International Journal of Endorsing
HEALTH SCIENCE RESEARCH

IJEHSR

Original Article

Frequency of H. pylori in liver cirrhosis patients with overt Hepatic encephalopathy at tertiary care hospital, Karachi.

Shaista Ahmed[1], Afshan Siddiqui[2], Sadia Iqbal[2], Rma Waqas[3], Jamal Ara[1] & Aneela Altaf Kidwai[1]

[1]Karachi Medical and Dental College, Karachi-Pakistan.
[2]Dow University of Health Sciences, Karachi-Pakistan.
[3]Karachi Medical and Dental College, Karachi-Pakistan.

Doi: 10.29052/IJEHSR.v10.i3.2022.343-348
Corresponding Author Email: drafshansiddiqui@gmail.com
Received 02/03/2022
Accepted 14/06/2022
First Published 01/07/2022

OPEN ACCESS

Abstract

Background: Ammonia is detoxified in the liver, and hepatic insufficiency due to cirrhosis leads to raised ammonia, causing symptoms of Hepatic Encephalopathy (HE). Studies proclaim that Helicobacter pylori (H. pylori) accelerate ammonia production. The study objective was to establish the frequency of H. pylori in liver cirrhosis patients with overt HE.

Methodology: This cross-sectional study was conducted in Medical Unit-I Abbasi Shaheed Hospital, Karachi, from May to November 2018. Liver Cirrhosis patients between the ages of 31-60 years were selected via non-probability sampling. Patients of any sex suffering from liver cirrhosis for six months, as proved by ultrasound and overt HE diagnosed using West Haven Criteria, were included in the study. Stool samples were collected from patients in a sterile manner. Results of stool for H. pylori antigen were recorded. Data were analyzed using SPSS version 16.0.

Results: Out of 135 patients with Liver Cirrhosis with overt HE, 42 (31.1%) suffered from H. pylori infection while 93 (68.9%) patients did not. The mean age of patients was 44.14 ± 8.49 years. Stratification of the age of patients with H. pylori infection showed significant results (p=0.00). The mean disease duration was 4.72 ± 1.24 years. Stratification based on disease duration with H. pylori infection revealed significant results (p=0.00). Stratified findings based on Child-Pugh classification and H. pylori infection were insignificant (p=0.50).

Conclusion: Our study reveals there is less frequency of H. pylori infection amongst liver cirrhotic patients. However, amongst those infected, many had a longer duration of disease. Our study indicates more cases of H. pylori infection with increasing age of liver cirrhosis patients. Furthermore, the relation between H. pylori infection and the Child-Pugh classification indicates that overt HE may be attributed to factors other than H. pylori infection.

Keywords

Helicobacter Pylori, Hepatic Encephalopathy, Liver Cirrhosis.

Check for updates

Introduction

Liver diseases cause significant disability, morbidity, and mortality around the world. The most common consequence of chronic liver diseases that majorly affects the disease burden is liver cirrhosis. It is characterized by fibrosis of the liver parenchyma, disruption of the normal architecture of the liver, and formation of nodules[1]. In developed countries, namely the United States, liver cirrhosis-related mortality has increased. Etiologically, this increase in mortality is attributed to the increased consumption of alcohol and the development of alcoholic cirrhosis[2]. Contrary to this, Hepatitis C virus (HCV) infection is the main reason behind liver cirrhosis in developing countries such as Pakistan[3]. It is estimated that approximately 10 million people are infected with HCV in Pakistan, and they are all at risk of developing cirrhosis and its associated complications[4].

Overall the H. pylori infection is about 50% of the universal population and is more in third world countries with low socioeconomy[5,6]. The role of H. pylori in the progression of liver diseases, including liver cirrhosis, is a matter of interest to researchers worldwide. Interestingly enough, H. pylori has also been implicated in the pathogenesis of HE, which is a common complication occurring in about 30-70% of patients of liver cirrhosis[7,8]. HE is characterized by brain dysfunction and is classified based on the symptoms using the West Haven criteria (WHC), which divides it into five grades; Minimal HE and Grade 1 are attributed to Covert HE, and Grade 2-4 are attributed to overt HE[9]. The symptoms may be subtle as sleep disturbances, minor mental status, and personality changes to severe symptoms such as disorientation and asterixis, which signify but are not pathognomonic of overt HE[10].

Development of complications is associated with poor prognosis in patients of liver cirrhosis. Using the presence of complications (Ascites and HE), serum bilirubin, serum albumin, prothrombin time, and INR, the Child-Pugh (CP) classification determines the prognosis and severity of liver cirrhosis and classifies it into three categories; CP A, B, and C, with C being the most severe[11]. Pakistan has been declared a cirrhotic state by WHO as the prevalence of cirrhosis secondary to Hepatitis B and C virus infection is very high[12]. However, local data assessing the relationship between H. pylori and liver cirrhosis and its complications are scarce. This study aims to find out the frequency of H. pylori among cirrhotic patients with overt HE in a local settinghighlighting the problem in our society and opening doors for future studies.

Methodology

This cross-sectional study was conducted in Medical Unit – I of Abbasi Shaheed Hospital, Karachi, after approval from the ethical and scientific review committee of Karachi Medical and Dental College (Ref No. 019/17, 2018) from May to November, 2018. The sample size for frequency in a population was calculated using the WHO Sample Size Calculator by taking the prevalence of H. pylori in liver cirrhosis patients with overt HE at 78.57%[13]. With a confidence interval of 95% and a confidence limit of 7%, the required sample size was 135.

The adopted sampling technique for the study was non-probability consecutive sampling. Patients aged 31-60 years of either sex and suffering from liver cirrhosis for six months, as proved by their ultrasound now with overt HE, were included in the study. Patients were diagnosed having over HE by a consultant physician according to WestHaven Criteria with ≥ 2 parameters. Patients with known Diabetes Mellitus Type II, hypothyroidism, hyperthyroidism, or current pregnancy were not included. Patients with a history of peptic ulcer disease, secondary peritonitis, congestive cardiac failure, myocardial infarction, chronic renal failure, hepatocellular carcinoma, H. pylori eradication therapy in the past four weeks,or proton pump inhibitors in the past ten days were excluded as well. Informed consent was obtained from all participants of the study.

The researcher collected stool sample in a sterile manner from participants after obtaining a brief history. Samples were sent to the laboratory for H. pylori stool antigen. Data was collected on Performa, and the findings were analyzed on SPSS

version 16.0. Continuous variables such as age and disease duration were expressed as mean and standard deviation. At the same time, categorical data such as gender, CP, and H. pylori infection status were described with frequency and percentages. Age, gender, duration of disease, and CP class were made into strata. The Chi-square test was applied on strata, and a p-value ≤ 0.05 was considered significant.

Results

Patients with H. pylori infection in liver cirrhosis with overt HE were 42 (31.1%), while 93 (68.9%) patients did not have a simultaneous infection. Stratification of the age of patients with H. pylori infection showed 21 (30.9%) patients in the 31-40 years age group, 21 (60%) patients in 41-50 years age group, and none of the patients were in the 51-60 years age group had H. pylori infection. This was a significant finding with a p-value of 0.000, as in table 1.

There were 63 (46.7%) males and 72 (53.3%) females. Gender-based stratification for H. pylori infection showed male patients with H. pylori infection were 20 (31.7%). While females with H. pylori infection were 22 (30.5%), P-value was 0.51, which was insignificant.

The mean duration of disease in our study was 4.72 ± 1.24 years. Stratification based on disease duration with H. pylori infection is shown in table 1; the P-value was 0.000, which was significant.

Table 1: Distribution of H. pylori along with different age groups, disease duration, and severity.

Variables		Total patient (N=135)	H. pylori Present	H. Pylori Absent	p-value
Age	31 – 40 years	68(58.4)	21(30.9)	47(69)	0.000*
	41 – 50 years	35(25.9)	21(60)	14(40)	
	51 – 60 years	32(23.7)	-	32(100)	
Disease duration	1 – 2 years	53(39.3)	14(26.4)	39(28.9)	0.000*
	3 – 4 years	41(30.4)	7(17.1)	34(82.9)	
	5 – 6 years	28(20.7)	21(75)	7(25)	
	7 – 8 years	13(9.6)	-	13(100)	
Child-Pugh Class	A	28(20.7)	9(32.1)	19(67.9)	0.500
	B	43(31.9)	16(37.2)	27(62.8)	
	C	64(47.4)	17(21.9)	47(73.4)	

*p-value ≤ 0.05 is significant

Discussion

Due to this work, we come up with the frequency of H. pylori infection, specifically in cirrhotic patients with HE. Despite the fact that several studies proclaim an association between H. pylori and liver cirrhosis, the pathogenesis remains less known[14,15]. Normally, ammonia is detoxified in the liver; however, in cirrhotic patients with hepatic insufficiency, detoxification does not occur, which leads to shunting of ammonia-rich blood into the systemic circulation. Once ammonia crosses the blood-brain barrier, it causes brain edema, leading to HE symptoms[16-18]. The usual sources of ammonia include; urea and protein metabolism, deamination of glutamine in the gut, and nitrogenous products from the diet, but H. pylori adds to the ammonia production and is therefore thought to have a causal relationship with HE.

In our study, the frequency of H. pylori

infection in cirrhotic patients with hepatic encephalopathy was 31.1%. This contradicts another study done in Pakistan showing the frequency of 68%[19]. Similarly, Mahendra et al.[20], Shrimali et al.[13], and Maheshwari et al.[21] reported the frequency to be 56.25%, 78%, and 71%, respectively. Another recent study from Karachi showed an increased frequency of H. pylori infection in cirrhotics with Minimal, Hepatic Encephalopathy (MHE) compared to patients who did not have MHE[22]. Differences in results may be attributed to using different parameters for detecting H. pylori infection.

One possible reason for the paradoxical results is that different testing techniques were used in these studies to detect H. pylori, including serological testing and a Urea breath test. In contrast, the H. pylori stool antigen test was used in our study. Although stool test is a routinely used test, the urea breath test is known to have the highest accuracy among all non-invasive tests[23]. Furthermore, all the tests have different sensitivities.

Recent studies are exploring the effects of H. pylori eradication on HE. Amer et al.[24], Razik et al.,[25] and Elmataway et al.[26], in their study, concluded that H. pylori eradication therapy was associated with both; improvement of symptoms of MHE and reduction in the ammonia level[24]. Contrary to this, a local study revealed no improvement in symptoms of MHE after H. pylori eradication[22]. As the results are inconclusive and controversial, this warrants a need for large multicenter studies.

Regarding age, both liver cirrhosis and H. pylori infection occurs more commonly in older people[27,28]. Elucidating a relationship between the age of the cirrhotic patient and H. pylori infection, our study showed a statistically significant association between the two (p=0.00). Studies have shown that the presence of anti-H. pylori antibodies were independently and significantly associated with HCV-related liver cirrhosis, suggesting that H. pylori has a role in disease progression[14]. A significant association between the age of the patient and H. pylori in our study might suggest that progression of liver cirrhosis due to H. pylori is more in the older age groups as compared to the younger age groups, which is plausible because H. pylori is implicated in the progression of a wide spectrum of other age-related diseases too; including musculoskeletal, respiratory, metabolic and cardiovascular disorders[29].

The Child's Pugh classification is commonly used to assess the severity andultimately the prognosis of liver disease[11]. Our study did not reveal a significant association between the Child-Pugh classification and H. pylori infection. Many studies have used this classification to assess the relationship between disease severity and H. pylori infection. The study by Mohamed et al. revealed that H. pylori infection did not improve or worsen the prognosis of the liver disease[30], which strengthens the result of our study.

This is a valuable addition to the local literature on this subject and highlights the issue in a local context, but we had a few limitations in our study. Firstly, we took patients only suffering from overt HE; thus, one result could not be generalized for all grades. Secondly, we could not conclude that all etiologies of cirrhosis had the same risk of H. pylori as we did not incorporate different etiologies of cirrhosis. Thus we need consideration of further studies to look for the actual burden in different etiologies of cirrhosis and to assess the effect of H. pylori eradication on HE. This might not only help us halt the disease progression but will also contribute to preventing complications which will eventually

positively impact the mortality and morbidity rates due to liver diseases in Pakistan.

Conclusion

In conclusion, our study reveals there is less frequency of H. pylori infection amongst liver cirrhotic patients in Tertiary Care Hospital of Karachi. However, amongst those with simultaneous H. pylori infection, many had a longer duration of Liver Cirrhosis. Our research also shows that as patients with liver cirrhosis age, there are more and more cases of Helicobacter pylori infection. Furthermore, our study shows an insignificant association between H. pylori infection and Child-Pugh classification, indicating overt HE can be attributed to other factors besides H. pylori infection.

Conflicts of Interest

The authors have declared that no competing interests exist.

Acknowledgement

The authors like to acknowledge the support and assistance provided by Mr. M. Shoaib Shah.

Funding

The author(s) received no specific funding for this work.

References

1. Pinzani M, Rosselli M, Zuckermann M. Liver cirrhosis. Best Pract Res Clin Gastroenterol. 2011;25(2):281-290.
2. Tapper EB, Parikh ND. Mortality due to cirrhosis and liver cancer in the United States, 1999-2016: observational study. bmj. 2018;362.
3. Abubakar II, Tillmann T, Banerjee A. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015;385(9963):117-171.
4. Ullah A, Rehman IU, Ahmad J, Gohar M, Ahmad S, Ahmad B. Hepatitis-C Virus and Cirrhosis: An Overview from Khyber Pakhtunkhwa Province of Pakistan. Viral Immunol. 2020;33(5):396-403.
5. Peek RM, Blaser MJ. Helicobacter pylori and gastrointestinal tract adenocarcinomas. Nat Rev Cancer. 2002;2(1):28-37.
6. Kim SS, Ruiz VE, Carroll JD, Moss SF. Helicobacter pylori in the pathogenesis of gastric cancer and gastric lymphoma. Cancer letters. 2011;305(2):228-238.
7. Fagoonee S, Pellicano R. Helicobacter pylori: molecular basis for colonization and survival in gastric environment and resistance to antibiotics. A short review. Infect Dis. 2019;51(6):399-408.
8. Flamm SL. Complications of cirrhosis in primary care: recognition and management of hepatic encephalopathy. Am J Med Sci. 2018;356(3):296-303.
9. Weissenborn K. Hepatic encephalopathy: definition, clinical grading and diagnostic principles. Drugs. 2019;79(1):5-9.
10. Dellatore P, Cheung M, Mahpour NY, Tawadros A, Rustgi VK. Clinical manifestations of hepatic encephalopathy. Clin Liver Dis. 2020;24(2):189-196.
11. Kok B, Abraldes JG. Child–Pugh Classification: Time to Abandon?. Semin Liver Dis. 2019;39(1):96-103.
12. Afzal MS. Are efforts up to the mark? A cirrhotic state and knowledge about HCV prevalence in general population of Pakistan. Asian Pac J Trop Med. 2016;9(6):616-618.
13. Shrimali L, Chadda VS, Singh VB, Soni PK, Nayak KC, Gupta BK. Study of prevalence of H pylori in hepatic encephalopathy due to various liver diseases. J Indian Acad Clin Med. 2001;2(3):195-197.
14. Okushin K, Tsutsumi T, Ikeuchi K, Kado A, Enooku K, Fujinaga H, Moriya K, Yotsuyanagi H, Koike K. Helicobacter pylori infection and liver diseases: Epidemiology and insights into pathogenesis. World J Gastroenterol. 2018;24(32): 3617–3625.
15. Feng H, Zhou X, Zhang G. Association between cirrhosis and Helicobacter pylori infection: a meta-analysis. Eur J Gastroenterol Hepatol. 2014;26(12):1309-1319.

16. Elwir S, Rahimi RS. Hepatic encephalopathy: an update on the pathophysiology and therapeutic options. J Clin Transl Hepatol. 2017;5(2):142-151.
17. Patidar KR, Bajaj JS. Covert and overt hepatic encephalopathy: diagnosis and management. Clin Gastroenterol Hepatol. 2015;13(12):2048-2061.
18. Wijdicks EF. Hepatic Encephalopathy. N Engl J Med. 2016;375(17):1660-1670.
19. Ahmad S, Mahmood A, Khan HH, Ullah H, Ayub G, Sajjad Ali M. Helicobacter pylori as Initiating Factor in Patients of Cirrhosis with Concomitant Hepatic Encephalopathy. Ann Med Medical Res. 2020; 3.;1031.
20. Singh MP, Yadav AK, Singh B, Gautam A. Prevalance of H. Pylori infection in patients of cirrhosis of liver with its etiological correlation. JMSR. 2022;10(2):60-66
21. Maheshwari BK. Frequency of Helicobacter pylori among hepatic encephalopathic patients in liver cirrhosis. JLUMHS. 2012;11(02):93-96.
22. Abid S, Kamran M, Abid A, Butt N, Awan S, Abbas Z. Minimal Hepatic Encephalopathy: Effect of H. pylori infection and small intestinal bacterial overgrowth treatment on clinical outcomes. Sci rep. 2020;10(1):1-7.
23. Skrebinska S, Mégraud F, Bessède E. Diagnosis of Helicobacter pylori infection. Helicobacter. 2018;23:e12515.
24. Amer ME, Abdel Khalik MA, Khedr MA, Massoud SA. Effect of helicobacter pylori eradicationon the pathogenesis of minimal hepatic encephalopathy in egyptian patients with liver cirrhosis. J Egypt Soc Parasitol. 2018;48(3):583-586.
25. Abdel-Razik A, Mousa N, Elhelaly R, Elzehery R, Hasan AS, Abdelsalam M, Seif AS, Tawfik AM, El-Wakeel N, Eldars W. Helicobacter pylori as an initiating factor of complications in patients with cirrhosis: a single-center observational study. Front Med. 2020;7:96.
26. Elmaltawy MA, Khayyal AS, Osama Aly M, Elghandour HA. The Role of Helicobacter Pylori Eradication on the Pathogenesis of Minimal Hepatic Encephalopathy in Egyptian Patients with Liver Cirrhosis. QJM. 2021;114(Supplement_1):hcab100-068.
27. Shi H, Xiong H, Qian W, Lin R. Helicobacter pylori infection progresses proximally associated with pyloric metaplasia in age-dependent tendency: a cross-sectional study. BMC gastroenterol. 2018;18(1):1-7.
28. Scaglione S, Kliethermes S, Cao G, Shoham D, Durazo R, Luke A, Volk ML. The epidemiology of cirrhosis in the United States. J clin gastroenterol. 2015;49(8):690-696.
29. Zendehdel A, Roham M. Role of Helicobacter pylori infection in the manifestation of old age-related diseases. Mol Genet Genomic Med. 2020;8(4):e1157.
30. Mohamed AA, Elshimy AA, El Sadik AO, Ezzat E, Nasar M, Elshaer SS, Sayed MM. Association between severity of liver disease, frequency of Helicobacter pylori infection, and degree of gastric lesion in Egyptian patients with hepatitis B virus infection. Am J Trop Med. 2018;98(1):221-226.