Causes of Meningitis in children in Diyala government / Iraq

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ABSTRACT

Background: Differentiating bacterial from nonbacterial meningitis is very important in deciding treatment. Bacterial meningitis is a life-threatening neurological condition and needs prompt parenteral antibiotics, compared to viral and aseptic meningitis, which carries relatively better outcome.

Aim of study: To identify the causes of meningitis in children aged ≤ 14 years' old in Diyala, Iraq.

Subjects and Methods: A descriptive study conducted in Al-Batool Teaching Hospital,Diyala, Iraq during a period from October 2017 to February 2018. It included all patients aged ≤ 14 years' old who admitted with primary diagnosis of meningitis, presented with clinical signs of meningitis. Patients were subjected to a detailed history, clinical examination and a laboratory and radiological investigation.

Results: The main cause of meningitis detected by cerebrospinal fluid was viral cause (74.3%), Coxsackie virus A16 IgM antibody was detected in 70% of cases. Age and duration of fever were significantly associated factors with cause of meningitis (P= 0.024 and P= 0.017 respectively). 45.7% of study patients were presented with fit, most of these fits were generalized in type (93.8%) and 56.3% of these fits lasted for less than 15 minutes.

Conclusion: Meningitis was caused mostly by mostly viral infection and Coxsackie virus A16 IgM antibody was the most common virus detected. Viral meningitis was associated with young age and short duration of fever. Cerebrospinal fluid protein was significantly higher in bacterial than in viral meningitis.

Keywords: Meningitis, viral, bacterial, Diyala, Iraq.

Introduction

Meningitis is an infection of the meninges and cerebrospinal fluid (CSF) surrounding the brain and spinal cord [(1)].According to etiology it can be divided into, bacterial, viral, parasitic, fungal, tuberculous and chronic meningitis [(2)]. Mortality in bacterial meningitis is 100% in untreated cases [(3)] and the most common agents of bacterial meningitis are: Streptococcus pneumonia, Neisseria meningitides, haemophilus influenza type B (Hib), group B Streptococcus, Streptococcus suis and E. coli [(4)]. Viral meningitis is common and in absence of a lumbar puncture cannot be differentiated from bacterial meningitis[(5).] Enteroviruses are commonest (46%), and herpes simplex virus type 1 is least common (4%) [(6).]

The estimated annual incidence of viral meningitis was 219/100,000 in infants under one year and 27.8/ 100,000 overall in children under 14 years[(7).] Parasitic meningitis caused by a free-living unicellular Naegleria fowleri (N. fowleri). Although occurs rarely, it nearly always results in death, with a fatality rate more than 95% (8). Fungal meningitis may be caused by; Candida albicans, Coccidioides, Histoplasma, Blastomyces and Aspergillus [(9,10).] Tuberculous meningitis is a devastating illness, with a particularly high morbidity and mortality in young children [(11).] Chronic meningitis is a clinical syndrome with a persistent or progressive signs and symptoms of meningitis associated with CSF pleocytosis and elevated protein concentrations for at least four weeks without improvement [(12).] Fungal infections are the common cause for chronic meningitis [(13)]. Neoplastic involvement of the CNS (as Leptomeningeal carcinomatosis) should be considered in the differential diagnosis for patients presenting with signs and symptoms of chronic meningitis [(14).]

Clinical presentation includes: headache, vomiting, anorexia, restlessness, altered state of consciousness, and irritability. Common signs include photophobia, neck pain and rigidity, bulging fontanelle (children < 18 months), stupor, coma, seizures, and focal neurologic deficits (Kernigs and Brudzinski sign) [(15)]. Meningitis is diagnosed by CSF analysis, Gram stain, and culture, CT scan for evidence of brain abscess or increased intracranial pressure (ICP), blood culture should be performed in all patients with suspected meningitis [(16)]. Supportive measures like, IV fluidinhypotension or shock, mechanical ventilation if needed, anticonvulsant in convulsion play a vital role in treatment [(17).] Empiric antimicrobials used in suspected meningitis need adequate CSF penetration and sensitivity against the most probable pathogens(18,19). Survivors of neonatal meningitis are at considerable risk for long-term neurologic impairment [(20).]Meningitis requires a high index of suspicion, prompt diagnosis, and rapid treatment [(21).] The aim of this study is to identify the causes of meningitis in children aged ≤ 14 years' old in Diyala, Iraq.

Patients and Methods

Study Design and Setting:

Adescriptive study conducted in Al-Batool Teaching Hospital, Diyala, Iraq during a period from October 2017 to February 2018.

Study Population and sample size:

Included all patients aged one day to 14 years' old who presented with clinical signs of meningitis. Patients > 14 years, operated hydrocephaly, and those who diagnosed as posttraumatic meningitis were excluded from this study. The total number of cases enrolled was 70. Diagnosis of meningitis was done according to clinical presentation (fever, neck pain, petechial rash with signs of increased intracranial pressure), physical examination (identifying neurologic

deficits, characteristic skin lesions (petechiae and purpura) and meningeal irritation (neck stiffness, Brudzinski and Kernig signs), and laboratory investigation (CSF analysis and culture which was obtained via a lumbar puncture). A questionnaire was used to gather the necessary information as demographic data, details about fever and fit, type of feeding, vaccination status, partial treatment by antibiotic and associated symptoms. Laboratory investigations as complete blood count, blood culture, and CSF culture and sensitivity (gram stain, analysis) (Normal value of CSF sugar is 45 – 80 mg/dl, CSF protein is 15 – 60 mg/100ml, and CSF cell count is 0 – 5 WBC and no RBC) and meningitis diagnosis depends on CSF analysis, culture. CT-scan was done to evaluate complications and fundoscopy for diagnosis of increased ICP. A qualitative determination of human coxsackievirus A16 (CVA16) antibody (IgM) concentration in serum was done by ELIZA kit.

Statistical Analysis:

The data analyzed using Statistical Package for Social Sciences (SPSS) version 25. The data presented as mean, standard deviation and ranges. Categorical data presented by frequencies and percentages. Pearson's Chi–square test was used to assess statistical association between some patients' characteristics and cause of meningitis. Independent t-test and (two tailed) was used to compare the continuous variables among study groups accordingly. A level of P – value less than 0.05 was considered significant.

Results:

This study involved 70 patients who were diagnosed as meningitis. The mean age of the patients was 3.29 ± 3.45 years; 57.1% were males; 54.3% were from urban areas; and 84.3% had fever for less than five days. Fit was presented in 54.3% of patients; 93.8% of patients were generalized type; fits in 56.3% of them lasted less than 15 minutes as shown in table (1).

Comparison between viral and bacterial meningitis by CSF sugar and protein is shown in table (2). The mean of CSF protein was significantly higher in bacterial meningitis than that in viral meningitis (66 versus 44.4, P=0.019). No significant difference between mean of CSF sugar in bacterial meningitis and that in viral meningitis (P=0.204).

Table 3 shows the distribution of study patients by investigation. In this study, the most common cause of meningitis by CSF culture was viral cause (74.3%) and in 61.4% of cases, the CSF was turbid in appearance. Coxsackie virus A16 IgM antibody was seen in 70% of cases and high WBC count was found in 78.6%.

Table 1: Distribution of study patients by general characteristics

Variable	No. (n=70)	Percentage (%)
Age (Years)		
< 1	27	38.6
1 – 5	27	38.6
6 - 10	12	17.1
> 10	4	5.7
Gender		
Male	40	57.1
Female	30	42.9
Residence		
Urban	38	54.3
Rural	32	45.7
Duration of fever (Days)		
< 5	59	84.3
≥ 5	11	15.7
Fit		
Yes	32	45.7
No	38	54.3
Type of fit	**n= 32**	
Generalized	30	93.8
Focal	2	6.2
Duration of fit (Minutes)	**n= 32**	
< 15	18	56.3
≥ 15	14	43.7

Table 2: Comparison between viral and bacterial meningitis by CSF sugar, protein and culture

Variable	Cause of meningitis		P- Value
	Bacterial Mean ± SD	Viral Mean ± SD	
CSF Sugar	55.82 ± 27.17	47.67 ± 21.13	**0.204**
CSF Protein	66 ± 32.96	44.4 ± 32.02	**0.019**

Table 3: Distribution of study patients by investigation

Investigation			No. (n= 70)	Percentage (%)
CSF Culture result	**Viral**		52	74.3
	Bacterial	**Streptococcus**	5	7.1
		Staphylococcus	2	2.9
		H. Influenza B	7	10.0
		N. meningitides	4	5.7
CSF Appearance	**Clear**		27	38.6
	Turbid		43	61.4
Coxsackie virus A16 IgM antibody	**Positive**		49	70.0
	Negative		21	30.0
CSF WBC Count	**Normal**		15	21.4
	High		55	78.6

The association between cause of meningitis and general characteristics of study patients is shown in table (4). Viral meningitis was the cause in all patients aged between 6 – 10 years (100%) with a significant association (P=0.024) between cause of meningitis and age.

There was no significant association (P= 0.477, P= 0.331, and P= 0.477) between cause of meningitis and all other characteristics.

Table 5 shows the association between cause of meningitis and characteristics of fever and fit. We noticed that the highest prevalence of viral meningitis was seen in patients with duration of fever less than five days (79.7%) with a significant association (P=0.017) between cause of meningitis and duration of fever.There was no significant association (P= 0.128, P= 0.631, and P= 0.888) between cause of meningitis and presence, duration and type of fit.

The association between cause of meningitis and certain investigation is shown in table (6). There was no significant association ($P \geq 0.05$) between cause of meningitis and both of WBC count and CSF appearance.

Table 4: The relation between cause of meningitis and general characteristics of study patients

Variable		Cause of Meningitis		Total (%) n= 70	P - Value
		Bacterial (%) n= 18	Viral (%) n= 52		
Age (Years)	**< 1**	8 (29.6)	19 (70.4)	27 (38.6)	**0.024**
	1 – 5	7 (25.9)	20 (74.1)	27 (38.6)	
	6 – 10	0 (0)	12 (100.0)	12 (17.1)	
	> 10	3 (75.0)	1 (25.0)	4 (5.7)	
Gender	**Male**	9 (22.5)	31 (77.5)	40 (57.1)	**0.477**
	Female	9 (30.0)	21 (70.0)	30 (42.9)	
Residence	**Urban**	8 (21.1)	30 (78.9)	38 (54.3)	**0.331**
	Rural	10 (31.3)	22 (68.7)	32 (45.7)	

Table 5: The relation between cause of meningitis and characteristics of fever and fit

Variable		Cause of Meningitis		Total (%) n= 70	P - Value
		Bacterial (%) n= 18	Viral (%) n= 52		
Duration of Fever (Days)	< 5	12 (20.3)	47 (79.7)	59 (84.3)	0.017
	≥ 5	6 (54.5)	5 (45.5)	11 (15.7)	
Fit	Yes	11 (34.4)	21 (65.6)	32 (45.7)	0.128
	No	7 (18.4)	31 (81.6)	38 (54.3)	
Type of fit		n= 11	n= 21	n= 32	0.631
	Generalized	10 (33.3)	20 (66.7)	30 (93.8)	
	Focal	1 (50.0)	1 (50.0)	2 (6.2)	
Duration of fit (Minutes)	< 15	6 (33.3)	12 (66.7)	18 (56.3)	0.888
	≥ 15	5 (35.7)	9 (64.3)	14 (43.7)	

Table 6: The relation between cause of meningitis and certain investigation

Investigation		Cause of Meningitis		Total (%) n= 70	P - Value
		Bacterial (%) n= 18	Viral (%) n= 52		
CSF WBC Count	High	16 (29.1)	39 (70.9)	55 (78.6)	0.216
	Normal	2 (13.3)	13 (86.7)	15 (21.4)	
CSF appearance	Turbid	11 (25.6)	32 (74.4)	43 (61.4)	0.974
	Clear	7 (25.9)	20 (74.1)	27 (38.6)	

Discussion

Meningitis continues to be a significant cause of childhood morbidity and mortality [22]. Worldwide, the risk of neurological sequelae in survivors following hospital discharge reach 20%, so early diagnosis and appropriate management of the child with meningitis is therefore critical [3].

In the present study, 74.3% of the patients presented with viral meningitis, which was the significant causative agent in all patients aged between 6 – 10 years (100%, P=0.024), which is consistent to an American study conducted in USA in 2000(23) and to a study in Kuwait (2010) [24], majority of cases of meningitis were aseptic. Different results found in an Iraqi study in 2017[25] and an Egyptian study in 2014 [26] in which the highest proportion of cases diagnosed as bacterial meningitis. Lower results observed in in Iran (2012), as CSF study detected viral meningitis in 33.3% of cases [27], while in Niger (2016) 29.2% of CSF study samples detect aseptic meningitis [28]. According to virology study in this study, Coxsackie virus A16 IgM antibody was detected in 70% of cases, different from Iranian one in 2011, in whom non-polio human enterovirus was the commonest detected virus in 43.3% of cases [29], and to another Iranian one in 2017, as found that extracellular vesicles (EV RNA) found in 59.6% of CSF samples [30]. These differences in viral prevalence rates may be due to poor hygiene and virulence of each type or a higher rate of false positive results obtained from viral study. Additionally, 78.6% of study patients had leukocytosis in line to that don in Egypt in 2011 in which WBC was significantly higher in bacterial meningitis(31). High percentage of bacterial meningitis in some countries compared to viral one in other countries are of multifactorial, but the most probable cause is the vaccination program. "There are effective vaccines against the three major bacterial pathogens responsible for bacterial meningitis, Streptococcus pneumonia, Haemophilus influenza, and Neisseria meningitis", also sample size involved in each study might affect the results [32].

In the present study, mean of CSF protein was significantly higher in bacterial than in viral meningitis, similarto a study in Portugal (2013) [33]. In contrary to the current results, American researchers in 2006 demonstrates that meningitis can occur in the presence of normal CSF WBC, glucose, and protein levels [34]. These differences might have attributed to several factors; as the sample size and duration at which lumber punctures done whether at the beginning of the disease or at late period and antibiotic usage.

In the current study, low duration of fever was significantly associated with viral meningitis (P=0.017) these results differed from Iranian study in 2008, as age, complex convulsion was statistically significant in cases who had meningitis [35] and in Tunis in 2010, in which convulsion duration age were a predicting factors for meningitis [36]. Finally, a British study in

2005 predicted that prolonged convulsion can be an important sign of meningitis in patients with convulsion and fever [37].

The differences in frequency of meningitis between the current work and previous studies can be attributed to differences in the age, vaccination status, geographic, cultural, and ethnic differences, as parents may not always permit lumbar punctures, and sometimes it is not successful. In conclusion, meningitis was caused mostly by viral infection and Coxsackie virus A16 IgM antibody was the most common virus detected. Viral meningitis was associated with young age and short duration of fever. Cerebrospinal fluid protein was significantly higher in bacterial than in viral meningitis. In conclusion, meningitis was caused mostly by viral infection and Coxsackie virus A16 IgM antibody was the most common virus detected. Viral meningitis was associated with young age and short duration of fever. Cerebrospinal fluid protein was significantly higher in bacterial than in viral meningitis.

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