Life Science Journal

Websites:
http://www.lifesciencesite.com
http://www.sciencepub.net

Emails:
editor@sciencepub.net
sciencepub@gmail.com

MARSLAND PRESS
Multidisciplinary Academic Journal Publisher

Evaluation of Fasting Serum Gastrin Level in Patients with Portal Hypertensive Gastropathy

Yasmine M Massoud[1], Rasha O Refaie[2], Walid Abdelhady[3], Hend M Hussein[1]

[1]Department of Tropical Medicine, Faculty of Medicine, Ain Shams University, Cairo, Egypt
[2]Department of Clinical Pathology, Faculty of Medicine, Ain Shams University, Cairo, Egypt
[3]Department of Internal Medicine, Faculty of Medicine, Helwan University, Cairo, Egypt.
Email: Yasminemassoud3@gmail.com

Abstract: Aim: To evaluate the fasting serum gastrin level in cirrhotic patients with and without portal hypertensive gastropathy and healthy population and To correlate the fasting serum gastrin level with the severity of hepatic decompensation, portal hypertension and portal hypertensive gastropathy. **Methods:** This study was performed in the Tropical Medicine department Ain Shams University Hospitals, in Cairo Egypt and included the following: The study included 79 participants. Fifty-four cirrhotic patients, whom were further divided into 25 cirrhotic patients with Portal hypertensive Gastropathy (PHG) diagnosed by esophago-gastro-duodenoscopy (EGD) and 29 cirrhotic patients without PHG excluded by EGD, and a third group of 25 healthy persons. Patients were subjected to Full history taking, general examination, local abdominal examination, liver function tests, HBs Ag and HCV ab. Fasting serum level of Gastrin was done by ELISA technique. **Results:** In the current study, the mean age of the healthy group was 32.9 years in comparison to 58.2 years and 56.07 years in cirrhotic patients with and without PHG. Esophageal varices and ascites were significantly more common in cirrhotic patients with PHG in comparison to cirrhotic patients without PHG. The comparison between the cirrhotic patients group with and without PHG and the healthy group regarding fasting serum gastrin level revealed that the best cut off value was found to be > 18.1 pg/ml with area under the curve (AUC), 0.900; Sensitivity, 90.74%; Specificity, 80%. As for the comparison between cirrhotic group with PHG and cirrhotic group without PHG regarding fasting serum gastrin level, it revealed that the best cut off value was found to be > 95.6 pg/ml with area under the curve (AUC), 0.786; Sensitivity, 56%; Specificity, 100%. **Conclusion:** Fasting serum gastrin level may serve as a non-invasive predictor of the presence of portal hypertensive gastropathy in cirrhotic patients.

[Yasmine M Massoud, Rasha O Refaie, Walid Abdelhady, Hend M Hussein. **Evaluation of Fasting Serum Gastrin Level in Patients with Portal Hypertensive Gastropathy.** *Life Sci J* 2019;16(12):65-70]. ISSN: 1097-8135 (Print) / ISSN: 2372-613X (Online). http://www.lifesciencesite.com. 9. doi:10.7537/marslsj161219.09.

Keywords: Portal Hypertensive Gastropathy (PHG), Gastrin Hormone, cirrhotic patients

1. Introduction

Portal hypertension is one of the dangerous complications of chronic liver disease. Portal hypertension can be defined as an increase of hepatic venous pressure gradient. Because of elevated pressures within the portal vein several complications can arise, including the development of esophageal and gastric varices, portal hypertensive gastropathy, ascites, hepatic encephalopathy as well as complications secondary to circulatory dysfunction, such as hepatorenal syndrome, Porto pulmonary syndrome and hepatopulmonary syndrome [1].

Portal hypertensive gastropathy is known to cause changes in the mucosa of the stomach in patients with portal hypertension; as far as we know the most common cause of this is complication is liver cirrhosis. The changes in the mucosa include friability of the mucosa and the presence of ecstatic blood vessels at the surface. Patients with portal hypertensive gastropathy may experience bleeding from the stomach, which may uncommonly manifest itself in vomiting blood or melena; however, portal hypertension may cause several other more common sources of upper gastrointestinal bleeding, such as esophageal varices and gastric varices. On endoscopic evaluation of the stomach, this condition shows the characteristic mosaic or "snake-skin" appearance of the mucosa of the stomach[2].

Portal hypertensive gastropathy has a prevalence rate of 20-80% in patients with portal hypertension and is more frequent in patients with severe liver disease and in patients who had a previous endoscopic treatment for varices. In patients with portal hypertension, PHG is often associated with the presence of esophageal and/or gastric varices. The mechanisms involved in the pathogenesis of PHG have not been fully elucidated However,

regulation of gastric nitric oxide, prostaglandins, tumor necrosis factor α (TNF-α), and epidermal growth factor (EGF) production may be involved[3].

The diagnosis of PHG, and by extension portal hypertensive enteropathy (similar mucosal changes at other sites of the gastrointestinal tract) is established when the characteristic endoscopic findings are observed in patients with portal hypertension. PHG is classified as mild when only the snake-skin mosaic pattern is present or severe when, in addition to the mosaic pattern, flat or bulging red marks or black-brown spots are observed. The clinical relevance of this classification has been established since patients with severe PHG are more likely to have acute bleeding or chronic anemia than patients with mild PHG[4].

Gastrin is the major hormonal regulator of gastric acid secretion. Its discovery at the turn of the century was based upon its profound effect on meal-stimulated acid secretion, making it one of the first hormones to be described[5]. Gastrin stimulates the parietal and pepsin cells, increases gastric mucosal blood flow, and has a trophic effect on the gastric, duodenal and colonic mucosa[6]. Its main roles include food-stimulated gastric acid secretion and trophic effects on the Enterochromaffin-like cells[7].

Progastrin and gastrin serum levels have been reported to be significantly higher in patients with cirrhosis of any Child-Pugh class compared to controls while there are no differences between controls and patients with non-cirrhotic chronic hepatitis B or C[8].

A higher incidence of gastric and duodenum ulcer was well recognized in patients with liver cirrhosis, but the mechanism has not been fully identified. It is found that fasting serum gastrin level is significantly elevated in patients with cirrhosis and portal hypertension[9].

2. Materials and Methods

Patients

This prospective case control study was conducted within the Department of Tropical Medicine and the endoscopy unit at Ain Shams University Hospitals (Cairo, Egypt), after approval from the Research and Ethics Committee of Ain Shams University was obtained in accordance with local research governance requirements. This study was performed in accordance with the 1964 Declaration of Helsinki and all subsequent revisions.

This study included 3 groups, 2 patient groups and a control group. Group 1: 25 cirrhotic patients with PHG diagnosed by esophago-gastro-duodenoscopy (EGD), Group 2: 29 cirrhotic patients without PHG excluded by EGD, and a third group of 25 healthy persons.

Patients were assessed by: Clinical, biochemical, and sonographic criteria of chronic liver disease. All included patients were subjected to the following: (1) Full medical history and thorough clinical examination. (2) Laboratory investigations including: Liver function tests to determine the levels of aspartate aminotransferase, alanine aminotransferase, serum bilirubin (total and conjugated), serum albumin, prothrombin time; detection of antibodies to the viral markers HBsAg, and HCV by enzyme linked immunosorbent assay (ELISA). Fasting Serum level of Gastrin hormone was done by a competitive inhibition enzyme immunoassay technique. ***Pelvi-Abdominal Ultrasound*** was done by ACUSON X700 Ultrasound System, with comment on the following:

Liver size: expressed as average, shrunken or enlarged.

Liver texture: classified as homogenous, bright or coarse.

Splenic size: expressed as average (absence of splenomegaly) or enlarged.

Presence or absence of splenic collaterals at the hilum, ascites.

Portal vein diameter. Hepatic veins patency.

Esophago-gastro-duodenoscopy for cirrhotic patients:

The upper endoscopy was done by the advanced video-endoscope used in the upper gastrointestinal tract (GF-Q240Z: Olympus Optical Co. Ltd, Tokyo, Japan). Comment was done on the following items:

- Esophageal mucosa and presence or absence of esophageal varices.
- Gastric mucosa and presence or absence of fundal varix or portal hypertensive gastropathy.
- 1st part of duodenum for the presence of signs of portal hypertensive enteropathy.

Exclusion criteria:

Patients who refused to be enrolled in the study, co-administration of proton pump inhibitors, patients with contraindications to perform EGD e.g. hepatic precoma and patients below 18 years old.

Methods

Sample: Two centimeters of venous blood were collected from candidates. A separator tube was used and samples were allowed to clot for two hours at room temperature or overnight at 4°C before centrifugation for 20 min at approximately 4000 rpm. Samples were stored in aliquot at -20°C for later use.

Principle of the test: This kit is for the quantitative level of Gastrin in the sample. Purified human Gastrin antibody was adopted to coat microtiter plate to make solid-phase antibody, then Gastrin was added to the wells. Gastrin antibody was combined with labeled HRP to form antibody-antigen complex. After washing completely, TMB substrate solution was added and became blue color at HRP enzyme-

catalyzed. Reaction was determined by the addition of stop solution and the color change was measured at wavelength of 450nm. The concentration of the Gastrin hormone in the sample was determined by comparing the O.D of the samples to a standard curve.

Judgment of assay result:

1-The standard concentration was taken as horizontal.

2-The O.D value was the vertical.

3-Standard curve was drawn on semi log graph paper.

4-The corresponding concentration was found out according to the O.D value by the sample curve, multiplied by the dilution multiple and the result was the actual concentration.

Statistical analysis

IBM SPSS statistics (V. 21.0, IBM Corp., USA, 2012) was used for data analysis. Data was collected and recorded on specific forms. Data validation was ensured before and after introduction to a PC where statistical analysis was performed.

ANOVA (Analysis of variance) was used to test the difference about mean values of lab parameters among presentations, multiple comparison between pairs of groups were performed using LSD (Post hoc range test) results were presented as mean and SD, non-parametric data as ALT, AST, BIL T, BIL D, PLT and ESR were analyzed using Kruskal Wallis Test (data presented as median and IQR).

Chi-Square test X^2 and Fisher's Exact Test were used to test the difference in proportions of variables among the presentations and gender (results were presented as percentages and the corresponding P value). Unpaired (student's) t test was used to test the difference about mean values of lab parameters among males and females, results were presented as mean and SD, nonparametric data as ALT, AST, BIL T, BIL D, PLT and ESR were analyzed using Mann-Whitney test (data presented as median and IQR).

Spearman's correlation coefficient tests the strength of association between variables $P<0.05$ will be taken as a significant.

3. Results

Our study included 79 candidates, 54 cirrhotic patients, whom were further divided into 25 cirrhotic patients with PHG and 29 cirrhotic patients without PHG, and a third group of 25 healthy persons. Fasting serum gastrin level was measured in all candidates in the three groups to correlate its level with the severity of hepatic decompensation, portal hypertension and portal hypertensive gastropathy. The mean age of the healthy group was 32.9 years in comparison to 58.2 years and 56.07 years in cirrhotic patients with and without PHG as shown in **(Table 1).** As for median level of fasting serum gastrin in relation to ascites, degree of esophageal varices and degree of PHG as parameters of portal hypertension in cirrhotic patients with PHG, esophageal varices and PHG were found to be statistically insignificant while mild ascites was found to have statistical significance in relation to the median level of fasting serum gastrin in comparison to cirrhotic patients with PHG with other grades of ascites as shown in **(Table 2, Figure 1).** Regarding the median level of fasting serum gastrin in relation to ascites and esophageal varices as parameters of portal hypertension in cirrhotic patients without PHG, none of these studied parameters were found to be significant (as denoted by a p value> 0.05) As shown in **(Table 3)**. Receiver-operating characteristic (ROC) curve was done to assess the fasting serum gastrin level in cirrhotic patients – with and without PHG – and among the healthy group, it was found that the best cut off value was>18.1 pg/ml with area under the curve (AUC), 0.900; Sensitivity, 90.74%; Specificity, 80%; PPV, 90.7%; NPV, 80.0%. as shown in **(Figure 2)**. Moreover, Receiver-operating characteristic (ROC) curve of fasting serum gastrin between cirrhotic patients with PHG and cirrhotic patients without PHG was done and it showed that the best cut off value was >95.6 pg/ml with area under the curve (AUC), 0.786; Sensitivity, 56%; Specificity, 100%; PPV, 100%; NPV, 72.5% as shown in **(Figure 3).**

Table (1): Comparison between the three groups regarding socio-demographic data:

		Cirrhosis with PHG	Cirrhosis without PHG	Healthy group	One Way ANOVA		Post hoc analysis		
		No. = 25	No. = 29	No. = 25	F/X^2*	P-value	P1	P2	P3
Age	Mean± SD	58.20 ± 9.46	56.07 ± 11.25	32.92 ± 9.74	47.743	0.000	0.448	**0.000**	**0.000**
	Range	27 – 71	32 – 75	19 – 54					
Sex	Female	8 (32.0%)	16 (55.2%)	10 (40.0%)	3.078*	0.215	0.088	0.556	0.266
	Male	17 (68.0%)	13 (44.8%)	15 (60.0%)					

*: Chi-square test

P > 0.05 Non Significant

P < 0.05 Significant

P1: Comparison between cirrhosis with PHG and cirrhosis without PHG

P2: Comparison between cirrhosis with PHG and control

P3: Comparison between cirrhosis without PHG and control

Table (2): Median level of fasting serum gastrin in relation to ascites, degree of esophageal varices and PHG as parameters of portal hypertension in cirrhotic patients with PHG.

		Fasting S. Gastrin		Mann-Whitney test	
		Median (IQR)	**Range**	**Z/K***	**P-value**
Ascites	Mild	**244.5** (113.8 – 515.5)	19 – 700	8.287*	**0.040**
	Moderate	36.45 (18.3 – 118)	12.1 – 122		
	No	89.05 (61.7 – 165)	61 – 215.2		
	Tense	141 (28.7 – 150)	28.7 – 150		
OV	I	73.8 (61.3 – 141)	18.3 –500	1.731*	0.630
	II	146 (86.65 – 222)	51.3 – 274		
	III	215.2 (19 – 700)	19 – 700		
	No	139 (44.85 – 187.5)	12.1 – 531		
PHG	Mild	61.55 (21.6 – 98.1)	12.1 – 274	4.334*	0.115
	Moderate	160 (67.6 – 215)	61.3 – 500		
	Severe	145.5 (118 – 215.2)	18.3 – 700		

*: Kruskal –Wallis; Data are presented as median (range) and range.

Table (3): Median level of fasting serum gastrin in relation to ascites and esophageal varices as parameters of portal hypertension in cirrhotic patients without PHG.

		Fasting S. Gastrin		Mann-Whitney test	
		Median (IQR)	**Range**	**Z/K***	**P-value**
Ascites	Mild	32.1 (11.2 – 33.2)	11.2 – 33.2	1.246	0.536
	Moderate	50.15 (25.45 – 81.7)	18.4 – 95.6		
	No	31.05 (19.4 – 65.3)	13.2 – 81		
OV	No	31.05 (19 – 49.7)	11.2 – 81	1.502	0.472
	I	48.9 (30.8 – 69.1)	18.4 – 95.6		
	II	43.2 (43.2 – 43.2)	43.2 – 43.2		

Data are presented as median (range).

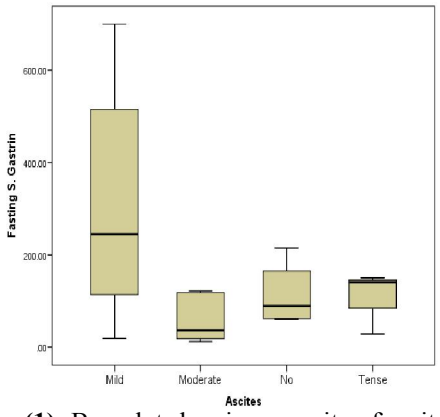

Figure (1): Box plot showing severity of ascites in cirrhotic patients with PHG

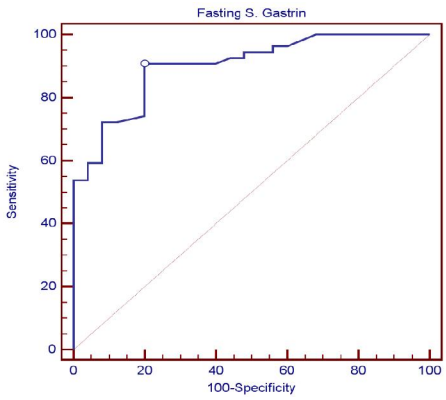

Figure (2): Receiver-operating characteristic (ROC) curve of Fasting S. Gastrin level between cirrhotic patients – with and without PHG – and healthy group

Cut off point	**AUC**	**Sensitivity**	**Specificity**	**+PV**	**-PV**
>18.1	0.900	90.74	80.00	90.7	80.0

Cut of point	AUC	Sensitivity	Specificity	+PV	-PV
>95.6 *	0.786	56.00	100.00	100.0	72.5

Receiver-operating characteristic (ROC) curve of fasting serum gastrin between cirrhotic patients with PHG and cirrhotic patients without PHG shows the best cut off value >95.6 pg/ml with area under the curve (AUC), 0.786; Sensitivity, 56%; Specificity, 100%; PPV, 100%; NPV, 72.5%.

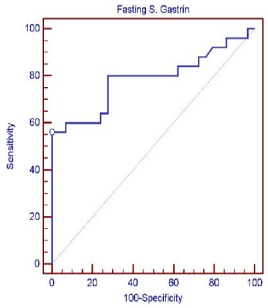

Figure (3): Receiver-operating characteristic (ROC) curve of Fasting S. Gastrin level between Cirrhotic patients with PHG and cirrhotic patients without PHG

4. Discussion

Portal hypertensive gastropathy leads to changes in the mucosa of the stomach in patients with portal hypertension. These changes in the mucosa include friability of the mucosa and the presence of ecstatic blood vessels at the surface. ***Drinane and Vijay (2015),*** concluded that patients with portal hypertensive gastropathy may experience bleeding from the stomach, which may uncommonly manifest itself in vomiting blood or melena. On endoscopic evaluation of the stomach, this condition shows a characteristic mosaic or "snake-skin" appearance to the mucosa of the stomach.

The prevalence of PHG in patients with portal hypertension has been reported to range from 20% to 80%. ***Spina et al. (1992),*** found that higher prevalence was associated with more advanced Child–Pugh class, the presence of GOVs, and previous endoscopic treatment with sclerotherapy or EVL. ***Biecker (2013),*** claimed that the incidence of chronic bleeding in patients with PHG is approximately 10%–15% at 3 years.

The pathogenesis of PHG is not well defined. In addition to the role of portal hypertension, ***Ripoll and Garcia-Tsao (2010),*** declared that gastric mucosa has increased susceptibility to injury by noxious factors and impaired healing.

Wang et al. (1955) and ***Konturek et al. (2003)*** has attributed high incidence of gastro-duodenal ulcers in patients with liver cirrhosis to elevated concentrations of plasma gastrin and progastrin accompanied by impaired urinary gastrin output. Furthermore, ***Lenz et al. (1987)*** found that cirrhotic patients exhibit abnormally high sensitivity to gastric secretory stimulants such as endogenous or exogenous gastrin. This study aimed to evaluate the value of fasting serum gastrin level in cirrhotic patients and healthy persons and to correlate it with the severity of hepatic decompensation, signs of portal hypertension with or without signs of portal hypertensive gastropathy, aiming to find its cinical usefulness as a diagnostic and/or prognostic marker.

Our study included 79 candidates, 54 cirrhotic patients, whom were further divided into 25 cirrhotic patients with PHG and 29 cirrhotic patients without PHG, and a third group of 25 healthy persons.

In our study, the mean age of the healthy group was 32.9 years in comparison to 58.2 years and 56.07 years in cirrhotic patients with and without PHG, respectively, which is statistically significantly as denoted by P2 and P3 values (0.000 and 0.000).

The mean age of the two cirrhotic groups was consistent with ***Bang et al. (2016)*** who found that the mean age was 51 years and 52 years in cirrhotic patients with and without PHG, respectively.

The mean age of the healthy group which was much younger than the other two groups, can be explained by the fact that the healthy group composed mainly of healthcare workers of the middle age period.

In the current study, fasting serum gastrin level was significantly higher in cirrhotic patients with PHG in comparison to the other two groups as shown by the P values (0.000 and 0.000). Its level was also higher in cirrhotic patients without PHG in comparison to the healthy group as shown by the P value (0.000). Mean fasting serum gastrin was 118 pg/dl, 32.1 pg/dl and 15.1 pg/dl in cirrhotic patients with PHG, cirrhotic patients without PHG and the healthy groups, respectively. The pathogenesis of PHG has been investigated. Several portal hemodynamic studies have shown that intrahepatic and extrahepatic portal venous outflow block plays an important role in the development of PHG***Iwao et al. (1992).*** This abnormal portal circulation probably results in gastric mucosal vasodilatation, although controversy exists as to the mechanism of gastric mucosal hyperemia (i.e., stasis vs overflow) ***Panés et al. (1992).***

Further, the vasodilative action of gastrin may also contribute to this abnormal gastric mucosal circulation ***Guth and Smith (1976).*** Gastric mucosal hyperemia associated with elevated serum gastrin level has been established in cirrhotic patients with portal hypertensive gastropathy (PHG) ***Shigemori et al. (1994).***

As for the median level of fasting serum gastrin in relation to ascites, esophageal varices and degree of PHG as parameters detecting portal hypertension among the group of cirrhotic patients with PHG, we concluded that the median level of fasting serum gastrin in cirrhotic patients with PHG who had mild ascites was found to have statistical significance as denoted by P value 0.040 in comparison with cirrhotic patients with PHG with other grades of ascites.

Surprisingly, neither the presence of OVs nor the degree of PHG were found to have any statistical significance regarding the level of fasting serum gastrin level among the cirrhotic patients with PHG.

It was also found that, neither the presence of esophageal varices nor the degree of ascites has any statistical significance regarding the level of fasting serum gastrin level among the cirrhotic patients without PHG. The comparison between the cirrhotic patients group – with and without PHG – and the healthy group regarding fasting serum gastrin level revealed that the best cut off value was found to be > 18.1 pg/ml with area under the curve (AUC), 0.900; Sensitivity, 90.74%; Specificity, 80%; Positive predictive value (PPV), 90.7%; Negative predictive value (NPV), 80.0%.

As for the comparison between cirrhotic group with PHG and cirrhotic group without PHG regarding fasting serum gastrin level, it revealed that the best cut off value was found to be > 95.6 pg/ml with area under the curve (AUC), 0.786; Sensitivity, 56%; Specificity, 100%; Positive predictive value (PPV), 100%; Negative predictive value (NPV), 72.5%.

These results were near to a study done by ***Lam (1976)*** who studied 40 cirrhotic patients and 20 healthy controls. The author reported that the mean fasting serum gastrin was 41.6 and 26.3 in cirrhotic patients and controls, respectively.

Moreover, ***Lauritsen et al. (1976),*** found that the fasting plasma gastrin in 50 cirrhotic patients was higher than in normal controls.

In contrast, ***Pointner (1975)*** found that fasting serum gastrin level was normal in 28 cirrhotic patients with mean value 30.1 ± 19.3 pg/ml in comparison to 39.7 ± 21.3 pg/ml in normal subjects.

In a study conducted by ***Quintero et al. (1987),*** it was found that cirrhosis is associated with high levels of fasting serum gastrin. 36% of cirrhotic patients with PHG had hypergastrinemia. Only 5% of cirrhotic patients without portal hypertensive gastropathy had hypergastrinemia. All patients without portal hypertension (controls) had normal serum gastrin levels. It was explained by the associated hypochlorhydia found in those patients. ***Sato et al. (1985)***, measured post-prandial plasma gastrin in 24 cirrhotic patients and found increased levels, whereas gastric acid output was normal.

Conclusion

Fasting serum gastrin level may serve as a non-invasive predictor of the presence of portal hypertensive gastropathy in cirrhotic patients.

Acknowledgments: The authors thank all staff members of Tropical Medicine department and the endoscopy unit at Ain Shams University Hospitals Cairo, Egypt.
Funding: None.

12/25/2019

Conflict of Interest: All Authors declare to have no conflict of interest.
Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.
Informed consent: Informed consent was obtained from all individual participants included in the study.

Correspondence Author
Dr. Yasmine Mahmoud Massoud
El-Abbassia Square, Tropical Medicine Department, Ain Shams University Hospital, Cairo11566, Egypt.
Email: Yasminemassoud3@gmail.com

References

1. Bloom S, Kemp W, Lubel J (2015): Portal hypertension: pathophysiology, diagnosis and management. Internal Medicine Journal; 45(1):16–26.
2. Drinane M and Vijay H (2015): Portal Hypertensive Gastropathy and Gastric Antral Vascular Ectasia. Chapter Complications of Cirrhosis; pp 111-119.
3. Fontana R, Sanyal A, Mehta S, et al. (2006): Portal Hypertensive gastropathy in chronic Hepatitis C patients with bridging fibrosis and compensated cirrhosis: results from the HALT-C Trial. Am J Gastroenterol; 101: 983–92.
4. Urrunaga NH and Rockey DC (2014): Portal hypertensive gastropathy and colopathy. Clin Liver Dis; 18(2):389.
5. Edkins JS (1905): On the chemical mechanism of gastric secretion. Proc R Soc Lond B Biol Sci; 76:376.
6. Mortensen NJ (1980): The anatomy of the gastrin cell. Ann R Coll Surg Engl; 62:462–9.
7. Waldum HL, Fossmark R, Bakke I, et al. (2004): Hypergastrinemia in animals and man: causes and consequences. Scand J Gastroenterol. 39:505–9.
8. Konturek SJ, Gonciarz M, Gonciarz Z, et al. (2003): Progastrin and its products from patients with chronic viral hepatitis and liver cirrhosis. Scand J Gastroenterol; 38:643–647.
9. Celinski K, Konturek PC, Slomka M, et al. (2009): Altered basal and postprandial plasma melatonin, gastrin, ghrelin, leptin and insulin in patients with liver cirrhosis and portal hypertension without and with oral administration of melatonin or tryptophan. J Pineal Res; 46(4):408-14.
10. Spina GP, Arcidiacono R, Bosch J, et al. (1992): Gastric endoscopic features in portal hypertension: final report of a consensus conference, Milan, Italy, J Hepatol; 21:461.
11. Biecker E (2013): Portal hypertension and gastrointestinal bleeding: diagnosis, prevention and management. World J Gastroenterol; 19:5035.
12. Ripoll C and Garcia‐Tsao G (2010): Management of gastropathy and gastric vascular ectasia in portal hypertension. Dig Liver Dis; 43(5):345-51.
13. Wang F, Leng X, Du R (1955): The level of serum gastrin and ulceration in cirrhotic patients with portal hypertension. Zhonghua Wai Ke Za Zhi; 33:351–352. 33.
14. Konturek SJ, Gonciarz M, Gonciarz Z, et al. (2003): Progastrin and its products from patients with chronic viral hepatitis and liver cirrhosis. Scand J Gastroenterol; 38:643–647.
15. Lenz HJ, Struck T, Greten H, et al. (1987): Increased sensitivity of gastric acid secretion to gastrin in cirrhotic patients with portocaval shunt. J Clin Invest; 79:1120–1124.
16. Bang CS, Kim HS, Suk KT, et al. (2016): Portal hypertensive gastropathy as a prognostic index in patients with liver cirrhosis. BMC Gastroenterol; 16:93.
17. Iwao T, Toyonaga A, Sumino M, et al. (1992): Portal hypertensive gastropathy in patients with cirrhosis. Gastroenterol; 102:2060-2065.
18. Panés J, Bordas JM, Pique JM, et al. (1992): Increased gastric mucosal perfusion in cirrhotic patients with portal hypertensive gastropathy. Gastroenterol; 103:1875-1882, 1992.
19. Guth PH and Smith E (1976): The effect of gastrointestinal hormones on the gastric microcirculation. Gastroenterol; 71:435-438, 1976.
20. Shigemori H, Iwao T, Ikegami M, et al. (1994): Effects of propranolol on gastric mucosal perfusion and serum gastrin level in cirrhotic patients with portal hypertensive gastropathy. Dig Dis Sci; 39(11):2433-8.
21. Lam SK (1976): Hypergastrinaemia in cirrhosis of liver. Gut; 17:700-708.
22. Lauritsen KB, Rehfeld JF, Christiansen LA, et al. (1976): Serum gastrin in cirrhosis. Stand J Gastroenterol; 37(Suppl): 33-4.
23. Pointner H (1975): Normal serum gastrin levels in patients with liver cirrhosis. Digestion; 13:212.
24. Quintero E, Pique JM, Bombi JA, et al. (1987): Gastric mucosal vascular ectastias causing bleeding in cirrhosis. A distinct entity associated with hypergastrinemia and low serum levels of pepsinogen I. Gastroenterol; 93:1054-61.
25. Sato T, Imamura M, Sasaki I, et al. (1985): Gastric acid secretion and gastrin and gastrin inhibitory polypeptide release in cirrhotic patients. Am J Gastroenterol; 80: 163-9.