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

Thesis

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قَالُوا سُبْحَانَكَ
لاَ عِلْمَ لَنَا
إِلاَّ مَا عَلَّمْتَنَا
إِنَّكَ أَنتَ
الْعَلِيمُ الْحَكِيمُ
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List of Abbreviations

AFP ..... Alpha Feto protein

AKI..... Acute kidney injury

AMR..... Antimicrobial resistance

ASPs ..... Antimicrobial stewardship programs

ATB ..... Antibiotics

AUROCs ..... 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..... Klepsiella Pneumonie

KPC..... Klepsiella Pneumonie carbapenemase

LERS..... Leukocyte esterase reagent strips

LR..... Likelihood ratio

LT..... Liver transplantation

LVP ..... Large volume paracentesis;

MDR..... Multidrug resistant

MELD ..... Modelfor End-Stage Liver Disease

MIP-1β ..... 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

SAAG ..... Serum to Ascites Albumin Gradient

SBP ..... Spontaneous bacterial peritonitis

SIRS ..... Systemic inflammatory response syndrome

SPP ..... Species

SSTI..... Skin and Soft Tissue infection

TB ..... Tuberculosis

TIPS ..... Transjugular intrahepatic portosystemic shunt

TLR ..... Toll-like receptor

TNF ..... Tumor necrosis factors

TREM-1 ..... Triggering receptor expressed on myeloid cells 1

TZP ..... Tazobactam–pipercillin

UNOS ..... United Network for Organ Sharing

US ..... Ultrasound

UTI ..... Urinary tract infection

VRE..... Vancomycin-resistant enterococci

WBC..... White blood cell

WHO ..... World 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.