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Helicobacter pylori as Initiating Factor in Patients of Cirrhosis with Concomitant Hepatic Encephalopathy

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Abstract

Objectives: To determine the prevalence of *Helicobacter pylori* seropositivity in patients of hepatic cirrhosis with hepatic encephalopathy.

Study design: Descriptive cross-sectional study.

Place and duration of study: This study was conducted at the Department of Medicine, Northwest General Hospital & Research Center, Peshawar, KPK, from 2nd June 2016 to 2nd December 2016.

Materials and Methods: The study was conducted at Northwest General Hospital & Research center from 2nd June 2016 to 2nd December 2016 on 137 patients after the permission of the hospital ethical committee. The collection of data regarding the patients with liver cirrhosis having encephalopathy presenting to the outpatient department/causality of this institute. The patients were informed and their written consent was taken from patients (age 15 and above) with full work-up of comprehensive clinical history and for physical examination. The 5 ml blood was obtained under aseptic condition, sent to the laboratory for *H. pylori* antibodies detection.

Results: The mean ages of the patients were 41.36 years ± 10.48 SD and 62 (45.55%) were female and 75 (54.75%) were male and *H. pylori*-positive was found in 94 (68.61%). Encephalopathy grade wise distribution of patients shows that 25 (18.25%) patients have grade 1, 33 (24.09%) were grade 2, 40 (29.2%) were grade 3 and 39 (28.47%) have grade 4 encephalopathy.

Conclusion: *Helicobacter pylori* antibodies showed a high titer in patients with Porto-systemic encephalopathy due to cirrhosis. This may suggest that presence of *Helicobacter pylori* may play some part or may amplify the pathogenesis of hepatic encephalopathy in patients with liver cirrhosis.

Keywords: *H. pylori*; Hepatic encephalopathy; ELISA; Liver disease

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Introduction

Hepatic encephalopathy or the portosystemic encephalopathy is one of the neuropsychiatric reversible syndrome which presents with brain function deterioration. Once the liver cells fail to detoxify the metabolic products especially the ammonia; which, then builds up in the blood and produces clinical manifestations of hepatic encephalopathy. Hepatic encephalopathy is clinically presented by a variety of abnormalities that affect the patient's attention, cognition, functional ability, personality changes, and intellectual abilities are also noted to be affected [1]. When hepatic encephalopathy develops due to liver cirrhosis patients may experience certain signs and symptoms such as confusion, forgetfulness, sweet musty breath odor, fatigue. Patients with hepatic encephalopathy can also advance into coma state which reflects its severity and poor prognosis. *Helicobacter pylori* are gram negative bacteria that mostly live and affect the human gastric mucosa resistant to the acidic medium and main cause of peptic ulcer and gastritis. However *H. pylori* are rich in urease enzyme which increases the production ammonia from gastric lumen into the blood circulation and reaches to the brain is the main cause of encephalopathy [2-14]. High level

of ammonia in blood is also being found in patients with hepatic encephalopathy which may play some role in contributing to its pathogenesis [2]. Electroencephalographic (EEG) abnormalities in hepatic encephalopathy patients which are non-specific and similar to those seen in uremia and acid-base disorders are also been observed [3]. New strategies are developed to diagnose and treat hepatic encephalopathy [15]. Hepatic encephalopathy having different types depending on the severity and their occurrence. Hepatic encephalopathy is classified into three subtypes which are Type A, Type B, and Type C [4,5]. Type A is associated with acute liver injury and has a fatal outcome [6]. This subtype leads to the swelling of astrocyte cells in the brain, which are responsible for the ammonia detoxification and once these cells lose its ability to function normally it could be a possible factor in contributing to the pathogenesis of Hepatic encephalopathy [7]. Type B hepatic encephalopathy being quite rare, in type B hepatic encephalopathy or bypass hepatic encephalopathy in which an abnormal connection is formed and toxins get to the systematic circulation without their detoxification [8]. Type C as one of the common Encephalopathy associated with cirrhosis. Type C is further subdivided into episodic, persistent, and minimal encephalopathy [9]. The key purpose of using these new descriptors was the entire scale misperception in the literature as to what constitutes as acute or chronic HE. As an alternative, most of it is been so called chronic HE reported in the old management literature was individualize or recurrent occurrences of HE in patients with chronic liver disease [10].

Methods and Materials

A descriptive cross-sectional study was conducted between 02nd June 2016 to 02nd December 2016 in the Northwest General Hospital & Research center, Peshawar, one of the largest health centers in Khyber Pakhtunkhwa. The WHO (World Health Organization) software was used for the sample size determination *via* consecutive (no probability) sampling [13]. The final sample size was 137, using 77.6% seropositivity of *H. pylori,* 95% confidence level, and with a 7% margin of error. Patients (male and female) aged 15 years or above included in the current study. All those patients with liver cirrhosis having encephalopathy from grade 1 to 4 (West Haven Criterion) on clinical grounds. Approval was taken from the hospital ethical committee to conduct the study, data was collected of all those patients with liver cirrhosis having encephalopathy presenting to outpatient department/causality of this institute. Patients were admitted in the Medical Unit of Northwest General Hospital & Research center for additional assessment. The attendants who came with the patients were asked to sign the consent for the relative study, which fulfilled the inclusion criteria. Patients age 15 and above had full workup of detailed medical history and physical examination carried out. The 5 ml blood was obtained under aseptic condition, sent to the laboratory for *H. pylori* antibodies detection. All investigation was done from the same laboratory and same microbiologist who was the fellow of CPSP. Complete material was documented into a perform for this study design. Strictly an exclusion criterion was tailed to control confounder and bias in the results of this study. Records were stored and examined by statistical program SPSS version 11. *H. Pylori* seropositivity was stratified among the age, sex and encephalopathy grades so that to see the effect modifiers. Frequency in percentages were calculated for all categorical variables like gender, age, encephalopathy grading and serum positivity for *H. Pylori* and Mean ± Standard Deviation was calculated for continuous variables like age. All the data were presented in tables and graphs.

Results

Total 137 patients were diagnosed with hepatic cirrhosis in the tertiary care hospitals based on clinical evaluation, liver panels and ultrasound features. The average age of the patients was 41.36 years ± 10.48 SD. The minimum age was 28 years and the maximum age was 73 years. The total number of patients was 137, out of which 75 (54.75%) were male and 62 (45.55%) were female (Figure 1). Majority of the patients 68 (49.64%) were in the age range 41 to 50 years, followed by 29 (21.17%) the patients in the age group 51 to 60 years, 5 (3.65%) were in the age range 20 to 30 years, 27 (19.71%) were in the age range 31 to 40 years and 8 (5.83%) were in the age more than 60 years (Table 1). *H. pylori*-positive was found in 94 (68.61%) and 43 (31.39%) have *H. pylori*-negative (Figure 2). It was noticed that elderly patients were more susceptible to get *H. pylori* infection while comparing them to the age group of younger patients. *H. pylori*-positive patients 48 (51.06%) were in the age range of 41 to 50 years followed by 17 (18.09%) in the range of 31 to 40 years of age (Table 2). Encephalopathy grade wise distribution of patients shows that 25 (18.25%) patients have grade 1, 33 (24.09%) were grade 2, 40 (29.2%) were grade 3 and 39 (28.47%) have grade 4 encephalopathy (Table 3).

Discussion

H. Pylori plays a vital role in contributing the factor for the pathogenesis of peptic ulcer and the debate is ongoing on its some role in hepatic encephalopathy. The statistics from the preceding studies have shown some link of relation having high levels ammonia were found in the gastric secretions and at the same time, the serum also showed quite increase in ammonia level, so it displayed that

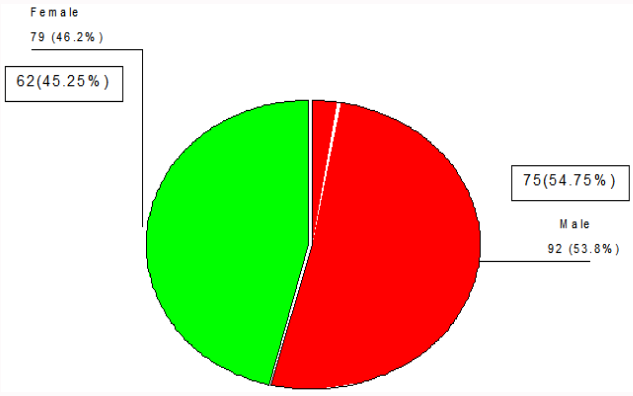

Figure 1: Gender distribution.

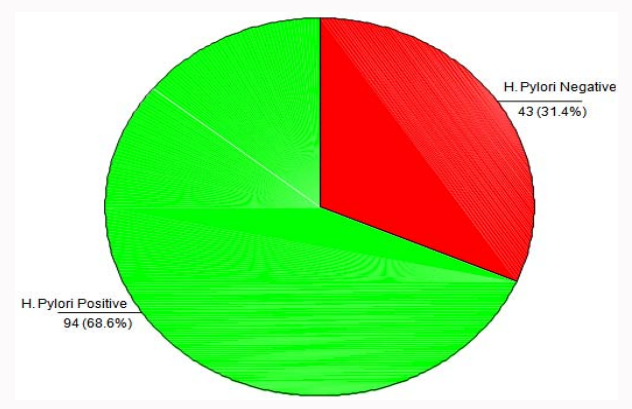

Figure 2: Cirrhotic patients having frequency of *H. Pylori.*

Table 1: Age wise distribution.

Age	No of patients	Percentage
20-30	7	2.13%
31-40	23	18.09%
41-50	69	51.06%
51-60	28	22.34%
>60	10	6.38%
Total	137	100%

Table 2: Age wise distribution of *H. Pylori.*

	H. Pylori		
Age	**Yes (%)**	**No (%)**	**Percentage**
20-30	2 (2.13%)	5 (11.6%)	7 (2.13%)
31-40	17 (18.09%)	6 (13.9%)	23 (18.09%)
41-50	48 (51.06%)	21 (48.8%)	69 (51.06%)
51-60	21 (22.34%)	7 (16.3%)	28 (22.34%)
>60	6 (6.38%)	4 (9.3%)	10 (6.38%)
Total	94 (100%)	43 (100%)	137 (100%)

Table 3: Distribution of encephalopathy grade.

	No of patients	Percentage
Grade 1	25	18.25
Grade 2	33	24.09
Grade 3	40	29.2
Grade 4	39	28.47
Total	137	100

the patients with cirrhosis were considerably higher in incidence when comparing the *H. pylori*-positive patients with those negative for the disease [16-18]. The main aim of the study was to search the effect of *H. pylori* in patients with hepatic encephalopathy. The study revealed that the frequency of *H. pylori* infection was much higher in the patients (68%) in those patients who presented with shunting of blood from the liver and development of the hepatic encephalopathy. The results can be compared to a similar study conducted by Siringo et al. [19] in Italy (76.5%) and (76%) stated by the Tsai et al. [20] in the Taiwanese population with liver cirrhosis having the prevalence of *H. pylori* infection. The prevalence of concomitant *H. pylori* infection in the patient presenting with hepatic cirrhosis was found to be 74% in Pakistan [21]. Chinese patients with PSE also have reported the high prevalence of *H. pylori* antibodies 71.4% from the studies shown by Xu in his wide data [22] and 67% Dasani et al. [23]. Depicted it in the American people. Some other studies were also conducted which concluded that there is a lower occurrence (20.3% to 60%) of *H. pylori* infection with PSE in patients with cirrhosis [24-30]. Numerous additional abdominal disorders are linked with *Helicobacter pylori* infection. Hepatic encephalopathy association with *H. pylori* infection may be due to its virulence factors; of them the ammonia produced by this pathogen *H. Pylori* in the stomach is one of the factors leading to its pathogenicity. When comparing the Cirrhotic patients with hepatic encephalopathy than those without it, the former show some extent of mutual interlinked relation with *H. pylori. H. pylori* which break down urea into ammonia and increase the PH in the stomach thus causing peptic ulcer, it can also lead to accumulation of ammonia in blood which might be too low or not that much significant in contributing to hepatic encephalopathy. However, blood ammonia level is improved in patients with hepatic encephalopathy after the specific treatment of *H. pylori* [31,32]. In our study, the severity of hepatic encephalopathy showed a concomitant rise in the *H. pylori* titer which was taken into account. This factor may be responsible for the deterioration of the patients with liver cirrhosis. The findings in the study of Guillermo et al. [33] don't correlate with our study. The study conducted by them revealed *H. pylori* seropositivity in hepatic Encephalopathy Gr-I (77.63%), Gr-II (78.13%), Gr-III (100.00%), Gr IV (75.00%). The primary purpose of our study was to include only four patients from Gr IV hepatic encephalopathy in our study. The study conducted by our group signified that the patients with liver cirrhosis and those who had developed the hepatic encephalopathy due to a higher level of ammonia had increased incidence of *H. pylori* seropositivity. The highest titer of the *H. Pylori* was demonstrated in patients who had a severe form of hepatic encephalopathy, clearly suggesting that *H. pylori* might play quite an essential role in leading to the development of hepatic encephalopathy. However, further studies should be conducted at a large level by recruiting a high number of cases for a better understanding.

Conclusion

In this study, cirrhotic patients with portosystemic shunting and hepatic encephalopathy had a higher incidence of *H. pylori* antibodies showing relation with this co-existing disorder. This may suggest that presence of *Helicobacter pylori* may have some part or may amplify to the pathogenesis of encephalopathy in patients with liver disease. However, bigger studies are required to establish *H. pylori* role as one of the reasons for portosystemic encephalopathy in patients with liver cirrhosis co-existing portosystemic shunting.

References

1. Abou-Assi S, Vlahcevic ZR. Hepatic encephalopathy. Metabolic consequence of cirrhosis often is reversible. Postgrad Med. 2001;109(2):52-4,7-60,3-5 passim.
2. Lockwood AH. Blood ammonia levels and hepatic encephalopathy. 2004;19(3-4):345-9.
3. Blei AT. Diagnosis and treatment of hepatic encephalopathy. Baillieres Best Pract Res Clin Gastroenterol. 2000;14(6):959-74.
4. Ferenci P. Hepatic encephalopathy. Gastroenterol Rep (Oxf). 2017;5(2):138-47.
5. Cordoba J, Blei AT. Treatment of hepatic encephalopathy. Am J Gastroenterol. 1997;92(9):1429-39.
6. Jalan R, Seery JP, Taylor-Robinson SD. Review article: Pathogenesis and treatment of chronic hepatic encephalopathy. Aliment Pharmacol Ther. 1996;10(5):681-97.
7. Butterworth RF. Complications of cirrhosis III. Hepatic encephalopathy. J Hepatol. 2000;32(1):171-80.
8. Ferenci P, Grimm G, Meryn S, Gangl A. Successful long-term treatment of portal-systemic encephalopathy by the benzodiazepine antagonist flumazenil. Gastroenterology. 1989;96(1):240-3.
9. Ferenci P, Lockwood A, Mullen K, Tarter R, Weissenborn K, Blei ATJH. Hepatic encephalopathy-definition, nomenclature, diagnosis, and quantification: Final report of the working party at the 11th World Congresses of Gastroenterology, Vienna, 1998. Hepatology. 2002;35(3):716-21.
10. Mullen K. Evidence-based medicine and HE treatment. 12th ISA Symposium Schlossberg, Germany. 2005.
11. Gerber T, Schomerus H. Hepatic encephalopathy in liver cirrhosis: Pathogenesis, diagnosis and management. Drugs. 2000;60(6):1353-70.

12. Lambert JR. The role of *Helicobacter pylori* in non ulcer dyspepsia. A debate--for. Gastroenterol Clin North Am. 1993;22(1):141-51.

13. Lazzaroni M, Bargiggia S, Sangaletti O, Maconi G, Boldorini M, Bianchi Porro G. Eradication of *Helicobacter pylori* and long-term outcome of functional dyspepsia. A clinical endoscopic study. Dig Dis Sci. 1996;41(8):1589-94.

14. Rinaldi V, Zullo A, Diana F, Capocaccia L. *Helicobacter pylori*, hyperammonemia, and hepatic encephalopathy: Is there a correlation? Am J Gastroenterol. 1997;92(4):723-4.

15. Gasbarrini A, Serricchio M, Tondi P, Gasbarrini G, Pola P. Association of *Helicobacter pylori* infection with primary Raynaud phenomenon. Lancet. 1996;348(9032):966-7.

16. Scotiniotis IA, Lucey MR, Metz DC. *Helicobacter pylori* infection is not associated with subclinical hepatic encephalopathy in stable cirrhotic patients. Dig Dis Sci. 2001;46(12):2744-51.

17. Zullo A, Rinaldi V, Folino S, Diana F, Attili AF. *Helicobacter pylori* urease inhibition and ammonia levels in cirrhotic patients. Am J Gastroenterol. 1998;93(5):851-2.

18. Plevris JN, Morgenstern R, Hayes PC, Bouchier IA. Hyperammonaemia in cirrhosis and *Helicobacter pylori* infection. Lancet. 1995;346(8982):1104.

19. Miglioli M, Corinaldesi R, Bolondi L, Siringo S, Vaira D, Menegatti M, et al. High prevalence of *Helicobacter pylori* in liver cirrhosis: Relationship with clinical and endoscopic features and the risk of peptic ulcer. Dig Dis Sci. 1997;42(10):2024-30.

20. Tsai CJ. *Helicobacter pylori* infection and peptic ulcer disease in cirrhosis. Dig Dis Sci. 1998;43(6):1219-25.

21. Qureshi H, Ahmed W, Kazi J, Zuberi SJ. *Helicobacter pylori* in portal hypertension. J Pak Med Assoc. 1993;43(11):249.

22. Xu C, Jiang X. Relationship between *Helicobacter pylori* infection and cirrhosis of liver. Hunan Yi Ke Da Xue Xue Bao. 1998;23(4):382-4.

23. Dasani BM, Sigal SH, Lieber CS. Analysis of risk factors for chronic hepatic encephalopathy: The role of *Helicobacter pylori* infection. Am J Gastroenterol. 1998;93(5):726-31.

24. Nilsson I, Lindgren S, Eriksson S, Wadstrom T. Serum antibodies to *Helicobacter hepaticus* and *Helicobacter pylori* in patients with chronic liver disease. Gut. 2000;46(3):410-4.

25. Huber M, Rossle M, Siegerstetter V, Ochs A, Haag K, Kist M, et al. Helicobacter pylori infection does not correlate with plasma ammonia concentration and hepatic encephalopathy in patients with cirrhosis. Hepato-gastroenterology. 2001;48(38):541-4.

26. Chang CS, Kao CH, Yeh HZ, Lien HC, Chen GH, Wang SJ. *Helicobacter pylori* infection and gastric emptying in cirrhotic patients with symptoms of dyspepsia. Hepatogastroenterology. 1999;46(30):3166-71.

27. Shimamoto C, Hirata I, Katsu K. Breath and blood ammonia in liver cirrhosis. Hepatogastroenterology. 2000;47(32):443-5.

28. Zullo A, Rinaldi V, Meddi P, Folino S, Lauria V, Diana F, et al. *Helicobacter pylori* infection in dyspeptic cirrhotic patients. Hepatogastroenterology. 1999;46(25):395-400.

29. Calvet X, Navarro M, Gil M, Mas P, Rivero E, Sanfeliu I, et al. Seroprevalence and epidemiology of *Helicobacter pylori* infection in patients with cirrhosis. J Hepatol. 1997;26(6):1249-54.

30. Zullo A, Rinaldi V, Meddi P, Hassan C, Winn S, Attili AF. *Helicobacter pylori* infection, plasma ammonia levels, and psychometric testing in cirrhotic patients. Am J Gastroenterol. 1999;94(8):2214-8.

31. Duseja A, Sachdev A, Dhiman R, Chawla Y. *Helicobacter pylori* and hepatic encephalopathy. Indian J Gastroenterol. 2003;22:31-2.

32. Zullo A, Hassan C, Morini S. Hepatic encephalopathy and *Helicobacter pylori*: A critical reappraisal. J clinic gastroenterol. 2003;37(2):164-8.

33. Gubbins GP, Moritz TE, Marsano LS, Talwalkar R, McClain CJ, Mendenhall CJ. *Helicobacter pylori* is a risk factor for hepatic encephalopathy in acute alcoholic hepatitis: The ammonia hypothesis revisited. The Veterans Administration Cooperative Study Group No. 275. Am J Gastroenterol. 1993;88(11):1906-10.