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Research Article

Colonic Mucosal Changes in Egyptian Patients with Liver Cirrhosis and Portal Hypertension

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Abstract

Background and Aims: In liver cirrhosis with portal hypertension, 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 cirrhotic and Portal Hypertension (PHT).

Patients and Methods: A prospective study done on 35 patients with liver cirrhosis and portal hypertension (proved by upper endoscopy and/or abdominal US). They were evaluated using full colonoscopy to detect changes in colonic mucosa and gastroscopy for presence of gastro-esophageal varices, and Portal Hypertensive Gastropathy (PHG) as well.

Results: Colonic lesions were found in 27 patients (77.1%), including hemorrhoids in 20 patients (57.1%), diffuse hyperaemic mucosa in 16 patients (45.7%), angiodysplastic lesions in 12 patients (34.3%) and rectal varices in 5 (14.3%). Bleeding per rectum was detected in 7 patients (20%), and it significantly correlated with the presence of hemorrhoids (P: 0.02). The prevalence of PHC and the presence of hemorrhoids increased with worsening Child-Pugh class (P: 0.01 and 0.02 successively). Conclusion: The prevalence of PHC and haemorrhoids increases with progression of liver disease and worsening of Child-Pugh in cirrhotic patients.

Keywords:

Colopathy; Liver cirrhosis;Portal hypertension

Abbreviations

PHC: Portal Hypertensive Colopathy
PHG: Portal Hypertensive Gastropathy
GI: Gastrointestinal
OV: OesophagealVarices
PHT: Portal Hypertension.

Introduction

Cirrhosis is the most common cause of portal hypertension. Various vascular abnormalities have been observed in the mucosa of upper gastrointestinal tract of cirrhotic patients, including gastro-esophageal varices and gastric antral vascular ectasia. These vascular lesions account for most of the upper gastrointestinal 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. The diagnostic criteria and clinical significance of this condition are confusing; this may be due to imprecise terminology, lack of uniform endoscopic descriptions, inter-observer variability and the absence of distinctive histopathologic features [2].

Outcome of the study

The primary outcome of the study was the evaluation of the prevalence and clinical significance of various forms of colonic mucosal changes in Egyptian patients with liver cirrhosis and portal hypertension; the secondary outcome was correlating

them with oesophagealvarices, portal hypertensive gastropathy and the severity of liver disease.

Patients and Methods

Study population

In this was prospective study, 60 patients with liver cirrhosis were screened, 35 patients were found eligible as they had proved portal hypertension (by upper endoscopy and/or abdominal ultrasound), they were admitted to Tropical Medicine andHepatology Department, Kasr-El-Aini Hospital, Cairo University from November 2012 to July 2013. The study was approved by the ethics committee of the department and the IRB. This study has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki, revised in 2000) for experiments involving humans.

Study methods

After an informed consent, all the patients were subjected to: (A) CBC and stools occult blood (B) Liver biochemical profile (total and conjugated billirubin, serum total proteins and albumin, PT and PC, AST, ALTand ALP) (C) Kidney function tests (blood urea and serum creatinine) (D) Abdominal ultrasonography (done in the ultrasonography unit, Tropical Medicine andHepatology Department, Kasr-El-Aini Hospital, Cairo University using a Toshiba ECOSEE 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: Done 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) Oesophagealvarices (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) Portal hypertensive gastropathy (PHG): present or absent and the grade (mild, moderate or severe), and (iv) presence of gastritis, duodenitis, ulcers and/or other lesions.

(F) Lower GI endoscopy: Done using a Pentax EC3440F colonoscope. All patients underwent full colonoscopy (up to the cecum), commenting on colonoscopic lesions: (a) Haemorrhoids which were classified as external and internal. Internal hemorrhoids are located above the dentate line, are covered by mucosa; external hemorrhoids are located below the dentate line, are covered by squamous epithelium. Internal haemorrhoids were further classified according to Banov et al. [4] into: 1st degree: bleeding with no prolapse; 2nd degree: prolapsed with spontaneous reduction/bleeding; 3rd degree: prolapsed requiring digital reduction / bleeding; and 4th degree: prolapsed cannot be reduced, strangulated. (b) Rectal varices were classified by Thakebet 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 sacculvarices. When viewed endoscopically, rectal varices occur in the rectum and hemorrhoids are located in the anal canal. (c) Angiodysplastic lesions; and finally (d) Hyperemic colonic mucosa. (G) Endoscopic biopsies from areas with lesions (ulcer, polyp, or mass) were taken and sent to the pathology department, Kasr El-Aini, Hospital, Cairo University, for histopathologic study. According to Biniet al. [6] portal hypertensive colopathy (PHC) is classified into three grades: Grade 1: erythema of the colonic mucosa, Grade 2: presence of vascular ectasia, Grade 3: presence of rectal varices.

Statistical methods

Quantitative variables were expressed as mean and standard deviation while qualitative data were expressed as frequency and percentage. Qualitative variable were analyzed using Chi-square or Fischer's exact test when appropriate. Quantitative variables were analyzed using the student's T-test or Friedman's test when appropriate. P value was expressed as the following: $P>0.05$ = non-significant, $P<0.05$ = significant and $P<0.01$ = highly significant

Results

The present study included 35 patients with liver cirrhosis andportal hypertension; they included 23 (65.7%) males and 12 (34.3%) females, their ages ranged from 18 to 80 years (51.5±11.8 years). Seventeen patients (48.6%) came from rural areas, and 18 patients (51.4%) from urban areas.

	No	%
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(n≤13mm)	(Mean)12.26	(SD)2.75
Splenomegaly	33	94.28
Spleen size	(Mean)16.58	(SD)2.75
Dilated SV(n<10mm)	6	17.1
Portosystemiccollateralls		
Splenic	6	17
Coronary vein	1	3
Paraumblical Vein	1	3
Ascites		
Mild	11	31.4
Moderate	10	28.6
Marked	9	25.7
No ascites	5	14.3

Table 1: Abdominal ultrasonographic data of the studied patients (number =35).

19 patients (54.3%) had history of contact with canal water, 8 of them received parentral anti-Schistosomal treatment, while 5 patients received oral anti-Schistosomal tablets, 3 patients received both treatments and 3 patients did not record any history of anti-Schistosomal treatment. Abdominal ultrasonographic data of the studied patients are showed in Table 1.

The studied patients were divided according to the Child-Pugh score into: 1 (2.9%) had Child A, 14 (40%) had Child B and 20 (57.1%) had Child C. Bleeding tendency (e.g. epistaxis, echymosis or bleeding gums) was detected in 10 patients (33.3%), 18 patients (51.4%) had haemetmesis, 13 patients (37.1%) had melena, and 7 patients (20%) had frank bleeding per rectum. Tables 2 and 3 showed upper and lower endoscopic data of the studied patients respectively.

Upper endoscopy	Number	%
Esophageal varices	29	83
G0	5	14
GI	11	31
GI-II	4	11
GII	6	17
GIII	5	14
GIV	3	8.6
PHG	26	74
Gastric Varices	4	11
Gastritis	1	2.9
GAVE*	1	2.9
Duodenitis	2	5.7

*Gastric Antral Vascular Ectasia

Table 2: Upper endoscopic findings of the studied patients (number =35).

By studying the relation between colonoscopic lesions and oesophagealvarices (OV), we found statistically significant relation (P value 0.02) between colonic hyperemia and OV (Figure 1), as in 16 patients (45.7%) with hyperemia, OV were detected in all of them and in 19 patients (54.3%) with no hyperemia, OV were detected in 14 of them. However, non-significant correlation was found between haemorrhoids and OV, as in 20 patients (57.1%) with haemorrhoids, OV were detected in 19 of them, and in 15 patients (42.9%) with no haemorrhoids, OV were detected in 11 of them (P value 0.14).

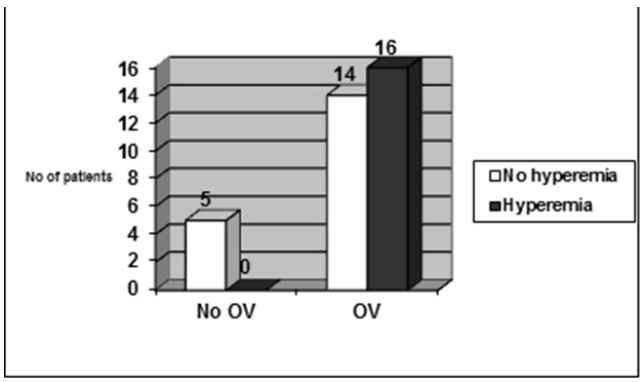

Figure 1: Relation between colonic Hyperemia and OesophagealVarices.

`Also, in 5 patients (14.3%) with rectal varices, OV were detected in all of them, and in 30 patients (85.7%) with no rectal varices, OV were detected in 25 of them; this correlation was statistically not significant (P value 1.0). Moreover, in 12 patients (34.3%) with angiodysplasia, OV were detected in 11 of them, and in 23 patients (65.7%) with no angiodysplasia, OV were detected in 19 of them; this correlation was statistically not significant (P value 0.64).

Colonoscopy	No	%
Normal	8	23
Multiple lesions	18	51
Haemorrhoids	20	57
Hyperemia	16	46
Angiodysplasia	12	34
Rectal varices	5	14
Others		
Inflammatory polyps	8	23
Inflammatory ulcers	2	5.7

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

By studying the relation between colonoscopic lesions and PHG, it was detected that the relation between colonic angiodysplasia and PHG was statistically significant (P value 0.02) as in 12 patients (34.3%) with angiodysplasia, PHG was detected in 7 of them, and in 23 patients (65.7%) with no angiodysplasia, PHG was detected in 19 of them (Figure 2).

But, in 20 patients (57.1%) with haemorrhoids, PHG was detected in 14 of them, and in 15 patients (42.9%) with no haemorrhoids, PHG was detected in 12 of them; this correlation was statistically not significant (P value 0.31).

Also, in 5 patients (14.3%) with rectal varices, PHG was detected in 4 of them, and in 30 patients (85.7%) with no rectal varices, PHG was detected in 22 of them; this correlation was statistically not significant (P value 1.0). Similarly, in 16 patients (54.3%) with hyperemia, PHG was detected in 10 of them, and in 19 patients (45.7%) with no hyperemia, PHG was detected in 13 of them; this correlation was statistically not significant (P value 0.25).

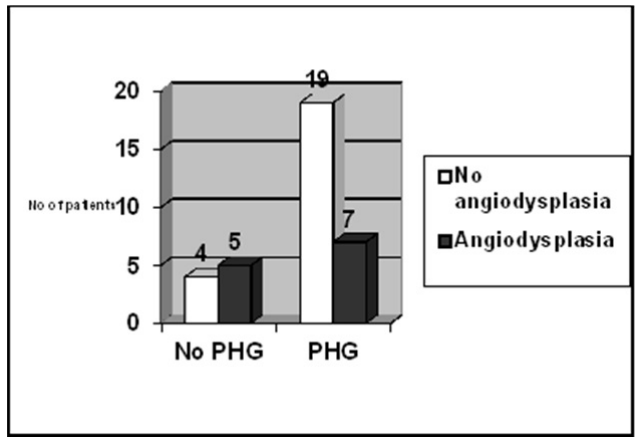

Figure 2: Relation between presence of colonic angiodysplasia and PHG.

The spectrum of lower GI bleeding (bleeding per rectum, melena and occult bleeding) was studied in relation to different colonoscopic lesions and it was found that in the 7 (20%) patients with history of bleeding per rectum, haemorrhoids were found in 6 of them (85.7%) and in 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 value 0.02).

But in the 7 patients with history of bleeding per rectum, rectal varices were detected in 2 (28.6%), hyperemia detected in 2 (28.6%) and angiodysplasia detected in none of them (0%). In 28 patients without history of bleeding per rectum, rectal varices were detected in 3 (10.7%), hyperemia detected in 14 (50%) and angiodysplasia detected in 12 (42.9%); these correlations were statistically not significant (P values 0.26, 0.42 and 0.07 respectively).

Also, in the 13 (37.1%) patients with melena, hemorrhoids were detected in 6 (46.2%) of them, rectal varices in 2 (15.4%), hyperemia in 7 (53.8%) and angiodysplasia in 4 (30.8%). And in the 22 (62.9%) patients without history of melena, hemorrhoids were detected in 14 (63.6%) of them, rectal varices in 3 (13.6%), hyperemia in 9 (40.9%) and angiodysplasia in 8 (36.4%), and these correlations were not significant (P values 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 value 0.08) or angiodysplasia (P value 0.4).

The stage of liver cirrhosis (estimated by Child-Pugh score) was studied in relation to colonoscopic lesions and it showed that the one patient (2.9%) with Child's score A had no haemorrhoids by colonoscopy, while the 14 patients (40%) with Child's score B, 12 of them (85.7%) had haemorrhoids; and the 20 patients (57.1%) with Child's score C, 8 of them (40%) had haemorrhoids; and this correlation was statistically significant (P value 0.02).

However, the single patient (2.9%) with Child's score A had no rectal varices, no hyperemia and no angiodysplasia; but the 14 patients (40%) with Child's score B, 2 of them (14.3%) had rectal varices, 9 (64.3%) had hyperemia and 5 (35.7%) had angiodysplasia. The 20 patients (57.1%) with Child's score C, 3 of them (15%) had rectal varices, 7 (35%) had hyperemia and 7 (35%) had angiodysplasia. These correlations were statistically not significant (P values 0.92, 0.16 and 0.71 respectively).

But when the lesions were studied collectively as Portal Hypertensive Colopathy (PHC), the correlation between PHC and Child-Pugh score was statistically significant (P value 0.01) (Table 4).

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

Table 4: Relation between Child-Pugh score and PHC.

Discussion

Portal hypertension diffusely affects the gastrointestinal 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 to 90% [8].

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

In our study, PHC in the form of haemorrhoids, anorectalvarices, angiodysplastic lesions or diffuse hyperemia was detected in 27 patients (77.1%), and there were 8 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. On the other hand, Bresci et al. [10] detected colonic lesions in 92% of their patients.

The prevalence of colonic lesions (haemorrhoids, rectal varices, angiodysplastic lesions and hyperemic colonic mucosa) in patients with cirrhotic portal hypertension has varied greatly; this discrepancy may be explained by differences in the patient populations studied (eg. viral vs. alcoholic cirrhosis), inter-observer variability among endoscopists, or differences in the indications for colonoscopy. Also, ViggianoandGostout[11] and Bresci et al. [9] found that there is confusion regarding the diagnostic criteria and clinical significance of colonic lesions in cirrhotic portal hypertension and attributed this to imprecise terminology, lack of uniform endoscopic descriptions, inter-observer variability, and the absence of distinctive histopathologic features.

Increase in the prevalence of PHC with worsening Child-Pugh class was observed in our study. Also there was a significant correlation between the presence of haemorrhoids and worsening of Child-Pugh class. This could be attributed to increased haemodynamic dysfunction in patients with more advanced liver disease. Also, Ghoshal et al. (2001), [12] Ito et al. (2005) [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% respectively. But it was lower than the result of Bresciet al. [10] who detected haemorrhoids in 70% of their patients.

Anorectalvarices were detected in 14.3% of patients in our study; also, Ito et al. [2] detected anorectalvarices 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 anorectalvarices was attributed by Thakeb et al. [5] to the absence of clear grading system and the different etiologies of liver cirrhosis or portal hypertension.

The prevalence of angiodysplastic lesions in patients with portal hypertension 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 hyperemic colonic mucosa in our study, was close to the studies of 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, 7 patients gave 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 not found with rectal varices, hyperemic mucosa or angiodysplastic lesions. Misra et al. [15],Ghoshal et al. [12] and El Kady et al. [13] found that rectal bleeding significantly correlated with the presence of haemorrhoids and with rectal varices also.

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

On the contrary, Ito et al. [2] detected that esophageal varices were not related to any of the colonic mucosal abnormalities. This could be explained by the possibility that increased portal pressure leading to gastro-esophageal varices, and portal hypertensive gastropathy might deviate the main brunt of portal hypertension towards the upper portion of gastrointestinal 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. But El Kady et al. [13] studied the correlation between the histopathologic evidence and colonoscopic features of PHC by taking biopsies from rectum and sigmoid colon. Thirty four patients (85%) had histopathological evidence of PHC, 27 patients of these had coexisting colonoscopic features of PHC. Evaluation of colonoscopic features of PHC revealed a sensitivity of 79%; specificity of 66.6%, PPV of 93% and a NPV of 36.4% taking histopathology as the gold standard for diagnosis.

In conclusion, the prevalence of portal hypertensive colopathy and haemorrhoids increases with the progression of liver cirrhosis and worsening of Child-Pugh grading. Being a potential source of acute lower GI bleeding, portal hypertensive colopathy requires additional studies not only to determine their frequency but also to understand their pathophysiology and establish proper universal endoscopic classification.

Conflict of Interest and Source of Funding

All authors disclose that there aren't any commercial associations or other arrangements (e.g.finSSSSancial compensation received, patient-licensing arrangements, potential to profit, consultancy, stock ownership, etc.) that may pose a conflict of interest in connection with this article.

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