Colonic mucosal changes in Egyptian patients with liver cirrhosis and portal hypertension

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Background and aims
In patients with liver cirrhosis and portal hypertension (PHT), portal hypertensive colopathy (PHC) is thought to be an important cause of lower gastrointestinal bleeding. This study aimed at evaluating the prevalence and clinical significance of colonic mucosal changes in Egyptian patients with liver cirrhosis and PHT.

Patients and methods
A prospective study was conducted on 35 patients with liver cirrhosis and PHT (proved by upper endoscopy and/or abdominal ultrasonography). They were evaluated using full colonoscopy to detect changes in colonic mucosa and using gastroscopy to detect the presence of both gastroesophageal varices and portal hypertensive gastropathy.

Results
Colonic lesions were found in 27 patients (77.1%), including haemorrhoids in 20 patients (57.1%), diffuse hyperaemic mucosa in 16 patients (45.7%), angiodysplastic lesions in 12 patients (34.3%) and rectal varices in five patients (14.3%). Bleeding per rectum was detected in seven patients (20%), and it significantly correlated with the presence of haemorrhoids ($P = 0.02$). The prevalence of PHC and the presence of haemorrhoids increased with the worsening Child–Pugh class ($P = 0.01$ and 0.02, respectively).

Conclusion
The prevalence of PHC and haemorrhoids increases with the progression of liver disease and worsening of the Child–Pugh grading in cirrhotic patients. However, haemorrhoids, rectal varices, hyperaemia and colonic angiodysplasia are not affected by the presence of portal hypertensive gastropathy.

Keywords:
colopathy, liver cirrhosis, portal hypertension

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Introduction

Cirrhosis is the most common cause of portal hypertension (PHT). Various vascular abnormalities have been observed in the mucosa of upper gastrointestinal (GI) tract of cirrhotic patients, including gastroesophageal varices and gastric antral vascular ectasia. These vascular lesions account for most of the upper GI bleeding in cirrhotic patients [1].

Similarly, vascular ectasia and varices may occur in the colonic mucosa of cirrhotic patients, a condition named portal hypertensive colopathy (PHC). The diagnostic criteria and clinical significance of this condition are confusing; this may be because of imprecise terminology, lack of uniform endoscopic descriptions, interobserver variability and the absence of distinctive histopathologic features [2].

This study aimed at evaluating the prevalence and clinical significance of various forms of colonic mucosal changes in Egyptian patients with liver cirrhosis and PHT and correlating them with oesophageal varices (OV), portal hypertensive gastropathy (PHG) and the severity of liver disease.

Patients and methods

This is a prospective study conducted on 50 patients with liver cirrhosis; 35 patients were selected as having proved PHT (by upper endoscopy and/or abdominal ultrasonography) and were admitted to the Tropical Medicine & Hepatology Department, Kasr-El-Aini Hospital, Cairo University from November 2007 to July 2008. The study was approved by the ethical committee of the department. This study was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki, revised in 2000) for experiments involving humans.

After taking informed consent, all patients were subjected to the following examinations:

(a) complete blood count and faecal occult blood test were performed;
(b) liver biochemical profile (total and conjugated bilirubin, serum total proteins and albumin, prothrombin time and stands for prothrombin concentration (PC), aspartate transaminase, alanine transaminase and alkaline phosphatase) was carried out;

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(c) kidney function tests (blood urea and serum creatinine) were performed;
(d) abdominal ultrasonography was performed in the Ultrasonography Unit, Tropical Medicine & Hepatology Department, Kasr-El-Aini Hospital, Cairo University using a Toshiba ECOSEE Japan instrument with a 3.5 MHz curved linear transducer. The hepatic functional reserve was assessed using the Pugh modification of the Child's criteria.
(e) Upper GI endoscopy was performed in the Gastrointestinal Endoscopy Unit, Kasr-El-Aini Hospital, Cairo University using an Olympus GF-240 videoscope or a Pentax EC3440F videoscope, commenting on:
  (i) OV — number and grade according to The Japanese Research Society for Portal Hypertension Classification [3], F1: small straight varices, F2: enlarged tortuous varices, less than 1/3 of lumen and F3: large coil-shaped varices more than 1/3 of lumen;
  (ii) gastric varices — number and size;
  (iii) PHG — present or absent and the grade (mild, moderate or severe); and
  (iv) the presence of gastritis, duodenitis, ulcers and/or other lesions.
(f) Lower GI endoscopy was performed using a Pentax EC3440F colonoscope. All patients underwent full colonoscopy (up to the caecum), commenting on colonoscopic lesions.
  (i) Haemorrhoids were classified as external and internal. Internal haemorrhoids are located above the dentate line and are covered by mucosa, whereas external haemorrhoids are located below the dentate line and are covered by squamous epithelium. Internal haemorrhoids were further classified according to Banov *et al.* [4] into first degree: bleeding with no prolapse; second degree: prolapsed with spontaneous reduction/bleeding; third degree: prolapsed requiring digital reduction/bleeding; and fourth degree: prolapse cannot be reduced or strangulated.
  (ii) Rectal varices were classified by Thakeb *et al.* [5] according to their diameter and shape into grade I: small-sized straight or infrequently tortuous varices; grade II: moderate-sized tortuous varices; and grade III: large-sized tortuous or saccular varices. When viewed endoscopically, rectal varices occur in the rectum and haemorrhoids are located in the anal canal.
  (iii) Angiodysplastic lesions and
  (iv) Hyperaemic colonic mucosa.
(g) Endoscopic biopsies from the areas with lesions (such as ulcer, polyp or mass) were taken and sent to the Pathology Department, Kasr-El-Aini Hospital, Cairo University, for histopathologic study.

According to Bini *et al.* [6], PHC is classified into three grades: grade I includes erythema of the colonic mucosa, grade II includes presence of vascular ectasia and grade III includes presence of rectal varices.

Statistical analysis

Quantitative variables were expressed as mean and SD, whereas qualitative data were expressed as frequency and percentage. Qualitative variables were analysed using the χ^2-test or Fisher's exact test as appropriate. Quantitative variables were analysed using Student's *t*-test or Friedman's test as appropriate. *P* value was expressed as the following: *P* value greater than 0.05 was considered nonsignificant, *P* value less than 0.05 was considered significant and *P* value less than 0.01 was considered highly significant.

Results

The present study included 35 patients with liver cirrhosis and PHT; they included 23 (65.7%) male patients and 12 (34.3%) female patients, ages ranging from 18 to 80 years (51.5 ± 11.8 years). Seventeen patients (48.6%) came from the rural areas and 18 patients (51.4%) from the urban areas. Nineteen patients (54.3%) had a history of contact with canal water; eight of them received parenteral anti-Schistosomal treatment, five patients received oral anti-Schistosomal tablets, three patients received both treatments and three patients did not record any history of anti-Schistosomal treatment. Abdominal

Table 1 Abdominal ultrasonographic data of the studied patients (*n* = 35)

	N (%)
Liver size	
Enlarged	2 (5.7)
Average	2 (5.7)
Shrunken	31 (88.6)
Coarse liver echo pattern	35 (100)
Attenuated HV	35 (100)
PV (normal ≤ 13 mm) [mean (SD)]	12.26 (2.75)
Splenomegaly	33 (94.28)
Spleen size [mean (SD)]	16.58 (2.75)
Dilated SV (normal<10 mm)	6 (17.1)
Splenic	6 (17)
Coronary vein	1 (3)
Paraumbilical vein	1 (3)
Mild	11 (31.4)
Moderate	10 (28.6)
Marked	9 (25.7)
No ascites	5 (14.3)

HV, hepatic vein; PV, portal vein; SV, splenic vein

ultrasonographic data of the studied patients are shown in Table 1.

The studied patients were divided according to the Child–Pugh score: one patient (2.9%) had Child score A, 14 (40%) had Child score B and 20 (57.1%) had Child score C. Bleeding tendency (e.g. epistaxis, ecchymosis or bleeding gums) was detected in 10 patients (33.3%), 18 patients (51.4%) had haematemesis, 13 patients (37.1%) had melaena and seven patients (20%) had frank bleeding per rectum. Tables 2 and 3 show upper and lower endoscopic data of the studied patients, respectively.

By studying the relationship between colonoscopic lesions and OV, we found statistically significant relationship (P = 0.02) between colonic hyperaemia and OV (Fig. 1); of the 16 patients (45.7%) with hyperaemia, OV were detected in all of them, and, of the 19 patients (54.3%) with no hyperaemia, OV were detected in 14 of them. However, nonsignificant correlation was found between haemorrhoids and OV; of the 20 patients (57.1%) with haemorrhoids, OV were detected in 19 of them, and, of the 15 patients (42.9%) with no haemorrhoids, OV were detected in 11 of them (P = 0.14).

In addition, of the five patients (14.3%) with rectal varices, OV were detected in all of them, and, of the 30 patients (85.7%) with no rectal varices, OV were detected in 25 of them; this correlation was statistically not significant (P = 1.0). Furthermore, of the 12 patients (34.3%) with angiodysplasia, OV were detected in 11 of them, and, of the 23 patients (65.7%) with no angiodysplasia, OV were detected in 19 of them; this correlation was statistically not significant (P = 0.64).

By studying the relationship between colonoscopic lesions and PHG, it was detected that the relationship between colonic angiodysplasia and PHG was statistically significant (P = 0.02); of the 12 patients (34.3%) with angiodysplasia, PHG was detected in seven of them, and, of the 23 patients (65.7%) with no angiodysplasia, PHG was detected in 19 of them (Fig. 2).

However, of the 20 patients (57.1%) with haemorrhoids, PHG was detected in 14 of them, and, of the 15 patients (42.9%) with no haemorrhoids, PHG was

Table 2 Upper endoscopic findings of the studied patients (n = 35)

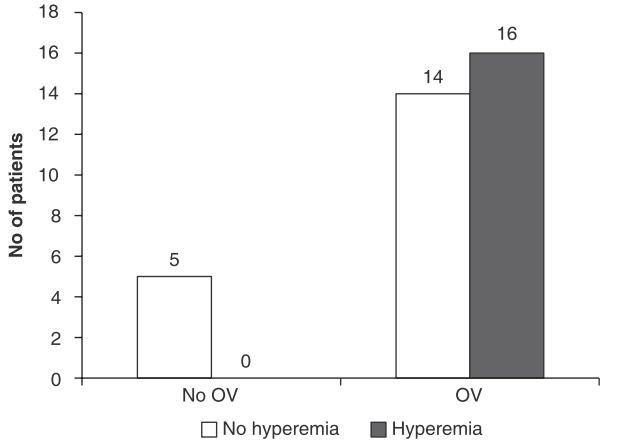
Upper endoscopy	*N* (%)
Oesophageal varices	29 (82.9)
G0	5 (14.3)
GI	11 (31.4)
GI–II	4 (11.4)
GII	6 (17.1)
GIII	5 (14.3)
GIV	3 (8.6)
PHG	26 (74.3)
Gastric varices	4 (11.4)
Gastritis	1 (2.9)
GAVE	1 (2.9)
Duodenitis	2 (5.7)

GAVE, gastric antral vascular ectasia; PHG, portal hypertensive gastropathy.

Table 3 Colonoscopic findings of the studied patients (n = 35)

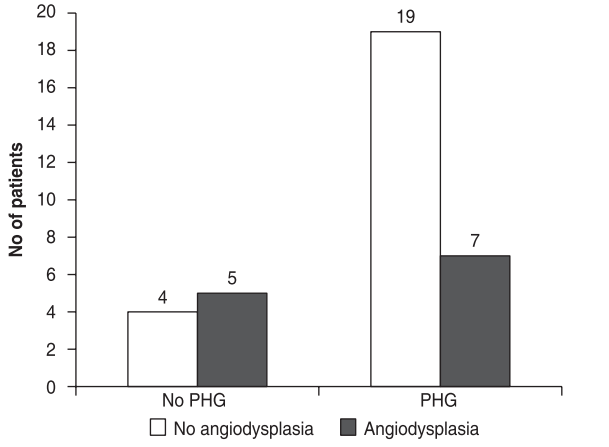
Colonoscopy	*N* (%)
Normal	8 (22.9)
Multiple lesions	18 (51.4)
Haemorrhoids	20 (57.1)
Hyperaemia	16 (45.7)
Angiodysplasia	12 (34.3)
Rectal varices	5 (14.3)
Others	
Inflammatory polyps	8 (22.9)
Inflammatory ulcers	2 (5.7)

Figure 1



Relationship between colonic hyperaemia and oesophageal varices (OV).

Figure 2



Relationship between the presence of colonic angiodysplasia and portal hypertensive gastropathy (PHG).

detected in 12 of them; this correlation was statistically not significant ($P = 0.31$).

In addition, of the five patients (14.3%) with rectal varices, PHG was detected in four of them, and, of the 30 patients (85.7%) with no rectal varices, PHG was detected in 22 of them; this correlation was statistically not significant ($P = 1.0$). Similarly, of the 16 patients (54.3%) with hyperaemia, PHG was detected in 10 of them, and, of the 19 patients (45.7%) with no hyperaemia, PHG was detected in 13 of them; this correlation was statistically not significant ($P = 0.25$).

The spectrum of lower GI bleeding (bleeding per rectum, melaena and occult bleeding) was studied with respect to different colonoscopic lesions and it was found that of the seven (20%) patients with history of bleeding per rectum, haemorrhoids were found in six of them (85.7%) and of the 28 (80%) patients with no history of bleeding per rectum, haemorrhoids were detected in 14 of them (50%); this correlation was statistically significant ($P = 0.02$).

However, of the seven patients with history of bleeding per rectum, rectal varices were detected in two (28.6%), hyperaemia in two (28.6%) and angiodysplasia in none of them (0%). Of the 28 patients without history of bleeding per rectum, rectal varices were detected in three (10.7%), hyperaemia in 14 (50%) and angiodysplasia in 12 (42.9%); these correlations were statistically not significant ($P = 0.26$, 0.42 and 0.07, respectively).

In addition, of the 13 (37.1%) patients with melaena, haemorrhoids were detected in six (46.2%) of them, rectal varices in two (15.4%), hyperaemia in seven (53.8%) and angiodysplasia in four (30.8%). Of the 22 (62.9%) patients without history of melaena, haemorrhoids were detected in 14 (63.6%) of them, rectal varices in three (13.6%), hyperaemia in nine (40.9%) and angiodysplasia in eight (36.4%); these correlations were not significant ($P = 0.31$, 1.0, 0.46 and 1.0, respectively).

It was also found that occult bleeding (low haemoglobin with positive occult blood test) was statistically not correlated to rectal varices ($P = 0.08$) or angiodysplasia ($P = 0.4$).

The stage of liver cirrhosis (estimated by the Child–Pugh score) was studied with respect to colonoscopic lesions and it showed that one patient (2.9%) with Child's score A had no haemorrhoids as shown by colonoscopy, whereas, of the 14 patients (40%) with Child's score B, 12 of them (85.7%) had haemorrhoids and of the 20 patients (57.1%) with Child's score C, eight of them (40%) had haemorrhoids; this correlation was statistically significant ($P = 0.02$).

However, the single patient (2.9%) with Child's score A had no rectal varices, no hyperaemia and no angiodysplasia but of the 14 patients (40%) with Child's score B, two of them (14.3%) had rectal varices, nine (64.3%) had hyperaemia and five (35.7%) had angiodysplasia. Of the 20 patients (57.1%) with Child's score C, three of them (15%) had rectal varices, seven (35%) had hyperaemia and seven (35%) had angiodysplasia. These correlations were statistically not significant ($P = 0.92$, 0.16 and 0.71, respectively).

When the lesions were studied collectively as PHC, the correlation between PHC and the Child–Pugh score was statistically significant ($P = 0.01$) (Table 4).

Discussion

PHT diffusely affects the GI tract. Portal colopathy is a clinical entity with liver cirrhosis, but the frequency and profile of distinct colonic mucosal lesions (portal colopathy) and rectal varices have been little studied in patients with liver cirrhosis [7]. The frequency of at least one of these features in cirrhosis has been estimated at 50–90% [8].

Although the colonic lesions are usually asymptomatic and clinically insignificant, they are a potential source of acute or chronic lower GI bleeding. Further investigation is needed to reduce the risk of bleeding and to offer alternative treatment models [7].

In our study, PHC in the form of haemorrhoids, anorectal varices, angiodysplastic lesions or diffuse hyperaemia were detected in 27 patients (77.1%), and there were eight patients (22.9%) with normal colonic mucosa. Similarly, Bresci *et al.* [9] and Ito *et al.* [2] detected colonic lesions in 82 and 66% of their studied patients, respectively. However, Bresci *et al.* [10] detected colonic lesions in 92% of their patients.

The prevalence of colonic lesions (such as haemorrhoids, rectal varices, angiodysplastic lesions and hyperaemic colonic mucosa) in patients with cirrhotic PHT has varied greatly; this discrepancy may be explained

Table 4 Relationship between the Child–Pugh score and portal hypertensive colopathy

	Colonoscopy			
	Normal	PHC	Total	*P* value
Child				
A	1	0	1	
B	0	14	14	0.01 (S)
C	7	13	20	
Total	8	27	35	

PHC, portal hypertensive colopathy.

by the differences in the patient populations studied (e.g. with respect to the underlying aetiology of liver cirrhosis), interobserver variability among endoscopists or differences in the indications for colonoscopy. In addition, Viggiano and Gostout [11] and Bresci *et al.* [9] found that there is a confusion with respect to the diagnostic criteria and clinical significance of colonic lesions in cirrhotic PHT and attributed this to imprecise terminology, lack of uniform endoscopic descriptions, interobserver variability and the absence of distinctive histopathologic features.

Increase in the prevalence of PHC with worsening Child–Pugh class was observed in our study. In addition, there was a significant correlation between the presence of haemorrhoids and worsening of the Child–Pugh class. This could be attributed to increased haemodynamic dysfunction in patients with more advanced liver disease. In addition, Ghoshal *et al.* [12], Ito *et al.* [2] and El Kady *et al.* [13] demonstrated the same correlation. However, this correlation was not proved by Bresci *et al.* [9].

In our study, haemorrhoids were detected in 57.1% of patients. This was higher than that reported by Ghoshal *et al.* [12] and Misra *et al.* [14] as they detected haemorrhoids in 21.5 and 37% of patients, respectively. However, it was lower than the result of Bresci *et al.* [10] who detected haemorrhoids in 70% of their patients.

Anorectal varices were detected in 14.3% of patients in our study. In addition, Ito *et al.* [2] detected anorectal varices in 12% of their patients. However, Bresci *et al.* [9] and Misra *et al.* [14] reported higher rates (31 and 40%, respectively). The wide range in the incidence of anorectal varices was attributed by Thakeb *et al.* [5] to the absence of clear grading system and the different etiologies of liver cirrhosis or PHT.

The prevalence of angiodysplastic lesions in patients with PHT has varied greatly; it was detected in 12 patients (34.3%) in our study. Bresci *et al.* [10], Bini *et al.* [6] and Ito *et al.* [2] detected it in 16, 13 and 36% of their patients, respectively.

The incidence of diffuse hyperaemic colonic mucosa in our study was close to the studies by Bini *et al.* [6], Ghoshal *et al.* [12], Misra *et al.* [14], Ito *et al.* [2] and Bresci *et al.* [9], as they reported it in 38, 36.6, 57, 42 and 54%, respectively.

In this study, seven patients had a history of bleeding per rectum, representing 20% of the patients included in the study and 25.9% of patients with colonic lesions. Significant correlation between rectal bleeding and presence of haemorrhoids has been found in our study, but no correlation was found with rectal varices, hyperaemic mucosa or angiodysplastic lesions. In the studies by Misra *et al.* [15], Ghoshal *et al.* [12] and El Kady *et al.* [13], rectal bleeding significantly correlated with the presence of haemorrhoids and also with rectal varices.

The presence of colonic hyperaemia significantly correlated with the presence of gastroesophageal varices in our study, whereas the presence of haemorrhoids, rectal varices and angiodysplasia did not correlate with the presence of gastroesophageal varices. In addition, the presence of colonic angiodysplasia correlated with the presence of PHG, whereas haemorrhoids, rectal varices and hyperaemia were not affected by the presence of PHG. In the study by El Kady *et al.* [13], significant correlation was found between the mere presence of OV and PHC, but none of the parameters (grades of OV, presence of gastric varices and congestive gastropathy or its severity) had a significant correlation with PHC. In addition, Bresci *et al.* [9] and Ghoshal *et al.* [12] detected that one of these colonic mucosal abnormalities significantly correlated with the presence of gastroesophageal varices and PHG.

In contrast, Ito *et al.* [2] detected that OV were not related to any of the colonic mucosal abnormalities. This could be explained by the possibility that increased portal pressure leading to gastroesophageal varices and PHG might deviate the main brunt of PHT towards the upper portion of the GI tract from its lower portion, thus decreasing the chance for the appearance of colonic mucosal abnormalities and vice versa.

In our study, histopathologic examination of colonic mucosa to study changes due to PHC was not performed. However, El Kady *et al.* [13] studied the correlation between the histopathologic evidence and colonoscopic features of PHC by taking biopsies from the rectum and sigmoid colon. Thirty-four patients (85%) had histopathological evidence of PHC and 27 of them had coexisting colonoscopic features of PHC. Evaluation of colonoscopic features of PHC revealed a sensitivity of 79%, specificity of 66.6%, positive predictive value of 93% and a negative predictive value of 36.4%, taking histopathology as the gold standard for diagnosis.

Conclusion

The prevalence of PHC and haemorrhoids increases with the progression of liver cirrhosis and worsening of the Child–Pugh grading. Being a potential source

of acute lower GI bleeding, PHC requires additional studies not only to determine their frequency, but also to understand their pathophysiology and establish proper universal endoscopic classification.

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The manuscript was read and approved by all authors.

Conflicts of interest

There are no conflicts of interest.

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