Prevalence of Helicobacter Pylori among Patients with Minimal Hepatic Encephalopathy and the Effect of its Eradication

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Abbreviation

BCAA ..... Branched chain amino acid
Cag PAI .....Cag pathogenicity island
CDR.....Cognitive drug research
CFF ..... Critical flicker frequency
CHESS..... Clinical hepatic encephalopathy scoring scale
EEG .....Electroencephalogram
GABA..... Gama amino butyric acids
H.pylori.....helicobactor pylori
HE..... Hepatic encephalopathy
HpSA .....H.pylori stool antigen
LOLA ..... L-ornithin L-aspartate
MHE ..... Minimal hepatic encephalopathy
miR-١٥٥.....Micro RNA-١٥٥
MMSE ..... Mini mental state examination
Mn..... Manganese
MyD٨٨.....Myeloid differentiation protein ٨٨
NCT .....Number connection test
NMDA..... Nmethyl-D aspartate
OHE..... Overt hepatic encephalopathy
PET..... Positron emission tomography
PHES ..... Psychometric hepatic encephalopathy score
RBANS..... Repeatable battery for assessment of neurological status
SD ..... Standard deviation
TIPS..... Transjagular intrahepatic porto-systemic shunt
Vac A.....Vacuolating cytotoxin A

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Introduction

Hepatic encephalopathy (HE) is a frequent complication of liver cirrhosis. Although the exact pathogenesis of hepatic encephalopathy is unknown, accumulation of ammonia from poor hepatic function and porto-systemic shunts has been implicated as a primary factor ***(Dubois et al., ٢٠٠٩).***

Some patients have minimal hepatic encephalopathy (MHE), which is not discernible at clinical examination but can be detected using sensitive tests of coordination, such as number connection tests (NCT), figure connection test (FCT) and line tracing test, electroencephalography and visual, auditory, and somatosensory evoked potentials ***(Agrawal et al., ٢٠١١).***

The term minimal hepatic encephalopathy (MHE) refers to the subtle changes in cognitive function, electrophysiological parameters, cerebral neurochemical/neurotransmitter homeostasis, cerebral blood flow, metabolism, and fluid homeostasis that can be observed in patients with cirrhosis who have no clinical evidence of hepatic encephalopathy ***(Nava and Delgadillo, ٢٠١١).***

Helicobacter pylori is the most common chronic bacterial infection in humans worldwide. The prevalence of H.pylori infection is high in developing countries (٨٠-٩٠٪) and lower in developed countries (١٠-٣٠٪) ***(Bureš and Kopáčová, ٢٠١١).***

H.pylori infection is an important factor of inducing high blood ammonia concentration and hepatic encephalopathy in cirrhotic patients. H.pylori eradication may be helpful for treatment and prevention of HE ***(Wang et al., ٢٠٠٦)***.

In patients with liver cirrhosis, there is a significant association between H. pylori infection and MHE. Anti-H. pylori therapy results in reduction in blood ammonia levels and improvement in MHE ***(Agrawal et al., ٢٠١١).***

The literature contains conflicting data, with several other studies showing ammonia levels do not significantly differ between cirrhotic patients with and without H pylori infection. Ammonia production in the stomach by H pylori urease appears to be inadequate to clinically affect ammonia disposal in the majority of cirrhotic patients ***(shu-jie et al., ٢٠٠٨).***

Aim of the Study

The aim of the present study is to assess the prevalence of H. pylori infection among patients with minimal and overt hepatic encephalopathy and to determine the effect of its eradication in those with minimal hepatic encephalopathy.

Hepatic Encephalopathy

Introduction

Hepatic encephalopathy (HE) is a neuropsychiatric syndrome in patients with liver disease and/or portosystemic shunting that affects quality of life and prognosis. HE is caused by disorders that affect the liver. These include disorders that reduce liver function (such as cirrhosis or hepatitis) and conditions in which blood circulation does not enter the liver ***(Garcia, ٢٠١١).***

HE can be classified as either overt or minimal. Overt HE is a syndrome of neurological and neuropsychiatric abnormalities that can be detected by bedside clinical tests. By contrast, patients with minimal HE (MHE) present with normal mental and neurological status upon clinical examination but specific psychometric tests yield abnormal results ***(Shawcross et al., ٢٠٠٧).***

Classification:

The World Congress of Gastroenterology has categorized HE based on underlying hepatic abnormalities, and for patients with cirrhosis it can be further subdivided by the duration and characteristics of neurologic dysfunction. The three types of HE are A, B, and C which are associated with acute liver failure,

porto-systemic Bypass without intrinsic liver disease, and Cirrhosis, respectively ***(Al Sibae and McGuire, ٢٠٠٩).*** (Table ١).

Table (١): Types of hepatic encephalopathy ***(Munoz, ٢٠٠٨)***

Type A	Encephalopathy from acute liver failure
Type B	Encephalopathy caused by portosystemic shunting, without intrinsic liver disease
Type C	Encephalopathy of cirrhosis associated with portosystemic shunting:
	Episodic: precipitated, spontaneous, or recurrent
	Resistant: mild, severe, treatment-dependent
	Minimal: previously known as "subclinical"

Encephalopathy has been further subdivided, based on duration and characteristics of neurologic dysfunction, into episodic, persistent, and minimal subtypes. Episodic HE occurs over a short time span and fluctuates in severity. Persistent HE is a chronic clinical condition of cognitive deficits that affects social and occupational functioning. Minimal HE is associated by subtle cognitive impairments of attention, response inhibition and executive function ***(Al Sibae and McGuire, ٢٠٠٩).***

Table (٢): Clinical presentation of hepatic encephalopathy ***(Seyan et al., ٢٠١٠)***

Encephalopathy	Definition
Acute	Acute liver dysfunction
Recurrent or episodic	Episodes of mental alteration in a patient with cirrhosis, even in the absence of known precipitating factor
Persistent	Neurological deficit that persists despite the reversal of liver injury, such as liver transplantation or the removal of a precipitating factor
Minimal (previously known as subclinical)	No evidence of overt encephalopathy, but subtle cognitive deficit might be detected with a neuropsychological

In cirrhotic patients who were followed from a time when the disease was compensated, HE represents, in fact, the second most frequent cause of decompensation after ascites and before variceal bleeding. HE is particularly frequent in patients undergoing porto-systemic shunt, and is considered an important prognostic factor for survival ***(Bajaj, ٢٠٠٨).***

A generic hypothesis proposes that the symptoms are caused by the loss of a "protective" mechanism exerted by the liver on brain functions. As an effect of liver failure and porto-systemic shunting, substances arising from the gut are able to reach the systemic circulation and the central nervous system, where they can exert a "toxic effect" on brain function ***(Riggio et al., ٢٠٠٨).***

The Astrocyte swelling hypothesis is able to explain one of the key features of HE. It has been recently proposed that neutrophils, in addition to ammonia, may be involved in the pathogenesis of HE. Thus, neutrophils can be a target for future anti-inflammatory therapeutic strategies in addition to ammonia lowering therapies ***(Shawcross et al., ٢٠١٠).***

HE is reversible with treatment. This relies on suppressing the production of the toxic substances in the intestine and is most commonly done with the laxative lactulose or with non-absorbable antibiotics. In addition, the treatment of any underlying condition may improve the symptoms. In particular settings, such as acute liver failure, the onset of encephalopathy may indicate the need for a liver transplant ***(Cash et al., ٢٠١٠).***