Diagnostic Value of Lactoferrin Ascitic Fluid Levels in Spontaneous Bacterial Peritonitis (SBP)

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Presented By

Mahmoud Roshdy Mohamed El-Ansary

M.B., B.Ch.

Misr University for Science and Technology

Under Supervision of

Dr. Faten Mostafa Ali

Professor of Medical Microbiology & Immunology

Faculty of Medicine - Ain Shams University

Dr. Iman Hussein Shehata

Assistant Professor of Medical Microbiology & Immunology Faculty of Medicine -Ain Shams University

Dr. Abd Elfatah Abd Elsalam

Professor of Internal Medicine Faculty of Medicine- Ain Shams University

Faculty of Medicine

Ain Shams University

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الدلالة التشخصية للاكتوفيرين فى سائل استسقاء البطن فى حالات الالتهاب البكتيرى التلقائى للغشاء البريتونى

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الطبيب:- محمود رشدى محمد الانصارى
بكالوريوس الطب و الجراحة العامة
جامعة مصر للعلوم و التكنولوجيا
تحت اشراف
الأستاذ الدكتورة
فاتن مصطفى على
استاذ الميكروبيولوجيا الطبية و المناعة
كلية الطب جامعة عين شمس
دكتورة
ايمان حسين شحاتة

أستاذ مساعد الميكروبيولوجيا الطبية و المناعة
كلية الطب جامعة عين شمس

الاستاذ الدكتور
عبد الفتاح عبد السلام
أستاذأمراض الباطنة
كلية الطب جامعة عين شمس

كلية الطب
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Contents

List of Table

List of figures

List of abbreviation

AF	Ascitic fluid
AUC	Area under the curve
BA	Bactericidal activity
BCG	Bovis Calmette Guerin
BSA	Bovine serum albumin
CF	Cystic fibrosis
CMI	Cell- mediated immunity
CNNA	Culture- negative neutrocytic ascites
CI	Confidence Interval
CS	Chondroitin sulfate
CSF	Cerebrospinal fluid
DNA	Deoxyribo nuclic acid
DTH	Delayed type hypersensitivity
ETEC	Enterotoxigenic E. coli
HA	Hydroxyapatite
HCV	Hepatitis C virus
HRP	Horseradish peroxidase
HRS	Hepatorenal syndrome

HLF	Human lactoferrin
IAC	International Ascitis Club
LAF	Lactoferrin
LDH	Lactate dehydrogenase
LPS	Lipopolysaccharide
MAb	Monoclonal antibody
MDR	Multidrug resistance
MNB	Monomicrobial Non-Neutrocytic Bacterascitis
MRSA	Methicillin resistant *Staph. aureus*
mCD 14	Membrane cluster of diffrantiation14
NADPH	Nicotinamide adenine dinucleotide phosphate
NK	Natural killer
OPD	O- phenylenediamine
OR	Odds Ratio
OVA	Ovalbumin
PMNL	Polymorphonuclear leucocyte
ROC	Receiver operating characteristics
ROS	Reactive oxygen species
SBP	Spontaneous bacterial peritonitis

sCD14	Soluble cluster of diffrantiation 14
SD	Standard deviation
SE	Standard Error
SIBO	Small intestinal bacterial overgrowth
SPSS	Statistical program for social science
SRBCs	Sheepred blood cells
TSI	Triple sugar iron
TF	Transferrin family
WBCs	White blood cells

Introduction

Spontaneous bacterial peritonitis (SBP) is a clinical syndrome in which ascitic fluid becomes infected in the absence of a recognizable cause of peritonitis (***Bernardi et al., 1992 and Wilis et aL., 2003).***

It is one of the most frequent bacterial infections in patients with decompensated liver cirrhosis and ascitis and is associated with high mortality (20-40%). Bacteraemia is thought to precede the development of SBP, mainly as a result of bacterial translocation from the intestinal lumen ***(Arroyo and Jimenz ., 2000).***

It may occur as a complication of any disease state that produces the clinical syndrome of ascitis, such as liver cirrhosis ***(Wilis and Potercucha., 2003).***

Decompensated and especially jaundiced patients have impaired reticuloendothelial function with reduced phagocytic activity, low ascitic fluid protein concentration, and opposing activity, all of which predispose to spontaneous infection of the ascitic fluid ***(Runyon 2003)***.

Most organisms causing SBP are derived from the intestinal microbial flora and *Escherichia coli* are the most frequently isolated organism ***(Guarner and Soriano., 1997).***

Empirical antibiotic therapy should be initiated before the results of ascitc fluid culture and must cover the most commonly isolated microbial organisms (***Rimola et aL., 2000).***

During recent years, quinolones are used for primary or secondary prophylaxis in high risk group cirrhotic patients to decrease the incidence of SBP. However, there is a concern that changes of the microbial causes of SBP may have occurred with increasing involvement of quinolone - resistant Gram negative and Gram positive bacteria (***Fernandez et al., 2002 and Parsi et aL., 2008).***

Furthermore, these epidemiological changes in microbial causes of SBP have been associated with the increasing number of invasive procedures and hospitalization of cirrhotic patients in intensive care units, which facilitate the prevalence of infections caused by resistant Gram positive bacteria like MRSA and resistant Gram negative *Pseudomonas* ***(Campiilo et aL., 2001and Wilis et aL., 2003).***

Diagnostic paracentesis is used commonly in cirrhotic patients with ascitis to detect the presence of SBP ***(Fernandez et* al., *2002).*** The diagnostic criterion of SBP is increase in polymorphonuclear cell (PMN) count than 250 cells/ml in the ascitic fluid. Lysis of the PMN during transport to the laboratory could occur leading to false negative results. Moreover manual measurement of the ascetic fluid PMN count is operator dependant, makes quality control difficult, and can delay the diagnosis ***(Runyon 2003).***

Therefore, there has been considerable interest in the development of a bedside test that can diagnose SBP rapidly ***(Nausbaum et aL., 2000).***

Lactoferrin (LAF) is a mammalian iron binding protein released by degranulating neutrophils that sequesters iron from pathogens, inhibiting their growth. Its presence in body fluids is proportional to the flux of neutrophils ***(Runyon 2004).***

Furthermore, LAF also has been shown to be remarkably stable and resistant to degradation when left in room temperature for extended periods of time. In patients with

cirrhosis and ascitis, LAF concentration in ascitic fluid represents a potential new test for diagnosing spontaneous bacterial peritonitis ***(Parsi et aL., 2008).***

Aim of work

1. This study aimed to evaluate the significant utility of LAF for the diagnosis of SBP by its titration in ascitic fluid.

2. Isolate the main aerobic causative organisms of SBP and identify the antibiotic sensitivity patterns of isolated organism to detect possible resistance to antimicrobials.

Patients and methods

This study included 60 decompensate liver patients with cirrhosis with suspicion of SBP admitted to Medical Department of Ain Shams University Hospitals and Yasine Abd El Gafar Charity Center for Hepatology fulfilling clinical suspected criteria of SBP represented by:-fever, chills, generalized abdominal pain, absent bowel sounds and rebound tenderness.

Exclusion criteria were: patients on antibiotic therapy associated renal or cardiac disease, peritoneal dialysis and abdominal surgery within 3 months of study entry, presence of other causes of neutrocytic ascitis such as pancreatitis, appendicitis, peritoneal carcinomatosis, and T.B.

Thirty six cirrhotic patients with ascitis with no clinical signs of SBP were included as a control group.

SBP patients and control group were subjected to:

- Detailed medical history
- Diagnostic paracentesis
- Analysis of ascitic fluid to assess :
    1. WBC's count (neutrophil)
    2. Glucose level.
    3. Protein level.
    4. pH.
    5. Specific Gravity.

- Culture of ascitic fluid using blood culture bottles.

-Isolation & Identification of isolates by conventional bacteriological methods according to ***(Colle et aL., 1996)***

-Antibiotic sensitivity pattern for the isolated bacterial pathogens by disk diffusion method ***(NCCLS 2003)***

-Measurement of LAF level in ascitic fluid by ELISA**.**

DEDICATION

TO MY FATHER (ALLAH BLESS HIM)

MY MOTHER

MY WIFE

FOR EVERYTHING THEY DID FOR ME ALL THROUGH THIS STUDY