

The study of Prognostic Factors in Resistant Spontaneous Bacterial Peritonitis in Cirrhotic Patients

Thesis

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

صدق الله العظيم

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List of Abbreviations

AFP	Alpha Feto protein
AKI	Acute kidney injury
AMR	Antimicrobial resistance
ASPs	Antimicrobial stewardship programs
ATB	Antibiotics
AUROC s	Area under the Receiver Operating Characteristic
BC	Blood culture
BCAA	Branched-chain amino acids;
BT	Bacterial translocation
BUN	Blood urea nitrogen
CAIDS	Cirrhosis-associated immune dysfunction syndrome
CI	Confidence interval
CNNA	Culture-negative neutrocytic ascites
CRP	C- Reactive protein
DIC	Disseminated Intravascular Coagulation
DNA	Deoxyribonucleic Acid
E. coli	Escherichia coli
EDTA	ethylenediaminetetraacetic
ELISA	Enzyme Linked immunesorbent Assay
ESBL	Extended-spectrum β -lactamase
ESLD	End-stage liver disease;
GI	Gastrointestinal
GNB	Gramnegative bacteria
HCC	Hepatocellular carcinoma
IL	Interleukins

IP Interferon- γ -induced protein
IV Intravenous
KP Klebsiella Pneumonie
KPC Klebsiella Pneumonie carbapenemase
LEERS Leukocyte esterase reagent strips
LR Likelihood ratio
LT Liver transplantation
LVP Large volume paracentesis;
MDR Multidrug resistant
MELD Model for End-Stage Liver Disease
MIP-1 β Macrophage inflammatory protein type 1 beta
MLN Mesenteric lymph nodes
MRP Multidrug resistant proteins
MRSA Methicillin-resistant Staphylococcus aureus
NGAL Neutrophil gelatinase-associated lipocalin
NK Natural Killer
NOD2 Nucleotide-binding oligomerisation domain 2
NSBB Nonselective beta-blocker
PCN Penicillin;
PCT Procalcitonin
PMN Polymorphonuclear cells
PPI Proton pumps inhibitors
RBC Red blood cells
RCT Randomized controlled trial
RES Reticuloendothelial system
RSBP Resistant spontaneous bacterial peritonitis

SAAGSerum to Ascites Albumin Gradient
SBPSpontaneous bacterial peritonitis
SIRSSystemic inflammatory response syndrome
SPPSpecies
SSTI.....Skin and Soft Tissue infection
TBTuberculosis
TIPSTransjugular intrahepatic portosystemic shunt
TLR.....Toll-like receptor
TNFTumor necrosis factors
TREM-1.....Triggering receptor expressed on myeloid cells 1
TZPTazobactam–piperacillin
UNOSUnited Network for Organ Sharing
USUltrasound
UTIUrinary tract infection
VRE.....Vancomycin-resistant enterococci
WBC.....White blood cell
WHOWorld Health Organization
XDR.....Extensive Drug Resistant

INTRODUCTION

The most common complication in cirrhosis is ascites that occurs in approximately 60% of patients with compensated cirrhosis in a ten-year period of diagnosis. The development of ascites is a landmark in the natural history of cirrhosis, since the mortality is 40% in one year and 50% in two years (**Runyon, 2009**). Moreover, it carries a poor prognosis and impairs quality of life recommending patient evaluation by a Liver Transplantation team as soon as possible (**Tandon P and Garcia-Tsao, 2008**).

Bacterial infections, such as spontaneous bacterial peritonitis (SBP), are worrisome in cirrhotic patients since it is known that 30% to 50% of them either have bacterial infection when admitted to a hospital or acquire them during this period with a mortality rate of near 25% in this population. SBP is one of the most common infection in cirrhotic patients (**Da Rocha Ribeiro et al., 2016**).

SBP has been considered a life-threatening infection that requires a prompt diagnosis and treatment. In-hospital mortality for the first SBP episode varies from 10% to 50%. The recurrence rate is also high and one-year mortality rate after the first episode of SBP has been estimated to be between 31% and 93%. The worse scenario in the prognosis

of a cirrhotic patient after an episode of infection has been proposed since that a new prognostic stage of cirrhosis, not reflected by the existing staging systems, should be defined, as the so-called “critically ill cirrhotic” (**Arvaniti et al., 2010**).

Cirrhotic patients have a higher risk of developing bacterial infections, sepsis, severe sepsis and therefore death. Alterations in microbiota and intestinal permeability, functional impairment of the reticuloendothelial system, neutrophilic dysfunction, impairment in opsonization of ascitic fluid and immune dysfunction are findings that make these patients susceptible to the emergence of infectious complications. Cirrhosis-associated immune dysfunction syndrome (CAIDS) is a multifactorial state of systemic immune dysfunction, which decreases the capacity of clearing cytokines, bacteria and endotoxins from circulation which associated with portosystemic shunts allow fewer bacteria and endotoxins to be cleared by the liver from circulation. The development of bacterial infection exacerbates pre-existing circulatory dysfunction, predisposes early onset of renal dysfunction, expressed by hepatorenal syndrome, and triggers an overstressed pro-inflammatory response which can lead to organ failure (acute on chronic liver failure) (**Nadim et al., 2015**).

In the past few years the epidemiology of bacterial infection in cirrhotic patients has changed dramatically. Initially, SBP occurred in up to 30% of patients with cirrhosis and ascites, and had an estimated in-hospital mortality of 20%. The prevalence of SBP in outpatients cirrhotic is estimated in 1.5% to 3.5% and in inpatients is about 10%. Recent studies have shown that 60% of bacterial infections are community acquired and 40% are nosocomial **(Pleguezuelo et al., 2013)**.

Furthermore, several studies from different geographical areas, have reported a significant increase in the number of infections caused by multiresistant bacteria. The SBP prophylaxis with quinolones and other types of antibiotics, invasive procedures during hospitalization and the stay of cirrhotic patients in healthcare facilities are associated with a change in bacterial flora in these patients. More recent studies highlight the increasing emergence of gram positive cepas as quinolone-resistant organisms **(Da Rocha Ribeiro et al., 2016)**.

AIM OF THE WORK

The aim of our study is:

- To evaluate the effect of certain prognostic factors namely Child -Pugh score, MELD Score and isolated organisms by bacterial cultures responsible for resistant spontaneous bacterial peritonitis in patients with liver cirrhosis.
- To Identify organisms that responsible for resistant SBP will guide in modification of antimicrobial treatment regimen and changing the antibiotic protocol administered to those patients.