Relation between fecal calprotectin concentration and severity of hepatitis c (HCV) related chronic liver disease

Thesis

Submitted for Partial Fulfillment of Master Degree
In Tropical Medicine

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بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم

صدق الله العظيم

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LIST OF ABBREVIATIONS

ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
Anti-LKM1	Anti Liver Kidney Muscle 1
anti-HCV	HCV antibody
ANA	Antinuclear Antibodies
ASMA	Anti Smooth Muscle Antibodies
ANCA	Anti-Nuclear Cytoplasmic Antibodies
BMI	Body Mass Index
bDNA	Branched DNA
CTL	Cytotoxic T lymphocytes
CHC	Chronic hepatitis C
ELISA	Enzyme Linked Immunoabsorbent Assay
ESR	Erythrocyte sedimentation rate
FCCs	Fecal calprotectin concentrations
GGT	Gamma-glutamyl transferase
HLA	Human Leukocytic Antigen
HIV	Human Immunodeficiency Virus
HBV	Hepatitis B Virus
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C virus
IL	Interleukin
MHC	Major Histocompatibility Complex
MELD	Model for End Stage Liver Disease
NAFLD	Nonalcoholic fatty liver disease
PCR	Polymerase Chain Reaction
RF	Rheumatoid Factor
RIBA	Recombinant Immunoblot Assay
ROC	Receiver Operating Characteristic

S	Significant
SD	The standard deviation
TLC	Total leukocytic count
TNF-α	Tumor Necrosis Factor alpha
TNF-γ	Tumor Necrosis Factor gamma
WBCs	White blood cells

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INTRODUCTION

Egypt has one of the highest prevalence rates of hepatitis C virus (HCV) infection in the world. The HCV epidemic appears to have been initiated by vigorous public-health campaigns using intravenous tartar emetic from the 1950s until 1982 to eradicate schistosomiasis (***Frank et al., 2000***). This iatrogenic mode of infection has now resulted in a high incidence of hepatic morbidity and mortality from the late complications of HCV infection, such as chronic hepatitis, cirrhosis and hepatocellular carcinoma (HCC) ***(Strickland et al., 2002; El-Zayadi et al., 2005***).

Complications of liver cirrhosis especially hepatic encephalopathy represent a major impact among hepatic patients. The prevalence of hepatic encephalopathy (HE) in patients with liver cirrhosis is considered high and can be diagnosed in up to 80% of all cirrhotic patients ***(McPhail et al 2010)***. Another study demonstrated that bacterial overgrowth is a responsible factor for minimal hepatic encephalopathy in cirrhotic patients ***(Gupta. et al 2010)***.

From the pathophysiological point of view, numerous alterations in intestinal flora, mucosal barrier functions and immunological defense mechanisms occur in cirrhotic patients ***(Wiest et al 2005)***; this leads to bacterial overgrowth ranging from 30% to 64% and seems to represent one of the main factors to trigger bacterial translocation ***(Bauer et al 2002, Gunnarsdottir et al 2003)***. The gut flora and bacterial translocation play an important role in the pathogenesis of certain complications of cirrhosis like hepatic encephalopathy ***(Garcia et al 2004)***.

Calprotectin is a calcium and zinc-binding peptide, proposed as a biomarker for various inflammatory diseases due its potential role in pathophysiology of inflammation and associated outcomes like tissue destruction, apoptosis and growth impairment. As an acute phase reactant, calprotectin increases more than 100 folds during inflamed conditions (***Golden et al 1996***).

Calprotectin is found in monocytes (***Rammes et al 1997***), keratinocytes (***Johne et al 1997***), muscle tissue (***Mortensen et al 2008***) and infiltrating tissue macrophages (***Newton et al 1998***). Calprotectin is also found abundant in neutrophils

(***Boussac et al 2000***) and it constitutes 30-60% of the cytosolic proteins (***Hessian et al 1993***).

Once get stimulated by an injury or cell disruption, neutrophils and monocytes start secreting calprotectin into the extra cellular fluid (***Stritz al 2004***). Accordingly, the presence of fecal calprotectin quantitatively relates to intestinal neutrophil migration ***(Vermeire et al 2006)*** and is therefore, it may be considered as a valid marker of intestinal inflammation ***(D' Inca et al 2008)***. As the gastrointestinal tract of cirrhotic patients shows various alterations of its mucosal barrier including infiltrates of neutrophils, calprotectin might be a promising diagnostic parameter to diagnose the onset of hepatic encephalopathy ***(Gundling et al 2011)***.

Aim of the Work

This study aims to assess the relation between fecal calprotectin concentration and severity of HCV related chronic liver disease.

Patients and Methods

Patients:

Study design: Prospective study.

Sample size: Sample size 50 cases.

This study will be performed in Ain shams university hospital and Alexandria university hospital.

The enrolled patients will be divided into 2 groups:

- **Group 1:** 30 patients with HCV related chronic liver disease who will be admitted to the hospital will be invited to enter this study.
- **Group 2:** 20 of healthy Control group.

Informed consent will be obtained from all patients who will be included in the study.