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Full Length Research Paper

Epidemiological profile of patients suspected with meningitis: A cross-sectional study among 1712 Egyptian patients

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Patients suspected with meningitis can fall into three main categories including meningitis, encephalitis or meningism. Each category has its own epidemiological features; however clinical presentations can be non-discriminating in many instances. Studying the epidemiological features of such cases can help in defining more clues for discriminating these categories. The aim of this study is to describe the epidemiology of acute meningitis, encephalitis and meningism in 1712 cases presented to Shebin EL-Kom Fever Hospital with suspected meningitis. A total of 1712 Egyptian patients suspected with acute meningitis admitted to Shebin El-Kom Fever Hospital were studied according to demographic features and disease outcome. Meningitis was diagnosed in 36.4% of cases, encephalitis in 17.3%, while the largest percentage of 46.3% was diagnosed as meningism. Meningitis was higher in pre and post school age groups. Encephalitis peak above 60 years and meningism was below 6 years. Each group showed significant male and rural area predominance (p >0.001). Encephalitis showed higher mortality as compared to meningitis and meningism. Age grouping can be useful to discriminate cases suspected with meningitis. CNS affection is a common disease in male gender, rural communities and summer season. Meningitis and encephalitis are serious diseases with lethal outcome.

Key words: Epidemiology, meningitis, encephalitis, meningism.

INTRODUCTION

Infection of the central nervous system manifested as meningitis and/or encephalitis can pose a serious public health problem especially during outbreaks. These infections are associated with significant morbidity and mortality despite advances in antimicrobial therapy (Rajnik and Ottolni, 2000). Meningitis is defined as inflammation of the membranes surrounding the brain and spinal cord, including the dura, arachnoid and pia mater. Encephalitis is the inflammation of the brain parenchyma (Braunwald et al., 2001). Meningism can be defined by the presence of meningeal signs without meningitis, for example, in young children with high fevers, upper lobe pneumonia, acute urinary tract infections, and subarachnoid hemorrhage (Bannister et al., 2006).

The clinical presentation of patients with meningitis include rapid onset of fever, headache, photophobia,

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nuchal rigidity, lethargy, malaise, altered mentation, seizure, or vomiting (van de Beek et al., 2006). As with meningitis, patients with encephalitis may exhibit a wide range of clinical features. With encephalitis, altered level of consciousness is much more common, including new psychiatric symptoms, cognitive defects, seizures, or focal neurologic deficits (Whitley et al., 1982).

The distinction between meningitis and encephalitis is not always clear clinically, as many of the symptoms and signs overlap, and the term meningoencephalitis is often used (Solomon et al., 2007). Added to this is the fact that there is a long list of infective agents that are responsible, and often even at discharge, many of these agents are not identified. In only a third to half of the causes of encephalitides are the pathogens identified even with the best laboratory facilities (Rotbart, 2000).

Herpes virus is the most common cause of encephalitis and has a bimodal age distribution, commonly occurring in patients younger than 20 and older than 50 years of age (Honda and Warren, 2009).

Bacterial meningitis is a significant problem in many other areas of the world, particularly in developing countries. In Dakar, Senegal, from 1970 through 1979, the average incidence was 50 cases per 100,000 population, with approximately 1 in 250 children developing bacterial meningitis during the first year of life (Greenwood, 1987). In African countries with high rates of human immunodeficiency virus (HIV) infection, many of meningitis cases are caused by *S. pneumoniae* with high mortality rates (Scarborough and Thwaites, 2008). Sub-Saharan Africa is known for epidemics of meningococcal meningitis, with incidence rates of 101 cases per 100,000 population in the period of 1981 to 1996 in Niger and up to 40 cases per 100,000 during an outbreak in Burkina Faso (de Gans and van de Beek, 2002).

The epidemiology of bacterial meningitis in Egypt has largely changed over the past decade due to the introduction of bivalent A/C polysaccharide vaccine into school-based vaccination programs (Schuchat et al., 1997). Diagnosing meningitis, especially in elderly and neonatal patients, can be challenging because of considerable variability in clinical manifestations. The sensitivity of the classic triad of bacterial meningitis (that is, fever, neck stiffness, and altered mental status) is approximately 40% (van de Beek et al., 2004). In severe cases, bacterial meningitis may present with coma, seizure, and focal neurologic deficits, which are associated with an unfavorable prognosis. Severity of symptoms may be influenced by host factors, such as age, anatomic abnormalities, concurrent illness, immune function, and causative pathogens (Flores-Cordero et al., 2003). Lumbar puncture should not delay initiation of antimicrobial therapy in cases in which bacterial meningitis is suspected. A delay in treatment is strongly associated with adverse outcome (Proulx et al., 2005).

Objectives

The aim of this study is to describe the epidemiology of acute meningitis, encephalitis and meningism in 1712 cases presented to Shebin EL-Kom Fever Hospital with suspected meningitis.

MATERIALS AND METHODS

This is a prospective, cross sectional study including 1712 patients who presented to Shebin El-Kom Fever Hospital in the period from July 2008 to June 2011.

Selection of patients

Patients were included according to the clinical suspicion of meningitis and had undergone a lumbar puncture. A standardized form for collecting information on demographic and clinical characteristics of enrolled patients was designed and completed for all patients' data which included:

- Demographic data: Age, sex, place of residence, and occupation.
- Symptoms: Fever, headache, vomiting, photophobia, and irritability.
- Symptoms of weak suckling, and high pitched crying in infants.
- Signs: Neck rigidity, Kernig sign, Brudzinski sign, altered conscious level, seizures, focal neurological signs, and skin rash and bulging anterior fontanel in infants.
- CSF analysis for chemical tests was done including total white cells count (neutrophils or lymphocytes), protein and glucose level and CSF/serum glucose. CSF culture was inoculated onto chocolate, blood and MacConkey agars and gram stain was performed. Ziehl Nielsen stain for mycobacterial tuberculosis and India ink preparation was done when tuberculous meningitis and cryptococcal meningitis was clinically suspected respectively.

Patients' classification

According to the results of the above studies and discharge diagnosis, patients were categorized into three groups:

- Group I (meningitis): Patients presenting with fever, meningeal symptoms and altered mental status, and with an abnormal number of white blood cells in CSF (number = 623 cases) (Torok et al., 2009).

- Group II (encephalitis): Acute onset of fever and a change in mental status and/or new onset of seizures, and a clear CSF (leukocyte count <80/mm^3, all were lymphocytes or without CSF pleocytosis) with no identification of bacteria by CSF culture or gram stain, and after exclusion of other causes of decreased mentation (number = 297 cases) (Jmor et al., 2008; MOPH report, 2000).

- Group III (meningism): Patients presented with meningeal signs but CSF examination was normal and the subsequent investigation and evolution of the disease revealed the true diagnosis (number = 792 cases) (Bannister et al., 2006).

Patients' consent

Informed written consent from each patient and local ethical committee approval were obtained before starting the data collection. With respect to patients' confidentiality, patients were represented in the study by code numbers. All personal data were concealed. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

Statistical analysis

Data were collected and statistically analyzed using SPSS version 11 statistical package. Comparison of qualitative data was performed with chi square (x^2) test. The quantitative data were described with mean, standard deviation (SD) or range and compared to ANOVA (analysis of variance). Pearson correlation was conducted to correlate continuous parameters. Spearman correlation coefficient test was used for correlation between non-parametric quantitative data. Also, Mann-Whitney test was used for comparison of non-parametric quantitative data among the three groups.

RESULTS

From the studied 1712 patients, the diagnosis of meningitis was in 36.4% (623 patients), encephalitis was 17.3% (297 patients), while the largest percentage (46.3%) was diagnosed as meningism (792 patients) as shown in Figure 1.

Seasonal data of the studied patients

There was a non-significant change in the total number of cases admitted to the hospital throughout the three years of this study and also within each of the three groups (p >0.05) as presented in Figure 2.

The studied patients did not show monthly variation in the incidence of cases between the three groups. While it was evident that all the three groups followed the same seasonal variation, that is, the lowest number of cases was reported in the winter months (January, February, and March) (106, 50 and 153 for meningitis, encephalitis and meningism respectively) and the largest numbers were seen in the summer months (June, July, and August) (215, 114 and 237 for meningitis, encephalitis and meningism respectively). This increased incidence of cases in each group that in summer season it was highly significant (p <0.0001) as plotted in Figure 3.

Demographic data of the studied patients

Meningitis cases were significantly higher in the age groups of children (>6 - 18 years), young adults (>18 - 40 years), and middle-aged patients (>40 - 60 years) with p value <0.001, <0.05 and <0.001 respectively. While encephalitis was significantly higher in elderly patients (>60 years old) with p value<0.001, meningism was of significance in infants (>1 month - 1 year) and children (>1 - 6 years) with p value <0.001 and <0.05 correspondingly compared to the other two diagnostic groups as in Table 1.

The variation in the incidence between different age groups in the three groups was highly significant (p<0.0001). Neonates (0 - 1 month) were the least affected age group in this study, presenting only 1% of the total cases, followed by the elderly (>60 years) with 9.6%.

Meningitis cases' distribution in relation to school age showed two peaks in preschool (0-6 years) and post school (>18) ages with significant difference of p value <0.001 (Figure 4).

Among each of the three studied groups, male preponderance was highly significant with p value <0.0001. Meningitis and encephalitis affected males more commonly than females, with a sex ratio of 1.5:1. However, a non-significant gender difference was found comparing between the three groups (p value >0.05) as shown in Table 2.

Similar results were observed concerning the patients' residence. Meningitis, encephalitis as well as meningism were higher in rural community (p <0.0001). Comparing the three groups together, no significant difference was observed.

Diseases outcome of the studied patients

Both meningitis and encephalitis carried a high mortality

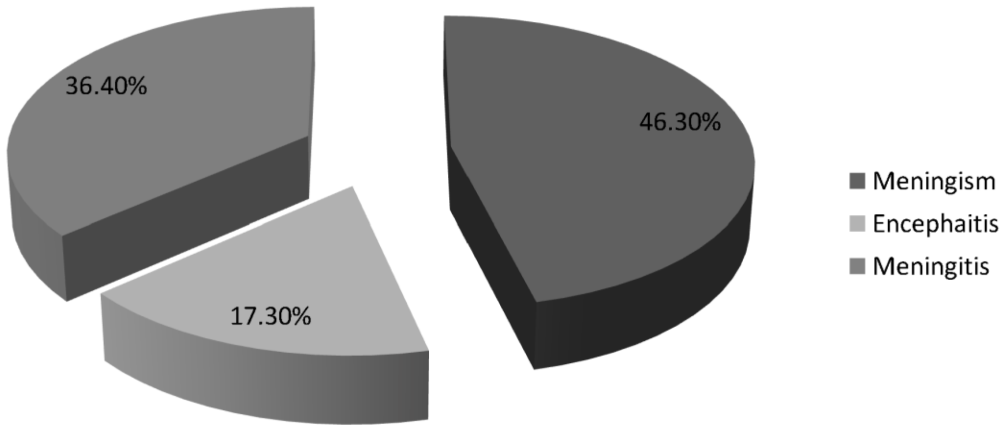

Figure 1. Distribution of the studied patients according to the diagnosis.

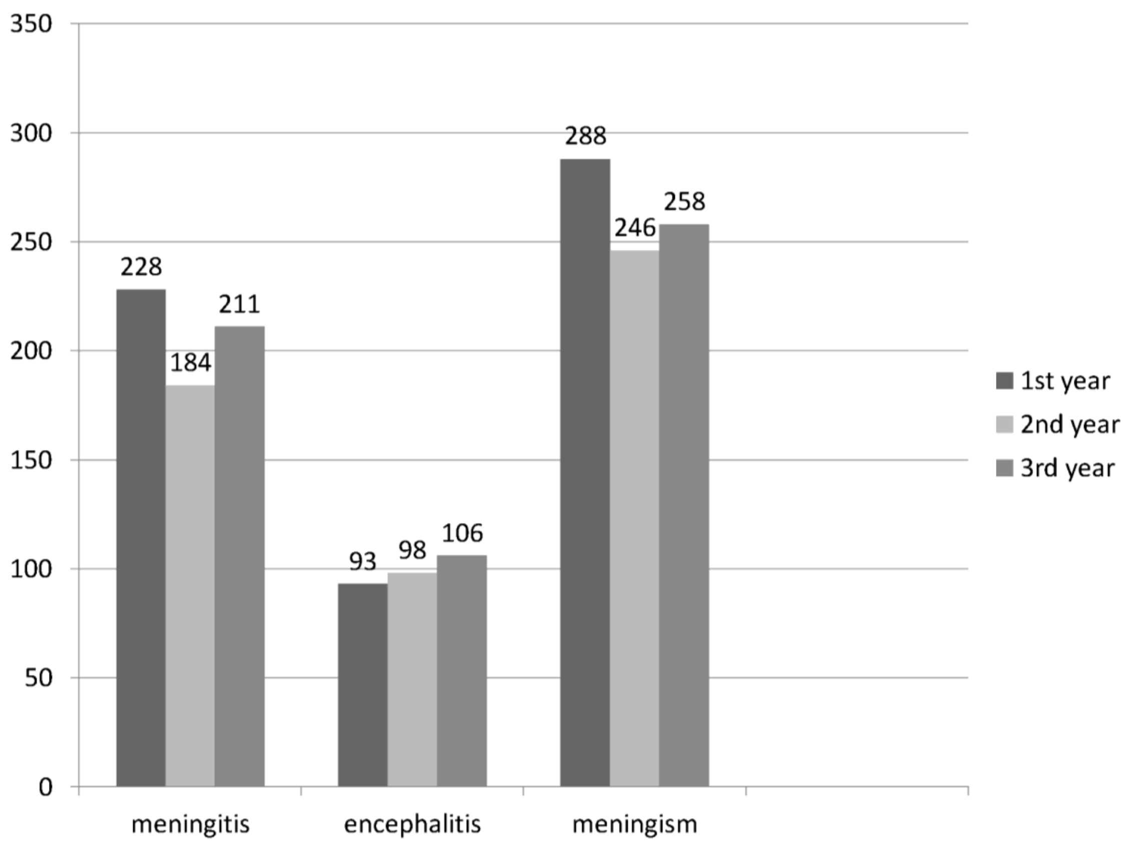

Figure 2. Yearly incidence of cases from all groups.

rate than the meningism group. However, mortality rate was significantly higher in patients with encephalitis (p<0.001) than the other two groups as shown in Table 3.

DISCUSSION

Central nervous system (CNS) infections are a

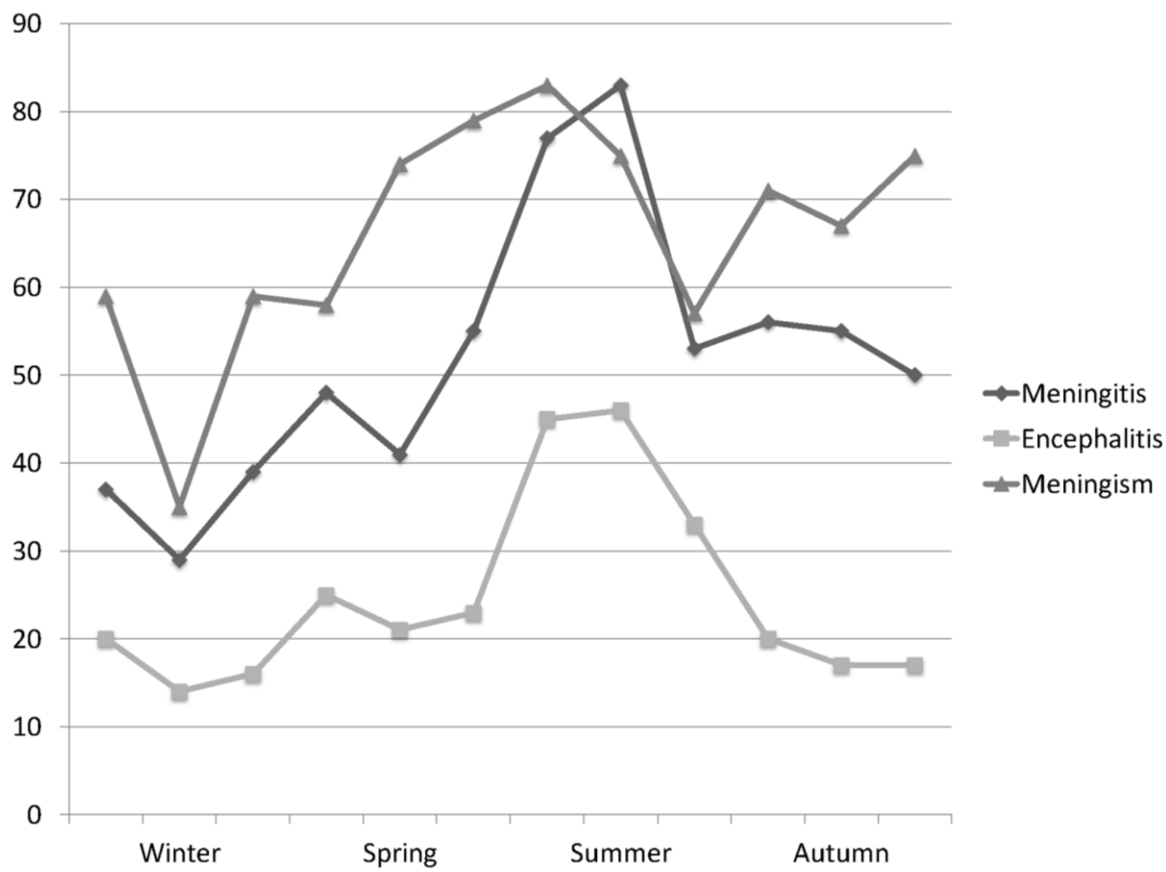

Figure 3. Seasonal incidence of cases in each group of the studied patients.

Table 1. Age distribution in each group of studied patients.

Age	Group I Meningitis (N=623)		Group II Encephalitis (N=297)		Group III Meningism (N=792)		Total (N= 1712)		P
	No.	%	No.	%	No.	%	No.	%	
0-1 m	7	1.1	2	0.7	9	1.1	18	1	>0.05
>1 m-1 y	140	22.5	61	20.5	282	35.6*	483	28.3	<0.001*
>1-6 y	98	15.7	46	15.5	172	21.7*	18.5	316	<0.05*
>6-18 y	98	15.7†	18	6.1	104	13.1	220	12.8	<0.001†
>18-40 y	126	20.2†	43	14.5	126	15.9	295	17.2	<0.05†
>40-60 y	108	17.3†	49	16.5	59	7.4	216	12.6	<0.001†
60 y	46	7.4	78	26.2‡	40	5.1	164	9.6	<0.001‡
p	<0.0001		<0.0001		<0.0001				

neurological emergency requiring urgent investigation and treatment (Solomon et al., 2007). Among the most common CNS infections are meningitis, in which the brain meninges are primarily affected, and encephalitis, when the brain parenchyma is primarily involved; however, the distinction between meningitis and encephalitis is not always clear clinically, as many of the symptoms and signs overlap, and the term meningoencephalitis is often used (Kennedy, 2005).

In this study, meningitis was diagnosed in 36.4% of

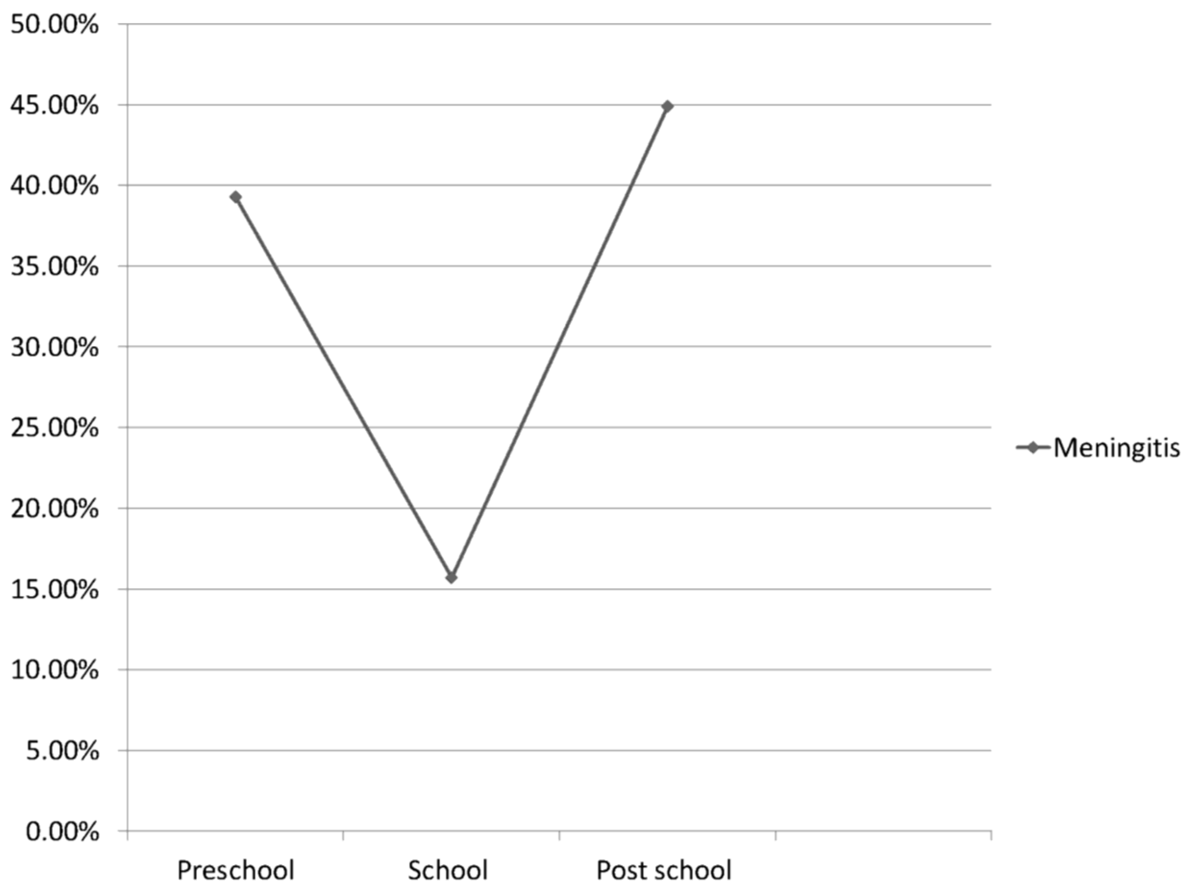

Figure 4. Age distribution of meningitis cases in relation to school age.

Table 2. Sex and residence distribution in each group of studied patients.

Demographic data	Group I Meningitis (N=623)		Group II Encephalitis (N=297)		Group III Meningism (N=792)		P
	No.	%	No.	%	No.	%	
Sex							
Male	374	60	173	58.2	451	56.9	
Female	249	40	124	41.8	341	43.1	>0.05
p	<0.0001		<0.0001		<0.0001		
Residence							
Urban	124	19.9	72	24.2	135	17	
Rural	499	80.1	225	75.8	657	83	>0.05
p	<0.0001		<0.0001		<0.0001		

cases, encephalitis in 17.3%, while 46.3% was diagnosed as meningism. The large number of patients diagnosed as meningitis during the study period reflects the high prevalence rate and endemicity of the disease in Egypt (Farag et al., 2005; Youssef et al., 2004; Girgis et al., 1993).

Table 3. Disease outcome in each group of studied patients.

Outcome	Group I Meningitis (n=623)		Group II Encephalitis (n=297)		Group III Meningism (n=792)		P
	No.	%	No.	%	No.	%	
Cured	523	83.9	198	66.7	780	98.5	<0.001*
Died	100	16.1	99	33.3*	12	1.5	

The big number of non-meningitis patients who underwent a lumbar puncture but their CSF examination was normal, that is, patients with meningism, can be explained by the fact that meningeal signs can occur without meningitis, for example in young children with high fevers, upper lobe pneumonia, acute urinary tract infections, and subarachnoid hemorrhage (Bannister et al., 2006).

In 2000, a project performed by the Ministry of Health and Population (MOHP) was carried out in 12 hospitals and it identified that 223 had acute bacterial meningitis of a total of 2455 persons suspected with acute meningitis (MOPH report, 2000). These figures are much lower than those shown in this study as our results represent a single center. This might be explained by improved patient awareness and diagnostic methods. This was contradictory to the total number of encephalitis cases, where our rates were less than that of MOHP. Nationally, a total of 1,725 encephalitis cases were reported in the year 2000 and 1151 cases in 2004. We only reported 297 cases in three years.

A study done between 1966 and 1989 which included 7,809 suspected meningitis patients revealed that encephalitis was evident in 12.5% of cases. However this study was done over a long duration and on urban population (Girgis et al., 1993).

A non-significant change in the total number of cases in the three diagnostic categories throughout the three years period of this study was found. No epidemic wave of either meningitis or encephalitis was reported in Egypt in the last few years and during study period. The last meningococcal outbreak occurred between 1987 and 1991. Since 1992, the Egyptian Ministry of Health initiated a school-based vaccination program against *N. meningitides*; the only major bacterial pathogen which causes epidemics of meningitis, since then, only sporadic cases occurred (Shaban et al., 2009). Also the last outbreak of Rift Valley encephalitis was in the year 2003 (Hanafi et al., 2011).

In this study, meningitis and encephalitis cases were found to peak during the summer months. Other studies from Egypt reported a seasonal peak in winter and early spring (Youssef et al., 2004). This may be explained by the decrease of meningococcal disease with its seasonal pattern which may have led to the prevalence of other pathogens which had no specific seasonal distribution.

In this study, meningitis occurred in all age groups. However, those under school age suffered a great disease burden (39.3% in pre-school children). Other studies documented a higher prevalence of meningitis in infants and children (Afifi et al., 2009; Campagne et al., 1999).

Beyond school age (>18 years), the incidence of meningitis was the highest (44.9%) in comparison to other age groups. The availability of effective vaccines against common pathogens causing meningitis have resulted in a shift of age incidence towards adulthood in countries that has implemented routine vaccination (Schuchat et al., 1997; Dery and Hasbun, 2007).

In our work significantly higher incidence of encephalitis was reported in elderly patients (26.2% in the age group >60 years). It has been reported that individuals at the extremes of age are at the highest risk, particularly for herpes encephalitis in a bimodal distribution of patients aged 5-30 years or older than 50 years (Howes, 2013). Lastly, meningism was reported mainly in infants and preschool children, this reflects that the manifestations of meningitis should not be a clue toward diagnosis in this age group without CSF examination.

In our study, meningitis affected males more commonly than females, with a sex ratio of 1.5:1. The same was seen in encephalitis and in meningism. This male preponderance was highly significant but not between each group. This is quite similar to an Egyptian study which showed more males than females in all etiologic groups, with the ratio for the total patient population being 1.6:1 (Girgis et al., 1993).

Mortality rate for meningitis was 16.1% in this study. In one study conducted in Turkey, the overall mortality was 425 out of 2,408 (17.6%) among patients with acute purulent meningitis [Arda et al., 2008]. In another study about bacterial meningitis in Niger, the overall mortality rate was 20.5% [Campagne et al., 1999]. For encephalitis, a significantly higher mortality rate (33.3%) was found in our series. Although patients with meningism did not had a CNS infection, yet 12 out of 792 patients (1.5%) died, as a complication to the causative disease.

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