**Scholars Journal of Applied Medical Sciences**
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

**Gastroenterology**

# Small Intestinal Bacterial Overgrowth among Patients with Cirrhosis

Patwary RI[1*], Rahman MM[2], Dutta R[3], Ahmed HI[4], Imam I[5], Islam MA[6]

[1]Dr. Md. Rezaul Islam Patwary, Assistant Registrar, Sheikh Russel National Gastroliver Institute and Hospital, Dhaka, Bangladesh
[2]Dr.Mohammad Mahatabur Rahman, Registrar, Sheikh Russel National Gastroliver Institute and Hospital, Dhaka, Bangladesh
[3]Dr. Rajib Dutta, Medical Officer, Sheikh Russel National Gastroliver Institute and Hospital, Dhaka, Bangladesh
[4]Dr. Habib Iftekhar Ahmad, Junior Consultant, OSD (DGHS), Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[5]Dr. Iftekhar Imam, Specialist, United Hospital Limited, Dhaka, Bangladesh
[6]Prof. Md. Ashraful Islam, Professor and Head, Department of Gastroenterology, Dhaka Medical College and Hospital, Dhaka, Bangladesh

**DOI:** 10.36347/sjams.2022.v10i04.030 | **Received:** 05.03.2022 | **Accepted:** 07.04.2022 | **Published:** 26.04.2022

***Corresponding author:** Patwary RI
Assistant Registrar, Sheikh Russel National Gastroliver Institute and Hospital, Dhaka, Bangladesh

**Abstract** **Original Research Article**

***Introduction:*** Acute chronic liver failure, spontaneous bacterial peritonitis, hepatic encephalopathy, and hepatorenal syndrome are a few of the grave complications of liver cirrhosis that may result in death. For years, small-intestinal bacterial overgrowth (SIBO) has been considered a predisposing factor for these complications in cirrhotic patients. However, data regarding SIBO in cirrhosis patients remain less focused in our country. Therefore, the study was designed to evaluate the risk of SIBO in patients with liver cirrhosis attending a tertiary care hospital, in Bangladesh. The aim of the study was to find out the association of small intestinal bacterial overgrowth (SIBO) with cirrhosis. ***Methods:*** This case-control study was carried out in the departments of Gastroenterology and Department of Hepatology, Dhaka medical college hospital during the period from September 2018 to October 2019 with a total of 136 patients equally divided into case and control groups. The case group consisted of patients with cirrhosis, while the control group comprised of healthy age-matched volunteers. ***Result:*** Among SIBO positive cases and control most common age group was 41-50 years of age. The majority were males observed in both the case (83.3%) and the control (66.7%) groups. The risk of SIBO was more in the cirrhotic patient as the odds ratio was > 1(OR= 7.8) with 95% CI 2.18-27.96. Overall frequency of SIBO was more among patients with higher CTP score {CTP-B (72.2%), CTP-C (27.8%)} with a p-value <0.05. ***Conclusion:*** Cirrhosis is associated with small intestinal bacterial overgrowth (SIBO). The frequency of SIBO also increases in cirrhotic patients with higher CTP scores.

**Keywords:** Cirrhosis, Liver, Gastrointestinal, Intestinal, Bacteria, Overgrowth.

**Copyright © 2022 The Author(s):** This is an open-access article distributed under the terms of the Creative Commons Attribution **4.0 International License (CC BY-NC 4.0)** which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

## INTRODUCTION

Cirrhosis is an advanced stage of liver fibrosis. It causes significant morbidity and mortality and contributes to a large economic and health burden. Patients with cirrhosis may be either in a compensated or decompensate state. The worldwide prevalence of cirrhosis is 4.5%-9.5% [1, 2]. In the USA alone, the prevalence of cirrhosis is 0.27% [3]. Cirrhosis has various complications including hepatic encephalopathy, bacterial infections (SBP, sepsis, pneumonia, UTI, cellulitis, SIBO), portal hypertension, hepatorenal syndrome, hepatopulmonary syndrome, and others [1, 4]. Among the many complications of cirrhosis, small intestinal bacterial overgrowths (SIBO) are one of the major causes of death. Identification and early treatment of SIBO in cirrhotic patients are essential in preventing grave complications like sepsis, spontaneous bacterial peritonitis (SBP), and remote organ injury such as acute-on-chronic liver failure, hepatorenal syndrome, hepatic encephalopathy. SIBO is defined as an overgrowth of $\geq 10^5$ colony-forming units (CFU) per ml of bacteria in the proximal small bowel [5]. It can be diagnosed by both direct tests (Culture-based methods) and indirect tests (breath tests). Indirect tests are noninvasive and less costly. For this reason, indirect tests are now widely employed as an alternative to direct tests. Some examples of indirect tests or breath tests are lactulose breath test (LBT), glucose hydrogen breath test (GHBT), glycine-1-14C-labeled glycocholate breath test, etc. Different tests have different sensitivity and specificity tests. The sensitivity and specificity of GHBT were observed to be 75% and 30% respectively in a 1996 study [6]. Numbers of factors are responsible for the development of SIBO in cirrhotic patients. Altered small bowel motility and

delayed intestinal transit are often seen in patients with cirrhosis due to autonomic neuropathy. Several studies also confirmed a prolongation of orocecal transit time and alterations of small intestinal motility in patients with cirrhosis. These observations are potential explanations for the higher prevalence of SIBO in cirrhosis [7-13]. In an Indian case-control study conducted in 2009, the prevalence of SIBO was 49% in the case group and 8% in the control group [5]. A systematic review and meta-analysis show the prevalence of SIBO was 35.80% and 8% in cirrhosis and control groups, respectively [14]. Patients who had both ascites and a serum bilirubin level of ≤2 mg/dL had an 82 percent risk of having SIBO, while those who had neither had just a 10% chance. Because data on the prevalence of SIBO in people with liver cirrhosis is scarce, it's impossible to tell how common SIBO is in the general population. SIBO is underdiagnosed in the general population. This is due to a number of factors. SIBO may not be accurately diagnosed by available examinations in certain patients who do not seek medical consultation. SIBO can be asymptomatic or present with just non-specific symptoms, and all symptoms may be misattributed to the underlying condition. The prevalence data in the literature for specific diseases and disorders varies significantly [15].

## OBJECTIVE

### General Objective

- To find out the association of small intestinal bacterial overgrowth (SIBO) with cirrhosis.

### Specific Objectives

- To find out the frequency of SIBO among patients with cirrhosis.
- To find out the frequency of SIBO among healthy controls.

## METHODS

This cross-sectional study was conducted at the Department of Gastroenterology and Department of Hepatology, Dhaka medical college hospital, Dhaka, Bangladesh. The study duration was 1 year, from September 2018 to October 2019. A total of 136 participants were selected for this study. The patients were divided into case and control groups, with 68 patients in each group. For the case group, patients were selected through consecutive selection, from those who had cirrhosis and were attending the out-patient or in-patient department of Gastroenterology and Department of Hepatology. Cirrhosis was diagnosed by clinical findings, imaging studies, and fibrosis scores. For the control group, 68 healthy volunteers were included in the study. Informed written consent was obtained from each participant from both groups, and ethical approval was obtained from the ethical review committee of the study hospital. The consenting patients were asked to come on a specific date with overnight fasting. Any patient taking antibiotics or lactulose was advised to stop antibiotics 7 days or lactulose 2 days before the study. From each case, the data was collected and recorded in a pre-designed data collection sheet. Following data collection, entire data were assessed for completeness, accuracy, and consistency before analysis was commenced. Data analysis was being carried out by using SPSS version 25.

### Inclusion Criteria

- Age over 18 years
- Case: Consecutive patients of cirrhosis
- Control: Healthy volunteers
- Patients who had given consent to participate in the study.

### Exclusion Criteria

- Patients with active GI bleeding.
- Hepatic encephalopathy in the previous 4 weeks.
- History of previous GI surgery.
- Patients on immunosuppressive, narcotics, probiotics, motility reducing or acid-suppressive drugs
- Unable to answer the criteria question.
- Exclude those affected with other chronic diseases etc.

## RESULTS

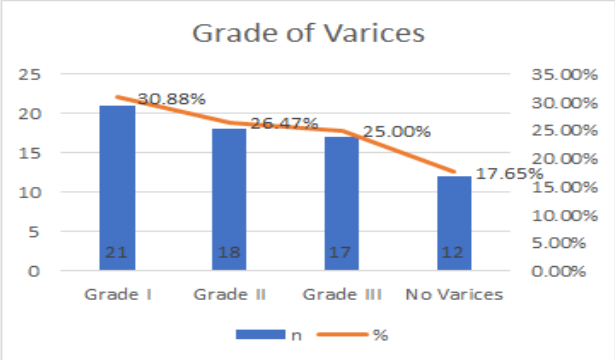


**Fig-1: Distribution of the case group participants by grading of varices (n=68)**

Figure 1 shows the distribution of the case group participants by the grade of varices of their cirrhosis. Here, among the 68 participants, 17.65% had no varices, 30.88% had grade I varices, 26.47% had Grade II varices, and the remaining 25% had grade III varices.

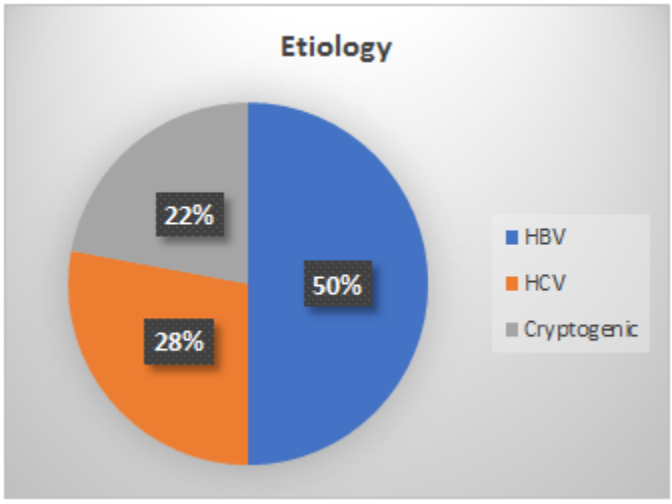


**Fig-2: Distribution of case group participants by etiology of cirrhosis (n=68)**

The figure shows the distribution of the 68 case group participants with cirrhosis by their etiology. Half the participants (32) had cirrhosis as a result of HPV (human papillomavirus), 28% of the patients had HCV (Hepatitis C Virus), and the remaining 22% had cirrhosis due to uncertain reasons, and were cryptogenic.

**Table -1: Distribution of SIBO positive and negative cases among case and control group participants (n=136)**

| Groups | SIBO Positive (n=21) | | SIBO Negative (n=115) | | OR | 95% CI | P value |
|---|---|---|---|---|---|---|---|
| | n | % | n | % | | | |
| Case Group | 18 | 26.5 | 50 | 73.5 | 7.8 | 2.18-27.96 | 0.001s |
| Control Group | 3 | 4.40% | 65 | 95.6 | | | |

In both the case and control group participants, the presence of SIBO was tested. In the case group, 26.5% of the initial cirrhosis patients had tested positive for SIBO, while 73.5% didn't. In the control group of 68 healthy volunteers with no cirrhosis, only 4.40% (n=3) had tested positive for SIBO, while 95.6% didn't. These findings show that cirrhosis increases the risk of SIBO by 7.8 times, and this difference was highly significant.

**Table-2: Age and gender distribution of SIBO positive cases of both groups (n=21)**

| Age and Gender | Case Group (n=18) | | Control Group (n=3) | |
|---|---|---|---|---|
| | n | % | n | % |
| **Age (in years)** | | | | |
| 18-30 | 2 | 11.1 | 0 | 0 |
| 31-40 | 3 | 16.7 | 1 | 33.3 |
| 41-50 | 8 | 44.4 | 2 | 66.7 |
| 51-60 | 5 | 27.8 | 0 | 0 |
| **Gender** | | | | |
| Male | 15 | 83.3 | 2 | 66.7 |
| Female | 3 | 16.7 | 1 | 33.3 |

Among the SIBO positive patients of both the case and the control group, the majority were from the age group of 41-50 years, 44.4% from the case group, and 66.7% from the control group. Male prevalence was higher in both the case and the control group. In the case group, 83.3% were male and only 3 (16.7%) were female. In the control group, 2 (66.7%) were male and 33.3% were female.

**Table-3: Social-demographic characteristics of SIBO positive patients from both groups (n=21)**

| Characteristics | Case Group (n=18) | | Control Group (n=3) | |
|---|---|---|---|---|
| | n | % | n | % |
| **Profession** | | | | |
| House wife | 3 | 16.7 | 1 | 33.3 |
| Service | 4 | 22.2 | 0 | 0 |
| Labor | 2 | 11.1 | 0 | 0 |
| Business | 4 | 22.2 | 0 | 0 |
| Cultivator | 5 | 27.8 | 2 | 66.7 |
| **Education** | | | | |
| Illiterate | 1 | 5.6 | 1 | 33.3 |
| Primary | 7 | 38.9 | 1 | 33.3 |
| Class 6-10 | 3 | 16.7 | 1 | 33.3 |
| Secondary | 5 | 27.8 | 0 | 0 |
| Graduate | 2 | 11.1 | 0 | 0 |
| **Economic** | | | | |
| <10000 | 6 | 33.3 | 3 | 100 |
| 10001-20000 | 6 | 33.3 | 0 | 0 |
| 20001-30000 | 5 | 27.8 | 0 | 0 |
| >30000 | 1 | 5.6 | 0 | 0 |

Among social-demographic characteristics, occupation of one-fourth (27.8%) of respondents were cultivators in the case group and 2(66.7%) in the control group. The educational status of more than one-third (38.9%) of respondents was up to the primary level in the case group, and 1(33.3%) in the control group. The monthly income of almost one third (33.3%) of respondents was <10000 in the case group, while all 3 (100%) of the control group participants had a monthly income of <10000.

**Table-4: Distribution of the case group participants by CTP score (n=68)**

| CTP Score | SIBO Positive (n=18) | | SIBO Negative (n=50) | | P value |
|---|---|---|---|---|---|
| | n | % | n | % | |
| CTP-A | 0 | 0.0 | 27 | 54.0 | 0.001[s] |
| CTP-B | 13 | 72.2 | 21 | 42.0 | |
| CTP-C | 5 | 27.8 | 2 | 4.4 | |

Almost three fourth (72.2%) of patients were CTP-B in SIBO positive group and 21(42.0%) in SIBO negative group. The difference was statistically significant ($p<0.05$).

## DISCUSSION

The present study was conducted with a total of 136 participants who were divided into two equal groups. 68 participants who had cirrhosis were included in the case group, while 68 age-matched healthy volunteers were included in the control group. Out of the 68 cases, the majority (30.88%) had grade I varices, 26.47% had grade II varices and 25% had grade III varices. The remaining case group participants had no varices. Among 68 cases of liver cirrhosis, Hepatitis B virus infection (50.0%) was the most common cause, followed by Hepatitis C virus in 27.9%, and for the remaining participants, the cause of cirrhosis was undetermined. A study by Pande *et al*. reported out of 62 cases 34% were due to the Hepatitis B virus, 26% due to alcohol, 21% due to cryptogenic, 16% due to Hepatitis C, and 3% due to other causes, which was somewhat similar to our studies [5]. A simple breath test was performed among both the case group and the control group participants to determine SIBO. Out of 68 cases, the majority (73.5%) didn't have small intestinal bacterial overgrowth and 26.5% had small intestinal bacterial overgrowth. Among the control group participants, 95.6% didn't have small intestinal bacterial overgrowth and only 4.4% had small intestinal bacterial overgrowth. The presence of cirrhosis increased the chances of SIBO by over 7 times compared to patients with no cirrhosis. While SIBO was once thought to be a malabsorptive illness linked to gut dysmotility, it has lately been linked to a number of clinical disorders, including cirrhosis [16]. The link between SIBO and cirrhosis was initially discovered in 1957 when cirrhotic patients' small intestines had higher levels of Streptococcus faecalis than healthy people [17]. Among the cases with SIBO, the majority (44.4%) were between 41-and 50 years. In the control group with SIBO, the majority (66.7%) were between 41-and 50 years ago. This high prevalence of SIBO among those

older than 41 years was similar to the findings of another study by Pande *et al*. [5] Out of 18 SIBO positive cases, the majority (83.3%) was male and 16.7% were female. In SIBO positive control group, 2 were male and 1 was female. This high prevalence of the male population among SIBO positive patients was in line with other similar studies [5, 18]. Majority of the SIBO positive cases (38.9%) were educated up to the primary level, while 33.3% of the control group SIBO positive patients had a similar level of education. This was similar to the findings of a 2016 study [19]. In cases with SIBO (n=18), the major occupation was cultivation, observed among 27.8% of the participants, followed by 22.2% who were in business and service, 16.7% who were housewives, and 11.1% were day laborers. And among the controls (n=3) with SIBO, the major occupation was cultivation, observed in 66.7%, and 33.3% were housewives. These findings were quite different from many other studies [20-23]. This might be due to the difference in demographics between the study regions. Among the SIBO positive case group participants (n=18), most of the respondents belonged to CTP – B (72.2%), followed by CTP-C (27.8%), and none from CTP-A. On the other hand, among SIBO negative cases, most of the respondents belonged to CTP-A (54.0%), followed by CTP-B (42.0%) and CTP-C (4.4%). This observation indicates that the prevalence of SIBO increased with the severity of the CTP score. Similar findings were also observed in a study by Pande *et al*. [5].

***Limitations of the Study***

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

## CONCLUSION

Cirrhosis is associated with small intestinal bacterial overgrowth (SIBO). The frequency of SIBO also increases in cirrhotic patients compared to non-cirrhosis patients.

## RECOMMENDATIONS

We recommend multi-center study with large sample size to draw a more reliable findings of the current issue.

***Funding:*** No funding sources

***Conflict of interest:*** None declared

***Ethical approval:*** The study was approved by the Institutional Ethics Committee

## REFERENCES

1. Melato, M., Sasso, F., & Zanconati, F. (1993). Liver cirrhosis and liver cancer. A study of their relationship in 2563 autopsies. *Zentralblatt fur Pathologie*, *139*(1), 25-30.
2. Lim, Y. S., & Kim, W. R. (2008). The global impact of hepatic fibrosis and end-stage liver disease. *Clinics in liver disease*, *12*(4), 733-746.
3. Scaglione, S., Kliethermes, S., Cao, G., Shoham, D., Durazo, R., Luke, A., & Volk, M. L. (2015). The epidemiology of cirrhosis in the United States. *Journal of clinical gastroenterology*, *49*(8), 690-696.
4. Graudal, N., Leth, P., Mårbjerg, L., & Galløe, A. M. (1991). Characteristics of cirrhosis undiagnosed during life: a comparative analysis of 73 undiagnosed cases and 149 diagnosed cases of cirrhosis, detected in 4929 consecutive autopsies. *Journal of internal medicine*, *230*(2), 165-171.
5. Pande, C., Kumar, A., & Sarin, S. K. (2009). Small-intestinal bacterial overgrowth in cirrhosis is related to the severity of liver disease. *Alimentary pharmacology & therapeutics*, *29*(12), 1273-1281.
6. Mac Mahon, M., Gibbons, N., Mullins, E., RR, O., Keane, C. T., Walsh, J. B., & Coakley, D. (1996). Are hydrogen breath tests valid in the elderly?. *Gerontology*, *42*(1), 40-45.
7. Chesta, J., Lillo, R., Defilippi, C., Jouanee, E., Massone, M. A., Maulén, M., & Zavala, A. (1991). Patients with liver cirrhosis: mouth-cecum transit time and gastric emptying of solid foods. *Revista medica de Chile*, *119*(11), 1248-1253.
8. Bode, C., Kolepke, R., Schäfer, K., & Bode, J. C. (1993). Breath hydrogen excretion in patients with alcoholic liver disease--evidence of small intestinal bacterial overgrowth. *Zeitschrift fur Gastroenterologie*, *31*(1), 3-7.
9. Quigley, E. M. M. (1952). HOME ADDRESS.
10. Fleckenstein, J. F., Frank, S. M., & Thuluvath, P. J. (1996). Presence of autonomic neuropathy is a poor prognostic indicator in patients with advanced liver disease. *Hepatology*, *23*(3), 471-475.
11. Chang, C. S., Chen, G. H., Lien, H. C., & Yeh, H. Z. (1998). Small intestine dysmotility and bacterial overgrowth in cirrhotic patients with spontaneous bacterial peritonitis. *Hepatology*, *28*(5), 1187-1190.
12. Sadik, R., Abrahamsson, H., Björnsson, E., Gunnarsdottir, A., & Stotzer, P. O. (2003). Etiology of portal hypertension may influence gastrointestinal transit. *Scandinavian journal of gastroenterology*, *38*(10), 1039-1044.
13. Madrid, A. M., Hurtado, C., Venegas, M., Cumsille, F., & Defilippi, C. (2001). Long-term treatment with cisapride and antibiotics in liver cirrhosis: effect on small intestinal motility, bacterial overgrowth, and liver function. *The American journal of gastroenterology*, *96*(4), 1251-1255.
14. Shah, A., Shanahan, E., Macdonald, G. A., Fletcher, L., Ghasemi, P., Morrison, M., ... & Holtmann, G. (2017, November). Systematic review and meta-analysis: prevalence of small

intestinal bacterial overgrowth in chronic liver disease. In *Seminars in liver disease* (Vol. 37, No. 04, pp. 388-400). Thieme Medical Publishers.

15. Bures, J., Cyrany, J., Kohoutova, D., Förstl, M., Rejchrt, S., Kvetina, J., ... & Kopacova, M. (2010). Small intestinal bacterial overgrowth syndrome. *World journal of gastroenterology: WJG*, *16*(24), 2978.
16. Bauer, T. M., Steinbrückner, B., Brinkmann, F. E., Ditzen, A. K., Schwacha, H., Aponte, J. J., ... & Blum, H. E. (2001). Small intestinal bacterial overgrowth in patients with cirrhosis: prevalence and relation with spontaneous bacterial peritonitis. *The American journal of gastroenterology*, *96*(10), 2962-2967.
17. Martini, G. A., Phear, E. A., Ruebner, B., & Sherlock, S. (1957). The bacterial content of the small intestine in normal and cirrhotic subjects: relation to methionine toxicity. *Clinical Science*, *16*, 35-51.
18. Yakoob, J., Abbas, Z., Khan, R., Hamid, S., Awan, S., & Jafri, W. (2011). Small intestinal bacterial overgrowth and lactose intolerance contribute to irritable bowel syndrome symptomatology in Pakistan. *Saudi Journal of Gastroenterology: Official Journal of the Saudi Gastroenterology Association*, *17*(6), 371.
19. Zhang, Y., Feng, Y., Cao, B., & Tian, Q. (2016). The effect of small intestinal bacterial overgrowth on minimal hepatic encephalopathy in patients with cirrhosis. *Archives of Medical Science: AMS*, *12*(3), 592.
20. Yang, C. Y., Chang, C. S., & Chen, G. H. (1998). Small-intestinal bacterial overgrowth in patients with liver cirrhosis, diagnosed with glucose H2 or CH4 breath tests. *Scandinavian journal of gastroenterology*, *33*(8), 867-871.
21. Bauer, T. M., Schwacha, H., Steinbrückner, B., Brinkmann, F. E., Ditzen, A. K., Kist, M., & Blum, H. E. (2000). Diagnosis of small intestinal bacterial overgrowth in patients with cirrhosis of the liver: poor performance of the glucose breath hydrogen test. *Journal of hepatology*, *33*(3), 382-386.
22. Bauer, T. M., Steinbrückner, B., Brinkmann, F. E., Ditzen, A. K., Schwacha, H., Aponte, J. J., ... & Blum, H. E. (2001). Small intestinal bacterial overgrowth in patients with cirrhosis: prevalence and relation with spontaneous bacterial peritonitis. *The American journal of gastroenterology*, *96*(10), 2962-2967.
23. Sadik, R., Abrahamsson, H., Björnsson, E., Gunnarsdottir, A., & Stotzer, P. O. (2003). Etiology of portal hypertension may influence gastrointestinal transit. *Scandinavian journal of gastroenterology*, *38*(10), 1039-1044.