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تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

Amyloid A in serum and ascetic fluid as a marker of spontaneous bacterial peritonitis

Thesis

Submitted in Partial Fulfillment for the Requirement of Master Degree

In Internal medicine

By

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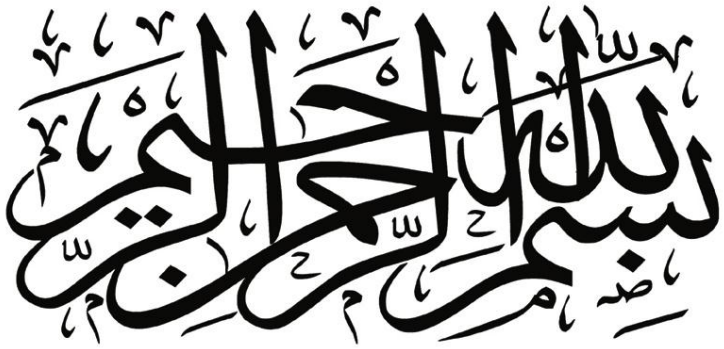

قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا
إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

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I'd like to dedicate this work to my lovely family; without them I'm nothing.

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AFLAC	Ascitic fluid lactoferrin
APP	acute phase protein
APR	the acute phase response
A-SAA	Acute-phase reactant serum amyloid
AUO	amyloid of unknown origin
C/EBP	CCAAT/enhancer-binding protein
CNNA	culture-negative neutrocytic ascites
CRP	C-reactive protein
DIC	disseminated intravascular coagulation
DRE	distal response element
EDTA	ethylene diamine tetraacetic acid
fMLP	formyl-methionyl-leucyl-phenylalanine
GRE	glucocorticoid-responsive elements
HDL	high-density lipoprotein
HMG1	high mobility group 1 box
IFN-γ	Interferon-γ
IL-1β	Interleukin-1β
LDL	low-density lipoprotein
M1	mediate feedback inhibition
MDSC	myeloid-derived suppressor cells
MMP	matrix metalloproteinase
MNB	
NLR	Neutrophil-to-lymphocyte ratio
NSBB	namely nonselective beta-blocker
PAMPS	Pattern recognition receptors on cell surfaces
PCR	
PMN	polymorphonuclear
PPI	Proton pump inhibitors
RAGE	receptor for advanced glycation end products
SAA	Serum amyloid A
SAAG	serum-ascites albumin gradient
SAF	SAA activating factor
SBP	Spontaneous Bacterial Peritonitis
SEF	SAA3 enhancer factor
SIRS	Systemic Inflammatory Response
SNP	single nucleotide polymorphism

TLR2	Toll-like receptor 2
TNF	tumor necrosis factor
US	ultrasound

ABSTRACT

Background; Diagnosis of Spontaneous Bacterial Peritonitis (SBP) depends mainly on ascetic fluid culture which may be negative in spite of the clinical suggestion of SBP and high ascetic fluid neutrophilic count, **Aim and objectives;** to assess the role of the clinical usefulness of the Amyloid A (serum and ascetic fluid) in patients with ascites (liver cirrhosis) and as a diagnostic marker for Spontaneous Bacterial Peritonitis, **Subjects and methods;** This is a Case-Control study, was conducted at Internal medicine and Gastroentrology outpatient clinics and ward in Ainshams University Hospitals and Shurook Hospital, on 50 patients divided into 2 groups; (group1): included 25 patients diagnosed with liver cirrhosis and ascites with spontaneous bacterial peritonitis (SBP), (group2): included 25 control subjects diagnosed with liver cirrhosis and ascites, **Result;** there was high statistically significant difference between the studied groups as regard amyloid, **Conclusion**; Although many research works showed the role of acute phase reactant (C-reactive protein (CRP) and Serum amyloid A (SAA)) in the inflammatory process and bacterial infections, this study focused on spontaneous bacterial peritonitis and assess the role of the clinical usefulness of the Amyloid A (serum and ascetic fluid) in patients with ascites (liver cirrhosis) and as a diagnostic marker for Spontaneous Bacterial Peritonitis, **Keywords; Ascitic fluid, bacterial infections, C-Reactive Protein (CRP), diagnostic marker, Serum Amyloid A (SAA), Spontaneous Bacterial Peritonitis (SBP).**

INTRODUCTION

Liver cirrhosis is a severe disease of the digestive system, associated with many complications, poor prognosis, and a high rate of morbidity and mortality worldwide. The main causes of chronic liver disease include infection by hepatitis B virus and hepatitis C virus, excessive alcohol consumption, primary biliary cirrhosis, and autoimmune liver disease ***(Bosch et al., 1999).***

Chronic liver disease frequently progresses to liver cirrhosis, following different processes that involve liver cell degeneration and extensive necrosis (**Lee et al., 1997).**

Cirrhosis is characterized by advanced fibrosis, scarring, and formation of regenerative nodules leading to architectural distortion. In the past cirrhosis was generally thought to be irreversible but recent studies have shown that treatments aimed at the underlying cause especially in earlier stages of the disease can improve or even reverse fibrosis ***(Salman et al., 2014).***

Ascites is the most common complication of cirrhosis ***(Ginés et al., 1987).*** It is also the most common complication that leads to hospital admission ***(Lucena et al., 2002).*** Approximately 15% of the patients with ascites will die in one year and 44% will die in five years ***(Groszmann et al., 2004).***

Ascites is defined as accumulation of more than 25 ml of fluid in the peritoneal cavity. In Western countries, development of ascites is in 75% of cases due to underlying cirrhosis but other less common etiologies of ascites such as malignancy, congestive heart failure, Budd

Chiari syndrome, tuberculosis and pancreatitis should be considered – especially if ascites is the first presenting symptom ***(Julie et al., 2015).***

Ascites is transudative and contains agents with a low immune activity, providing a good environment for pathogen growth. The risk factors for the incidence and mortality of patients with spontaneous bacterial peritonitis (SBP) have been comprehensively described. A high bilirubin level, a low ascitic fluid protein concentration, and an episode of variceal haemorrhage are strongly associated with SBP occurrence ***(Dever et al., 2015).***

Spontaneous peritonitis is one of the most common infectious complications, with mortality from 10% to 46% at 1 year in cirrhotic patients with ascites ***(Chun-Hong Huang et al., 2019).***

Spontaneous bacterial peritonitis is the most frequent bacterial infection in patients with cirrhosis. The reported incidence varies between 7% and 30% in hospitalized patients with cirrhosis and ascites ***(Sebastián et al., 2019).***

The factors that predisposes cirrhotics to infections are not well defined but following mechanism have been suggested (1) portal hypertension results in creation of porto-systemic anastomosis, diverting blood that would normally go to the liver and thus impairing detoxification; (2) dysfunction of reticuloendothelial system; (3) impaired neutrophil phagocytosis; and (4) bacterial translocation resulting from bacterial overgrowth and intestinal barrier dysfunction ***(Salman et al., 2014).***

Commonly used diagnostic parameters like C-reactive protein and Systemic Inflammatory Response (SIRS) criteria have limited value

secondary to decreased number of baseline polymorphnuclear leucocytes, elevated heart rate at baseline, baseline hyperventilation and blunted elevation of body temperature. This can delay diagnosis and worsen outcomes thus a high level of suspicion is warranted ***(Cazzaniga et al., 2009 and Levy et al., 2010).***

Serum amyloid A (SAA) plays a critical role in acute or chronic and is used in clinical laboratories as an indicator of inflammation. The elevated SAA is closely related to inflammation-mediated diseases, such as liver diseases, autoimmune diseases, metabolism-related diseases, amyloidosis, and tumors ***(Liu Q et al., 2019).***

Serum amyloid A (SAA) protein is a major acute phase protein (APP), which belongs to the apolipoprotein family ***(Lannergard et al., 2003)***. Serum amyloid A (SAA) are associated with high-density lipoprotein (HDL) in plasma. Different isoforms of SAA are expressed constitutively (constitutive SAAs) at different levels or in response to inflammatory stimuli (acute phase SAAs). These proteins are produced predominantly by the liver ***(Uhlar et al., 1999).***

SAA was also found as one of the major acute-phase proteins that are produced in large quantities by hepatocytes and released to blood circulation in response to trauma, infection, late-stage malignancy and severe stress ***(Yu Fan et al., 2019).***

During the acute phase response (APR), many cytokines induce its production by hepatocytes mainly but extrahepatic production has also been documented. For many years, SAA was a protein without function, but today is known that, in the course of acute inflammation, it stimulates the immune cell chemotaxis and cytokines production, inhibits bacterial