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**An Epidemiological Study of Meningitis Pattern and
Some Risk Factors in Egyptian Children (2:12 years).
In Selected fever Hospital**

Thesis submitted for PhD degree in Childhood Studies
(Child Health and Nutrition)

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Contents

- List of Abbreviations
- List of Tables
- List of Figures
- List of Appendices
- Acknowledgment
- Aim of work
- Abstract
- Review of Literature
- Patients and Methods
- Results
- Discussion
- Conclusion and Recommendation
- Summary
- References
- Pictures
- Summary
- Arabic Summary

List of tables:

Table 1: Geographical distribution of meningitis cases in Egypt.

Group "1"

Table 2: Gender distribution of the studied cases.

Table 3: Age group distribution of the studied cases.

Table 4: Number and percent of the studied meningitis cases attending school.

Table 5: Number and percent of meningitis cases who were in contact with ill relative.

Table 6: Number and percent of the studied meningitis cases that had their temperature measured at time of admission.

Table 7: Number and percent of the studied meningitis cases present with bulging fontanels.

Table 8: Different clinical presentation of the studied meningitis cases.

Table 9: Number and percent of meningitis cases who used antibiotic before admission to the hospital.

Table 10: Antibiotic used in treatment.

Table 11: CSF tapping.

Table 12: Appearance of the patients' CSF.

Table 13: CSF culture.

Table 14: The prognosis of the studied meningitis cases.

Group "2"

Table 15: Distribution of cases according to their age.

Table 16: Gender distribution of cases.

Table 17: Meningitis cases who were in contact with ill relative.

Table 18: School attendance.

Table 19: Clinical presentation of meningitis cases.

Table 20: Number and percent of studied meningitis cases distributed according to use of antibiotic in their treatment.

Table 21: CSF tapping.

Table 22: Appearance of the patients' CSF.

Table 23: Results of gram stain.

Table 24: Results of CSF culture versus Gram Stain.

Table 25: Causative agent of meningitis cases.

Table 26: Results of CSF Culture.

Table 27: Results of TB Culture.

Table 28: Prognosis of studied cases.

Table 29: Interleukin 6 level in cases whose causative agent was Strept. Pneumonia.

Table 30: Interleukin 6 level in cases whose causative agent was N. meningitides.

Table 31: Interleukin 6 level in non bacterial cases.

Table 32: Interleukin 6 level in dead meningitis cases.

Table 33: Interleukin 6 level in meningitis cases complicated by Neurological disorders.

Table 34: Summary table.

List of Figures

Figure 1 : Aseptic meningitis cases – by month	96
Figure 2 : Aseptic meningitis cases – by age group	96
Figure 3 : Number of cases & case fatality rate of meningococcal disease outbreak.....	99
Figure 4 :	104
Figure 5	106
Figure 6: geographical distribution of meningitis cases in different Egyptian governorates	125
Figure 7: distribution of cases according to their age in relation to their CSF appearance (group 1).....	132
Figure 8: distribution of cases according to their age in relation to their CSF appearance (group 2)	141

Appendices	160
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Appendix 1: <i>Antimicrobial agents</i>	161
Appendix 2 : <i>Antiviral agents</i>	164
Appendix 3 : <i>Antifungal agents</i>	166
Appendix 4 : <i>Antitubercular agents</i>	168
Appendix 5 : <i>Anticonvulsants</i>	171
Appendix 6: <i>Antiemetics agents</i> –.....	172
Appendix 7: Interleukin 6 level in our meningitis cases	174
Appendix 8: Questionnaire	176

Index

	Page
I – Review of literature	
• Meningitis	10
• Causes & types of meningitis	17
• Acute Bacterial meningitis	17
• Aseptic meningitis	21
• Acute viral meningitis	23
• Chronic meningitides	25
• Chronic Bacterial meningitis	25
• Spirochetal Meningitis	27
• Fungal meningitis	28
• Parasitic meningitis	30
• Investigation of meningitis	31
• Management of meningitis	36
• Meningococcal meningitis	48
• Haemophilus meningitis	57
• Neonatal meningitis	71
• Viral meningitis	79
• Case definition of aseptic meningitis	95
• Epidemics of meningitis	97
• Immunization	100
• Meningococcal septicemia	104
• Interleukin 6	107
• Lumber puncture	110
II – Patients and Methods.....	106
III – Results	121
○ Current situation in Egypt in 3 years	122
○ Descriptive results	124
○ Active surveillance results	134
○ Interleukin 6 results	143

IV – Discussion	148
V –Conclusion and Recommendation	159
VI – References	177
VII –Pictures	184
VIII –Summary	185
IX – Arabic Summary	189

Abbreviations

Abbreviation

CDC: Central disease control and prevention
CMV: Cytomegalovirus
CNS: Central nervous system
CSF: Cerebrospinal fluid
CT: Computerized tomography
EBV: Epstein bar virus
ELISA: Enzyme Linked Immunosorbent Assay
HIP: Vaccine
HiP: Haemophilus influenza type B
HSV: Herpes simplex virus
ICP: Increasing intracranial pressure
IL: Interleukine
IM: Intra-muscular
IV: Intra-venous
LP: Lumber puncture
L. Monocytogens: Listeria Monocytogens
MRI: Magnetic resonance imaging
N: Neisseria
NPEV: Nonpolio- enterovirus
PG: Prostaglandin
SLE: Systemic lupus erythrematosis
TB: Tuberculosis
TNF: Tumor necrosis factor
WBC: White blood cells
WHO: World health organization

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Aim of the study

- Determination of epidemiological profile of all admitted cases of meningitis in the age group (**2: 12** years old) in selected period of time (1998 : 2000), in three selected Egyptian fever hospitals
- To study the effects of some risk factors that may play a role in distribution and occurrence of the disease
- Evaluation of IL 6 level in the CSF samples of meningitis cases in order to detect if it can be used as a useful diagnostic marker for differentiation between bacterial, non-bacterial and aseptic causes of meningitis

Abstract

Community-acquired meningitis is associated with high morbidity and mortality. Age is a major risk factor in bacterial meningitis.

There is a controversy of data about the current situation of meningitis between Egyptian children aged from two to twelve years age, regarding epidemiological profile, risk factors, clinical presentations and CSF analysis. Also the lack of clear recommendation about the use of interleukin 6 level as a rapid screening test for differentiation between causative agents of different types of meningitis (bacterial and non-bacterial types of meningitis) challenged us to under take this study.

The study was done on two group,

First group : Represented by 1077 Egyptian children aged 2: 12 years old who were admitted in selected three fever hospital in three years period of time suffering from different symptoms and signs of meningitis and confirmed by CSF culture as meningitis cases.

Second part : Represented by 84 Egyptian children aged 2: 12 years old who were admitted in selected two fever in sex months.

We found that, 60% of cases were males, 44% of cases aged 8: 12 years, 36% of cases 4: 8 years old, and 19% from 2:4 years old. 42% attending schools, and 69% were in contact to a relative of the same illness. Fever was the main clinical presentation (95%), followed by nausea and vomiting (81%), stiffness of neck (65%), seizers (54%), headache (77%), photophobia (40%), pharyngitis (37%), finally rash and petechiae were represented by 3.3% and 1.4% of total cases respectively.

CSF samples from almost all patients examined for its appearance were clear indicating non-bacterial cases (65%), turbid denoting bacterial meningitis (22.4%) or bloody (5.7%) suggesting tuberculous meningitis.

Studying the antibiotics used by patients without medical advise, we found that 40% of cases use antibiotic before hospital admission.

The mortality rate in this group was 8.1%, while 75% of the total cases improved without complications.

The CSF samples in the active surveillance part of the study examined by ELISA technique for detection of interleukin 6 level denoting that, IL6 levels in the non bacterial cases which represent 32% of the total 84 cases were ranged from 0.41 pg/dl to 7.9 pg/dl, while in bacterial cases its level was ranged from 1.7 pg\dl to 2.9 pg\dl. 34 % Of them were female.

Review of literature

Meningitis

Introduction

Meningitis is the inflammation of meninges resulting in meningeal symptoms (e.g., headache, nuchal rigidity, and photophobia) and an increased number of white blood cells in the cerebrospinal fluid (CSF). This is caused by either infectious or noninfectious causes (e.g. nonsteroidal anti-inflammatory drugs, antibiotics) or carcinomatosis.

Depending on the duration of symptoms, meningitis is classified as acute or chronic. Acute meningitis denotes the evolution of symptoms within hours to several days, while chronic meningitis has an onset of weeks to months but at least 4 weeks.

Aseptic meningitis is a broad term that denotes a nonpyogenic cellular response. Patients characteristically have an acute onset of meningeal symptoms. After an extensive workup, many of these cases are found to have a viral etiology and then can be reclassified as acute viral meningitis (e.g., enterovirus meningitis, herpes simplex virus [HSV] meningitis), it can also be caused by bacterial, fungal, mycobacterial, and parasitic agents.(Archer, 1993)

Pathophysiology:

There are three major pathways by which the infectious agent (i.e., bacteria, virus, fungus, and parasite) gains access to the central nervous system (CNS) and causes disease.

Initially, the infectious agent colonizes or establishes a localized infection in the host. This may be in the form of colonization or infection of the skin, nasopharynx, respiratory tract, gastrointestinal tract, or genitourinary tract. Most

meningeal pathogens are transmitted through the respiratory route, as exemplified by the nasopharyngeal carriage of *Neisseria meningitidis* (meningococcus) and nasopharyngeal colonization with *S pneumoniae* (pneumococcus).

From this site, the organism invades the submucosa by circumventing host defenses (e.g., physical barriers, local immunity, phagocytes/macrophages) and gains access to the CNS by:

(1) Invasion of the bloodstream (i.e. bacteremia, viremia, fungemia, parasitemia) and subsequent hematogenous seeding of the CNS, which is the most common mode of spread for most agents (e.g. meningococcal, cryptococcal, syphilitic, and pneumococcal meningitis);

(2) A retrograde neuronal (i.e. olfactory and peripheral nerves) pathway (e.g. *Naegleria fowleri*, *Gnathostoma spinigerum*); or

(3) Direct contiguous spread (i.e. sinusitis, otitis media, congenital malformations, trauma, direct inoculation during intracranial manipulation).

Certain respiratory viruses are thought to enhance the entry of bacterial agents into the intravascular compartment. Once inside the bloodstream, hematogenous seeding into distant sites occurs, including the CNS. The infectious agents inside the CNS likely survive because host defenses (e.g. immunoglobulin, neutrophils and complement components) appear to be limited in this body compartment.

The pathophysiology include the pivotal role of cytokines (e.g., tumor necrosis factor-alpha [TNF-alpha], interleukin [IL]-1), chemokines (IL-8), and other proinflammatory molecules in the pathogenesis of pleocytosis and neuronal damage during bacterial meningitis. Increased CSF concentrations of TNF-alpha, IL-1, IL-6, and IL-8 are characteristic findings in patients with bacterial meningitis. Increasing intracranial pressure (ICP) may involve proinflammatory molecules as well as mechanical elements.

The proposed interplay among these mediators of inflammation is as follows:

- The exposure of cells (e.g. endothelium, leukocytes, microglia, astrocytes, and meningeal macrophages) to bacterial products released during replication and death incites the synthesis of cytokines and proinflammatory mediators.
- TNF-alpha and IL-1 are the most prominent among the cytokines that initiate this inflammatory cascade. TNF-alpha is a glycoprotein derived from activated monocytes-macrophages, lymphocytes, astrocytes, and microglial cells. IL-1, previously known as endogenous pyrogen, is also produced primarily by activated mononuclear phagocytes and is responsible for the induction of fever during bacterial infections. Both