

Acute Meningitis in Children: Clinical and Laboratory Profiles

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الخلاصة

إلتهاب السحايا سبب معتد به للمرضية والفناء في الأطفال حول العالم. إن التشخيص والمعالجة المبكرة الطريق الأكثر أهمية في منع المضاعفات. لحساب التردد وأنواع إلهاب السحايا، ولوصف المتثاببات السريرية والمختبرية، وتحليل الفناء والمضاعفات المبكرة من إلهاب سحايا الطفولة..

مائة طفل بعمر 1 شهر - 15 سنة رقدوا في مستشفى الزهراء التعليمي مع الشكّ السريري لاصابتهم بالتهاب السحايا أثناء الفترة من الأول كانون الثاني 2009 إلى الأول من كانون الثاني 2010، شملتهم هذه الدراسة.

وأخضعوا إلى الفحص السريري ولفحص الدم والسائل الدماغي الشوكي (فحوصات كيميائية حيوية، جرثومية، ومصلية).

ثلاثون من المرضى كان لديهم إلهاب سحايا جرثومي، 34 % كان لديهم إلهاب سحايا فيروسي، 36 % إلهاب سحايا جرثومي معالج جزئياً. أغلب المرضى ادخلوا للمستشفى كانون الثاني وشباط. الحمى كانت أكثر الأعراض موجياً (94%)، يليها القيء (64 %)، إلهاب سيء أو شهية سيئة (65 %). تهيج وانتفاخ اليافوخ كانت العلامات الرئيسية في أولئك الأطفال تحت عمر السنة الواحدة. تيبس الرقبة وعلامة إيجابية علامة كيرنك كانت من العلامات الرئيسية في الأطفال فوق عمر السنة الواحدة. دراسات السائل الدماغي الشوكي للمرضى المصابين بالتهاب السحايا الجرثومي كانت كالاتي: [صبغة كرام كانت إيجابية في 18 (60%) مريض، زرع السائل الدماغي الشوكي كان إيجابي في 22 (73 %) مريض، البروتين المتفاعل (سي) كان إيجابي في 23 (77 %) مريض]. البروتين المتفاعل (سي) في مصل الدم كان إيجابي في 16 (53%) مريض من المرضى المصابين بالتهاب السحايا الجرثومي. المستدمية النزلية كانت المسبب الرئيسي لإلهاب السحايا الجرثومي. المضاعفات الرئيسية كانت تشنجات متكرراً (27 %) من إلهاب السحايا الجرثومي، (8 %) من إلهاب السحايا الفيروسي، (5 %) من إلهاب السحايا الجرثومي المعالج جزئياً..

تطلبت الدخول إلى وحدة العناية المركزة. وان معدل الوفيات العام كان 8%. حالتين اثبتت الدراسة ان المستدمية النزلية نوع (بي) هي العامل المسبب البارز لإلهاب السحايا الجرثومي. وان الحمى كانت أكثر الأعراض موجياً، وان تشنجات راجع كان أكثر المضاعفات تكراراً لكل الاعمار ولكل انواع السحايا. ان البروتين المتفاعل (سي) في السائل الدماغي الشوكي، ان البروتين المتفاعل (سي) في مصل الدم كانا إيجابيين بصورة رئيسية في المرضى المصابين بالتهاب السحايا الجرثومي.

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Abstract

Background: Meningitis is a significant cause of morbidity and mortality in children around the world . Early diagnosis and treatment are the most important way in prevention of the complications.

Objective: To estimate the frequency and types of meningitis, to describe various clinical and laboratory parameters, and to analyze mortality and early complications of childhood meningitis.

Patients and methods: One hundred Children aged 1 month-15 years admitted to AL-Zahra Teaching Hospital in Wassit, with clinical suspicion of meningitis during the period from 1st January 2009 to 1st January 2010 were included in this study. They were subjected to clinical examination , blood tests and cerebrospinal fluid tests (CSF) which include: biochemical, bacteriological, and serological tests.

Results: Thirty of the patients had bacterial meningitis, 34% had viral meningitis, 36% had partially treated bacterial meningitis. Majority of the patients admitted in January and February. Fever was the most common presenting symptom (94%) , followed by vomiting in 64%, poor feeding or appetite in 65%. Irritability and bulging fontanel were the main signs in those children below one year. Neck stiffness and positive kernig sign were the main signs in children above one year. The results of Cerebrospinal fluid studies in patients with bacterial meningitis were as following : (gram stain was positive in 18 (60%) patients, culture was positive in 22 (73%) patients, C-reactive protein (CRP) was positive in 23 (77%) patients). Serum C-reactive protein was positive in 16 (53%) patients with bacterial meningitis. Haemophilus influenza (H.influenza) was the main causative agent of bacterial meningitis. The main complication was recurrent convulsion (27% of bacterial meningitis,8% of viral meningitis, 5% of partially treated bacterial meningitis).Two cases required admission to intensive care unit. The overall mortality rate was 8%.

Conclusion: H. influenza type B is the leading causative agent of bacterial meningitis. Fever was the most common presenting signs , recurrent convulsion was the most frequent complication in all

age groups and in all types of meningitis. Positive C- reactive protein in the Serum and CSF was mainly found in patients with bacterial meningitis.

Key words: meningitis, children, C-reactive protein, lumbar puncture.

Introduction

Meningitis is defined as inflammation of the membranes that surround the brain and spinal cord . Depending on the course of illness, meningitis can be classified to: acute, recurrent and chronic meningitis. ^(1,2) Meningitis also can be divided into septic and aseptic meningitis. Septic meningitis was defined as the acute onset of meningitis and documented bacterial infection in the CSF or blood . Aseptic meningitis was defined as the acute onset of meningitis and the absence of any bacterial meningitis criteria . Bacterial meningitis is one of the most potentially serious infections occurring in infants and older children. ^(3,4,5)

Etiology: *Group B streptococci* (GBS) followed by *Escherechia coli* (*E.coli*) are the two most common causes of neonatal meningitis, while *Streptococcus pneumonia*, *Neisseria meningitidis*, and *Haemophilus influenzae type B* (*HiB*) are the most common causes of bacterial meningitis in infants and young children. ^(6,7)

Epidemiology: The peak incidence of meningitis is 3 to 12 months old, with decreasing incidence after 2 years of age. The greatest mortality and morbidity occurs between birth and 4 years of age . ^(8,9,10)

pathogenesis: Meningitis is usually caused by viruses or bacteria when the infection passes into the blood stream and then into the cerebrospinal fluid that surrounds the brain and spinal cord, it can affect the nerves and travel to the brain and/or surrounding membranes, causing inflammation. ^(11,12)

Clinical features:

(1).**Non-specific findings:** which include (fever, anorexia, poor feeding, , myalgia, arthralgia, hypotension, petechiae, macular rash). ^(13,14)

(2). **Meningeal irritation:** which include (neck stiffness, back pain, Kernig sign, Brudzinski sign).⁽¹⁵⁾

(3). **Increased intracranial pressure (ICP):** is suggested by headache, vomiting, bulging fontanel, widening of the sutures, oculomotor or abducent nerve palsy, hypertension with bradycardia and apnea .⁽¹⁶⁾

Diagnosis: Early diagnosis and prompt management are essential, not only to save life but also to prevent further complications. CSF analysis and culture remains the definitive method for diagnosis of meningitis. Analysis of CSF should include: gram-stain and culture, WBC count and differential, glucose and protein concentration.^(17,18)

Treatment: A child with rapidly progressing disease of less than 24 hours duration, in the absence of increased ICP, should receive antibiotics as soon as possible after lumbar puncture (LP) is performed. If there are signs of increased ICP or focal neurologic findings, antibiotics should be given without performing LP and before obtaining a computerized tomography (CT) scan.^(19,20)

Patients and Methods

Study design: This is a prospective descriptive study conducted for the period from 1st January 2009 to 1st January 2010 in AL-Zahra Teaching Hospital to assess the different patterns, clinical presentations and early complications of meningitis in children aged 1 month-15 years.

Study sample: Forty Out of one hundred children admitted to AL-Zahra Teaching Hospital with a clinical suspicion of meningitis were included as they match the inclusion criteria.

Inclusion criteria: Children (1 month-15 years) presented with signs and symptoms suggestive of meningitis admitted to the AL-Zahra Teaching Hospital during the period of the study in whom LP was done and it was not traumatic and CSF contained >5 WBC/mm³.

Exclusion criteria: Some patients were excluded for the following reasons:

1. Age \leq 30 days, because the clinical presentation and the laboratory profiles of CSF are different in this age group from older children.
2. If LP not done for any reason.
3. If CSF- WBC \leq 5/mm³.
4. If LP was traumatic.
5. If CSF had mixed bacterial growth.
6. If CSF grew coagulase negative staphylococci.
7. Presence of shunt within the central nervous system.
8. Presence of a known immunodeficiency.
9. Presence of a chronic neurological disease (e.g. cerebral palsy).

Bacterial meningitis was considered when any of the following criteria was present :⁽²¹⁾

- 1 . Positive CSF culture for known bacterial pathogen.
2. Positive CSF antigen study or gram stains in conjunction with a CSF WBC of $>$ 10/mm³.
3. Positive blood culture in conjunction with CSF- WBC of $>$ 100/mm³.
4. In the absence of bacterial isolate, CSF WBC of $>$ 4000/mm³.

Partially treated bacterial meningitis was considered if there is a history of antibiotic use before LP, negative CSF culture, negative gram stain and CSF pleocytosis (CSF WBC $>$ 5/mm³) with neutrophil predominance .⁽²²⁾

Viral meningitis was considered when there is no history of use of antibiotic before LP , CSF pleocytosis (CSF WBC $>$ 5/mm³) mainly of lymphocytes and negative csf culture for a known bacterial pathogen.⁽²²⁾

- CSF glucose was considered low when it was \leq 40mg/dl, CSF protein was considered high when it was \geq 100mg /dl, CSF cell (neutrophil or lymphocyte) predominance was considered when it was \geq 50% of total WBC count in CSF.^(23,24)

Statistical analysis of data:

- The data were processed using the statistical package for the social science (SPSS version 15). **P.value** was calculated by Chi-square test and considered significant when it was ≤ 0.05 .

Results

The mean age was 2.84 ± 3.47 years (range 1 month-15 years). There were 43 patients (32 male, 11 female) who were more than one month to one year, 57 patients (19 male, 38 female) who were more than one year to fifteen years of age. Males were 51 (51%) of the patients, females were 49 (49%) of the patients with male to female ratio of 1.04:1. Thirty (30%) of the patients had bacterial meningitis, Thirty- four (34%) had viral meningitis, thirty- six (36%) had partially treated bacterial meningitis. Twelve (40%) of patients with bacterial meningitis were under one year, eighteen (60%) were above 1 year. Seventeen (50%) of the patients with viral meningitis were under one year, and seventeen were above one year. Males affected more than females in bacterial and partially treated bacterial meningitis, but females affected more in viral meningitis.

In those under one year, the major symptoms were: fever in 40 (93%), vomiting in 27 (62%) and the major signs were: irritability in 22 (51%), lethargy in 20 (46%), bulging fontanel in 17 (39%). In those above one year, the major symptoms were: fever in 54 (94%), vomiting in 37 (64%) and the major signs were: neck stiffness in 34 (59%), positive Kernig sign in 16(28%).

The diagnosis of bacterial meningitis was based on a positive CSF-culture and CSF- gram stain in 15 cases (50%), positive CSF gram stain alone in 3 cases (10%), positive CSF culture alone in 7cases (23%) and positive CSF pleocytosis (WBC > 4000/mm) with neutrophil predominance in 5 cases (17%).

CSF glucose was low (<40 mg/dl) in 33 of cases (28 cases bacterial meningitis, 1 cases viral meningitis, 4 cases partially treated bacterial meningitis). The mean CSF glucose was 66 ± 27.88 mg/dl (minimal was 11mg/dl, maximal 188mg/dl).

CSF protein was high (≥ 100 mg/dl) in 51 of cases (27 cases bacterial meningitis, 8 cases viral meningitis, 16 cases partially treated bacterial meningitis). The mean CSF protein was 47 ± 62.36 mg/dl (minimal was 4 mg/dl, maximal was 471 mg/dl). CSF pleocytosis (CSF-WBC $\geq 5/\text{mm}^3$) with neutrophil predominance (neutrophil $\geq 50\%$ of CSF- WBC) was found in 65 of cases (25 cases bacterial meningitis, 4 cases viral meningitis, and 36 cases partially treated bacterial meningitis). CSF pleocytosis with lymphocyte predominance (lymphocyte $> 50\%$ of CSF-WBC) was found in 35 cases (5 cases bacterial meningitis, 30 cases viral meningitis).

CSF was gram-stain positive in 18 (60%) case of bacterial meningitis . CSF- culture was positive in 22 (73%) cases of bacterial meningitis, and the underlying organisms were: *Hemophilus influenzae* 8 cases (36%), *Streptococcus pneumoniae* 3 cases (14%) , *Neisseria meningitidis* 3 cases (14%), *E.coli* 4 cases (18%), *Enterococcus* 2 cases (9%) , *Group B Streptococci* 2 cases (9%) .

CSF- CRP was positive in 28 cases [23 (77%) cases of bacterial meningitis, 2 (6%) cases of viral meningitis, and 3 (8%) cases of partially treated bacterial meningitis].

Mean blood WBC count in meningitis was $9.000 \pm 7.420/\text{mm}^3$ (minimal $1.000/\text{mm}^3$, maximal $17.000/\text{mm}^3$). Fifteen (15%) cases had WBC less than $4000/\text{mm}^3$, 63% had WBC $4000-11000/\text{mm}^3$, and 22% had WBC count more than $11000/\text{mm}^3$.

Serum CRP was positive in 31 cases [16 (53%) cases of bacterial meningitis, 6 (18%) cases of viral meningitis, 9 (22%) cases of partially treated bacterial meningitis].

CSF-CRP, serum-CRP, CSF -gram stain, and CSF- culture were mainly positive in those not used antibiotic before admission. Positive CSF-CRP, serum CRP, and CSF- gram stain were mainly occurred in those had positive CSF culture.

During the period of hospitalization, the complications that happened were as following : **Recurrent convulsion** in 8 (27%) cases of bacterial meningitis, 3 (8%) cases of viral meningitis, and 2 (5%) cases of partially treated bacterial meningitis), **Subdural**

effusion in 7 (23%) cases of bacterial meningitis, 1 case (3%) of viral meningitis, **Brain atrophy** in 5 cases (17%) of bacterial meningitis, 1 case (3%) of viral meningitis,

Cerebral infarction in 3 cases (10%) of bacterial meningitis, 1 case (3%) of viral meningitis, **Communicating hydrocephalus** in 2 cases (7%) of bacterial meningitis.

Minimal duration of hospitalization of overall cases was 6 days, maximal duration was 20 days. Only 2 (2%) cases required admission to intensive care unit because of recurrent apnea. Death occurred in 5 (17%) cases of bacterial meningitis, 3 (9%) cases of viral meningitis and no cases in partially treated bacterial meningitis.

Table 1. Age distribution according to the sex .

Age	Male (n=51)		Female (n=49)		Total	P. value
	No.	(%)	No.	(%)		
1mo-1yr	32	(74)	11	(26)	43	<0.0001
>1yr-15yr	19	(33)	38	(67)	57	

Table 2 .Types of meningitis according to the age Group.

Type of meningitis	Age				Total	P. value
	1mo-1yr (n=43)		>1yr-15yr (n=57)			
	No.	(%)	No.	(%)		
Viral meningitis	17	(50)	17	(50)	34	0.595
Partially treated bacterial meningitis	14	(39)	22	(61)	36	
Bacterial meningitis	12	(40)	18	(60)	30	

Table 3. Types of meningitis according to the sex.

Type of meningitis	sex				Total	p. value
	Male (n=51)		Female (n=49)			
	No.	(%)	No.	(%)		
Viral meningitis	15	(45)	19	(55)	34	0.6
Partially treated bacterial meningitis	20	(56)	16	(44)	36	
Bacterial meningitis	16	(53)	14	(47)	30	

Table 4. Clinical features according to the types of meningitis.

Clinical features	Bacterial meningitis		Viral meningitis		Partially treated bacterial meningitis		Total
	No.	(%)	No.	(%)	No.	(%)	
Convulsion	22	(73)	18	(52)	7	(19)	47
Fever	29	(97)	32	(94)	33	(92)	94
Positive Kernig sign	10	(33)	6	(18)	3	(8)	7
Neck stiffness	23	(77)	11	(32)	6	(17)	40
Bulging fontanel	17	(57)	3	(9)	3	(8)	23
Vomiting	23	(77)	22	(65)	19	(53)	64
Headache	9	(30)	8	(23)	4	(11)	21
Irritability	16	(53)	7	(20)	10	(28)	33

Table 5. The laboratory findings according to the types of meningitis.

CSF findings		Bacterial meningitis		Viral meningitis		Partially treated bacterial meningitis	
		No.	(%)	No.	(%)	No.	(%)
CSF culture	+	22	(73)	0	(0)	0	(0)
	-	8	(27)	34	(100)	36	(100)
CSF pleocytosis	Lymphocyte predominant	5	(17)	30	(88)	0	(0)
	PMN predominant	25	(83)	4	(12)	36	(100)
CSF CRP	+	23	(77)	2	(6)	3	(8)
	-	7	(23)	32	(94)	33	(97)
Gram stain	+	18	(60)	0	0	0	(0)
	-	12	(40)	34	(100)	36	(100)
CSF glucose	≤ 40 mg/dl	28	(94)	1	(3)	4	(11)
	>40 mg/dl	2	(6)	33	(97)	32	(89)
CSF protein	<100 mg/dl	27	(90)	8	(24)	16	(44)
	≥100mg/dl	3	(10)	26	(76)	20	(56)
Hematological findings							
Serum CRP	+	16	(53)	6	(18)	9	(25)
	-	16	(47)	28	(82)	27	(75)
Hb level	≤ 10 gm/dl	9	(30)	12	(35)	10	(28)
	>10 gm/dl	21	(70)	22	(65)	26	(72)
WBC count	< 4000/mm ³	4	(14)	3	(9)	8	(22)
	4000-11,000/mm ³	19	(63)	21	(62)	23	(64)
	>11,000/mm ³	7	(23)	10	(29)	5	(14)
Platelet count	<150,000/mm ³	13	(43)	3	(10)	5	(14)
	150-450,000/mm ³	12	(40)	27	(79)	28	(78)
	>450,000/mm ³	5	(17)	4	(11)	3	(8)

Discussion

This study showed that the mean age of children with meningitis was 2.84 ± 3.47 years (range: 1 month-15 years), approximate the result (mean age 3 years) found by Husain EH, et al. ⁽²⁵⁾ Males were affected more than females, with male to female ratio of 1.04:1, this agree with result of Nashwan NJ. study ⁽²⁶⁾ Bacterial meningitis mainly occurred in those older than one year (60%). This in agreement with result of 66.3% of Farag HF, et al. In this study, fever was the most frequent presenting symptom (97%) of bacterial meningitis, 94% of viral meningitis, and 92% of partially treated bacterial meningitis. Franco, et al ⁽²⁷⁾ revealed fever in 92% in children with bacterial meningitis.

In this study The most common presenting signs in children aged less than one year with meningitis were irritability (51%)and bulging fontanel (39%). Franco C, et al reported bulging fontanel in 27%, irritability in 54% in those under 6 months with bacterial meningitis.

In this study The most common presenting signs in those older than one year with meningitis were neck stiffness (59%), seizure (51%), and positive Kernig sign (28%).

In this study, seizure was present in 73% of bacterial meningitis, 52% of viral meningitis. Seizure in bacterial meningitis was reported in 42% in Nashwan NJ.study, and 30% in Tunkel AR⁽²⁸⁾ study.

CSF glucose was low (<40mg/dl) in 94% of bacterial meningitis, 3% of viral meningitis, and 11% of partially treated bacterial meningitis. CSF protein was high (>100 mg/dl) in 90% of bacterial meningitis, 24% of viral meningitis and 44% of partially treated bacterial meningitis.

Somunen P, Kallio MJ ⁽²⁹⁾ found that mean CSF glucose was 52 mg/dl and mean CSF protein was 180 mg/dl in children with bacterial meningitis.

In this study, CSF gram stain was positive in 18 (60%) cases with bacterial meningitis. The sensitivity of gram stain was 60%, specificity and positive predictive value were 100%, and negative

predictive value was 85%. Chinchankar N, et al⁽³⁰⁾. reported positive CSF gram stain in 67% of bacterial meningitis.

CSF culture was positive in 22 (73%) cases of bacterial meningitis. The sensitivity of CSF culture was 73%, specificity and positive predictive value 100%, negative predictive value 90%. CSF culture was positive in 30% of Wisam E.⁽³¹⁾ study (40% Hib, 40% *Streptococcus pneumoniae*, 10% *Neisseria meningitidis*, 10% *E. coli*), in 35% of Sahai S, et al⁽³²⁾ study and 79% of Berkley J, et al⁽³³⁾. Study.

It was clear that H. influenzae is the most common microorganism responsible for bacterial meningitis in our study and in studies which were done in developing countries because Haemophilus influenzae vaccine is not available in our country and in these countries.

In our study, CSF-C-RP was positive in 77% of bacterial meningitis, 6% of viral meningitis, and 8% of partially treated bacterial meningitis. The sensitivity of CSF-CRP in bacterial meningitis was 77% , specificity 93% , positive predictive value 82%, and negative predictive value 90%. Pemde HK, et al⁽³⁴⁾. found that CSF-CRP was positive in 100% of bacterial meningitis and negative in 95% of viral meningitis. John M, et al⁽³⁵⁾. showed that CSF-CRP was positive in (91%) of bacterial meningitis. Abramson JS, et al⁽³⁶⁾. showed that CSF-CRP was positive in 97% of patients with bacterial meningitis with sensitivity of 97%, a specificity of 86%, positive predictive value of 77%, and negative predictive value of 99%.

Serum CRP in our study was positive in 53% of patients with bacterial meningitis, 18% of patients with viral meningitis, and 25% of patients with partially treated bacterial meningitis. Tankhiwale S.⁽³⁷⁾. showed that serum CRP was positive in 88% of bacterial meningitis.

Conclusions

1. Meningitis is one of the most serious infections in children, causing high rate of morbidity and mortality.
2. Males affected more than females in bacterial meningitis while females more affected in viral meningitis.
3. Bacterial meningitis was more common in children older than one year than those under one year.
4. H. influenzae type B is the leading causative agent of bacterial meningitis.
5. Fever was the most common presenting symptom in all age groups and in all types of meningitis followed by vomiting and poor feeding or appetite..
6. Irritability, lethargy and bulging fontanel were the most common presenting signs in those under one year. Neck stiffness and positive kernig sign were the most presenting signs in children older than one year.
7. Recurrent convulsion was the most frequent complication in bacterial and viral meningitis.
8. Positive CSF-CRP , serum –CRP mainly occurred in bacterial meningitis and may be a useful supplement for rapid diagnosis of bacterial meningitis.

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