Frequency of Complement Deficiency in Pediatric Patients with Bacterial Meningitis

Thesis

Submitted for Partial Fulfillment of Master Degree in Pediatrics

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SUMMARY

Meningitis; is an inflammation of the membranes that surround the brain and spinal cord, thereby involving the arachnoid, the pia mater, and the interposed cerebrospinal fluid (CSF).

The meningitis syndrome may be caused by a variety of infectious agents, as well as non infectious diseases and other etiologies.

There are some risk factors that predispose the individual to meningitis. Host risk factors can be grouped into four categories: age, demographic/socioeconomic factors, exposure to pathogens, and immunosuppressant.

Immunodeficiency increase risk for bacterial meningitis whether primary or secondary immune deficiency. The absence of an opsonic or bactericidal antibody is a major risk factor in most cases of meningitis caused by group B streptococcus, E coli, Hib, S pneumoniae, and N meningitides.

The goal of the study to estimate the frequency of complement deficiencies in pediatric patients with meningitis, allowing early diagnosis and rapid treatment.

In this study we used CH50 assay as an effective screening test for a complete deficiency of component of the

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Mai Salah Abdelaziz

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List of Abbreviations

ABM	*Acute bacterial meningitis.*
AD	*Autosomal dominant inheritance,*
aHUS	*Atypical hemolytic uremic syndrome.*
AID	*Activation-induced cytidine deaminase.*
AR	*Autosomal recessive.*
ASC	*Apoptosis-associated speck-like protein with a caspase recruitment domain*
ATLD	*Ataxia- telangiectasia-like disease.*
BTK	*Burton tyrosine kinase.*
BLKN	*B cell linker protein.*
BUN	*Blood urea nitrogen.*
CARD	*Caspase recruitment domain.*
CBC	*Complete blood count.*
CGD	*X-linked chronic granulomatous disease.*
CH50	*Serum hemolytic complement.*
CIAS1	*Cold-induced autoinflammatory syndrome 1.*
CIE	*Counter-immuno-electrophoresis.*
CINCA	*Chronic infantile neurologic cutaneous and articular syndrome.*
CMCC	*Chronic mucocutaneous candidiasis.*
CNS	*Central nervous system.*
CR3	*Complement receptor 3.*
CSF	*Cerebrospinal fluid.*
CT	*Cat scan.*
CVID	*Common variable immunedeficiency.*
DAF	*Decay accelerating factor.*
DIC	*Disseminated intravascular coagulopathy.*

E coli	*Escherichia coli*
EDA-ID	*Anhidrotic ectodermal dysplasia with immunodeficiency.*
EKG	*Eckocardiogram.*
ESR	*Erythrocytes sedimentation rate.*
FCN3	*Frame shift mutation of the ficolin-3 gene.*
FH	*Family history.*
FHL	*Familial hemophagocytic lymphohistiocytosis.*
FTT	*Failure to thrive.*
GLU	*Glucose.*
GNEBM	*Gram-negative enteric bacillary meningitis.*
GPI	*Glyco phosphatidylinositol.*
H	*Haemophilus.*
Hb	*Hemoglobin.*
HAE	*hereditary angioedema.*
Hib	*Haemophilus influenza type b.*
HIV	*Human immune deficiency virus.*
HSE	*Herpes simplex encephalitis.*
HPV	*= human papilloma virus;*
ICOS	*Inducible co stimulator.*
ICP	*Intracranial pressure.*
ICU	*Intensive care unit.*
Ig	*Immunoglobulin.*
IPEX	*Immune dysregulation, polyendocrinopathy, enteropthy, X-linked inheritance.*
IRAK4	*Interleukin-1 Receptor Associated kinase 4 deficiency.*
LP	*Lumbar puncture.*

MAC	*Membrane attack complex.*
MASP-2	*Mannan- binding lectin-associated protease 2.*
MBL	*Mannose-binding lectin.*
MBP	*Mannan-binding protein.*
MCP or CD46	*Membrane cofactor protein.*
MOHP	*Ministry of health and population.*
MRI	*Magnetic resonance imaging.*
N	*Neisseria.*
NK	*Natural killer cells.*
NF-Kb=	*nuclear factor Kappa B*
NOMID	*Neonatal onset multisystem inflammatory disease.*
NS	*Non significant.*
NT	*Neutrophil.*
P	*Properdin.*
PAPA	*Pyogenic sterile arthritis, pyoderma gangrenosum, acne syndrome*
PCR	*Polymerase chain reaction.*
PCV7	*Seven-valent pneumococcal conjugate vaccine.*
PID	*Primary immunodeficiency diseases.*
PLT	*Platelets.*
PNH	*Paroxysmal nocturnal hemoglobinuria.*
PSTPIP1	*Proline/serine/threonine phosphatase-interacting protein 1.*
PTN	*Protein.*
S	*Streptococcus.*
SCID	*Severe combined immune deficiencies.*
SNHL	*Sensorineural hearing loss.*

SLE	*Systemic lupus erythematosus.*
TCCD	*Terminal complement component deficiency.*
THC	*Total hemolytic complement.*
TIR	*Toll and Interleukin 1 Receptor*
TLC	*total leucocytes count.*
TLR	*Toll-like receptor.*
TRAPS	*TNF receptor-associated periodic syndrome.*
UNG	*Uracil-DNA glycosylase.*
USA	*United states of America.*
VODI	*Hepatic venoocculusive disease with immunodeficiency.*
VP	*Ventriculoperitoneal.*
VZV	*Varicella-zoster virus.*
WAS	*Wiskott-Aldrich syndrome*
WBCs	*White blood cells.*
XL	*X-linked inheritance.*
XLA	*X-linked agamma globulinemia.*
XLP1	*X-linked lymphoproliferative syndrome.*

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INTRODUCTION

Bacterial meningitis, an inflammation of the meninges affecting the pia, arachnoids, and subarachnoid space that happens in response to bacteria and bacterial products, continues to be an important cause of mortality and morbidity in neonates and children ***(de Louvois et al., 2005).***

In the United States, the overall incidence of bacterial meningitis is about 2 to 10 cases per 100,000 populations per year ***(Lavoie and Caucier, 2006)***. The incidence is greatest in pediatric patients, especially infants, with attack rates in neonates at about 400 per 100,000 .While In Japan, the incidence rate of bacterial meningitis is estimated to be between 10 and 13 per 100,000 in children aged less than 5 years ***(Loring, 2004).***

Predisposing factors for bacterial meningitis can be broadly categorized into congenital and acquired conditions and further divided into anatomical abnormalities, immune - deficiencies, and chronic para-meningeal infections. Complement deficiencies are generally associated with an increased risk of bacterial infections but have also been linked to autoimmune disorders, because Complement plays a particularly important role in the defense against encapsulated bacteria including Neisseria meningitidis, Neisseria

gonorrhoeae, S pneumoniae, and H influenza ***(Truedsson et al., 2007).***

Complement deficiency is a form of primary immunodeficiency disorder; deficiency in any component of the complement system can lead to immune-compromise and overwhelming infection and sepsis, deficiency can be inherited or acquired and complete or partial ***(Agrawal et al., 2006).*** Complement deficiencies form about 2 % of all primary immunodeficiency disorders ***(Sjoholm et al., 2006).***

The CH_{50} assay is an effective screening test for a complete deficiency of component of the classical pathway. Complete deficiency generally yields a very low or undetectable CH_{50} ***(Khajoee et al., 2003)***.

The management of complement deficient patients involves education of the patient in vigilance for early signs of infection and vaccination against the organisms to which the patient is susceptible ***(Mehta et al., 2010).***

AIM OF THE WORK

The work aims to assess the frequency of complement deficiencies among pediatric patients with bacterial meningitis. Allows recognition of such a risk factor paves the way for proper diagnosis and prompt treatment.