Frequency, Clinical Profile, Bacteriologic Patterns and Outcome of Ascitic Fluid Infection in Patients with Chronic Liver Disease in Tropical Medicine Department at Ain Shams University Hospitals

Thesis

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Hazem Ahmed Kamal

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List of Abbreviations

Abb.	Full term

ADA .....*Ascitic Fluid Deaminase Activity*
ADH.....*AntiDiuretic Hormone*
AFI.....*Ascitic Fluid Infection*
AIH .....*AutoImmune Hepatitis*
AKI .....*Acute Kidney Injury*
AMA.....*AntiMitochondrial Antibody*
ANA .....*AntiNuclear Antibody*
AP .....*Alkaline Phosphatase*
CBC.....*Complete Blood Count*
CCM .....*Cirrhotic Cardiomyopathy*
CLD.....*Chronic Liver Disease*
CNNA .....*Culture-Negative Neutrocytic Ascites*
CRP.....*C-Reactive Protein*
DAMPs .....*Danger Associated Molecular Patterns*
DHS .....*Demographic Health Survey*
DILI .....*Drug Induced Liver Injury*
DNA .....*DeoxyriboNucleic Acid*
E. Coli.....*Escherichia coli*
ELISA .....*Enzyme Linked Immunosorbent Assay*
ERCP .....*Endoscopic Cholangiopancreatography*
FLI .....*Fatty Liver Index*
FVLM .....*Factor V Leiden Mutation*
GGT .....*Gamma-Glutamyltranspeptidase*
HBcAg .....*Hepatitis B Core Antigen*
HBsAg .....*Hepatitis B Virus Envelope*
HBV .....*Hepatitis B Virus*
HCC .....*Hepatocellular Carcinoma*
HCV .....*Hepatitis C Virus*
HIS .....*Hepatic Steatosis Index*

List of Abbreviations (Cont...)

Abb.	Full term
HPS	*Hepato-Pulmonary Syndrome*
HRS	*Hepatorenal Syndrome*
HSCs	*Hepatic Stellate Cells*
HVPG	*Hepatic Venous Pressure Gradient*
IFL	*Indirect Immunofluourescence*
IgM	*Immunoglobulin M*
INR	*International Normalized Ratio*
LDH	*Lactate Dehydrogenase*
LERS	*Leukocyte Esterase Reagent Strips*
LFS	*Liver Fat Score*
LKM	*LiverKidney Microsome*
LVP	*Large Volume Paracentesis*
MELD	*Model for End-stage Liver Disease*
MNB	*Monomicrobial Non-Neutrocytic Bacterascites*
MRCP	*Magnetic Resonance Cholangiopancreatography*
MRSA	*Methicillin-Resistant Staphylococcus Aureus*
MTHFR	*Methylene Tetrahydrofolate Reductase*
NAFLD	*Nonalcoholic Fatty Liver Disease*
NASH	*Non-Alcoholic Steatohepatitis*
NAT	*Nucleic Acid Tests*
NF-κB	*Nuclear Factor-Kappa B*
NO	*Nitric Oxide*
PAMPs	*Pathogen Associated Molecular Patterns*
PBC	*Primary Biliary Cirrhosis*
PCR	*Polymerase Chain Reaction*
PMN	*Polymorphonuclear Leukocytes*
PNPLA3	*Patatin-Like Phospholipase Domain-Containing 3*
PPHT	*Portopulmonary Hypertension*

List of Abbreviations (Cont...)

Abb.	Full term
PSC	*Primary Sclerosing Cholangitis*
PTEN	*Phosphatase and Tensin Homolog*
RNA	*RiboNucleic Acid*
SAAG	*Serum-Ascites Albumin Gradient*
SBP	*Spontanous Bacterial Peritonitis*
SBEM	*Spontaneous Bacterial Empyema*
SLA/LP	*SolubleLiver Antigen/Liver-Pancreas*
SMA	*Smooth Muscle Antibody*
T2DM	*Type 2 Diabetes Mellitus*
TIPS	*Transjugular Intrahepatic Portosystemic Shunt*
TLR-4	*Toll-Like Receptor 4*
TyG	*Triglyceride × Glucose*
VAI	*Visceral Adiposity Index*
VEGF	*Vascular Endothelial Growth Factor*
WHO	*World Health Organization*

ABSTRACT

The ascitic culture and sensitivity taken from the studied patients showed that 74% of patients with infected ascites had culture negative neutrocytic ascites, 22% of patients with infected ascites had monomicrobial bacterascites and 4% of patients with infected ascites had polymicrobial bacterascites. *E.coli* was the most frequently isolated micro-organism (7%).

As regards the upper gastrointestinal endoscopy, 30% of patients with infected ascites had no esophageal varices or fundal varices, 33% had small or medium sized esophageal varices and 26% had large risky esophageal varices banded. Also, 7% of patients with infected ascites had fundal varices injected.

Among the 27 studied patients with infected ascites, 12 patients responded to the first-line antibiotic therapy (third generation Cephalosporins), 10 patients responded to the second-line antibiotic therapy (9 patients responded to Meropenem where two of them were culture-based and one patient responded to Piperacillin/Tazobactam), three patients responded to culture-based Linezolide and one patient responded to culture-based Ciprofloxacin and one patient was asymptomatic Non-neutrocitic bacterascites who did not receive antibiotic treatment.

Keywords: Hepatitis B Virus Envelope - Hepatitis B Core Antigen - Factor V Leiden Mutation - Fatty Liver Index

INTRODUCTION

Ascites is a common problem in patients with chronic liver disease. Almost 60% of patients with cirrhosis will develop ascites ***(Ginés et al., 2010).*** The main pathophysiology of ascites is progressive increase in portal venous pressure as a result of increased intrahepatic resistance caused by cirrhosis ***(Fortune and Cardenas, 2017).*** Portal hypertension increases the hydrostatic pressure at the sinusoidal level and causes some hemodynamic changes including the splanchnic vasodilation, reduced systemic resistance, increased plasma volume and cardiac output. These alterations stimulate the renin-angiotensin-aldosterone system leading to renal sodium and water retention that result in ascites ***(Gentilini and Laffi, 1992).***

Patients with chronic liver disease and cirrhosis frequently develop infections of the ascitic fluid. Spontaneous bacterial peritonitis (SBP) is defined as an ascitic fluid infection without an evident intraabdominal surgically treatable source, it primarily occurs in patients with advanced cirrhosis ***(Sheer and Runyon, 2005).*** The diagnosis is established by positive ascitic fluid bacterial culture and elevated ascitic fluid absolute polymorphonuclear leukocyte (PMN) count (≥250 cells/mm^3). SBP occurs in one third of patients with cirrhosis and is associated with hospital mortality of 20% to 40% ***(Ekser and Mangus, 2016).*** Patients who recover an attack of SBP have an increased risk of recurrence of 40% to 70% in one year and poorer survival on follow-up ***(Sheer and Runyon, 2005).***

Other variants of ascitic fluid infections include culture-negative neutrocytic ascites, monomicrobial non-neutrocytic bacterascites and polymicrobial bacterascites ***(Runyon, 2009).***

Culture-negative neutrocytic ascites (CNNA) is diagnosed when a patient had an elevated ascitic fluid absolute PMN count (≥250 cells/mm^3) with a negative ascitic fluid culture and no evident intraabdominal surgically treatable source of infection ***(Pelletier et al., 1990).*** However, negative cultures maybe attributed to various factors such as inadequate culture techniques, inadequate ascitic fluid volume or unrecognized antibiotics intake ***(Kim et al., 2010).***

Monomicrobial non-neutrocytic bacterascites (MNB) usually represents the colonization phase of ascitic fluid infection. The floras are similar to those of SBP ***(Runyon, 1990).*** MNB may progress to SBP in 62 to 86 % of cases. Progression from MNB to SBP can occur very rapidly with 50 to 170-fold rise in PMN count within 40 to 70 minutes ***(Runyon, 2009).***

Polymicrobial bacterascites is caused by a traumatic paracentesis in which the bowel is injured by the paracentesis needle and bacteria leak, usually transiently, from the gut into the ascitic fluid. This complication is recognized when multiple bacteria are seen on Gram stain or grow on culture of non-neutrocytic ascites (ie, PMN count <250 cells/mm^3) ***(Sagar et al., 2016).***

The three variants of infected ascites are distinguished from classic SBP largely by ascitic fluid analysis. It is important to recognize these variants in at-risk patients who do not fulfil classical definitions of SBP.

The bacterial isolates in SBP may differ from the isolates detected in neutrocytic ascites, monomicrobial non-neutrocytic bacterascites and polymicrobial bacterascites. Gram-negative organisms are the most common organisms in SBP ***(Fiore et al., 2017).***

Third generation cephalosporins are commonly used as emperical treatment of infected ascites with cirrhosis as they cover both enterobactericae and non-enterococcal streptococci ***(Fernández and Gustot, 2012).*** The development of multidrug resistant strains raise the need to investigate other antibiotic regimen based on the prevalence and the antimicrobial resistance pattern of the infection ***(Acevedo, 2015).***

AIM OF THE WORK

The aim of this study is to assess the frequency, clinical profile, bacteriological patterns and outcome of spontaneous bacterial peritonitis and other variants of ascitic fluid infections in patients of liver cirrhosis admitted to Tropical Medicine department at Ain Shams University hospitals. The study also investigated the bacterial isolates and antibiotic sensitivity and resistance patterns in different variants of ascitic fluid infections.