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Research Article

PREVALENCE AND CLINICAL SIGNIFICANCE OF SMALL INTESTINAL BACTERIAL OVERGROWTH IN PATIENTS WITH CHRONIC LIVER DISEASE

John.S*., Kani Shaikh Mohamed., Sabarinathan Ramanathan., Premkumar Karunakaran., Ratnakar Kini., Mohammed Ali., Pugazhendhi Thangavel and Veeraraghavan Krishnamoorthy

Institute of Medical Gastroenterology, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai, Tamil Nadu, India

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A B S T R A C T

Aim: To study the prevalence of small intestinal bacterial overgrowth (SIBO) in chronic liver disease patients. To analyze its relationship with the etiology, severity and complications (Spontaneous bacterial peritonitis, hepatic encephalopathy) of chronic liver disease.
Materials & methods: Cases were 60 chronic liver disease patients (20 CHILD-A, 20 CHILD-B, 20 CHILD-C). 60 Controls were healthy persons who were not on any recent medications like antibiotics or probiotics. All patients underwent routine laboratory investigations, upper gastrointestinal endoscopy and glucose hydrogen breath test as per the protocol. **Results:** 60 cirrhotic cases were included in our study. 20 numbers included in each child status A, B and C. 44 males and 16 females were included in both cases and controls. The age ranged between 28 to 71 years (mean age - 51.42 years), 22 to 65 years (mean age - 50.47 years) among cases and controls respectively. 44 (73.30%) males and 16 (26.70%) females were present in both case and control group. Considering etiology of CLD was found to be 30 ethanol related, 9 HBV related, 5 HCV related and 16 cryptogenic. Child Turcot Pugh score varied from 6 to 12 with mean value 8.3. Model For End Stage Liver Disease score value ranged from 7 to 16 with mean 10.14. GHBT was positive in 20 out of 60 patients (33.3%). In controls only 2 out of 60 were positive for hydrogen breath test. Comparing the GHBT between two groups p value was found to be <0.001 which was statistically significant. GHBT glucose hydrogen breath testwas positive in 12 (20%) alcoholic liver disease, 1(1.7%) HBV related, 2 (3.3%) HCV related and 5 (8.3%) cryptogenic CLD. Presence of SIBO was not correlated with the etiology of liver disease (p value 0.435). Prevalence of SIBO among CTP class A was 20% (4/20), CTP class B was 35% (7/20), CTP class C was 45% (9/20). The prevalence of SIBO increased with the severity of liver disease (p = 0.013). Increased prevalence of small intestinal bacterial overgrowth in patients with decompensated (CTP score more than 7) cirrhosis than in patients with compensated cirrhosis was noted. **Conclusion:** Small intestinal bacterial overgrowth was prevalent in about 33% of cirrhotic patients. The frequency of small intestinal bacterial overgrowth increases with severity of liver disease. Severity of portal hypertension does not correlate with small intestinal bacterial overgrowth. Presence of ascites and high serum bilirubin can reliably predict presence of small intestinal bacterial overgrowth.

INTRODUCTION

The gut microflora[1] consists of about 10^{14} microrganisms. Number of factors influences the composition of gut flora including age, dietary habits, immunological factors, intraluminal pH[1-3] are plays a important role in maintaining the composition of intestinal microflora. Distribution of bacterial species is not uniform in the gastrointestinal tract. Gastric acidity helps to maintain a sterile environment in the stomach. Bacterial concentration gradually increases in the small intestine. Aerobic bacterias predominant in the small bowel.

Corresponding author:* **John.S
Institute of Medical Gastroenterology, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai, Tamil Nadu, India

While anaerobic organisms[4] predominantly seen in the colonic flora. Gastric acidity, anatomical integrity of the digestive tract, peristaltic activity of the bowel, immunglobulin A[4,5] are plays a major role in maintaining the balance between the intestinal microflora and host environment. When these mechanisms fails bacterial over growth occurs. In many studies, small intestinal bacterial over growth (SIBO) is defined as the microbiological presence of more than10^5 colony forming units (CFU) per ml of small bowel aspirate. Various studies showed the relationship between the derangement of gut flora and increased prevalence of SIBO in cirrhotic patients.[5,6] Decrease in small bowel motility and increasein adrenergic activity in cirrhotic patients may lead to bacterial overgrowth.[5-7]

In addition to the range of symptoms and consequences of SIBO per se, increasing evidence suggests tha tderangement of intestinal flora is of substantial clinical relevance to

patients with cirrhosis. Increase in bacterial translocation of gut flora from the intestinal lumen and failure of immune defence mechanisms to remove these translocating microorganisms leads to an increased potential for bacterial infections like spontaneous bacterial peritonitis (SBP).[8]

Only few studies available regarding SIBO in cirrhotic patients. In patients with cirrhosis complicated by SBP there is increased prevalence of small intestinal bacterial overgrowth[9] demonstrated in some studies.

This study compared the presence of small intestinal bacterial over growth in cirrhotic patients with healthy controls. Both compensated and decompensated cirrhotic patients were included in this study. In this study glucose hydrogen breath test used to diagnose SIBO. Various clinical and biochemical parameters compared in between hydrogen breath test positive and negative groups. Identifying SIBO in cirrhotic patients would help in prevention of some of the serious complications of cirrhosis in near future.

MATERIALS AND METHODS

This is a Cross-sectional case control study, was carried out in the institute of Medical Gastroenterology of Rajiv Gandhi Government General Hospital, Chennai, India from June 2014 to March 2015. 60 cases and 60 controls were included. Both out-patientand in-patient with cirrhosis irrespective of etiology were included in the study.Cases were 60 chronic liver disease patients (20 CHILD-A, 20 CHILD-B, 20 CHILD-C).60 Controls were healthy persons who were not on any recent medications like antibiotics or probiotics. The exclusion criteria were hepatic encephalopathy (HE) grade, hepatorenal syndrome (HRS), hepatopulmonary syndrome (HPS) active/recent gastrointestinal (GI) bleed, inflammatory bowel disease (IBD), chronic diarrhea due to any other cause, intestinal obstruction, history of (h/o) GI surgery (except appendectomy), chronic pancreatitis, chronic proton pump inhibitor (PPI) intake, probiotics, steroid therapy or any other chronic drug therapy, sepsis in four weeks before the study, hepatocellular carcinoma or any other malignancy, pregnancy, patients with comorbidities like diabetes mellitus, systemic hypertension, coronary artery disease, chronic kidney disease, chronic obstructive pulmonary disease, rheumatological or neurological disorder

Duration of illness, h/o UGI bleed, alcohol intake, blood transfusion, tattooing, extra marital sexual contact were noted. On clinical evaluation signs of chronic liver disese & decompensation features like ascites, pedal edema, jaundice, upper gastrointestinal (UGI) bleed, encephalopathy were noted. Cirrhosis was diagnosed by history, liver function tests, imaging methods like ultrasonography of abdomen. Etiology and severity of disease was diagnosed by these methods. The biochemical studies included serum bilirubin, AST, ALT, albumin levels, PT(INR), serum creatinine,viral markers (HbsAg, anti HCV, HIV I&II) and ascetic fluid analysis. Portal hypertension was diagnosed by endoscopic evidence of varices and portal vein doppler study the Model for End-Stage Liver Disease (MELD) & Child-Turcotte-Pugh (*CTP*) score were calculated.

Glucose Hydrogen Breath Test (GHBT)

The Gastro+ Gastrolyzer (Bed font- UK) is a breath hydrogen monitor used to measure hydrogen levels in expired breath. A D-piece sampling system enables end expired breath to be sampled easily and hygienically, using disposable cardboard mouthpieces. With the use of colour touch screen results can be obtained in a tabular or graphical format. Accuracy of the Gastro+ breath hydrogen monitor may be affected by temperature. Readings may be lower if the device is used at a lower temperature than it was calibrated. Readings may be higher at high temperature. Press and hold the on/off button until the display becomes active. When home screen display comes insert the D-piece into the instrument and fit a new mouthpiece. Touch the icon to start a breath test. The breath hold count down will begin. Ask patient to inhale deeply and hold their breath until the display counts down to zero. At the end of the count down, the patient is asked to blow slowly into the mouthpiece.The ppm value starts to rise in the display screen. Highest level will remain on the screen. Value to be noted, then remove and dispose the mouthpiece. To allow fresh air to circulate around the sensor, remove the D piece in between the tests. To perform another breath test touch the icon at the bottom of the screen. Ask the subjects to avoid slowly absorbed carbohydrate diets like bread, potato, corn and fibre diet in the previous night. Slowly absorbable carbohydrate diets causes delayed excretion of hydrogen in the breath that leads to false negative result. Basal breath specimens were obtained after the overnight fast. Cigarette smoking and physical exercise were restricted for about 2 hours before and during the test. Both leads to hyperventilation and casuses changes in breath hydrogen content. The subjects are then asked to brush their teeth and rinse their mouths with an antiseptic solution followed by tap water. This was done to eliminate an early hydrogen peak due to action of oral cavity bacteria on test sugars. Basal breath hydrogen level was measured by averaging the four basal values.

Subjects are then ingested 100 grams glucose dissolved in 100 mL of water. Thereafter, breath hydrogen was measured by a device every 15 minutes for 2 hours. An increase in hydrogen excretion, in parts per million (ppm), following glucose administration, was calculated by subtracting the fasting value from the highest value of hydrogen excretion obtained. A rise of breath hydrogen by more than 12 ppm above basal value following glucose administration was considered positive for SIBO. On subjects with average value of basal breath hydrogen more than 20 ppm, the test was repeated on the next day to confirm the high basal breath hydrogen levels and this was also considered as positive.

Statistical Analyses

Positive hydrogen breath test in cirrhotic patients was compared with healthy controls. Correlation between the presence of SIBO and the severity and etiology of liver disease was analysed. Association between small intestinal bacterial overgrowth and portal hypertension was also analysed. The results were expressed as mean with standard deviation (or) median with range. Comparisons between cases and controls were performed by using Student's t test, Pearson's chi-square test with Yates' continuity correction. p

value < 0.05 considered significant. Statistical analyses were performed using the SPSS 15 statistical package.

RESULTS

60 cirrhotic cases were included in our study. 20 numbers included in each child status A, B and C. 44 males and 16 females were included in both cases and controls (Fig 1).

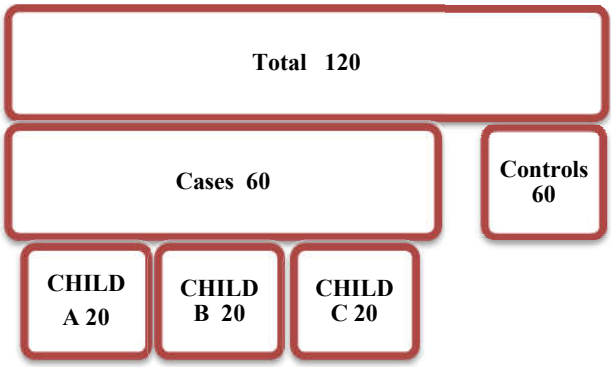

Figure 1 Study design

The age ranged between 28 to 71 years (mean age - 51.42years), 22 to 65 years (mean age - 50.47 years) among cases and controls respectively. 44 (73.30%) males and 16 (26.70%) females were present in both cases and control group (Table 1).

Table 1 Baseline characteristics of the cases and controls

Parametesr	Cases (n=60)	Controls (n=60)
Male	44 (73.3%)	44 ((73.3%)
Feamale	16 (26.7%)	16 (26.7%)
Mean age (years)	51.42 ± 10.44	50.47 ± 10.65

Considering etiology of CLD was found to be 30 ethanol related, 9 HBV related, 5 HCV related and 16 cryptogenic chronic liver disease cases included in this study. Of the 60 cases included in this study 65% had ascites. Of the 60 cases past h/o hepatic encephalopathy present in 4 patients, h/o spontaneous bacterial peritonitis: 8 patients, h/o bloating, 13 patients and h/o chronic diarrhea present in 6 patients. Bilirubin level varied from 1 to 6.2mg/dl with mean 2.6mg/dl. Albumin level varied between 2.4 to 3.6 g/dl with mean 2.97 g/dl. INR value ranged from 1.1 to 2.3 seconds with mean value 1.45 seconds. Portal vein doppler study detect collaterals in 51.6% of cases. Large varix was found in 60% of cases. Child Turcot Pugh score varied from 6 to 12 with mean value 8.3. Model for End Stage Liver Disease score value ranged from 7 to 16 with mean 10.14. Baseline characteristics of the cases shown in table 2.

Table 2 Baseline characteristics of the cases

Parameter	Cases (n=60)
Etiology of cirrhosis of liver	
Alcohol related	30
HBV related	9
HCV related	5
Cryptogenic	16
Lab parameters	
Bilirubin (mg/dl)	2.6
Albumin (g/dl)	2.97
INR	1.45
Clinical parameters	
Ascites present	39
Hepatic encephalopathy	4
Spontaneous bacterial peritonitis	8
Bloating	13
Diarrhoea	6
Portal vein collaterals	31
Oesophageo gastro duodenoscopy	
Small esophageal varix(< 5 mm)	24
Large esophageal varix(> 5 mm)	12
CTP score	8.3
Child status	
A	20
B	20
C	20
MELD score	10.14

CTP= Child-Turcotte-Pugh; HBV= Hepatitis B virus; HCV= Hepatitis C virus; INR= International normalised ratio, MELD= Model for End-Stage Liver Disease

RESULTS OF BREATH TEST ANALYSIS

GHBT was positive in 20 out of 60 patients (33.3%). In controls only 2 out of 60 were positive for hydrogen breath test. Comparing the GHBT between two groups p value was found to be <0.001 which was statistically significant. In the 60 cases 20 were GHBT positive, of which 11 (18.3%) had high baseline value more than 20 ppm and the remaining 9 (15 %) positive by rising criteria. In the 60 controls 2 were hydrogen breath test positive, of which one had high baseline value and another had positive by rising criteria (p value<0.001). Among the 20 HBT positive group, 15 were males. GHBT was positive in 12 (20%) alcoholic liver disease, 1(1.7%) HBV related, 2 (3.3%) HCV related and 5 (8.3%) cryptogenic CLD (Table 3).

Table 3 Association of small intestinal bacterial overgrowth with the etiology of chronic liver disease

Etiology	Positive HBT (%)	Negative HBT (%)
Alcohol	20%	30%
HBV	1.70%	13.30%
HCV	3.30%	5%
Cryptogenic	8.30%	18.30%

P value 0.435; HBT=Hydrogen Breath Test; HBV= Hepatitis B virus; HCV= Hepatitis C virus

Presence of SIBO was not correlated with the etiology of liver disease (p value 0.435). As shown in Table 4 prevalence of SIBO among CTP class A was 20% (4/20), CTP class B was 35% (7/20), CTP class C was 45% (9/20).

Table 4 Correlation of small intestinal bacterial overgrowth and the severity cirrhosis

Parameters	Child A	Child B	Child C
HBT Positive	4 (6.7%)	7 (11.7%)	9 (15%)
HBT Negative	16 (26.7%)	13 (21.7%)	11 (18.3%)
Total	20 (33.3%)	20 (33.3%)	40 (66.7%)

P value = 0.013; HBT=Hydrogen Breath Test

The mean CTP score in HBT positive group was 8.65 and in HBT negative group was 8. The prevalence of SIBO increased with the severity of liver disease (p = 0.013). Positive GHBT was not correlated with albumin, PT (INR) and MELD score with P value 0.259, 0.707, 0.135 respectively.

Table 5 Correlation with laboratory parameters with hydrogen breath test

Parameter	HBT Positive	HBT Negative	P VALUE	Significant
Bilirubin	2.995	2.222	0.023	YES
Albumin	2.915	3.033	0.259	NO
INR	1.47	1.435	0.707	NO
MELD	10.65	9.63	0.135	NO

Values are shown as mean; HBT=Hydrogen Breath Test; INR= International normalised ratio; MELD= Model for End-Stage Liver Disease

On the other hand, serum bilirubin value correlated with hydrogen breath test positivity (P =0.023) (Table 5). In HBT positive group 85% (17/20) had ascites. In HBT negative group 55% (22/40) had ascites (p value 0.022). Thus indicated that increased prevalence of SIBO was seen in cases with ascites. Past h/o SBP present in 4 cases in both HBT positive and negative group (p value 0.283). Past h/o hepatic encephalopathy present 2 cases in both HBT positive and negative group (p value 0.464). h/o bloating was present in 40% (8/20) of cases with HBT positive and 20% (5/40) cases with HBT negative with statistically significant (p value < 0.015) was found. h/o chronic diarrhea present in 5% (1/20) of HBT positive group & 5% (5/40) of HBT negative group. Statistically not significant p value 0.36. In HBT positive group 65% (13/20) had collaterals. In HBT negative group 45% (18/40) had collaterals (p = 0.089). In hydrogen breath test positive group 14/20 (70%) had esophageal varix. In the negative group 22/40 (55%) had esophageal varix (p = 0.069) (Table 6).

Table 6 Association clinical characteristics and hydrogen breathe test

	HBT Positive	HBT Negative	P Value
Ascites present	17(28.3%)	22(36.7%)	
Ascites absent	3(5%)	18(30%)	0.022
SBP Present	4(6.7%)	4(6.7%)	
SBP Absent	16(26.7%)	36(60%)	0.283
HE Present	2(3.3%)	2(3.3%)	
HE Absent	18(30%)	38(63.3%)	0.464
Bloating present	8(13.3%)	5(8.3%)	
Bloating absent	12(20%)	35(58.3%)	0.015
Diarrhea present	1 (5%)	5 (5%)	0.361
Portal vein Collaterals	65% (13/20)	45% (18/40)	0.089

HBT=Hydrogen Breath Test; SBP= Spontaneous bacterial peritonitis; HE= Hepatic encephalopathy

Increased prevalence of small intestinal bacterial overgrowth in patients with decompensated (CTP score more than 7) cirrhosis than in patients with compensated cirrhosis was noted. In compensated cirrhosis, 4 out of 20 (20%) had SIBO. In decompensated cirrhosis, 16 out of 40 (40%) had SIBO with statistically significant p value 0.03 was found. Univariate analysis showed that small bowel bacterial overgrowth was significantly associated with the presence of ascites, high serum bilirubin value, high CTP score, decompensated state of liver disease. On multivariate analysis presence of SIBO was independently associated with presence of ascites, high serum bilirubin.

DISCUSSION

Martini *et al* in1957[37] first reported the association between the cirrhosis and small intestinal bacterial overgrowth. Since then, several studies have confirmed the high prevalence of SIBO among patients with chronic liver disease.[38,39] Small intestinal bacterial overgrowth in cirrhotic patients may predispose to complications like hepatic encephalopathy and spontaneous bacterial peritonitis. Correlation between the small intestinal bacterial overgrowth and portal hypertension and severity of cirrhosis is not known. Diagnosis of small intestinal bacterial overgrowth can be done by various methods. Diagnostic gold standard is aspiration and culture of small bowel contents. Aspiration of small bowel contents is invasive, requiring intubation of the small bowel and a laboratory equipped with isolating anaerobes. Now non invasive Glucose hydrogen breath test is commonly used to diagnose small intestinal bacterial overgrowth because it is simple to use and substrates are cheap. Various studies comparing jejunal aspirate and glucose hydrogen breath test showed that sensitivity of the glucose hydrogen breath test for diagnosing small intestinal bacterial overgrowth in between 62% to 93%.[40,41] Chesta *et al*[38] done a study to diagnose small intestinal bacterial overgrowth in cirrhotic patients. Jejunal culture and lactulose hydrogen breath test was done to diagnose bacterial overgrowth. Jejunal culture positive in 64% and lactulose hydrogen breath test positive in 45% of cirrhotic patients. Similar study done by Bauer *et al*[42] showed that 61% of cirrhotic patients had small intestinal bacterial overgrowth diagnosed by small bowel culture. Study concluded that glucose hydrogen breath test correlates poorly with jejunal aspirate and culture. For diagnosing small intestinal bacterial overgrowth breath hydrogen measured in the fasting state and after glucose administration every 15 minutes upto 2 hours.

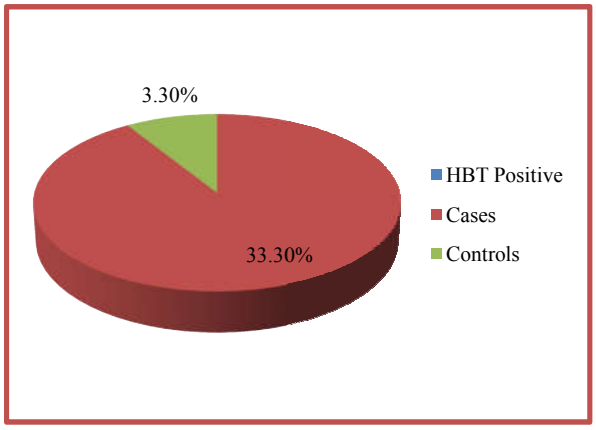

Figure 2 Positive hydrogen breath test (HBT) among cases and controls

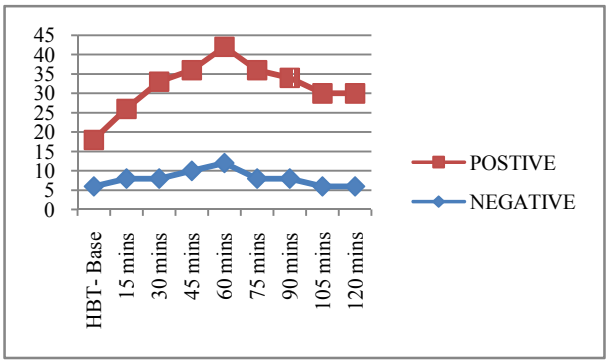

Figure 3 Graph showing positive and negative hydrogen breath test

Rise of breath hydrogen by more than 12 ppm above basal level (or) a average high baseline breath hydrogen value of more than 20 ppm used as a criteria to diagnose Small bowel bacterial overgrowth (Fig 3).[40,41,43] In this study 60 patients of cirrhosis (Child A: 20,Child: B 20, Child C: 20) of mixed etiology were included. Prevalence of small intestinal bacterial over growth compared with 60 age and sex matched controls. Association between the various biochemical parameters of liver disease with presence of small intestinal bacterial over growth was analysed. Patients with recent GI bleed, hepatic encephalopathy, septicemia, pulmonary disease excluded from this study. Probiotics, proton pump inhibitors, antibiotics, lactulose were stopped before the study. In this study as shown in fig.2, 33.3% (20/60) of cases with cirrhosis

have small intestinal bacterial over growth compared to 3.3% (2/60) healthy controls (p value < 0.001).

A study done by Morencos *et al* [44] and Yang *et al* [45] showed that prevalence of small intestinal bacterial overgrowth depends on the patients Child status. Prevalence of small intestinal bacterial overgrowth higher in Child C than Child A patients. Madrid *et al* [46] conducted a small intestinal motility study in cirrhotic patients. The study showed that absence of cyclic activity, increase in frequency and amplitude of contractions and increase in clustered contraction more commonly seen in Child C status. This altered small bowel motility may predispose to bacterial overgrowth. In this study, small intestinal bacterial over growth was more prevalent in Child C than Child A cirrhosis. Child A - 20% (4/20), Child B - 35% (7/20), Child C - 45% (9/20). Small intestinal bacterial over growth was more common in patient with decompensated state (40%), than in compensated state (20%) (p value = 0.03). A study conducted by Morencos *et al* [44] showed that prevalence of small intestinal bacterial overgrowth in patient with cirrhosis was about 30% compared to healthy controls. 89 alcoholic cirrhosis patients and 40 healthy controls included in that study. Alcohol may plays a role in the development of small intestinal bacterial overgrowth. Sadik *et al*[47] conducted a small bowel motility study in patients with alcoholic cirrhosis and non alcoholic cirrhosis. He found that small intestinal resistance time was longer in alcoholic cirrhosis and male gender compared to non alcoholic cirrhosis. So etiology and gender may plays a role inintestinal transit time. A study conducted by Bode etal[48] showed that small intestinal bacterial overgrowth was more common alcohol abuse patients. Study done by Chesta *et al*[50] and Yang *et al*[51] showed that etiology of the cirrhosis not plays arole in small intestinal bacterial overgrowth. In this study hydrogen breath test positive in 12 (20%) alcoholic liver disease, 1(1.7%) HBV related, 2 (3.3%) HCV related and 5 (8.3%) cryptogenic CLD (p value: 0.435). So etiology of cirrhosis not correlated with small intestinal bacterial overgrowth development. A study conducted by Morencos *et al* [44] showed that alcoholic cirrhosis with ascites had high prevalence of small intestinal bacterial overgrowth compared with alcoholic cirrhosis with out ascites. But a study conducted by Yang*et al* [45] failed to show the relationship with small intestinal bacterial overgrowth and ascites. Morencos *et al*[44] study showed that in patients with spontaneous bacterial overgrowth there was high prevalence of small intestinal bacterial overgrowth compared to patients with out spontaneous bacterial overgrowth (31% vs 9%). But a study done by Bauer *et al* [42] showed no relationship between small intestinal bacterial overgrowth and spontaneous bacterial overgrowth. In this study ascites present in 85% of cases HBT positive group compared to 55% in negative group (P value 0.022). So the presence of ascites correlated with small intestinal bacterial overgrowth. Only 8 patients had history of spontaneous bacterial peritonitis in this study of which, four cases in each HBT positive and HBT negative group. So there was no correlation between the spontaneous bacterial peritonitis and small intestinal bacterial overgrowth. Patients with hepatic encephalopathy cases were excluded from this study as per study design. Past h/o encephalopathy present in 4 cases (2 each in HBT + ve and HBT - ve group). No correlation between the small intestinal bacterial overgrowth and past h/o hepatic encephalopathy. A study done by Gunnarsdottir *et al*[49] showed that portal hypertension plays a important role in the development of small intestinal bacterial overgrowth. In that study 33% of cirrhotic patients with portal hypertension had small intestinal bacterial overgrowth. No patients without portal hypertension had small intestinal bacterial overgrowth. Pande*et al*[28] found that no correlation between portal hypertension and small intestinal bacterial overgrowth. In this study portal hypertension documented by the presence of varices and portal doppler study. In hydrogen breath test positive group 14/20 (70%) had varix. In the negative group 22/40 (55%) had varix (p =0.069 not significant). In HBT positive group 65% (13/20) had collaterals by PV Doppler study. In HBT negative group 45% (18/40) had collaterals (p = 0.089). So presence of esophageal varices and portal vein collaterals did not correlated with small intestinal bacterial overgrowth. In a Pande *et al*[28] study serum bilirubin value more than 2, Child Pugh score and ascites were correlated with small intestinal bacterial Overgrowth. In this study Child Pugh score, serum bilirubin, and ascites correlated with with the presence of small intestinal bacterial overgrowth. Serum albumin level and prothrombin time not correlating with small intestinal bacterial overgrowth. Best cut off of serum bilirubin obtained was 1.85 mg⁄ dl. At this level of serum bilirubin predicted small intestinal bacterial overgrowth sensitivity 82%, specificity 67%, positive predictive value 82%, negative predictive value 70%.

There are some limitations in this study. Jejunal aspiration and culture, which is considered the gold standard to diagnose small intestinal bacterial overgrowth was not done, due to technical difficulties. Patients with and without small intestinal bacterial overgrowth were not prospectively followed up to document differences in outcome.

A proportion of individuals have bacteria that do not produce hydrogen but produce other gases such as methane and hydrogen sulphide therefore these patients may not be detected with the breath test. Estimation of methane may be useful in such situation. Methane estimation not done in this study. Since glucose is absorbed completely in the upper small intestine, it may not be able to diagnose small intestinal bacterial overgrowth of the distal small intestine. So this study may under estimate the distal small bowel bacterial over growth. Some normal individuals may have slow transit through the small intestine leading to prolonged testing, up to 5 hours. But this study was done upto 2 hours only, so it may lead to false negative result in these patients.

The results of this study, using glucose hydrogen breath test in cirrhotics, showed that small intestinal bacterial over growth was more prevalent in patients with cirrhotic patients than healthy subjects. The prevalence of small intestinal bacterial over growth increases with severity of liver disease. Presence of ascites and high serum bilirubin were independently associated with presence of spontaneous bacterial overgrowth. Prospective studies are needed to document difference in outcome between patients with and without small intestinal bacterial overgrowth.

CONCLUSION

Small intestinal bacterial overgrowth was prevalent in about 33% of cirrhotic patients. The frequency of small intestinal bacterial overgrowth increases with severity of liver disease. Severity of portal hypertension does not correlate with small

intestinal bacterial overgrowth. Presence of ascites and high serum bilirubin can reliably predict presence of small intestinal bacterial overgrowth.

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