# Peptic ulcer in chronic hepatitis

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## Abstract

**Two hundred fifty patients with chronic hepatitis (mean age 31.58 years) were examined endoscopically for the presence of peptic ulcer. All patients were subjected to routine blood counts, LFT and liver biopsy. Simultaneously 100 normal volunteers (mean age 30.20 years) were also examined as control. Patients were segregated into chronic passive, chronic lobular and chronic active hepatitis on histopathological findings. Duodenal ulcer was seen in 17/94 (18.09%), 15/58 (25.86%) & 31/98 (31.63%) patients and gastric ulcer was seen in 3/94 (3.19%), 2/58(3.45%) & 4/98 (4.08%) patients with chronic passive, lobular and active hepatitis respectively. In the control group, duodenal and gastric ulcers were seen in 7/100 (7.00%) and 2/100 (2.00%) of subjects respectively. The occurrence of duodenal ulcer in chronic persistent hepatitis as compared to the control was significantly high (P = 0.0336). The occurrence of duodenal ulcer in chronic active hepatitis as compared with chronic persistent hepatitis (P = 0.0454) and control (P = 0.00002) was significantly high. No statistically significant difference was seen in occurrence of gastric ulcer between the control group and chronic hepatitis.**


## Introduction

Peptic Ulcer (PU) is a disease that is influenced by many factors, many of them are known but search is still on for the others. The frequency of peptic ulcer in cirrhosis has been reported to be fivefold higher than that of normal population[1,2]. To our knowledge no study has been done to show the relation of PU in chronic hepatitis. The aim of the present case control study is to see the occurrence of PU in patients with various types of chronic hepatitis (CH).

## Materials & Methods

**Subject:** Consecutive patients of either sex with CH were endoscopically examined for the presence of PU during the period between JUly 1990 & March 1993. The diagnosis of CH was confirmed by clinical, biochemical and histopathological methods. Patients with known acid peptic ulcer disease were excluded from the study. During the period 250 eligible patients were evaluated. Each gave informed written consent; the study has approval of hospital ethical committee for investigative studies in humans.

An age and sex matched group of volunteers was also examined endoscopically for peptic ulcer as control (CON). These volunteers had negative medical history for acid peptic disease and were not alcoholics.

**Definitions**[3,4]: Chronic Persistent Hepatitis: was defined as hepatitis for more than six months with lymphocytic infiltrate limited to the limiting plate and absence of piecemeal necrosis and bridging fibrosis.

Chronic lobular Hepatitis: was defined as hepatitis for more than six months with features of acute hepatitis on histopathology.

Chronic Active Hepatitis: was defined as hepatitis for more than six months having lymphocytic infiltration extending into the portal tracts, with piecemeal necrosis and bridging fibrosis.

Peptic Ulcer: was defined as presence of a carter of 5 mm. within the duodenum or stomach covered with a fibrinous base.

## Endoscopic Procedures

All endoscopies were performed by consultant gastroenterologist using an Olympus OES QX10 endoscope. Endoscopy was done by observing standard precautions[5] and procedure[6].

**Statistical Analysis:** The occurrence of PU in various types of CH was analyzed by chi-square test" ($x^2$) for proportions and Fisher's exact test. Odds ratio and 95% confidence interval (CI) were also calculated. A "p value" of less than 0.05 was considered significant.

## Results

Two hundred and fifty patients with CH were studied. These included 136 males (mean age 32.76 years) and 114 females (mean age 30.18 year). Patients were categorized into CPH (n = 94; mean age 34.08 years), CLH (n = 58; mean age 27.87 years) and CAH (n = 98; mean age 31.37 years), histopathologically. Hundred normal subjects (mean age 30.20 years) were also examined as control. Duodenal

ulcer (DU) was seen in 17/94 (18.09%), 15/58 (25.85%) & 31/98 (31.63%) patients and gastric ulcer (GU) was seen in 3/94 (3.19%), 2/58 (3.45%) % 4/98 (4.08%) patients with CPH, CLH & CAH respectively. In control (CON) group DU was seen in 7 (7.00%) and GU was seen in 2 (2.00%) of the subjects. The occurrence of DU in CPH as compared to the CON was significantly high (P = 0.0336). The occurrence of DU in CLH as compared to CPH and CAH v/s CLH although higher, were not statistically significant (P = 0.3484) and (P = 0.5604) respectively. However the occurrence of DU in CAH as compared with CPH (P = 0.0454) and CON (P = 0.00002) was significantly high. No statistically significant increase in occurrence of GU was noted in CAH as compared to CON (P = 0.6817). The statistical analysis is detailed in Table - I.

**TABLE - I**
**Statistical analysis of DU in CH.**

| | $X^2$ STA-X TISTICS | P Value | ODDS RATIO | 95% CONFIDENCE INTERVAL |
|---|---|---|---|---|
| CPH & CON | 4.5172 | 0.0336[+-] | 2.9332 | 1.0744 & 8.2736 |
| CLH & CPH | 0.8792 | 0.3484 | 1.58 | 0.6688 & 3.7311 |
| CAH & CLH | 0.339 | 0.5604 | 1.3263 | 0.6056 & 2.9245 |
| CAH & CPH | 4.0017 | 0.0454 | 2.0957 | 1.0136 & 4.3606 |
| CAH & CON | 17.808 | 0.00002 | 6.1471 | 2.4017 & 16.3757 |

Statistically Significant (P 0.05).

## Discussion

Chronic Liver diseases are increasing in our part of the world and so are their complications. Many of them are known but search is on for others. One of them is peptic ulcer. Some studies have been done to see the relationship of PU with cirrhosis but, to our knowledge, no study has been done to see its relationship with CH. These studies were conducted in the western countries[7,8,9], in which the most common cause of cirrhosis, is alcohol related, while in our country it is post infective. thus no data exists on the frequency of PU in CH in our country. In a recent study done in patients undergoing ERCP a higher frequency of peptic ulcer is documented in both obstructed and hepatocellular jaundice[10]. In another study 216 male cirrhotic patients were endoscopically examined as a part of routine workup for liver transplant. The prevalence of DU was found 7.8% that was significantly higher than the control (2.2% p 0.005)[11].

The cause of peptic ulcer in obstructed jaundice is attributed to the absence of bile in the duodenum, which leads weakened inhibiting effect of secretion on the serum gastrin content, resulting in hypergastrinemia and hyperacidity[12].

Various causes for peptic ulceration in chronic liver disease have been postulated. Porto-systemic anastomosis allows an ulcerogenic factor to enter the systemic circulation bypassing the liver[2,13]. Decrease in the gastroduodenal mucosal defence is another[14] In contrast to obstructed jaundice, peptic ulcer in chronic liver disease does not occur due to hyperacidity, but occur in reduced gastric acid output and high levels of serum gastrin[13,15,16]. The hypergastrinemia is probably due to hypochlorhydria[15], than due to reduced hepatic clearance, as liver does not play a significant role in the clearance of gastrin[17].

Out study showed that the occurrence of duodenal ulcer increases as the CH progress. The occurrence being lowest in CPH (18.09%) and highest in CAH (31.635). All of our patients with DU were asymptomatic, thus possibility of DU has to be kept in mind in patients with CH.

Twice yearly endoscopic examination of patients with CH is recommended. Improving the mucosal defence with prostaglandins, sucraflate or colloidal bismuth[18] would be more beneficial as compared to the reduction of the gastric acid secretion. Further studies are needed to see the relation of CH with PU and various treatment options.

In summary, we document an increased occurrence of DU in CPH as compared to the control and in CAH as compared to CPH and a non significant rise in the occurrence of GU in CH.

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## References

1 Conn HC, Atterbury CE. Cirrhosis. In: Diseases of the Liver. 6th ed. L Schiff, ER Schiff (eds.). Philadelphia, JB Lippencott, 1987: 753.

2. Phillips MM. Ramsby GR, Conn HO: Portocaval anastomosis and peptic ulcer: A non-association. Gastroenterology 1975; 68: 121- 31.

3. Shela Sherlock & James Dooley. Diseases of liver & biliary System. 9th Ed. Blackwell Scientific Publications. London 1993: 293-321.

4.O'Brien MJ, Gottlieb LS. The liver and Biliary Tract. In: Robbins SL, Cotran RS and Kumar. Pathologic Basis of Disease. 4th Ed. Wb Saunders Company.

5. Weller IVD, Williams CB, Jeffries DJ et al. Cleaning and disinfection of equipment for gastrointestinal flexible endoscopy: Interim recommendations of a Working Party of British Society of Gastroenterology. Gut 1988; 29: 1134-1151.

6. Kirk Rm Diagnostic upper gastrointestinal endoscopy. In: Dudley H. Paries WJ and Cartes DC eds. Rob & Smiths' Operative Surgery 4th Ed. Butterworths London 1983: 1-7.
7. Lipp Wf, Lipsitz MH. The clinical significance of the coexistence of peptic ulcer and portal cirrhosis, with special reference to the problem of massive hemorrhage. Gastroenterology 1952; 22: 181-191.
8. Swisher WP, Baker I A, Bennet HC. Peptic ulcer in Laennec's cirrhosis. Am J Dig Dis. 1955; 22: 291-94.
9. Kirt AP, Dooley JS, Hunt RH. Peptic Ulceration in patients chronic liver disease. Dig. Dis Sci 1980; 25: 756-60.
10. Bastid C, Telleches I, Sahel J. Does jaundice increase the frequency of gastroduodenal ulcerations? Hepatogastroenterology 1990; 37(6): 612-4.
11. Rabinovits M, Schade RR, Dindzan V, van Theiel DH and Gavaler JS. Prevalence of duodenal ulcer in cirrhotic males referred for liver transplantation. Does the etiology of cirrhosis make a difference. Dig Dis Sci March 1990; 35(3): 321-326.
12. Upyrev AV, Gusev Elu, Ilichev VA, Gorchakov VK and Muratova CA. Acute peptic lesions of the gastroduodenal mucosa in patients with obstructive jaundice (abst). Khirugiia Mosk 1989;(1): 42-6
13. Langman MJS, Cooke AR. Gastric and duodenal ulcer and their associated diseases. Lancet 1976; 2: 680-83.
14. McCormack TT, Sims J, Eyre-Brock I, Kennedy H, Goepel J, Johnson AG, triger DR. Gastric lesions in portal hypertension: inflammatory gastritis or congestive gastropathy? Gut 1985; 26: 1226-32.
15. Lam SK. Hypergastrinemia in cirrhosis of the liver. Gut 1976; 17. 700-8.
16. Kataev SS, Shifrin OS, Golovanova OIu, Tsvetkova IT & Lebedev SP. Hepatogenic ulcer - Various aspects of its pathogenesis (abst). Klin Med Mosk 1989 Jun; 67(6): 32-6.
17. Strunz UT, Thombson MR, Flashoff J, Grassman MI. Hepatic inactivation of gastrins of various chain lengths in dogs. Gastroenterology 1978; 74: 550-53.
18. Lam SK & Sabesin SM. Acid Cytoprotection and peptic ulcer. AM J Med Sept 28, 1987; 83(Suppl 38): 1-3.

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# World Health Assembly calls for action to protect INNS

The system that identifies each pharmaceutical substance included in marketed pharmaceutical products by a unique, universally recognised genetic name is of crucial importance to international communication in medicine WHO's programme on the selection of International Nonproprietry Names (INN) is intended to maintain and protect this system, and since 1950 names have been selected for approximately 6,000 pharmaceutical substances.

The procedure for selecting INNs allows manufacturers to contest names that are either identical or similar to their licensed trade marks. In contrast, trade mark applications are disallowed only when they are identical to an INN. Because of the competitive promotion of products no longer protected by patients, INNs now require greater protection. Rather than marketing such products by generic name many companies apply for a trade mark derived from an INN and, in particular, including the INN common stem. The 1991 WHO Expert Committee on the Use of Essential Drug[1] warned that "This practice endangers the principle that INNs are public property, it can frustrate the rational selection of further INNs for related substances and it will ultimately compromise the safety of patients by promoting confusion in drug nomenclature".

It was against this background that the Forty-sixth World Health Assembly in May 1993 adopted a resolution drawing attention to the dangers inherent in the situation and calling for action. The resolution acknowledges the fundamental contribution of international nonproprietary names to effective communication in medicine, and expresses satisfaction with the increasing contribution of generic products to national drug markets in both developed and developing countries. However, it warns that the current trend to market generic products under trade marks or brand names derived from INNS may compromise the safety of patients by creating confusion in prescribing and dispensing medicines and by interfering with the orderly development of the nomenclature for INNS.

The resolution calls on Member States:

"to enact rules or regulations, as necessary, to ensure that international nonproprietary names (or the equivalent nationally approved generic names) used in the labelling and advertising of pharmaceutical products are always displayed prominently;

"to encourage manufacturers to rely on their corporate name and the international nonproprietary names, rather than on trade marks, to promote and market multi-source products introduced after patient expiration;

"to develop policy guidelines on the use and protection of international nonproprietary names, and to discourage the use of names derived from INNS, and particularly names including established INN stems as trade marks."