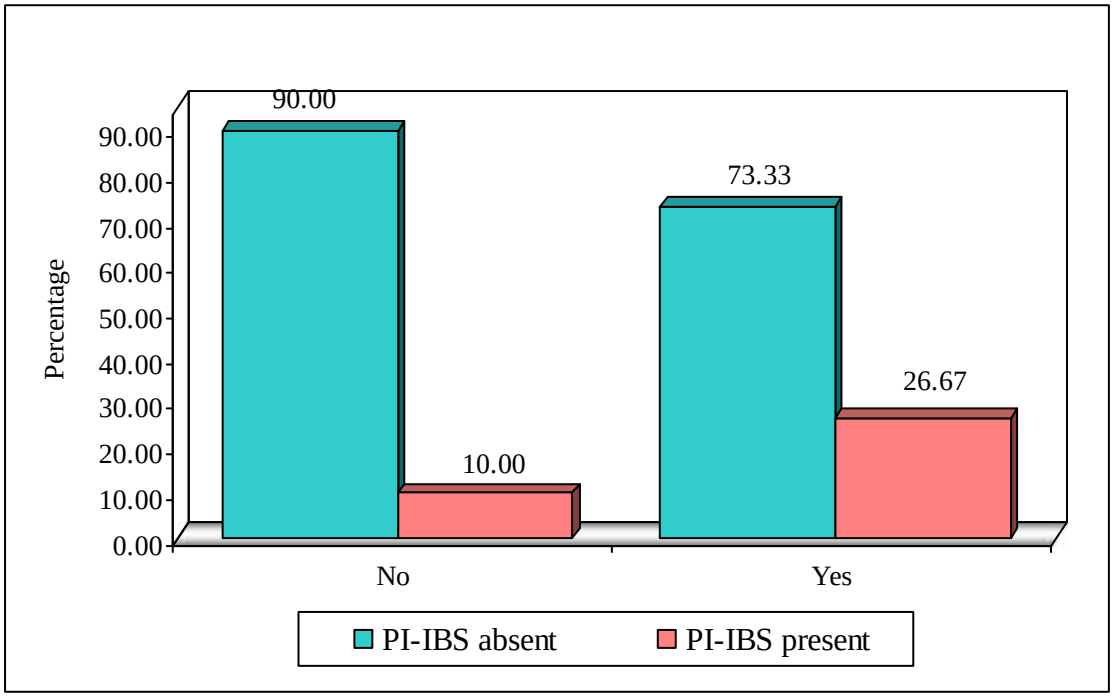


In this study, 9.52% of the patients without fever developed PI-IBS, but 29.11% of the patients with fever during the episode of AGE developed PI-IBS. However, fever was not statistically significant as a risk factor for development of PI-IBS. (p-value: 0.0650)

Table 10: Incidence of PI-IBS by Vomiting

Vomiting	PI-IBS absent	%	PI-IBS present	%	Total	%
No	9	90.00	1	10.00	10	10.00
Yes	66	73.33	24	26.67	90	90.00
Total	75	75.00	25	25.00	100	100.00
Chi-square=1.3330, p=0.2480, NS						

Figure 10: Incidence of PI-IBS by Vomiting

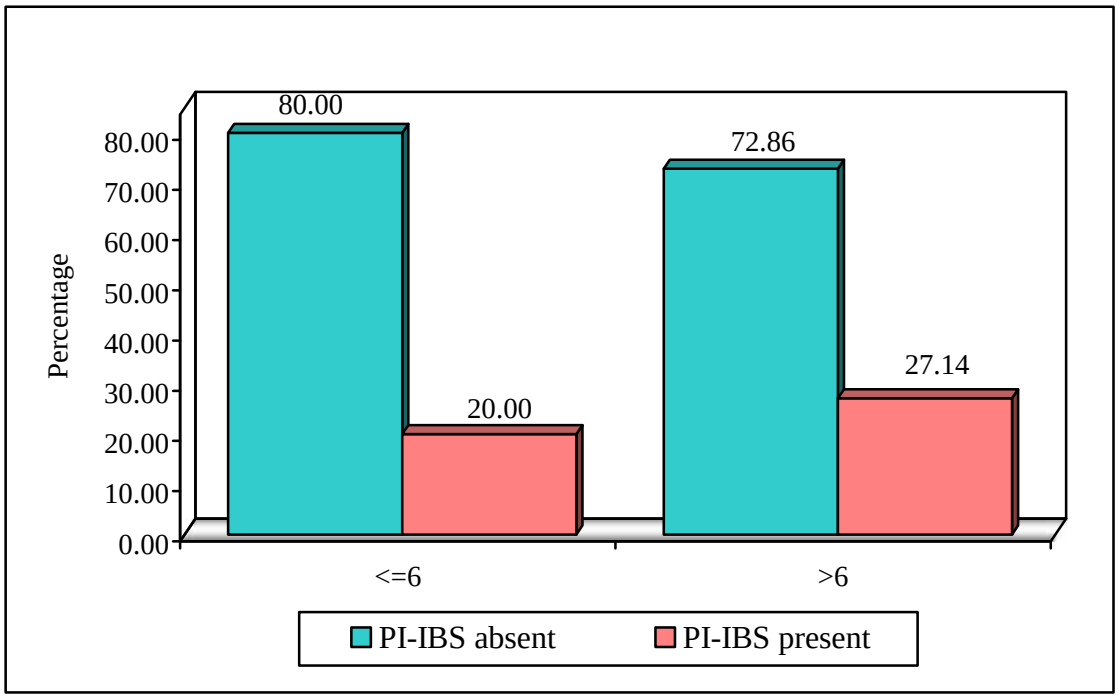


10% of the patients without vomiting and 26.67% of those with vomiting developed PI-IBS. Vomiting was not statistically significant as a risk factor for development of PI-IBS. (p-value: 0.2480)

Table 11: Incidence of PI-IBS by no. of stools per day

No. of stools	PI-IBS absent	%	PI-IBS present	%	Total	%
<=6 per day	24	80.00	6	20.00	30	30.00
>6 per day	51	72.86	19	27.14	70	70.00
Total	75	75.00	25	25.00	100	100.00
Chi-square=0.5710, p=0.4500, NS						

Figure 11: Incidence of PI-IBS by no. of stools per day

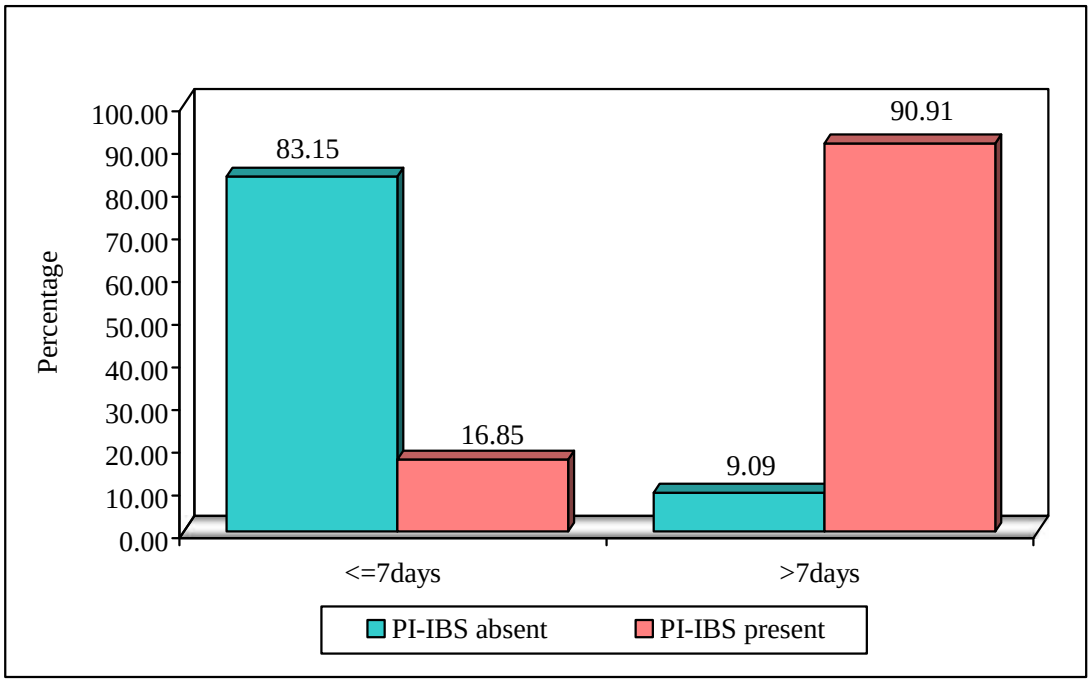


In this study, 30% patients had less than or equal to 6 stools per day. 20% of these developed PI-IBS. 70% patients had more than 6 stools per day. 27.14% of these developed PI-IBS. No. of stools per day was not a significant risk factor for development of PI-IBS in our study. (p-value: 0.4500)

Table 12: Incidence of PI-IBS by Duration of AGE (days)

Duration of AGE	PI-IBS absent	%	PI-IBS present	%	Total	%
<=7days	74	83.15	15	16.85	89	89.00
>7days	1	9.09	10	90.91	11	11.00
Total	75	75.00	25	25.00	100	100.00
Chi-square=28.6350, p=0.0001, S						

Figure 12: Incidence of PI-IBS by Duration of AGE (days)

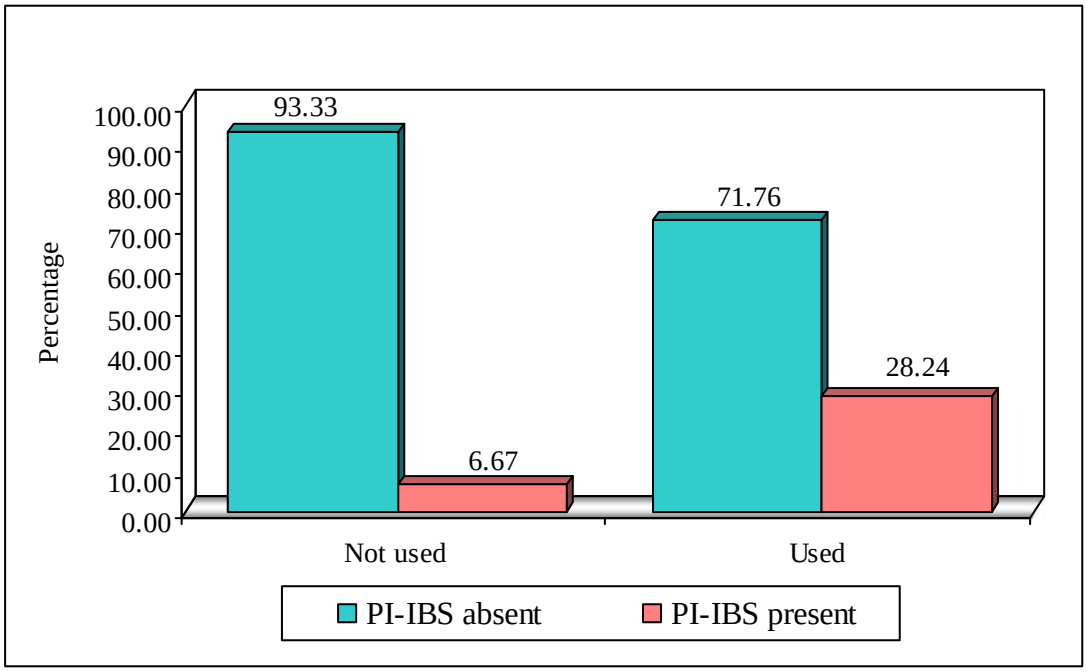


16.85% of the patients who had the episode of AGE for less than or equal to 7 days developed PI-IBS. However, 90.91% of those with AGE lasting for more than 7 days developed PI-IBS. Hence duration of AGE more than 7 days is statistically significant for development of PI-IBS. (p-value: 0.0001)

Table 13: Incidence of PI-IBS by Antibiotics use

Antibiotics	PI-IBS absent	%	PI-IBS present	%	Total	%
Not used	14	93.33	1	6.67	15	15.00
Used	61	71.76	24	28.24	85	85.00
Total	75	75.00	25	25.00	100	100.00
Chi-square=3.1630, p=0.0750, NS						

Figure 13: Incidence of PI-IBS by Antibiotics use

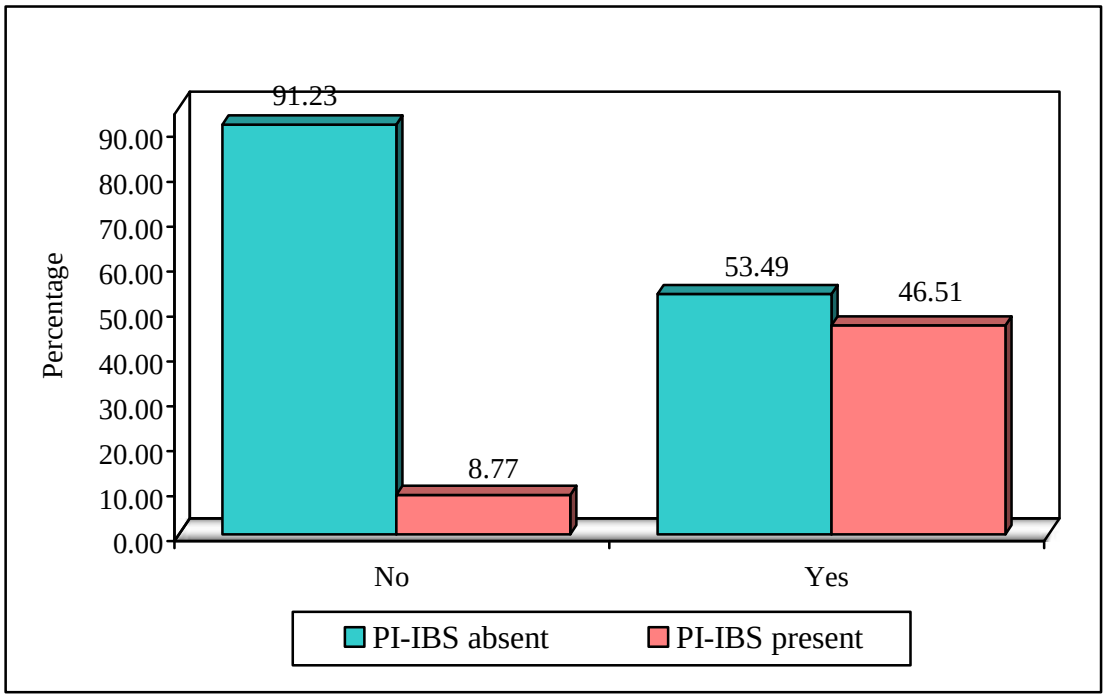


85% of the patients had used antibiotics for the current episode of AGE in this study. 28.24% of these developed PI-IBS. However, 6.67% of those who did not use antibiotics developed PI-IBS. Use of antibiotics did not prove statistically significant for development of PI-IBS in our study. (p-value: 0.0750)

Table 14: Incidence of PI-IBS by Abdominal cramps

Abdominal cramps	PI-IBS absent	%	PI-IBS present	%	Total	%
No	52	91.23	5	8.77	57	57.00
Yes	23	53.49	20	46.51	43	43.00
Total	75	75.00	25	25.00	100	100.00
Chi-square=18.6180, p=0.0001, S						

Figure 14: Incidence of PI-IBS by Abdominal cramps

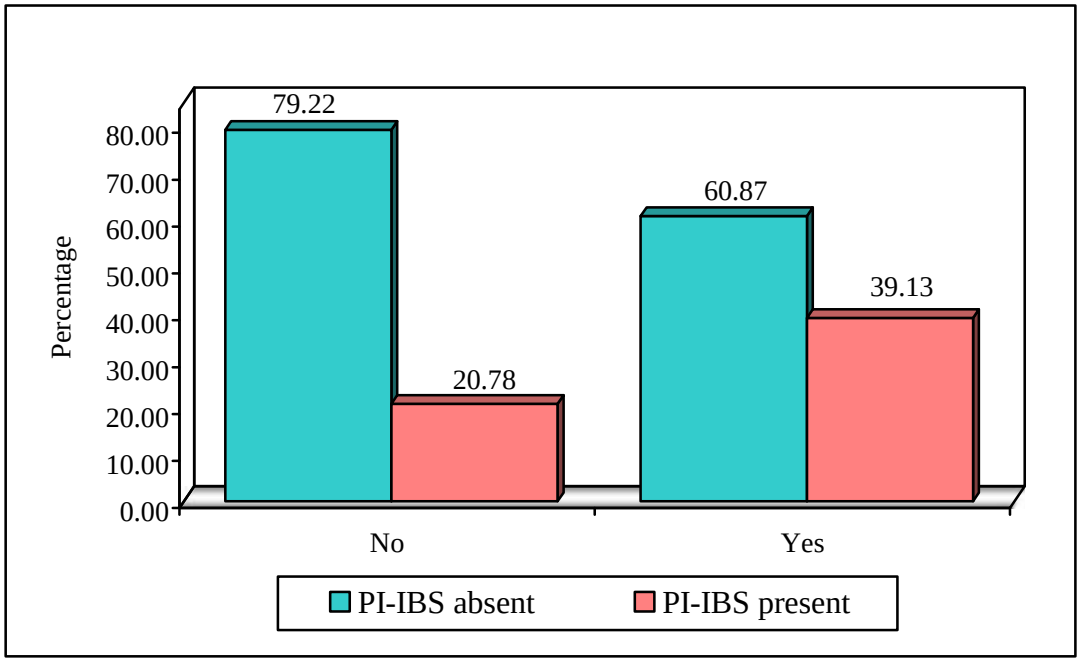


46.51% of the patients with abdominal cramps during the episode of AGE developed PI-IBS. Only 8.77% of those without abdominal cramps developed PI-IBS. Presence of abdominal cramps during AGE is statistically significant for development of PI-IBS. (p-value: 0.0001)

Table 15: Incidence of PI-IBS by Anxiety

Anxiety	PI-IBS absent	%	PI-IBS present	%	Total	%
No	61	79.22	16	20.78	77	77.00
Yes	14	60.87	9	39.13	23	23.00
Total	75	75.00	25	25.00	100	100.00
Chi-square=3.1810, p=0.0750, NS						

Figure 15: Incidence of PI-IBS by Anxiety

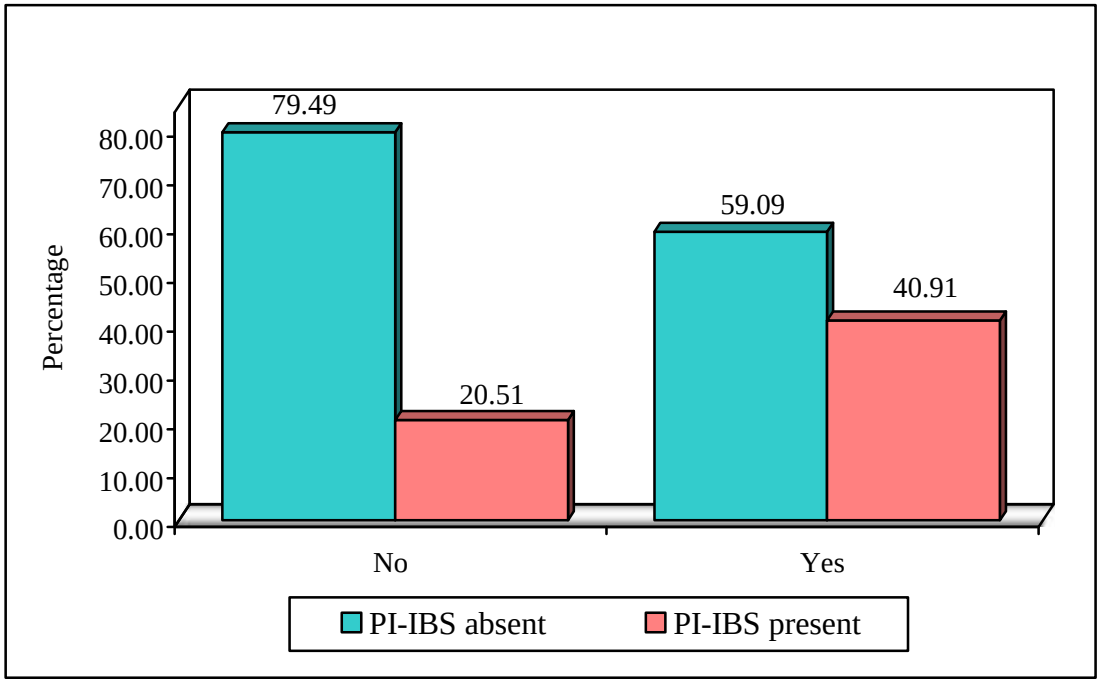


20.78% of the patients without anxiety and 39.13% of the patients with anxiety developed PI-IBS. Anxiety was not statistically significant for development of PI-IBS. (p-value: 0.0750)

Table 16: Incidence of PI-IBS by Depression

Depression	PI-IBS absent	%	PI-IBS present	%	Total	%
No	62	79.49	16	20.51	78	78.00
Yes	13	59.09	9	40.91	22	22.00
Total	75	75.00	25	25.00	100	100.00
Chi-square=3.8070, p=0.0500, S						

Figure 16: Incidence of PI-IBS by Depression

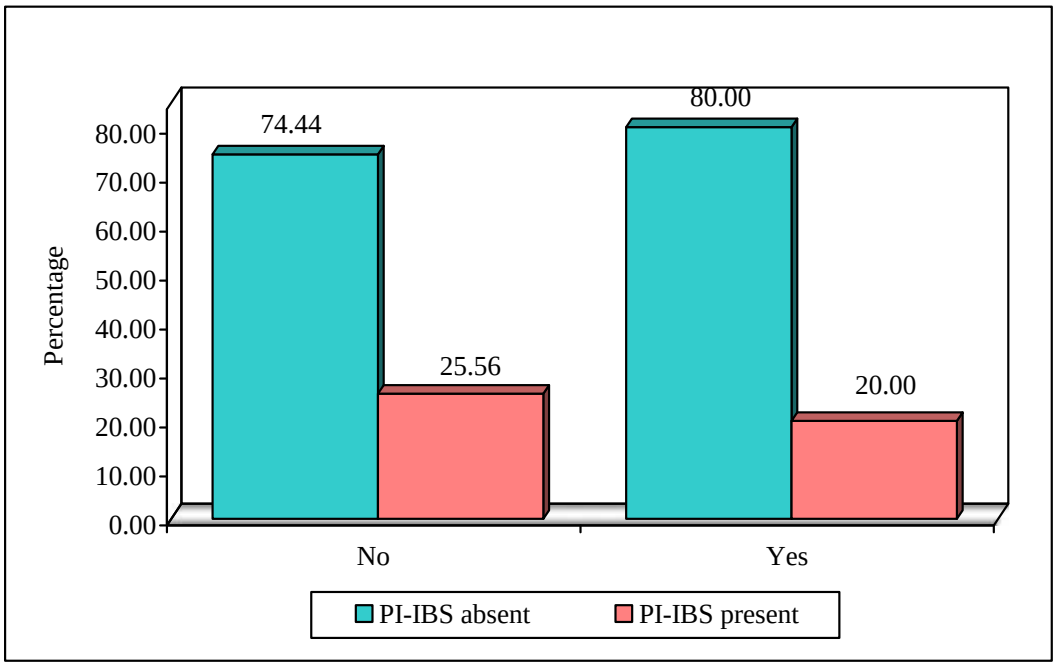


40.91% of the patients with depression during the episode of AGE developed PI-IBS. 20.51% of those without depression developed PI-IBS. Depression is a statistically significant risk factor for development of PI-IBS in our study. (p-value: 0.0500)

Table 17: Incidence of PI-IBS by Contact with livestock

Contact with livestock	PI-IBS absent	%	PI-IBS present	%	Total	%
No	67	74.44	23	25.56	90	90.00
Yes	8	80.00	2	20.00	10	10.00
Total	75	75.00	25	25.00	100	100.00
Chi-square=0.1480, p=0.7000, NS						

Figure 17: Incidence of PI-IBS by Contact with livestock

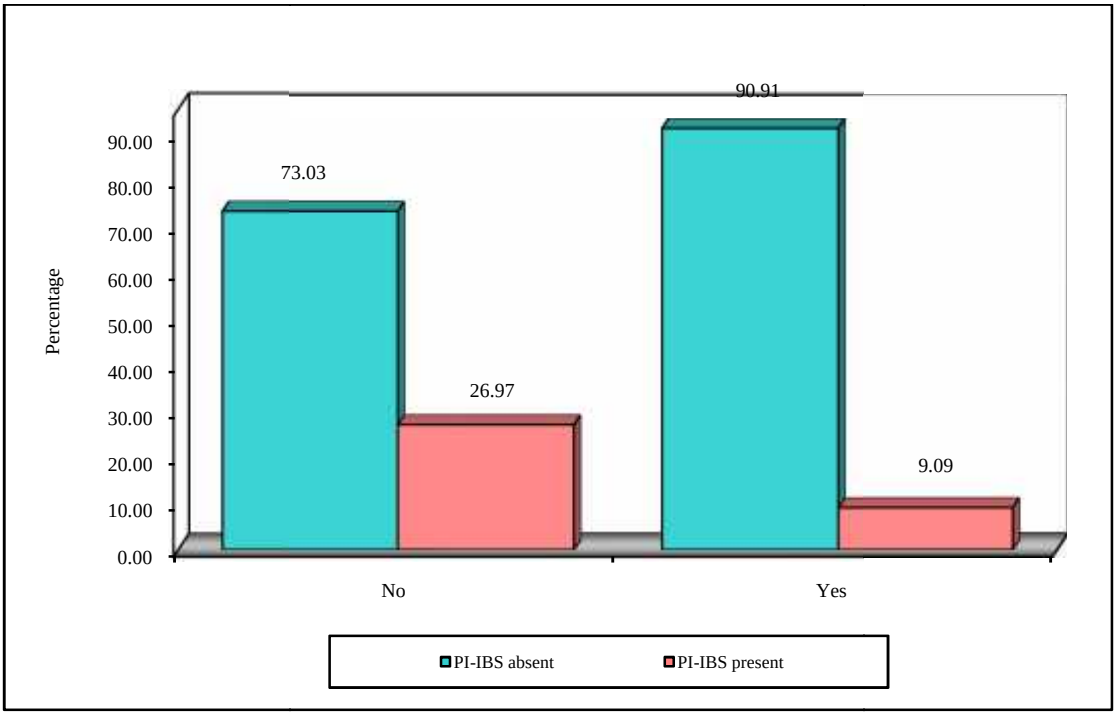


90% of our patients did not have contact with livestock. 25.56% of these developed PI-IBS. 20% of those with contact with livestock developed PI-IBS. Contact with livestock is not statistically significant as a risk factor for development of PI-IBS in our study. (p-value: 0.7000)

Table 18: Incidence of PI-IBS by Stool occult blood

Stool occult blood	PI-IBS absent	%	PI-IBS present	%	Total	%
No	65	73.03	24	26.97	89	89.00
Yes	10	90.91	1	9.09	11	11.00
Total	75	75.00	25	25.00	100	100.00
Chi-square=1.6680, p=0.1960, NS						

Figure 18: Incidence of PI-IBS by Stool occult blood

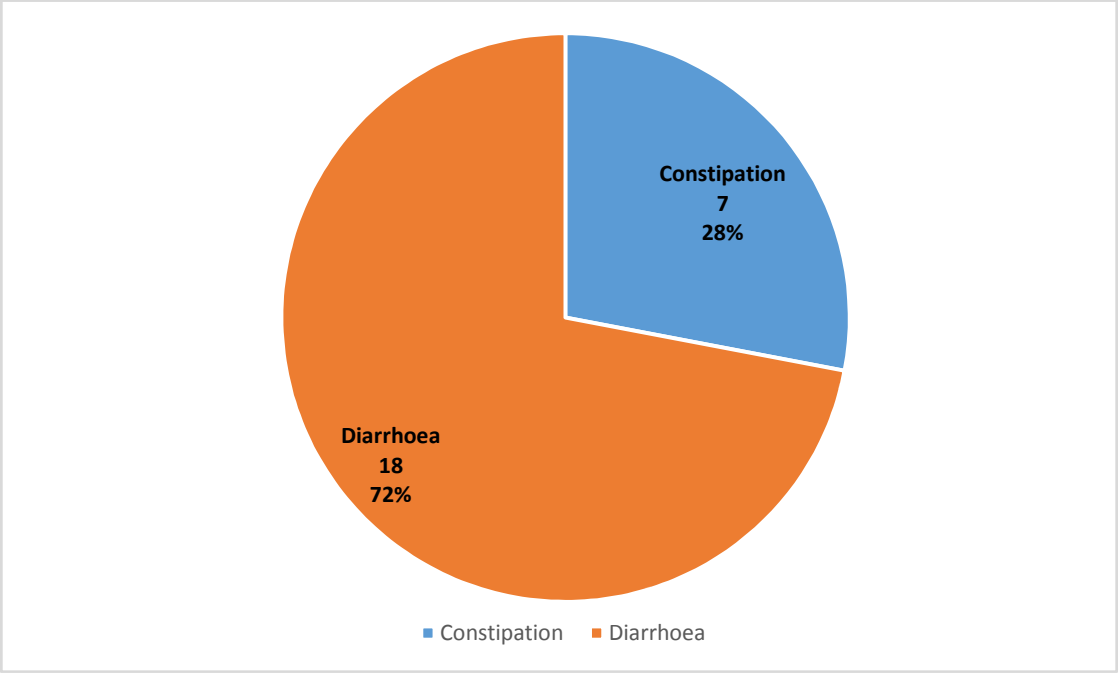


In this study, 89% of the patients had stools negative for occult blood. 26.97% of these developed PI-IBS. However, 9.09% of those with stools positive for occult blood developed PI-IBS. Hence, Occult blood in stool is not a statistically significant risk factor for development of PI-IBS. (p-value: 0.1960)

Table 19: IBS type (C vs D)

IBS type developed	No of patients	% of patients
Constipation	7	28.00
Diarrhoea	18	72.00
Total	25	100.00

Figure 19: IBS type (C vs D)

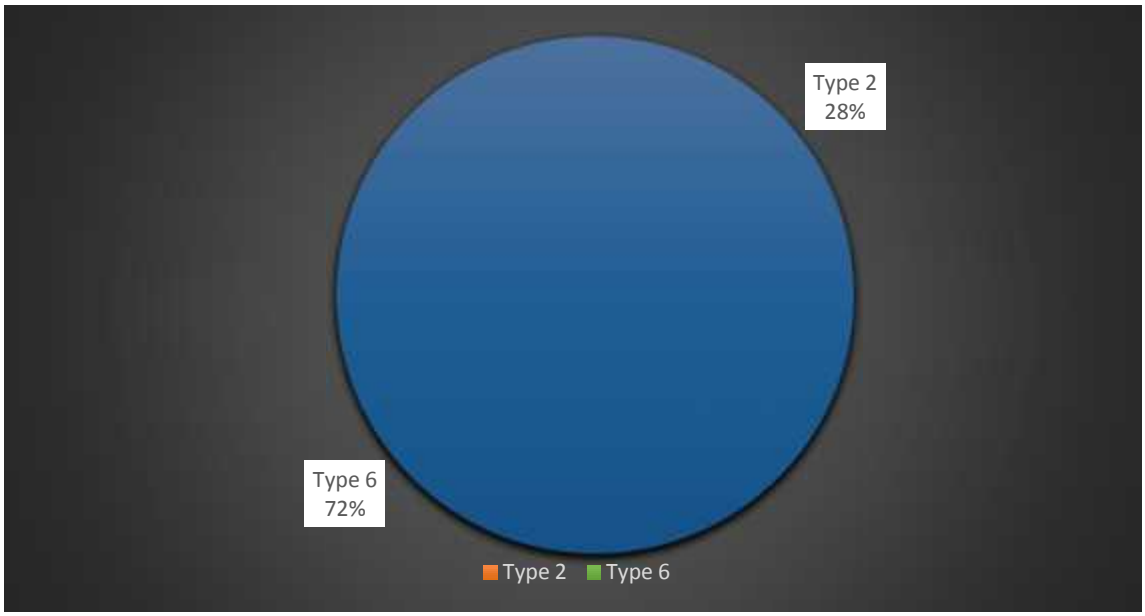


In our study, out of the 25 patients who developed PI-IBS, 28% had IBS-C (constipation predominant) and 72% had IBS-D (diarrhea predominant).

Table 20: Bristol stool type at 6months

Bristol stool type at 6months	No of patients	% of patients
2	7	28%
6	18	72%
Total	25	100.00

Figure 20: Bristol stool type at 6months



Out of the 25 patients who developed PI-IBS, 28% patients were passing Bristol stool type 2 at 6 months follow up. 72% were passing Bristol stool type 6.

Table 21: Multiple logistic regression analysis for incidence of PI-IBS

Independent factors	Unadjusted OR	95% CI for OR		p-value	Adjusted OR	95% CI for OR		p-value
		Lower	Upper			Lower	Upper	
Age groups (<=60 vs>60yrs)	0.12	0.04	0.40	0.0010*	0.33	0.07	1.57	0.1630
Sex (Male vs female)	0.39	0.21	0.72	0.0030*	1.11	0.32	3.91	0.8710
Fever (No vs Yes)	0.41	0.25	0.67	0.0001*	0.62	0.16	2.47	0.5010
Vomiting (No vs Yes)	0.36	0.23	0.58	0.0001*	0.28	0.06	1.32	0.1080
No. of stools per day (<=6 vs>6)	0.37	0.22	0.63	0.0001*	0.45	0.12	1.74	0.2500
Antibiotics (Not use vs Use)	0.39	0.25	0.63	0.0001*	0.89	0.14	5.72	0.9010
Duration of AGE (<=7 vs>7))	10.00	1.28	78.12	0.0280*	71.55	3.83	1337.58	0.0040*
Abdominal cramps (No vs Yes)	0.87	0.48	1.58	0.6480	5.07	1.42	18.18	0.0130*
Anxiety (No vs Yes)	0.64	0.28	1.49	0.3010	2.19	0.53	9.13	0.2820
Depression (No vs Yes)	0.69	0.30	1.62	0.3960	2.68	0.65	11.08	0.1730
Contact with livestock (No vs Yes)	0.25	0.05	1.18	0.0800	0.69	0.07	6.91	0.7520
Stool occult blood (No vs Yes)	0.10	0.01	0.78	0.0280*	0.17	0.02	1.88	0.1480

*p<0.05; *OR:* Odds Ratio; *AGE*: Acute gastroenteritis

On multivariate logistic regression analysis, duration of acute gastroenteritis (>7 days) (AOR 71.55; 95% CI; 3.83-1337.58; p-value=0.0040) and presence of abdominal cramps (AOR 5.07; 95% CI; 1.42-18.18; p-value=0.0130) were found to be significantly influencing the development of PI-IBS at 6 months, when compared to the other risk factors.

DISCUSSION

A total of 100 patients with acute gastroenteritis were enrolled in this prospective study, conducted in KLES Dr.Prabhakar Kore Hospital and MRC, with the objectives of finding out the incidence of Post-infection Irritable Bowel Syndrome and to study the risk factors associated with it. As IBS is a common diagnosis in the out-patient department, a prospective study helps us better in establishing acute gastroenteritis as an etiology for developing IBS, minimizing recall bias and enhancing the quality of follow-ups and hence the data regarding risk factors obtained. Although AGE is very common in tropical countries with poor hygiene, information on PI-IBS is very scarce from these countries.

In the present study, our patients ranged from 18 years to 86 years of age. For feasibility of studying association of age with PI-IBS, in accordance with Thabane Risk Score scale, we divided the patients into 2 groups- <=60 years and > 60 years. 72% of our patients were aged <=60 years and 28% were older than 60 years. Mean age of our study subjects was 46.12 years at the time of AGE episode. This is similar to The Walkerton Health Study where mean age of the study population was 46.6 years.[6]

50% of the patients with AGE in our study were males, and the remaining females. The Walkerton Health Study had 44.5% males which is similar to our study.[6] Females are reported to seek healthcare more in the western studies, however the opposite is usually seen in India. 68% of the patients were males in the report of Indian Society of Gastroenterology Task Force for clinical profile of IBS in India in 2008.[23]

80 out of our 100 patients had pus cells in stool on microscopic examination at the time of admission. Barr et al in 2014, have given recommendation to identify

infectious diarrhoea which infer the presence of fecal pus cells as inflammatory diarrhoea.[75] Absence of fecal leucocytes does not exclude infection as a cause of acute gastroenteritis.

None of the 100 patients with AGE in our study complained of bloody stool, however stool occult blood was positive in 11% of the patients.

We found the incidence of PI-IBS to be 25% by ROME IV criteria in our study. Gwee et al, in 1996 had studied a group of 75 patients with AGE, 20 of which had PI-IBS at 6 months (26.6%).[26] Our study was comparable to this result. The Walkerton Health Study had also reported about 30% incidence of PI-IBS in subjects with AGE.[6] Recently, in a study with 136 patients of acute gastroenteritis in Orissa, incidence of PI-IBS was reported to be 25.7% at 6 months by ROME III criteria.[40] However in a study by Borgaonkar et al, only 3.7% incidence of PI-IBS in community subjects was noted.[76] This was diagnosed by Manning and Rome I criteria, which currently are obsolete.

In the present study, females developed PI-IBS more than males(14 vs 11), however it was not statistically significant. Klem et al, in a systematic review and meta-analysis in 2017 had reported females are 2.2 times more likely to develop PI-IBS.[22] Marshal et al had also suggested females to be more likely of the two sex to develop PI-IBS. Ruigomez et al and Wensaas et al have also reported PI-IBS to be more prevalent in females but, it may not be statistically significant.[27,28]McKendrick et al found in their study that women were almost 5 times more as compared to men amongst those who had persistent symptoms after AGE.[18]

Age less than or equal to 60 years was found to be statistically significant in our study for development of PI-IBS. This is comparable to majority of the studies conducted to study risk factors associated with development of PI-IBS. Younger age

was associated with PI-IBS in studies conducted by Parida et al, Marshall et al, Thabane et al.[6,40]Ji et al on the contrary, did not find any significant difference in ages between patients who did and did not develop PI-IBS.[38]

Presence of fever and vomiting was not found to be statistically significant for development of PI-IBS in our study, however more number of patients with fever and vomiting did develop PI-IBS. Thabane et al had also reported the presence of fever, and vomiting as a risk factor for development of PI-IBS.[30]

Duration of acute gastroenteritis of more than 7 days and presence of abdominal cramps were two independently significant risk factors(p=0.0001), associated with development of PI-IBS. Similar observations were made by Parida et al, Thabane et al, Ji et al.[30,38,40] Singh et al, in an Indian study, have validated the same with duration of AGE and abdominal cramps getting more points in a PI-IBS risk score.[46] A study by Kowalcyk et al also described these two factors as statistically significant for development of PI-IBS.[41]

We observed that more number of patients who had consumed antibiotics during the episode of AGE went on to develop PI-IBS, however it was not statistically significant (p=0.0750). Paula et al had studied the relation between antibiotic use and functional GI disorders.[36] Maxwell et al had also made observations similar to our study in terms of the part played by antibiotics in development of PI-IBS.[77] Psychological disorders like depression and anxiety have been long associated with functional gastrointestinal disorders. In our study, patients with depression (according to Hospital Anxiety and Depression Scale proforma) were found to have statistically significant risk of developing PI-IBS (p=0.050). Patients with anxiety were also found to have increased risk of developing PI-IBS but it was not statistically significant (p=0.0750). HADS proforma was published in 1983, and was accepted for self-

assessment of emotional disorders in hospital setting.[78]Wouters et al observed that both anxiety and depression led to increased risk of developing PI-IBS. Sykes et al also found that anxiety predisposed to development of IBS.[79]

In the present study, 18 out of 25 patients (72%) who developed PI-IBS had diarrhoea predominant phenotype(IBS-D). The remaining 28% had constipation predominant IBS (IBS-C). Parida et al, found that all 35 who developed PI-IBS out of 136 patients with AGE, had diarrhoea predominant IBS.[40] Correspondingly, all those who had developed IBS-D had reported Bristol type 6 stool in our study, and those who had developed IBS-C had Bristol type 2 stool. In a review of clinical and epidemiological perspectives of IBS in India, Rahman et al observed that majority of patients could not be classified as IBS-C or IBS-D and were put into a mixed category IBS-M as most of them could not define their symptoms in accordance with frequency of stool criteria for constipation or diarrhoea.[4] However, the patients in our study who developed PI-IBS could be categorised as having IBS-C or IBS-D.

On univariate analysis, we found that fever, younger age, vomiting, prolonged duration of AGE were significant risk factors. However on multivariate analysis, prolonged duration of diarrhoea i.e. more than 7 days (AOR 71.55; 95% CI; 3.83-1337.58; p-value=0.0040) and abdominal cramps (AOR 5.07; 95% CI; 1.42-18.18; p-value=0.0130) were significant for development of PI-IBS. Direct contact with livestock was not found significant in development of PI-IBS. This is comparable to the studies conducted by Parida et al[40] and Thabane et al.[30]

Our study did not show any stool cultures with growth of enteropathogens, hence we could not relate the type of organism causing AGE as a risk factor for development of PI-IBS. Salmonella and Campylobacter causing AGE have been found to commonly predispose to PI-IBS.[80] As most of our patient's had consumed

antibiotics prior to hospital admission, it may have influenced the result of stool cultures. Besides, as we know that PI-IBS runs in families, we could not perform genetic analysis of patients to determine genetic risk factors for development of PI-IBS. It may also be necessary to get an upper and a lower GI scopy done for the patients to rule out organic causes of diarrhoea completely, to yield more accurate results.

CONCLUSION

Post-infection Irritable Bowel Syndrome is an established problem that should be looked for in patients of acute gastroenteritis. One-fourth of the patients in the present study developed PI-IBS by ROME IV criteria, with IBS-D type being more than IBS-C type. Hence we found increased risk of developing IBS following an acute gastrointestinal infection. We also found that identification of risk factors like female gender, younger age, prolonged duration of diarrhoea(>7 days), presence of abdominal cramps, psychological disorders like anxiety, depression during the episode of AGE are important in predicting development of PI-IBS. The patients can be counselled about the persistence of symptoms even after the episode of AGE has subsided, so that they can seek healthcare appropriately.

Since there are very few prospective studies like ours, there is not enough known about prevalence and management of PI-IBS in India. The symptoms of PI-IBS are often treated as new episodes of subsequent AGE, sometimes due to the patients visiting multiple physicians with the same problems. It is suggested to study a larger cohort, with inclusion of genetic risk factors in order to extrapolate the statistics to the general population. Physicians should keep a high suspicion for PI-IBS, in patients with predisposing risk factors.

The possibly involved molecular mechanisms in the pathogenesis of PI-IBS should be investigated for better understanding of the disease, and to plan and strategize therapeutic options. Targeting the gut microbiota and its alteration is currently a topic of focus, and is proving to be promising in management of PI-IBS.

SUMMARY

In the present prospective study, 100 patients with acute gastroenteritis in KLES Dr. Prabhakar Kore Hospital & MRC were followed up for development of Post-infection IBS after 6 months of the initial AGE episode. The risk factors known to predispose individuals to PI-IBS were also studied, by means of a questionnaire.

We found that one-fourth of our patients i.e. 25 out of 100 patients developed IBS at 6 months, hence showing increased risk of IBS after an episode of AGE. Diarrhoea predominant IBS were more common than Constipation predominant IBS. In our study, 50% of the patients were males and remaining were females, 72% of the patients were less than or equal to 60 years of age.

Females developed PI-IBS more than males in our study (14 vs 11), and more number of patients with age less than or equal to 60 years developed PI-IBS. More number of patients with fever and vomiting during AGE developed PI-IBS, however these weren't statistically significant. Number of stools passed per day during the episode of AGE was not significant as a risk factor. Prolonged duration of diarrhoea i.e. more than 7 days and presence of abdominal cramps were both statistically significant risk factors for development of PI-IBS (p-value=0.0001).

More number of patients who consumed antibiotics during AGE developed PI-IBS. More number of patients with depression or anxiety developed PI-IBS, however only depression was statistically significant (p-value=0.050). Contact with livestock was not a significant risk factor for PI-IBS.

On multiple logistic regression analysis, only presence of abdominal cramps (p-value=0.0040) and prolonged duration of diarrhoea (p-value=0.0130) were found to be statistically significant for development of PI-IBS at 6 months.

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ANNEXURE- I

ETHICAL COMMITTEE CERTIFICATE

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed – to- be- University)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (GoI)
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http//www.jnmc.edu
E-Mail : dome@jnmc.edu
Phone: (+ 91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ 38 **Date: 24/11/2018**

To,

REG. NO.: BG0118007

PG student in Medicine,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"INCIDENCE AND RISK FACTORS ASSOCIATED WITH DEVELOPMENT OF POST INFECTIOUS IRRITABLE BOWEL SYNDROME (IBS): A ONE YEAR PROSPECTIVE LONGITUDINAL STUDY AT KLES DR. PRABHAKAR KORE HOSPITAL AND MRC, BELGAUM",** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Arathi Darshan)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Roopa M Bellad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

38

ANNEXURE-II

INFORMED CONSENT

TITLE OF RESEARCH AND STUDY: Incidence and Risk factors associated with development of Post infection Irritable Bowel Syndrome (IBS): A One year Prospective longitudinal study

Principal Investigator:-

REG. NO.: BG0118007

Post Graduate Student,

Department Of General Medicine,

JNMC, Belagavi.

Guide:-

Dr. _____

Professor & Head of Department,

Department of General Medicine,

JNMC, Belagavi.

Introduction and Purpose:-

This study is aimed at determining the incidence of post infection IBS and the risk factors associated with it, with the help of questionnaire, examination and routine investigations.

Procedure:

If you agree to be part of the research study, you will be asked the relevant history and will be subjected to relevant clinical examination and investigations. You will also have to give blood samples for the necessary investigations.

Risk and Benefits:

This study doesn't carry any risks per se as nothing out of the ordinary shall be carried out. This study will benefit the population in general as development of IBS then could be anticipated after consideration of the risk factors, and easily evaluated and treated. The investigator cannot assure any direct benefits to the participants in the study.

Alternatives:

Taking part in this study is voluntary. You may choose not to take part in this study. If you decide to take part you can later change your mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. The study doctor or sponsor may stop your participation in this study at any time. If you choose not to take part in the study, you will receive the standard treatment for patients with your condition.

Privacy and Confidentiality:

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

Institution / Sponsor's policy:

Does not apply to this research

Financial incentives for participation:

You will not be paid / offered any gifts /incentives for participating in the study.

Authorization to publish the results:

The results of the study would be forwarded to the KLE University, Belagavi as part of requirement towards the completion of MD degree, review and publishing.

In case of the queries during study or in future you may contact following persons,

REG. NO.: BG0118007
Investigator,
PG in General Medicine,
JNMC, Belagavi.

Dr._____
Professor & Head of Department,
Dept of General Medicine,
JNMC, Belagavi.

CONSENT FORM

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicates that I have read this consent form, or it has been read to me and has been explained to me in my vernacular language and all my questions have been answered. I will be given a copy of this consent form.

Signature / Left Thumb print of the Participant or legally authorized representative

Participant's name :…….....

Signature / Left thumb impression:……...

of the participant

Name of the legally authorized

representative / guardian :……..

Signature / Left thumb impression:…….....

Witness' name :…….....

Signature / Left thumb impression: …….....

Investigator's name and signature:…….....

Date:

Place:

ತಿಳುವಳಿಕೆಯುಳ್ಳಒಪ್ಪಿಗ

ಸಂಶೋಧನಮತ್ತುಅಧ್ಯಯನದಶೀರ್ಷಿಕ: ಪೋಸ್ಟ್ಕಾಂಕ್ಯಾಮಿಕಕರಳಿಸುವಕರುಳಿನಸಿಂಡ್ರೋಮ್ (ಐಬಿಎಸ್) ಅಭಿವೃದ್ಧಿಗಸಂಬಂಧಿಸಿದಘಟನಮತ್ತುಅಪಾಯಕಾರಿಅಂಶಗಳು: ಒಂದು ವರ್ಷದ ನಿರೀಕ್ಷಿತ ರೇಖಾಂಶದ ಅಧ್ಯಯನ

ಪ್ರಧಾನತನಿಖಾಧಿಕಾರಿ: -

REG. NO.: BG0118007

ಸ್ನಾತಕೋತ್ತರವಿದ್ಯಾರ್ಥಿ,
ಜನರಲ್ಮೆಡಿಸಿನ್ಇಲಾಖೆ,
ಜೆಎನ್ಎಂಸಿ, ಬೆಳಗಾವಿ.

ಗೈಡ್: -

ಡಾ.,_____

ಇಲಾಖೆಯಪ್ರೊಫೆಸರ್ಮತ್ತುಮುಖ್ಯಸ್ಥ,
ಜನರಲ್ಮೆಡಿಸಿನ್ಇಲಾಖೆ,
ಜೆಎನ್ಎಂಸಿ, ಬೆಳಗಾವಿ.

ಪರಿಚಯಮತ್ತುಉದ್ದೇಶ: - ಈಅಧ್ಯಯನವುಪೋಸ್ಟ್ಕಾಂಕ್ಯಾಮಿಕ IBS ಮತ್ತುಅದರೊಂದಿಗೆಸಂಬಂಧಿಸಿದಅಪಾಯಕಾರಿಅಂಶಗಳವಿಚಾರಣೆಯನ್ನುಪ್ರಶ್ನಾರ್ಥಕ, ಪರೀಕ್ಷೆಮತ್ತುವಾಡಿಕೆಯತನಿಖೆಗಳಸಹಾಯದಿಂದಗುರಿಪಡಿಸುತ್ತದೆ.

ವಿಧಾನ: ಸಂಶೋಧನಾಅಧ್ಯಯನದಭಾಗವಾಗಿರಲುನೀವುಒಪ್ಪಿಕೊಂಡರೆ, ನಿಮಗೆಸೂಕ್ತವಾದಇತಿಹಾಸವನ್ನುಕೇಳಲಾಗುವುದುಮತ್ತುಸಂಬಂಧಿತವೈದ್ಯಕೀಯಪರೀಕ್ಷೆಮತ್ತುತನಿಖೆಗಳಿ[illegible] ಗೆಒಳಪಡಿಸಲಾಗುತ್ತದೆ. ಅಗತ್ಯವಿದ್ದರೆಹೆಚ್ಚುವರಿರಕ್ತಮಾದರಿಗಳನ್ನುಕೂಡಸೇರಿಸಬೇಕು.

ಅಪಾಯಮತ್ತುಪ್ರಯೋಜನಗಳು:

ಈಅಧ್ಯಯನದಪ್ರಕಾರಯಾವುದೇಸಾಮಾನ್ಯಅಪಾಯಗಳುಸಂಭವಿಸುವುದಿಲ್ಲಮತ್ತುಸಾಮಾನ್ಯವಾದವುಗ[illegible] ಳನ್ನುಕೈಗೊಳ್ಳಲಾಗುವುದಿಲ್ಲ.
ಈಅಧ್ಯಯನದಪ್ರಕಾರಐಬಿಎಸ್ನಬೆಳವಣಿಗೆಯುಅಪಾಯಕಾರಿಅಂಶಗಳಪರಿಗಣನೆಯನಂತರನಿರೀಕ್ಷಿಸಬ[illegible] ಹುದುಮತ್ತುಸುಲಭವಾಗಿಮೌಲ್ಯಮಾಪನಮತ್ತುಚಿಕಿತ್ಸೆನೀಡಲಾಗುತ್ತದೆ.
ತನಿಖಾಧಿಕಾರಿಗಳುಅಧ್ಯಯನದಲ್ಲಿಪಾಲ್ಗೊಳ್ಳುವವರಿಗೆಯಾವುದೇನೇರಪ್ರಯೋಜನಗಳನ್ನುಭರವಸೆನೀಡ[illegible] ಲಾರರು.

ಪರ್ಯಾಯಗಳು:ಈಅಧ್ಯಯನದಲ್ಲಿಪಾಲ್ಗೊಳ್ಳುವುದುಸ್ವಯಂಪ್ರೇರಿತವಾಗಿರುತ್ತದೆ.
ಈಅಧ್ಯಯನದಲ್ಲಿಭಾಗವಹಿಸದಿರಲುನೀವುಆಯ್ಕೆಮಾಡಬಹುದು.
ನೀವುಪಾಲ್ಗೊಳ್ಳಲುನಿರ್ಧರಿಸಿದರೂನೀವುನಂತರನಿಮ್ಮಮನಸ್ಸನ್ನುಬದಲಿಸಬಹುದುಮತ್ತುಅಧ್ಯಯನದಿಂದ
ಹಿಂತೆಗೆದುಕೊಳ್ಳಬಹುದು.
ನಿಮ್ಮನಿರ್ಧಾರಪ್ರಸ್ತುತಅಥವಾಭವಿಷ್ಯದಆರೋಗ್ಯರಕ್ಷಣಅಥವಾನೀವುಸ್ವೀಕರಿಸುವಇತರಸೇವಗಳನ್ನುಬದ
ಲಿಸುವುದಿಲ್ಲ.ಅಧ್ಯಯನದವೈದ್ಯರುಅಥವಾಪ್ರಾಯೋಜಕರುಈಅಧ್ಯಯನದಲ್ಲಿನಿಮ್ಮಭಾಗವಹಿಸುವಿಕಯ
ನ್ನುಯಾವುದೇಸಮಯದಲ್ಲಿನಿಲ್ಲಿಸಬಹುದು. ನೀವುಅಧ್ಯಯನದಲ್ಲಿಪಾಲ್ಗೊಳ್ಳಬಾರದೆಂದುಆಯ್ಕೆಮಾಡಿದರೆ,
ನಿಮ್ಮಸ್ಥಿತಿಯರೋಗಿಗಳಿಗೆನೀವುಪ್ರಮಾಣಿತಚಿಕಿತ್ಸೆಯನ್ನುಸ್ವೀಕರಿಸುತ್ತೀರಿ.

ಗೌಪ್ಯತೆಮತ್ತುಗೌಪ್ಯತೆ:
ಈಅಧ್ಯಯನದಸಮಯದಲ್ಲಿನಿಮ್ಮಬಗ್ಗೆಸಂಗ್ರಹಿಸಿದಎಲ್ಲಾಮಾಹಿತಿಯನ್ನುಕಾನೂನುಅನುಮತಿಸುವಮಟ್ಟಗ
ಗೌಪ್ಯವಾಗಿಡಲಾಗುತ್ತದೆ.
ಕೋಡ್ಸಂಖ್ಯೆಗಳುನಿಮ್ಮನ್ನುಈಸಂಶೋಧನಾದಾಖಲೆಯಲ್ಲಿಗುರುತಿಸುತ್ತದೆ.ಈಅಧ್ಯಯನದಮಾಹಿತಿಯುಪ್ರ
ಕಟವಾಗಬಹುದುಆದರೆನಿಮ್ಮಗುರುತುಯಾವುದೇಪ್ರಕಟಣೆಯಲ್ಲಿಗೌಪ್ಯವಾಗಿರುತ್ತದೆ.

ಸಂಸ್ಥೆ / ಪ್ರಾಯೋಜಕರನೀತಿಗಳು:ಈಸಂಶೋಧನೆಗಅನ್ವಯಿಸುವುದಿಲ್ಲ

ಭಾಗವಹಿಸುವಿಕೆಗಾಗಿಪರಿಹಾರಕಾಸಿನಪ್ರೋತ್ಸಾಹ:
ಅಧ್ಯಯನದಲ್ಲಿಪಾಲ್ಗೊಳ್ಳಲುನಿಮಗೆಯಾವುದೇಉಡುಗೊರೆಗಳು /
ಪ್ರೋತ್ಸಾಹಕಗಳನ್ನುನೀಡಲಾಗುವುದಿಲ್ಲ.

ಫಲಿತಾಂಶಗಳನ್ನುಪ್ರಕಟಿಸಲುಅಧಿಕಾರ:ಅಧ್ಯಯನದಫಲಿತಾಂಶಗಳನ್ನುಎಮ್ಡಿಪದವಿ,
ವಿಮರ್ಶೆಮತ್ತುಪ್ರಕಾಶನಮಾಡಿಸಲುಅಗತ್ಯವಿರುವಭಾಗವಾಗಿಕವಿಲಿಇವಿಶ್ವವಿದ್ಯಾಲಯ,
ಬೆಳಗಾವಿಗೆಫಾರ್ವರ್ಡ್ಮಾಡಲಾಗುವುದು

ಅಧ್ಯಯನದಸಮಯದಲ್ಲಿಅಥವಾಭವಿಷ್ಯದಲ್ಲಿಪ್ರಶ್ನೆಯಸಂದರ್ಭದಲ್ಲಿನೀವುಈಕೆಳಗಿನವ್ಯಕ್ತಿಗಳನ್ನುಸಂಪರ್ಕಿ
ಸಬಹುದು,

1.**REG. NO.: BG0118007**
ತನಿಖಾದಾರ,
ಪಿಜಿಇನ್ಜನರಲ್ಮೆಡಿಸಿನ್,
ಜೆಎನ್ಎಂಸಿ, ಬೆಳಗಾವಿ.
8884213593

2. **ಡಾ.** _____
ಇಲಾಖೆಮುಖ್ಯಸ್ಥರು
, ಜನರಲ್ಮೆಡಿಸಿನ್ವಿಭಾಗ,
ಜಎನ್ಎಂಸಿ, ಬೆಳಗಾವಿ.
9448371125

ರಸಚ್ಛ್ಯಡನಲ್ಲಿಪಾಲ್ಗೊಳ್ಳಲುಒಪ್ಪಿಗ

ಈಅಧ್ಯಯನದಲ್ಲಿಪಾಲ್ಗೊಳ್ಳಲುನಾನುಸ್ವಯಂಪ್ರೇರಿತವಾಗಿಒಪ್ಪುತ್ತೇನೆ.ನಾನುಯಾವುದೇಸಮಯದಲ್ಲಿಹಿಂ
ಪಡೆಯಬಹುದು.ಈಫಾರ್ಮ್‌ಅನ್ನುಸಹಿಮಾಡುವಮೂಲಕನನ್ನಯಾವುದೇಕಾನೂನುಹಕ್ಕುಗಳನ್ನುನಾನುಬಿ
ಟ್ಟುಕೊಡುವುದಿಲ್ಲ.

ಕೆಳಗೆನನ್ನಸಹಿನಾನುಈಸಂಪೂರ್ಣಒಪ್ಪಿಗೆಯನ್ನುಓದಿದ್ದೇನೆಅಥವಾನನಗೆಓದುತ್ತಿದ್ದೇನೆಎಂದುಸೂಚಿಸಿದ
, ಮತ್ತುನನ್ನದೇಶೀಯಭಾಷೆಯಲ್ಲಿನನಗೆಎವೆರೆಸಲಾಗಿದಮತ್ತುನನ್ನಎಲ್ಲಪ್ರಶ್ನೆಗಳಿಗೆಉತ್ತರಿಸಿದ.
ಈಸಮ್ಮತಿಯರೂಪದಪ್ರತಿಯನ್ನುನನಗೆನೀಡಲಾಗುವುದು.

ಸಹಿ / ಪಾಲ್ಗೊಳ್ಳುವವರಅಥವಾಕಾನೂನುಬದ್ಧವಾಗಿಅಧಿಕೃತಪ್ರತಿನಿಧಿಗಳಎಡತಮ್ಮುದ್ರಣ .

ಪಾಲ್ಗೊಳ್ಳುವವರಹಸರು: . . . . . .

ಸಹಿ / ಎಡತಮ್ಮುರುತು: . . . . . .

ಕಾನೂನುಬದ್ಧವಾಗಿಅಧಿಕೃತಪ್ರತಿನಿಧಿಹಸರು :

. . . . . .

ಸಹಿ / ಎಡತಮ್ಮುರುತು : . . . . . .

ಎಟ್ನೆಸ್ಟಸರು : . . . . . .

ಸಹಿ / ಎಡತಮ್ಮುರುತು :

. . . . . .

ತನಿಖಾಧಿಕಾರಿಹಸರುಮತ್ತುಸಹಿ :

. . . . . .

ದಿನಾಂಕಮತ್ತುಸ್ಥಳ :

. . . . . .

माहितीपूर्णसंमती

संशोधनआणिअभ्यासाचेशीर्षक: पोस्टसंक्रामकइररेबलबावेलसिंड्रोम (आयबीएस) च्याविकासाशीसंबंधितघटनाआणिजोखीमघटक:एकवर्षाचाभावीरेखांशाचाअभ्यास

मुख्यअन्वेषक: -
REG. NO.: BG0118007
पदव्युत्तरविद्यार्थी,
सामान्यऔषधविभाग,
जेएनएमसी, बेळगाव.

मार्गदर्शन:-
डॉ. _____,
विभागाचेप्राध्यापकआणिप्रमुख,
सामान्यऔषधविभाग,
जेएनएमसी, बेळगाव

परिचयआणिउद्देश:प्रश्नावली,
परीक्षाआणिनियमिततपासणीच्यामदतीनेपोस्टसंक्रामकआयबीएसआणित्याच्याशीसंबंधित जोखीमघटकांचीघटनाठरवण्याचाहेतूआहे.

प्रक्रिया : आपणसंशोधनअभ्यासाचाभागबनण्याससहमतअसल्यास, आपल्यालासंबंधितइतिहासविचारलेजाईलआणिसंबंधितक्लिनिकलतपासणीआणितपासणीअधीनकेलेजाईल. आवश्यकतपासणीसाठीआपल्यालारक्तनमुनेदेखीलद्यावेलागतील.

जोखीमआणिफायदे :
याअभ्यासामध्येकोणत्याहीप्रकारचेधोकेनसतातजेणेकरूनसाधारणगोष्टीबाहेरुनकेल्याजाणार नाहीत.

याअभ्यासामुळेआयबीएसच्याविकासाससर्वसाधारणपणेलोकसंख्येलाफायदाहोईल,
नंतरजोखीमघटकांचाविचारकेल्यानंतरआणिसहजतेनेमूल्यांकितकेलेजाऊशकतेआणित्यावरउ
पचारकेलेजाऊशकते.
अन्वेषणकर्त्यानेअभ्यासातसहभागीनाकोणतेहीथेटलाभआश्वासनदेऊशकतनाही.

पर्याय:याअभ्यासातभागघेतस्वैच्छिकआहे. आपणयाअभ्यासातभागनघेण्याचेनिवडूशकता
आपणभागघेण्याचानिर्णयघेतल्यासआपणनंतरआपलेमनबदलूआणिअभ्यासमागेघेऊशकता.
आपलानिर्णयआपल्यालामिळालेलीवर्तमानकिंवाभविष्यातीलआरोग्यसेवाकिंवाइतरसेवाबदल
णारनाही.अभ्यासडॉक्टरकिंवाप्रायोजककोणत्याहीवेळीयाअभ्यासातआपलासहभागथांबवूशक
तात.
जरआपणअभ्यासातभागनघेण्याचेनिवडलेतरआपणआपल्यास्थितीच्यारूग्णांसाठीमानकउप
चारप्राप्तकराल.

गोपनीयताआणिगुप्तता:
याअभ्यासाच्यादरम्यानआपल्याविषयीगोळाकेलेलीसर्वमाहितीकायद्यानेपरवानगीअसलेल्या
मर्यादेपर्यंतगोपनीयठेवलीजाईल. कोडशोधआपणासयाशोधरेकॉर्डेमध्येओळखतील.
याअभ्यासातूनमाहितीप्रकाशितकेलीजाऊशकतेपरंतुआपलीओळखकोणत्याहीप्रकाशनामध्ये
गोपनीयअसेल.

संस्था / प्रायोजकधोरण:यासंशोधनावरलागूहोतनाही

सहभागासाठीआर्थिकप्रोत्साहन:
अभ्यासातभागघेण्यासाठीआपल्यालाकोणत्याहीभेटवस्तू / प्रोत्साहनदेय / देऊकेलेजाणारनाहीत.

परिणामप्रकाशितकरण्यासाठीअधिकृतता:एमडीप्दवी,
समीक्षाआणिप्रकाशनपूर्णेकरण्यासाठीआवश्यकतेचाएकभागम्हणूनअभ्यासनिष्कर्षांचेपरिणा
मकेएलईविद्यापीठ, बेळगावयांनापाठवलेजातील
अभ्यासादरम्यानच्याप्रश्नांच्याबाबतीतकिंवाभविष्यातआपणखालीलव्यक्तीशीसंपर्कसाधूशक
ता,

1. REG. NO.: BG0118007 तपासक जनरलमेडिसिनमध्येपीजी जेएनएमसी, बेळगाव.	**2. डॉ.** _____ विभागाचेप्राध्यापकआणिप्रमुख, सामान्यऔषधविभाग, जेएनएमसी, बेळगाव.

संशोधनअभ्यासातसहभागीहोण्यासाठीसहमती

खालीदिलेल्याओळीवरसहीकरुनमीयाअभ्यासातभागघेण्यासस्वेच्छेनेसहमतआहे.मीकोणत्या हीवेळीमागेघेऊशकतो.मीयाफॉर्मवरस्वाक्षरीकरुनमाझ्याकोणत्याहीकायदेशीरअधिकारांनासोड तनाही.खालीमाझ्यास्वाक्षरीनेसूचितकेलेआहेकीमीहेसंपूर्णसंमतीफॉर्मवाचलेआहेकिवातेमलावा चलेगेलेआहेआणिमलामाझ्यास्थानिकभाषेतस्पष्टकेलेगेलेआहेआणिमाझ्यासर्वप्रश्नांचीउत्तरे दिलीआहेत. मलायासंमतीफॉर्मेचीएकप्रतदिलीजाईल.

सहभागीकिवाकायदेशीरअधिकृतप्रतिनिधीचेस्वाक्षरी / डावाथंबप्रिंट.

सहभागीचेनाव: . . . . . .

स्वाक्षरी /
डावाथंबप्रभाव: . . . . . .

कायदेशीरअधिकृतप्रतिनिधीचेनाव :

. . . . . .

स्वाक्षरी / डावाथंबप्रभाव: . . . . . .

साक्षीदारांचीनावे : . . . . . .

स्वाक्षरी /
डावाथंबप्रभाव: . . . . . .

तपासकर्तेचेनावआणिस्वाक्षरी :

. . . . . .

तारीखआणिठिकाण: . . . . . .

सूचितसहमति

अनुसंधानऔरअध्ययनकाशीर्षक: पोस्टसंक्रामकइर्रेबलबाउलसिंड्रोम (आईबीएस) केविकाससेजुड़ेघटनाएंऔरजोखिमकारक: एकसालकेसंभावितअनुदैर्ध्यअध्ययन

मुख्यजॉचकर्ता:-
REG. NO.: BG0118007
स्नातकोत्तरछात्र,
सामान्यचिकित्साविभाग,
जेएनएमसी, बेलगाम।

मार्गदर्शक:-
डॉ _____
विभागकेप्रोफेसरऔरप्रमुख,
सामान्यचिकित्साविभाग,
जेएनएमसी, बेलगाम।

परिचयऔरउद्देश्य: - इसअध्ययनकाउद्देश्यप्रश्नसंक्रामकआईबीएसऔरप्रश्नावली, परीक्षाऔरनियमितजांचकीसहायतासेइसकेसाथजुड़ेजोखिमकारकोंकीघटनाओंकानिर्धारणकर नाहै।

प्रक्रिया: यदिआपशोधअध्ययनकाहिस्साबननेकेलिएसहमतहैं, तोआपकोप्रासंगिकइतिहाससेपूछाजाएगाऔरप्रासंगिकनैदानिक परीक्षाऔरजांचकेअधीनकियाजाएगा।आपकोआवश्यकजांचकेलिएरक्तकेनमूनेभीदेनाहोगा।

जोखिमऔरलाभ: इसअध्ययनमेंकोईजोखिमनहींहैक्योंकिसामान्यसेकुछभीनहींकियाजाएगा।

इसअध्ययनसेआमतौरपरआबादीकोआईबीएसकेविकासकेरूपमेंलाभमिलेगा, फिरजोखिमकारकोंपरविचारकरनेकेबादअनुमानलगायाजासकताहै, औरआसानीसेमूल्यांकनऔरइलाजकियाजासकताहै।जांचकर्ताप्रतिभागियोंकोअध्ययनमेंकिसी भीप्रत्यक्षलाभकाआश्वासननहींदेसकताहै।

विकल्प:

इसअध्ययनमेंभागलेनास्वैच्छिकहै।आपइसअध्ययनमेंभागनलेनेकाचयनकरसकतेहैं।यदिआ पभागलेनेकाफैसलाकरतेहैंतोआपबादमेंअपनामनबदलसकतेहैंऔरअध्ययनसेवापसलेसकतेहैं। आपकानिर्णयवर्तमानयाभविष्यकीस्वास्थ्यदेखभालयाआपकोप्राप्तहोनेवालीअन्यसेवाओंकोन हींबदलेगा।अध्ययनडॉक्टरयाप्रायोजककिसीभीसमयइसअध्ययनमेंआपकीभागीदारीकोरोकस कताहै।यदिआपअध्ययनमेंभागनहींलेनाचुनतेहैं, तोआपकोअपनीहालतवालेरोगियोंकेलिएमानकउपचारप्राप्तहोगा।

गोपनीयताऔरगोपनीयता:

इसअध्ययनकेदौरानआपकेबारेमेंएकत्रकीगईसभीजानकारीकानूनद्वाराअनुमतसीमातकगोप नीयरखीजाएगी।कोडसंख्याआपकोइसशोधरिकॉर्डमेंपहचानलेगी।इसअध्ययनसेजानकारीप्रका शितकीजासकतीहैलेकिनआपकीपहचानकिसीभीप्रकाशनमेंगोपनीयहोगी।

संस्थान / प्रायोजककीनीति:इसशोधपरलागूनहींहोताहै

भागीदारीकेलिएवित्तीयप्रोत्साहन: अध्ययनमेंभागलेनेकेलिएआपकोकोईउपहार / प्रोत्साहननहींदियाजाएगा / पेशनहींकियाजाएगा।

परिणामप्रकाशितकरनेकेलिएप्राधिकरण:अध्ययनकेनतीजेएमडीडिग्री, समीक्षाऔरप्रकाशनकेपूराहोनेकीआवश्यकताकेहिस्सेकेरूपमेंकेएलईविश्वविद्यालय, बेलगामकोभेजेजाएंगे।

अध्ययनकेदौरानयाभविष्यमेंपूछताछकेमामलेमेंआपनिम्नलिखितव्यक्तियोंसेसंपर्ककरसकते हैं,

REG. NO.: BG0118007 अन्वेषक, सामान्यचिकित्सामेंपीजी, जेएनएमसी, बेलगाम।	**2. डॉ_____** विभागकेप्रोफेसरऔरप्रमुख, सामान्यचिकित्साविभाग, जेएनएमसी, बेलगाम।

अनुसंधानअध्ययनमेंभागलेनेकीसहमति

मैंस्वेच्छासेनीचेदीगईरेखापरहस्ताक्षरकरकेइसअध्ययनमेंभागलेनेकेलिएसहमतहूं।मैंकिसीभी समयवापसलेसकताहूं।मैंइसफॉर्मपरहस्ताक्षरकरकेअपनेकिसीभीकानूनीअधिकारकोनहींछोड़र हाहूं।नीचेदिएगएमेरेहस्ताक्षरसेसंकेतमिलताहैकिमैंनेइसपूरेसहमतिफॉर्मकोपढ़ाहैयायहमुझेप ढ़ागयाहै,

औरमुझेमेरीस्थानीयभाषामेंसमझायागयाहैऔरमेरेसभीसवालोंकेजवाबदिएगएहैं।मुझेइससहम तिपत्रकीएकप्रतिदीजाएगी।

प्रतिभागीयाकानूनीरूपसेअधिकृतप्रतिनिधिकेहस्ताक्षर / बाएंथंबप्रिंट।

प्रतिभागीकानाम: .....

हस्ताक्षर / बाएंथंबइंप्रेशन: ....

कानूनीरूपसेअधिकृतप्रतिनिधिकानाम: .....

हस्ताक्ष / बाएंथंबइंप्रेशन: ....

गवाहकानाम: ....

हस्ताक्षर / बाएंथंबइंप्रेशन: .....

जांचकर्ताओंकानामऔरहस्ताक्षर: .....

ANNEXURE III – PROFORMA

"Incidence and Risk factors associated with development of Post infection Irritable Bowel Syndrome (IBS): A One year Prospective Longitudinal Study"

Name **Age (y)** **Sex** M/F =1/0
IP no.:
Address:
Phone No
Date of filling this proforma: Filled by:
Symptoms:

Parameters of Acute gastroenteritis

1. When did it start (give exact date)? ☐
2. On what date did the patient get admitted ? ☐
3. How many stool/d? ☐
4. Watery? ☐ Yes/No =1/0
5. Bloody? ☐ Yes/No =1/0
6. Vomiting? ☐ Yes/No =1/0
7. Fever? ☐ Yes/No =1/0
8. Is the stool culture positive? ☐ Yes/No =1/0
9. If yes, nature of the organism? ☐
10. Did you take antibiotic? ☐ Yes/No =1/0

11. If yes, what drug?
12. If yes, for how many days?
13. If yes, in what dose?
14. In how many days in total, did it resolve?
15. Abdominal Cramping?Y
16. Direct contact with livestock ?Y

Psychiatric evaluation(According to HADS questionnaire)

IBS questionnaire (to be filled up once at admission to know these symptoms by recall before onset of diarrhea, once at 6 months after onset of diarrhea)

		At onset	**After 6 months**
17. Visible abdominal distension:	Yes/No =1/0		
18. Bloating/feeling of abdominal distension > ¼ of days	Yes/No =1/0		
19. Relief of pain with bowel movement	Yes/No =1/0		
20. More frequent stools with onset of pain	Yes/No =1/0		
21. Loose stools at onset of pain	Yes/No =1/0		
22. Urgency> ¼ of defecations	Yes/No =1/0		
23. Passage of mucus per rectum	Yes/No =1/0		
24. Passage of mucus> ¼ of defecations	Yes/No =1/0		
25. Feeling of incomplete evacuation	Yes/No =1/0		
26. Feeling of incomplete evacuation > ¼ of defecation	Yes/No =1/0		
27. Straining >1/4 of defecation	Yes/No =1/0		
28. Pain relieved with defecation	Yes/No =1/0		
29. Abnormal stool frequency;			
a. Stool > 3/day	Yes/No =1/0		
b. Stool ≤3/day	Yes/No =1/0		
30. Abnormal stool form;			
a. Lumpy/hard	Yes/No =1/0		

b. Loose/watery Yes/No =1/0

31. Did you experience these symptoms for at least 3-months? (need not be continuous)? Yes/No =1/0 ☐

32. Did these symptoms appear at least once per week for at least two months? Yes/No=1/0 ☐

33. How do you feel about your bowel movement ☐

1=constipation 2=diarrhea 0=none

How many times do you pass stool/**week?** ☐

34. How long are you suffering from these symptoms? (Months) ☐

35. Indicate if you have any of the following symptoms

(A). Do you pass blood with stool? Yes/No = 1/0 ☐ ☐

(B). Do you have lack of desire to eat? Yes/No = 1/0 ☐ ☐

(C) Did you loose weight recently without attempting to do so? Yes/No = 1/0 ☐ ☐

36. Do you have any of these symptoms (Dyspeptic)

(a). Postprandial fullness Yes/No = 1/0 ☐ ☐

(b). Epigastric pain Yes/No = 1/0 ☐ ☐

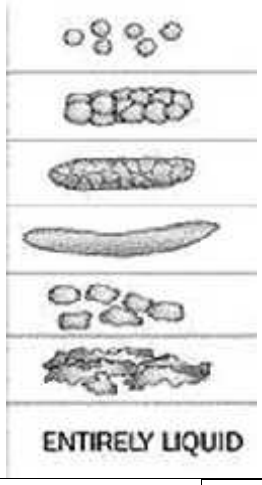
(c). Early satiety Yes/No = 1/0 ☐ ☐

(d). Epigastric burning Yes/No = 1/0 ☐ ☐

38. How many months ago did these dyspeptic symptoms start? ☐ ☐

39. For how many months (in total) did you suffer from the above dyspeptic symptoms since their onset? ☐ ☐

40. Indicate type of the stool that you commonly pass ☐ ☐

	Separate hard lumps, like nuts, hard to pass	1
	Sausage-shaped but lumpy	2
	Like sausage but with cracks on its surface	3
	Like sausage or snake, smooth & soft	4
	Soft blobs with clear cut edges (passed easily)	5
	Fluffy pieces with ragged edges, a mushy stool	6
	Watery, no solid pieces	7

Physical Examination

Investigations

Normal/Abnormal = 1/0
If abnormal, indicate abnormalities

(A). Hb…….g/dl

(**B)**.

Height Weight

ESR…….mm/hr**(E).**Stool microscopy……

(F). Stool occult blood ☐ 1= positive 0= negative

At 6-months after onset of diarrhea, if symptomatic)

Lactose tolerance test **LTT Report** ☐ (positive = 1, negative = 0)

a. Fasting blood sugar…….g%/dl
b. 30 min. PP sugar……..g%/dl

Symptom development ☐ Yes /No=1/0

a. Feeling of gas/abdominal bloating ☐ Yes /No=1/0

b. Loose motion ☐ Yes /No=1/0

c. How many times did you have loose motion? ☐ Yes /No=1/0

d. Abdominal pain ☐ Yes /No=1/0

Hospital Anxiety and Depression Scale (HADS)

Tick the box beside the reply that is closest to how you have been feeling in the past week. Don't take too long over you replies: your immediate is best.

D	A		D	A	
		I feel tense or 'wound up':			**I feel as if I am slowed down:**
	3	Most of the time	3		Nearly all the time
	2	A lot of the time	2		Very often
	1	From time to time, occasionally	1		Sometimes
	0	Not at all	0		Not at all
		I still enjoy the things I used to enjoy:			**I get a sort of frightened feeling like 'butterflies' in the stomach:**
0		Definitely as much		0	Not at all
1		Not quite so much		1	Occasionally
2		Only a little		2	Quite Often
3		Hardly at all		3	Very Often
		I get a sort of frightened feeling as if			

ANNEXURE IV

KEY TO MASTER CHART

M – Male

F – Female

1 – Yes

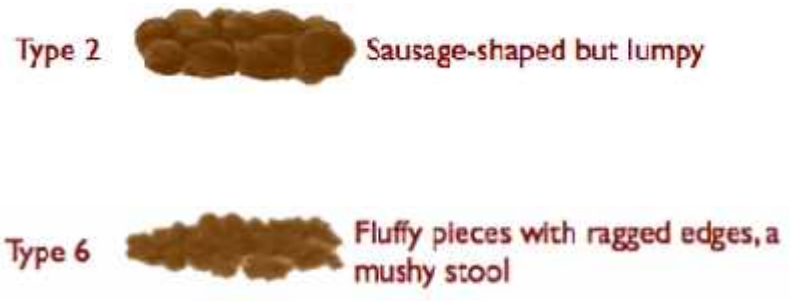
0 – No

IBS type if developed:

C- Constipation predominant IBS

D- Diarrhoea predominant IBS

Bristol Stool type



S. no	IP no.	Age (years)	Sex	Fever	Vomiting	Diarrhoea	Watery stool	No. of stools per day	Bloody stool	Stool culture	Stool routine	Antibiotics	Duration of AGE (days)	Abdominal cramps	Anxiety	Depression	Contact with livestock	IBS at onset	Functional dyspepsia	Chronic diarrhoea	Hb (g/dL)	ESR (mm/hr)	Stool occult blood	IBS at 6 months	IBS type if developed	Bristol Stool Type	Lactose Intolerance
1	940226	68	F	1	1	1	1	8	0	negative	pus cell+	1	2	1	1	0	0	0	0	0	9.5	61	0	0		4	
2	939876	53	M	1	1	1	1	6	0	negative	pus cell+	1	2	1	0	0	0	0	0	0	14.7	32	0	0		4	
3	942351	47	F	1	1	1	1	8	0	negative	pus cell+	1	2	1	1	0	0	0	0	0	13.7	18	0	1	D	6	0
4	943114	64	M	1	1	1	1	6	0	negative	pus cell+	1	3	0	0	0	0	0	0	0	10.3	19	0	1	C	2	0
5	945836	38	M	1	1	1	1	6	0	negative	pus cell+	1	3	0	0	0	1	0	0	0	13.2	31	0	0		4	
6	946061	26	F	1	0	1	1	8	0	negative	pus cell+	1	4	0	0	0	0	0	0	0	11.4	35	0	0		4	
7	946800	31	M	1	1	1	1	6	0	negative	Normal	0	2	0	0	0	0	0	0	0	16	9	0	0		4	
8	946564	20	F	0	1	1	1	7	0	negative	pus cell+	1	4	1	0	0	0	0	0	0	12.1	26	0	0		4	
9	946945	31	M	1	1	1	1	7	0	negative	pus cell+	1	6	0	0	0	0	0	0	0	14.4	10	0	0		5	
10	946921	80	M	1	1	1	1	8	0	negative	Normal	1	3	0	1	1	0	0	0	0	12.8	11	0	0		4	
11	947754	24	M	0	1	1	1	6	0	negative	pus cell+	1	6	1	0	0	0	0	0	0	17.1	46	1	0		4	
12	955363	62	F	1	1	1	1	6	0	negative	Normal	1	3	0	0	1	0	0	0	0	14.6	11	0	0		4	
13	955312	29	M	1	1	1	1	5	0	negative	Normal	1	3	0	0	0	0	0	0	0	16	30	0	0		4	
14	953770	61	F	1	0	1	1	6	0	negative	pus cell+	1	3	0	0	0	0	0	0	0	13	17	0	0		4	
15	954188	21	F	0	1	1	1	8	0	negative	Normal	1	3	1	0	0	0	0	0	0	13.8	12	0	0		4	
16	955023	80	F	1	1	1	1	8	0	negative	Pus cell+	1	6	1	0	1	0	0	0	0	7.8	22	0	1	D	6	0
17	956322	64	F	1	0	1	1	8	0	negative	Pus cell+	1	6	0	0	0	0	0	0	0	10	18	1	0		4	
18	961053	22	M	1	0	1	1	6	0	negative	Pus cell+	1	5	1	0	0	1	0	0	0	16.9	20	1	0		3	
19	959428	72	F	1	1	1	1	7	0	negative	Pus cell+	1	3	0	0	0	0	0	0	0	11.7	60	0	0		4	
20	962576	75	F	1	1	1	1	6	0	negative	Pus cell+	1	3	1	0	1	0	0	0	0	12	31	0	1	C	2	0
21	959368	55	F	0	1	1	1	6	0	negative	Pus cell+	1	3	0	0	0	0	0	0	0	11.1	30	0	0		4	
22	962647	32	F	1	0	1	1	8	0	negative	Pus cell+	1	3	1	0	0	0	0	0	0	9.9	45	0	0		4	
23	956521	26	F	1	0	1	1	8	0	negative	Normal	1	4	1	0	0	0	0	0	0	11	12	0	1	D	6	0
24	966741	75	F	1	1	1	1	9	0	negative	Normal	1	2	1	1	1	0	0	0	0	11.3	22	0	0		4	
25	966517	60	M	1	0	1	1	6	0	negative	Pus cell+	1	2	0	0	0	0	0	0	0	11.8	26	0	0		4	
26	964080	22	F	0	1	1	1	8	0	negative	Pus cell+	1	2	1	0	0	0	0	0	0	12.5	11	0	1	D	6	0
27	924854	22	F	1	1	1	1	10	0	negative	Normal	1	3	0	0	0	0	0	0	0	12.2	17	0	0		4	
28	968235	29	F	0	1	1	1	6	0	negative	Normal	1	3	0	0	0	0	0	0	0	11.6	32	0	1	C	2	0
29	969110	68	M	1	1	1	1	6	0	negative	Pus cell+	1	3	1	0	0	0	0	0	0	14.1	33	1	0		4	
30	969394	86	F	1	1	1	1	8	0	negative	Pus cell+	1	4	0	0	0	1	0	0	0	10	12	0	0		4	
31	968979	50	F	0	1	1	1	6	0	negative	Normal	1	2	0	0	0	0	0	0	0	11.6	20	0	0		4	
32	954894	23	F	1	1	1	1	7	0	negative	pus cell+	1	4	0	0	0	0	0	0	0	11.8	19	0	0		4	
33	955007	20	F	1	1	1	1	7	0	negative	pus cell+	1	4	1	0	0	0	0	0	0	13.3	40	0	0		4	
34	970022	45	M	1	1	1	1	7	0	negative	pus cell+	1	3	1	0	0	0	0	0	0	11.7	18	0	0		5	
35	970189	20	M	1	1	1	1	8	0	negative	pus cell+	1	3	0	1	1	0	0	0	0	13	31	0	0		4	
36	969938	75	F	1	1	1	1	6	0	negative	pus cell+	1	3	0	0	0	0	0	0	0	12.7	18	0	0		4	
37	970015	74	F	1	1	1	1	6	0	negative	pus cell+	1	3	0	0	1	0	0	0	0	13.6	29	0	0		4	
38	970020	45	F	1	1	1	1	5	0	negative	pus cell+	1	3	1	0	0	1	0	0	0	7.7	49	0	0		4	
39	980027	45	F	1	1	1	1	6	0	negative	pus cell+	1	3	1	0	0	0	0	0	0	10.3	8	0	0		4	
40	970598	23	F	1	1	1	1	8	0	negative	pus cell+	1	4	0	0	0	0	0	0	0	12.8	12	0	0		4	
41	980800	43	M	1	1	1	1	8	0	negative	RBC+	1	5	1	1	0	0	0	0	0	9.2	23	1	1	D	6	0
42	986590	76	M	1	1	1	1	7	0	negative	Normal	1	2	1	1	1	0	0	0	0	10.2	18	0	0		4	
43	984825	42	F	1	1	1	1	7	0	negative	Normal	1	3	0	0	0	0	0	0	0	6.3	20	0	1	C	2	0
44	984998	55	M	1	1	1	1	9	0	negative	Pus cell+	1	2	1	0	1	0	0	0	0	10.2	12	0	0		4	
45	973443	55	M	1	0	1	1	6	0	negative	Pus cell+	0	2	0	1	0	0	0	0	0	9.4	58	0	0		4	
46	972808	50	M	1	1	1	1	6	0	negative	Pus cell+	1	3	1	0	1	0	0	0	0	5.8	46	0	0		4	
47	987981	21	F	1	1	1	1	6	0	negative	Pus cell+	1	3	1	0	1	0	0	0	0	10.4	16	0	1	D	6	0
48	988005	20	F	1	1	1	1	8	0	negative	Pus cell+	1	8	1	0	1	0	0	0	0	12.4	18	0	1	D	6	0
49	988261	20	F	1	1	1	1	7	0	negative	Pus cell+	1	3	1	0	0	0	0	0	0	12.4	22	1	0		4	
50	942347	51	F	1	1	1	1	9	0	negative	Pus cell+	1	8	1	1	0	0	0	0	0	11.3	42	0	1	D	6	0

S. no	IP no.	Age (years)	Sex	Fever	Vomiting	Diarrhoea	Watery stool	No. of stools per day	Bloody stool	Stool culture	Stool routine	Antibiotics	Duration of AGE (days)	Abdominal cramps	Anxiety	Depression	Contact with livestock	IBS at onset	Functional dyspepsia	Chronic diarrhoea	Hb (g/dL)	ESR (mm/hr)	Stool occult blood	IBS at 6 months	IBS type if developed	Bristol Stool Type	Lactose Intolerance
52	938340	62	F	1	1	1	1	6	0	negative	Pus cell+	1	2	0	0	0	0	0	0	0	13.2	24	0	0		4	
53	936016	52	M	1	1	1	1	6	0	negative	Pus cell+	1	3	0	0	0	0	0	0	0	13.2	12	0	0		4	
54	938592	29	M	1	1	1	1	10	0	negative	Normal	1	9	1	0	0	0	0	0	0	16.2	10	0	1	D	6	0
55	939074	34	M	1	1	1	1	10	0	negative	Pus cell+	0	10	1	1	0	0	0	0	0	11.7	8	0	1	C	2	0
56	938248	55	M	1	1	1	1	9	0	negative	Normal	1	3	0	0	0	0	0	0	0	11.8	12	0	0		4	
57	939866	45	F	1	1	1	1	10	0	negative	Pus cell+	1	3	0	0	0	0	0	0	0	13.6	16	0	0		4	
58	936861	65	M	1	1	1	1	8	0	negative	pus cell+	1	6	1	0	0	0	0	0	0	11.1	39	0	0		4	
59	925247	78	F	0	1	1	1	12	0	negative	Pus cell+	1	5	1	0	0	0	0	0	0	11.5	34	0	0		4	
60	941170	39	F	1	1	1	1	8	0	negative	Pus cell+	1	4	0	1	0	0	0	0	0	6.4	16	0	1	D	6	0
61	931249	55	M	0	1	1	0	6	0	negative	Pus cell+	0	5	0	0	1	0	0	0	0	10.9	24	1	0		4	
62	923602	49	M	1	1	1	1	6	0	negative	Pus cell+	1	3	0	0	0	0	0	0	0	9.6	20	1	0		4	
63	932275	67	M	1	1	1	1	8	0	negative	Pus cell+	0	5	0	0	0	0	0	0	0	13.3	36	0	0		4	
64	931345	34	M	1	1	1	1	8	0	negative	Pus cell+	1	9	1	0	1	0	0	0	0	14.6	16	0	1	D	6	0
65	932545	80	F	0	1	1	1	8	0	negative	Pus cell+	0	10	0	0	0	0	0	0	0	10.3	72	1	0		4	
66	933551	58	F	1	1	1	1	8	0	negative	Pus cell+	1	5	0	0	1	0	0	0	0	9.4	62	0	0		4	
67	933762	84	M	1	1	1	1	10	0	negative	Pus cell+	0	3	0	1	0	0	0	0	0	8.9	88	1	0		4	
68	934137	44	M	1	1	1	1	10	0	negative	Normal	1	7	1	1	1	0	0	0	0	14.9	42	0	1	D	6	0
69	934154	39	M	1	1	1	1	8	0	negative	Pus cell+	1	5	0	0	0	0	0	0	0	12.2	12	0	0		4	
70	933200	56	M	1	1	1	1	5	0	negative	Pus cell+	1	5	0	0	0	0	0	0	0	9.9	65	0	0		4	
71	929328	62	M	1	1	1	1	8	0	negative	Pus cell+	0	5	0	0	0	0	0	0	0	11.8	22	0	0		4	
72	934818	30	F	0	1	1	1	10	0	negative	Pus cell+	1	5	1	1	0	0	0	0	0	11.4	34	0	0		4	
73	935318	63	F	1	1	1	1	12	0	negative	Pus cell+	0	5	0	0	0	0	0	0	0	13.7	18	0	0		4	
74	934638	54	M	0	1	1	1	10	0	negative	Normal	1	5	0	1	1	0	0	0	0	12.7	36	0	0		4	
75	936208	44	F	1	1	1	1	8	0	negative	Pus cell+	1	7	1	0	1	0	0	0	0	6.7	38	0	1	D	6	0
76	936493	18	M	1	1	1	1	9	0	negative	Pus cell+	0	5	0	0	0	0	0	0	0	15.6	12	0	0		4	
77	936931	44	M	1	1	1	1	7	0	negative	Pus cell+	1	8	1	0	0	1	0	0	0	13.6	14	0	1	C	2	0
78	936930	23	M	1	0	1	1	10	0	negative	Pus cell+	1	5	0	1	0	0	0	0	0	13.8	26	0	0		4	
79	936737	20	F	1	1	1	1	8	0	negative	Pus cell+	1	8	0	1	0	0	0	0	0	11.4	16	0	1	D	6	0
80	936987	44	M	1	1	1	1	10	0	negative	Pus cell+	0	6	0	0	0	0	0	0	0	9.2	20	0	0		4	
81	926218	54	F	1	0	1	1	10	0	negative	Pus cell+	1	3	0	0	0	0	0	0	0	12.6	12	0	0		4	
82	925969	21	M	1	1	1	1	5	0	negative	Pus cell+	1	3	1	0	0	0	0	0	0	16.1	22	0	0		4	
83	928258	25	F	1	1	1	1	6	0	negative	Normal	1	9	1	1	0	0	0	0	0	12.6	23	0	1	D	6	0
84	928696	63	M	0	1	1	1	8	0	negative	Pus cell+	1	5	0	0	0	1	0	0	0	9.9	32	0	0		5	
85	929101	67	M	0	1	1	1	8	0	negative	Pus cell+	1	3	0	0	0	0	0	0	0	7.8	42	0	0		4	
86	930130	54	M	0	1	1	1	10	0	negative	Pus cell+	1	4	0	1	0	0	0	0	0	14.3	16	0	0		3	
87	930123	44	M	1	1	1	1	8	0	negative	Pus cell+	1	8	1	0	1	0	0	0	0	11.1	23	0	1	D	6	0
88	930982	72	M	0	1	1	1	10	0	negative	Pus cell+	0	3	0	0	0	1	0	0	0	17.3	10	0	0		4	
89	917991	69	M	0	1	1	1	10	0	negative	Pus cell+	1	3	0	0	0	0	0	0	0	16.6	16	0	0		4	
90	915986	68	M	1	1	1	1	12	0	negative	Pus cell+	1	6	0	0	0	0	0	0	0	11.1	20	0	0		4	
91	921230	48	M	1	1	1	1	6	0	negative	Normal	1	8	1	0	0	0	0	0	0	13.3	17	0	1	C	2	0
92	920911	22	F	0	1	1	1	10	0	negative	Pus cell+	0	5	0	1	0	0	0	0	0	12.2	20	0	0		4	
93	921679	19	F	1	1	1	1	12	0	negative	Pus cell+	1	5	0	0	1	0	0	0	0	13.5	13	0	0		4	
94	922362	54	M	0	1	1	1	14	0	negative	Pus cell+	1	3	0	1	0	1	0	0	0	8	26	1	0		4	
95	922439	20	F	0	1	1	1	10	0	negative	Pus cell+	1	3	0	0	0	0	0	0	0	12	16	0	0		4	
96	922678	21	F	1	1	1	1	16	0	negative	Pus cell+	0	5	0	0	0	0	0	0	0	11	22	0	0		4	
97	922716	26	M	1	1	1	1	7	0	negative	Normal	1	7	1	0	1	1	0	0	0	15.2	12	0	1	D	6	0
98	922789	38	M	1	1	1	1	10	0	negative	Pus cell+	1	6	1	0	0	1	0	0	0	13.6	24	0	0		5	
99	922570	21	F	0	1	1	1	12	0	negative	Pus cell+	0	3	1	0	0	0	0	0	0	11.8	16	0	0		4	
100	923627	38	M	1	1	1	1	10	0	negative	Pus cell+	1	3	1	1	0	0	0	0	0	12.8	28	0	1	D	6	0