# INTRODUCTION

Meningitis is life threatening disease common in tropical areas and also in Egypt and has world-wide distribution ***(Adly et al., 1986).*** Meningitis is inflammation of the protective membranes covering the brain and spinal cord, known collectively as meninges. The inflammation may be caused by infection with viruses, bacteria, or other microorganisms ***(Ginsberg, 2004).***

Microorganisms reach the meninges either by direct extension from the ears, nasopharynx, cranial injury or congenital meningeal defect, or by blood-stream spread ***(Kumar and Clark, 2002).***

Meningitis can lead to serious long-term consequences such as deafness, epilepsy, hydrocephalus and cognitive deficits, especially if not treated quickly ***(Sáez-Liorens and McCracken, 2003 and Van de Beek et al., 2006).***

Prognostic factors of sequelae may be of value in selecting patients for more intensive therapy and identifying possible candidates for new treatment strategies ***(Grimwood et al., 2007).*** Prognostic factors depend on the pathogen, age of patient, general condition and the severity of acute illness ***(Ginsberg, 2004).***

***Prognostic factors include:***

- Patient with severe neurological impairment on presentation
- Pneumococcal meningitis has higher rate of mortality 21% and morbidity15%.
- Patients with associated diseases like hepatic and renal patients.
- Early treatment initiation and uninterrupted continuation, severity on presentation, seizures, stroke, cranial nerve involvement, cerebrospinal fluid cell count and lactate levels, hyponatremia, and coinfection are all found to be important prognostic factors for outcome ***(Flavia et al., 2012).***

In adults with community acquired bacterial meningitis, the survival benefit from adjunctive dexamethasone therapy is obtained in the acute phase of the disease and remain for years ***(Daan et al., 2013).***

In patients with community acquired bacterial meningitis early and adequate administration of antibiotic therapy in relation to overt signs of meningitis was independently associated with favorable outcome, defined as mild or no disability ***(Lepur and Barsic, 2010).***

# AIM OF THE WORK

*This study aims to evaluate:*

The different prognostic factors affecting patients presenting with acute bacterial meningitis.

# MENINGITIS

## Definition:

Meningitis is defined as inflammation of the meninges, the lining of the brain and spinal cord, and is characterized by an abnormal number of white blood cells (WBCs) in the cerebrospinal fluid (CSF). The meningitis may be caused by a variety of infectious agents, as well as noninfectious diseases and other aetiologies ***(Nudelman & Tunkel, 2009).***

## Classification of meningitis:

Meningitis has been divided into bacterial meningitis and aseptic meningitis. Bacterial or pyogenic meningitis is an acute meningeal inflammation secondary to bacterial infection that generally evokes a polymorphonuclear response in the CSF. Aseptic meningitis refers to a meningeal inflammation without evidence of pyogenic bacterial infection on Gram's stain or culture, usually accompanied by a mononuclear pleocytosis. Aseptic meningitis is subdivided into two categories: nonbacterial meningeal infections (typically viral or fungal meningitis), and noninfectious meningeal inflammation from systemic diseases (such as sarcoidosis), neoplastic disease (leptomeningeal carcinomatosis or neoplastic meningitis), or drugs ***(Mace, 2008).***

## Risk factors for meningitis:

### *1- Age*

- Extremes of age: elderly (age > 60 years); young children (age < 5 years), especially infants/neonates ***(Chavez-Bueno & McCracken, 2005)***.

### *2- Demographics/socioeconomic*

- Male gender.
- African American ethnicity.
- Low socioeconomic status.
- Crowding: military recruits, crowded dormitories.

***(Chavez-Bueno & McCracken, 2005)***

### *3- Exposure to pathogens*

- Recent colonization.
- Household/close contact with meningitis patient.
- Contiguous infection: sinusitis, mastoiditis, otitis media.
- Bacterial endocarditis.
- Intravenous drug abuse.
- Dural defect: status post neurosurgery, central nervous system (CNS) trauma, congenital defect.
- Ventriculoperitoneal shunt, other CNS devices.
- Cochlear implants.

***(Chavez-Bueno & McCracken, 2005)***

## *4- Immunosuppression Status post splenectomy*

- Hematologic disorders: sickle cell disease, thalassemia major.
- Malignancy.
- Diabetes.
- Alcoholism/cirrhosis
- Immunologic disorder: complement deficiencies, immunoglobulin deficiency.
- HIV.
- Immunosuppressive drug therapy.

## Causes of meningitis:

**Table (1):** Causes of meningitis *(Allen et al., 2010).*

| **I - Bacterial causes of meningitis** | | |
|---|---|---|
| Age of onset | Common | Less common |
| Neonate | - Gram-negative bacilli (Escherichia coli, Proteus)<br>- Group B streptococci | - Listeria monocytogenes |
| Pre-school child | - Haemophilus influenza<br>- Neisseria meningitidis<br>- Streptococcus pneumoniae | - Mycobacterium tuberculosis |
| Older child and adult | - Neisseria meningitidis<br>- Streptococcus pneumoniae | - Listeria monocytogenes<br>- Mycobacterium tuberculosis<br>- Staphylococcus aureus (skull fracture)<br>- Haemophilus influenza |
| **II – Viruses** | | |
| - Enteroviruses (echo, Coxsackie, polio) - Influenza<br>- Mumps - Epstein-Barr<br>- Herpes simplex -Varicella zoster<br>- Lymphocytic choriomeningitis -HIV<br>- Mollaret's meningitis (herpes simplex virus type 2) | | |
| **III – Fungi** | | |
| - Cryptococcus neoformans -Blastomyces<br>- Candida -Coccidioides<br>- Histoplasma -Sporothrix | | |
| **IV - Protozoa and parasites** | | |
| - Toxoplasma - Cysticercus<br>- Amoeba | | |
| **V - Non-infective ('sterile') Malignant disease** | | |
| -Breast cancer –Leukaemia<br>-Bronchial cancer – Lymphoma | | |
| **VI - Inflammatory disease (may be recurrent)** | | |
| -Sarcoidosis -Behçet's disease<br>-SLE | | |

# BACTERIAL MENINGITIS

Definition: Bacterial meningitis (BM) is the inflammation of the meninges (the pia, arachnoid, and subarachnoid space) that occurs when bacteria invade this normally sterile compartment ***(Ziai & Lewin, 2008).***

Bacterial meningitis is a neurological emergency. Patients with documented bacterial meningitis or those in whom there is a strong possibility of bacterial meningitis should be admitted to the intensive care unit. Timely recognition of bacterial meningitis and initiation of therapy are critical to outcome ***(Roos & Van de Beek, 2010).***

Delay in the diagnosis and initiation of effective antibiotic treatment can affect the clinical outcome adversely. Thus, rapid and accurate clinical evaluation is required to determine the suspicion of bacterial meningitis and the need for lumbar puncture ***(Curtis et al., 2010).***

Despite advanced medical care and the availability of effective antibiotic treatment, morbidity in children with bacterial meningitis remained high and fatality rates are reported to be as high as 6.9% ***(Thigpen et al., 2011).***

## Epidemiology & Incidence:

The incidence of bacterial meningitis is 4 to 6 cases per 100,000 persons in the developed world, and the condition is at

least 10 times more common in the developing world, where it is nearly uniformly fatal because of the limited availability of antibiotics ***(Scarborough & Thwaites, 2008).***

Despite recent decrease in the occurrence of meningitis brought about by vaccination programs against Haemophilus influenza type-B and Streptococcus pneumonia in the developed world, the incidence of meningitis is still unacceptably high ranging between 3 and 10 per 100,000 people ***(Liu et al., 2012a).***

The polysaccharide-encapsulated bacteria Neisseria meningitides (the meningococcus), Haemophilus influenzae typeb (Hib) and Streptococcus pneumonia (the pneumococcus) are leading causes of serious bacterial infections. Together, they account for most cases of bacterial pneumonia and meningitis worldwide ***(Pollard et al., 2009).***

## Epidemiology of bacterial meningitis in Egypt:

### *I- Streptococcus pneumoniae:*

Streptococcus pneumoniae is known to give rise to several severe infections. In Egypt it was described as the leading cause of bacterial meningitis ***(Afifi et al., 2007).*** Reflecting a change in the epidemiology of the disease where N. meningitidis was for a long time the main etiological agent causing bacterial meningitis ***(Girgis et al., 1993).***

Several studies were conducted between 1965 and 2004 on the epidemiology of pneumococcal meningitis, and revealed a constant rise in the number of S. pneumoniae meningitis in Egypt ***(Shaban & Siam, 2009).***

A longer comprehensive epidemiological study (ES) 1966–1989 on 7,809 patients admitted to the Abbassia Fever hospital (AFH), reported that 7.3% of patients that suffered from meningitis were due to pneumococcal infection and the peak in the number of cases were during Jan-April. The mean age of the patients was 11.7 with 41% mortality; this is five times greater than the mortality caused by N. meningitidis which was the leading cause of bacterial meningitis during this period. Expectedly, 68% of the mortality cases reported was less than one year of age ***(Girgis et al., 1993).***

A study that included 14 hospitals in Egypt to determine the epidemiology of bacterial meningitis in 11,070 patients suspected with the disease during epidemiological study (ES) 1998–2004 identified S. pneumoniae to be the leading cause, responsible for 42% of the 843 culture-positive bacterial meningitis cases, and 6% of 1,784 culture-negative CSF specimens tested by PCR. This epidemiological study used molecular tools to address the etiological agent of the disease when conventional methods failed ***(Afifi et al., 2007).***

The high percentage of culture negative samples was reported in many studies in Egypt. This was explained by the

high frequency of patients receiving on the counter antimicrobial drugs prior to professional evaluation ***(Youssef et al., 2004).***

## *II- Neisseria meningitidis:*

Meningococci are aerobic, Gram-negative, encapsulated bacteria. Asymptomatic nasopharyngeal carriage occurs in 5–10% of adults, with especially high rates reported in adolescents and young adults ***(Rosenstein et al., 2001).***

Six meningococcal serogroups, A, B, C, W-135, X, and Y cause the majority of disease worldwide and are considered epidemiologically important by the WHO ***(Tan et al., 2010).***

Neisseria meningitidis was for long reported as the leading cause for bacterial meningitis in Egypt based on studies conducted between 1965–1989 ***(Girgis et al., 1993).*** Recently it was described as the second or third leading cause after S. pneumoniae ***(Afifi et al., 2007).*** Egypt has experienced periodic nationwide outbreaks of meningococcal meningitis for several decades ***(Nakhla et al., 2005).***

The decrease in the number of meningococcal meningitis may due to the introduction of school-based vaccination program using the bivalent A/C polysaccharide vaccine for children upon entry of primary school and a second dose of vaccine 3 years after school entry with a coverage of more than 95% in the past 5 years. Other possible factors that may have

resulted in the decrease in the incidence of meningococcal meningitis is the mandatory meningococcal vaccination for all persons before leaving to attend the Hajj in addition to the immunization programs of military recruits ***(Nakhla et al., 2005).***

## *III- Haemophilus influenzae:*

H. influenzae is a Gram-negative cocco-bacillus responsible for a wide variety of respiratory infections and potentially life-threatening invasive diseases, such as meningitis and bacteraemia ***(Jordens & Slack, 1995).***

Hib meningitis is more common in infants with agammaglobulinemia, immunoglobulin G (IgG2) subclass deficiency, or various degrees of asplenia due to sickle cell anemia or other causes, as well as those with cancer, HIV infection, chronic pulmonary or renal disease, or immunosuppression due to organ transplant or other causes ***(Chandrasekar et al., 2013).***

Sparse epidemiology studies are available addressing the pathogenicity of H. influenzae. It was less implicated in meningitis in earlier studies conducted in Egypt ***(Girgis et al., 1993),*** but one study epidemiological study (ES) 1998–2004, defined H. influenza serotype b as the main cause of pneumonia in children below 5 year ***(Afifi et al., 2007).***

## Pathogenesis of bacterial meningitis:

In bacterial meningitis, bacteria reach the meninges by one of two main routes: through the blood stream or through direct contact between the meninges and either the nasal cavity or the skin. In most cases, meningitis follows invasion of the blood stream by organisms that live upon mucous surfaces such as the nasal cavity. This is often in turn preceded by viral infections, which break down the normal barrier provided by the mucous surfaces. Once bacteria have entered the bloodstream, they enter the subarachnoid space in places where the blood-brain barrier is vulnerable such as the choroid plexus. Meningitis occurs in 25% of newborns with bloodstream infections due to group B streptococci; this phenomenon is less common in adults ***(Sáez-Llorens & McCracken, 2003).***

Patients who suffer from skull fractures possess abnormal openings to the sinuses, nasal passages, and middle ears. Organisms that usually live in the human respiratory system without causing disease can pass through openings caused by such fractures, reach the meninges, and cause infection. Similarly, patients who underwent surgical procedures or who have had foreign bodies surgically placed within their skulls (such as tubes to drain abnormal amounts of accumulated CSF) have an increased risk of meningitis ***(Prober et al., 2002).***

The infection stimulates an immune response causing the pia-arachnoid membrane to become congested and infiltrated with inflammatory cells. A thin layer of pus forms and this may later organise to form adhesions. These may cause obstruction to the free flow of CSF leading to hydrocephalus, or they may damage the cranial nerves at the base of the brain. The CSF pressure rises rapidly, the protein content increases, and there is a cellular reaction that varies in type and severity according to the nature of the inflammation and the causative organism. An obliterative endarteritis of the leptomeningeal arteries passing through the meningeal exudate may produce secondary cerebral infarction ***(Allen et al., 2010).***

## Recurrent bacterial meningitis

May be caused by persisting anatomical defects either congenital or acquired, or by disorders of the immune system, anatomical defects allow continuity between the external environment and the nervous system. The most common cause of recurrent meningitis is skull fracture particularly fractures that affect the base of the skull or extend towards the sinuses and petrous pyramids. A literature review of 363 reported cases of recurrent meningitis showed that 59% of cases are due to such anatomical abnormalities, 36% due to immune deficiencies (such as complement deficiency, which predisposes especially to recurrent meningococcal meningitis) and 5% due to ongoing infections in areas adjacent to meninges ***(Tebruegge & Curtis, 2008).***

## Diagnosis of bacterial meningitis:

The rapid onset and progression of the disease and potentially lethal outcome makes it vital to diagnose the disease early ***(Knight & Glennie, 2010).*** Acute bacterial meningitis must be considered in the differential diagnosis of persons of any age presenting with fever and headache or signs of meningeal irritation or acute central nervous system dysfunction. Presentations can be subtle at the extremes of age or in patients who have received partially effective antibiotic therapy ***(Overturf, 2010).***

## Clinical Features of bacterial meningitis:

The clinical presentation of patients with meningitis include rapid onset of fever, headache, photophobia, nuchal rigidity, lethargy, malaise, altered mentation, seizure and vomiting ***(Van de Beek et al., 2006).***

In a study of 696 adults with culture-proven acute bacterial meningitis, the classic triad of fever, neck stiffness, and altered mental status was present in only 44% of episodes; however, 95% of episodes were characterised by at least two of the four symptoms of headache, fever, neck stiffness, and altered mental status ***(Van de Beek et al., 2004).***

The clinical features of acute bacterial meningitis usually develop over 24–48 hours but their nature varies according to the age of the patient. The triad of headache, neck stiffness, and