Cerebrospinal fluid Lipocalin 2 as a marker for detection of acute bacterial meningitis

Thesis

Submitted for Partial Fulfillment of Master Degree in Tropical Medicine

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2017

وَقُل رَّبِّ
زِدْنِي عِلْمًا
صدق الله العظيم
سورة طه الآية (١١٤)

Praise to be done to ALLAH, without his help nothing could be reached.

My deepest thanks to Professor Doctor Eman Mahmoud Fathy Barakat, Professor of Tropical Medicine, Faculty of Medicine, Ain Shams University to whom I am indebted and who cared about every detail written down in this work. It was impossible for me to finish this work without her wise instructions, her guidance and her way of thinking. She has sincerely directed me to set my foot on the right track to accomplish this work.

My deepest thank to Doctor Mohamed Salaheldin Abdelhamid, Lecturer of Tropical Medicine, Faculty of Medicine, Ain Shams University who helped me achieve my goal in this work with his meticulous supervision, valuable instructions, sincere efforts, fruitful encouragement, outstanding support and generous help. I doubt that I will ever be able to convey my appreciation.

Warm gratitude is paid to Doctor Doaa Zakaia Zaky, Lecturer of Tropical Medicine, Faculty of Medicine, Ain Shams University, for her keen help and cooperative guidance in take this work to light.

I'm also grateful to **Doctor Menat Allah Ali Shaaban** Lecturer of Clinical and Chemical Pathology, Faculty of Medicine, Ain Shams University for kind supervision and support throughout this work.

Last but not least, allow me to send my deepest gratitude, my great appreciation and sincere thanks to **My Family**.

List of Contents

Title	Page No.
List of Contents	I
List of Abbreviations	II
List of Tables	IV
List of Figures	VI
Introduction	1
Aim of the Work	7
Etiology, Pathophysiology and Epidemiology of Meningitis	8
Lipocalin 2 (NGAL)	39
Patients and Methods	54
Results	62
Discussion	86
Summary	97
Conclusion	101
Recommendations	102
References	103
الملخص العربى	1

List of Abbreviations

Abb.		Full Term
Bl. P.	:	Blood Pressure
BUN	:	Blood Urea Nitrogen
CDC	:	Centers for Disease Control and Prevention
CML	:	Chronic Myeloid Leukemia
CNS	:	Central Nervous System
COPD	:	Chronic Obstructive Pulmonary Disease
Creat	:	Creatinine
CRP	:	C-reactive Protein
CSF	:	Cerebrospinal Fluid
CT	:	Computed Tomography
DCL	:	Disturbed Conscious Level
DIC	:	Disseminated Intravascular Coagulation
E-coli	:	Escherichia coli
eGFR	:	estimated Glomerular Filtration Rate
ELISA	:	Enzyme-Linked Immunosorbent Assay
ENT	:	Ear, Nose and Throat
ESR	:	Erythrocyte Sedimentation Rate
HIV	:	Human Immunodeficiency Virus
HLA	:	Human Leukocyte Antigen
ICP	:	Intra Cranial Pressure
ICU	:	Intensive Care Unit
IL-1	:	Interleukin-1
K	:	Serum potassium
MRI	:	Magnetic Resonance Imaging
Na	:	Serum Sodium
NGAL	:	Neutrophil Gelatinase-Associated Lipocalin
PCR	:	Polymerase Chain Reaction
PLT	:	Platelets count
RBCs	:	Red Blood Cells
RBS	:	Random Blood Glucose
RR	:	Respiratory Rate
SGOT	:	Serum Glutamic Oxaloacetic Transaminase
SGPT	:	Serum Glutamate Pyruvate Transaminase

List of Abbreviations

Abb.		Full Term
SLE	:	Systemic Lupus Erythematosus
S. Pneumonia	:	Streptococcus pneumoniae
TLC	:	Total Leukocyte Count
WBCs	:	White Blood Cells
WHO	:	World Health Organization

List of Tables

Table No.	Title	Page No.
Table (1):	CSF picture of meningitis according to etiologic agent	28
Table (2):	Empirical antimicrobial therapy for patients with bacterial meningitis	33
Table (3):	Comparison between groups according demographic data.	62
Table (4):	Comparison between groups according to initial presentation.	63
Table (5):	Comparison between groups according to vital signs.	64
Table (6):	Comparison between groups according to signs of meningeal irritation.	66
Table (7):	Comparison between groups according to CBC, CRP and ESR.	67
Table (8):	Comparison between groups according to blood chemistry.	70
Table (9):	Comparison between groups according to CSF analysis.	71
Table (10):	Culture distribution in group I	72
Table (11):	Comparison between group I and group II according to the disease outcome.	772
Table (12):	Comparison between groups according to NGAL level	73
Table (13):	Relation between disease outcome and NGAL level in group I.	74
Table (14):	Relation between disease outcome and NGAL level in group II	75
Table (15):	Correlation between NGAL level and other parameters in group I,	77

Table (16): Correlation between NGAL level and other parameters in group II,. 78
Table (17): Comparison between positive culture and negative culture according to clinical data in group I..... 79
Table (18): Comparison between patients with positive and negative culture in group I according to NGAL level. 81
Table (19): Comparison between patients with positive culture and group II (aseptic meningitis) according to NGAL level..... 82
Table (20): Comparison between patients with negative culture in group I and group II (aseptic meningitis) according to NGAL level..... 83
Table (21): Diagnostic Performance of NGAL in Discrimination between patients of septic and aseptic..... 85

List of Figures

Figure No.	Title	Page No.
Figure (1):	Schematic representation of the lipocalin fold	42
Figure (2):	Comparison between groups according to vital signs.	65
Figure (3):	Comparison between groups according to temperature	65
Figure (4):	Comparison between groups according to signs of meningeal irritation.	66
Figure (5):	Comparison between groups according to CRP level.	68
Figure (6):	Comparison between groups according to TLC level.	68
Figure (7):	Comparison between groups according to ESR.	69
Figure (8):	Comparison between groups according to blood chemistry.	70
Figure (9):	Comparison between groups according to patient's outcome.	73
Figure (10):	Comparison between groups according to NGAL level ..	74
Figure (11):	Comparison between disease outcome and NGAL level in group I.	75
Figure (12):	Comparison between disease outcome and NGAL level in group II	76
Figure (13):	Comparison between positive culture and negative culture according to clinical data in group I.	80
Figure (14):	comparison between positive culture and negative culture in group I according NGAL level..	81
Figure (15):	Comparison between patients with positive culture and group II according to NGAL level	82

Figure (16): Comparison between patients with negative culture in group I and group II according to NGAL level. …..83

Figure (17): Comparison between positive, negative culture and group II according to NGAL in group I…….. 84

Figure (18): Roc curve diagnostic performance of NGAL level in discrimination between patients of septic and aseptic meningitis……...…….. 85

Introduction

Meningitis is a disease caused by the inflammation of the protective membranes covering the brain and spinal cord known as the meninges. The inflammation is usually caused by an infection of the fluid surrounding the brain and spinal cord. ***(CDC, 2014).***

Bacterial meningitis is a life-threatening infection of the central nervous system. Mortality is approximately 20% in high-income countries despite available treatment with antibiotics and dexamethasone, and is several times higher in low-income countries ***(Adriani, 2015).*** Glimåker et al., in a study over 712 patients found that the information about hearing disability or neurological deficits at follow-up 2–6 months after discharge was reported in 535 patients and in similar frequencies during the 2 study periods (85% in 2005–2009 and 81% in 2010–2012). The risk of sequelae was significantly associated with gender, age, etiology, and mental status on admission ***(Glimåker et al., 2015).***

There are several mechanisms by which the organisms gain entry to the CSF, most commonly by hematogenous spread, but also can occur by contiguous spread (e.g., sinusitis, mastoiditis, otitis media) and infrequently by direct entry due to Penetrating CNS trauma ***(mace 2008).***

Several risk factors and predisposing conditions have been identified that increase susceptibility for bacterial meningitis.

Such risk factors can consist of medical conditions resulting in immunodeficiency, host genetic factors or anatomical defects of the natural barriers of the central nervous system ***(Adriani, 2015).***

Clinical disease observed in patients with meningitis can vary with the host's age and underlying immune status, and can span the spectrum of an asymptomatic CSF pleocytosis to an illness causing an alarming degree of neurological impairment. Despite this heterogeneity, however, most patients with meningitis present with fever accompanied by complaints of headache, stiff neck, malaise, anorexia, and vomiting**. *(Irani, 2008).***

Acute complications are common with meningitis. Patients may have an altered mental status or even be comatose. They may present in shock and/or disseminated intravascular coagulation (DIC) frequently are associated with meningococcal meningitis. Apnea and/or respiratory failure/distress can occur. Seizures occur in about one-third of patients who have bacterial meningitis. Focal seizures should raise concern for complications such as subdural empyema, brain abscess, or increased intracranial pressure, and suggest a need for neuroimaging. The syndrome of inappropriate antidiuretic hormone (SIADH) can occur, so the electrolytes and fluid status should be monitored closely ***(Mace, 2008).***

Lumbar puncture is frequently performed, because cerebrospinal fluid (CSF) is a priceless diagnostic window to the central nervous system (CNS). Commonly performed tests on CSF include protein and glucose levels, cell counts and

differential, microscopic examination, and culture. Additional tests such as opening pressure, supernatant color, latex agglutination, and polymerase chain reaction also may be performed***. (Seehusen et al., 2003).***

The diagnosis of bacterial meningitis rests on CSF examination performed after lumbar puncture. Opening pressure is generally in the range of 200–500 mm H2O. The CSF appearance may be cloudy, depending on the presence of significant concentrations of WBCs, RBCs, bacteria, and/or protein. In untreated bacterial meningitis, the WBC count is elevated, usually in the range of 1000– 5000 cells/mm3, although this range can be quite broad (100 to 110,000 cells/mm3). Bacterial meningitis usually leads to a neutrophil predominance in CSF, typically between 80% and 95%; ~10% of patients with acute bacterial meningitis present with a lymphocyte predominance (defined as more than 50% lymphocytes or monocytes) in CSF. The CSF glucose concentration is 40 mg/dL in approximately 50%–60% of patients; a ratio of CSF to serum glucose of 0.4 was 80% sensitive and 98% specific for the diagnosis of bacterial meningitis (***Tunkel et al., 2004).***

Meningitis is considered viral if the viral culture, serological testing, pleocytosis, or reverse transcriptase polymerase chain reactions were positive, and the bacterial culture was negative ***(Dubos et al., 2008)***.