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Research Paper

Etiology, Clinical, and Laboratory Profiles of Meningitis a Sample of Children

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ABSTRACT:

BACKGROUND:

Meningitis is a significant cause of morbidity and modality 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-l5 years admitted to children Welfare Teaching Hospital with clinical suspicion of meningitis during the period from 18 September 2007 to 15 March 2008 were included in this study. They were subjected to clinical examination, blood tests, cerebrospinal fluid tests (biochemical, bacteriological, and serological).

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 kerning 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 1n 22 (73%) patients, C-reactive protein was positive in 23(77%) patients).

Serum C-reactive protein was positive in 16(53%) patients with bacterial meningitis. 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 Cerebrospinal fluid was mainly found in patients with bacterial meningitis.

KEY WORDS: meningitis, children, C - reactive protein, lumbar puncture.

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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, chronic meningitis. [1,2] Meningitis also can be divided into septic, 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 followed by E. coli are the two most common causes of neonatal meningitis, while Streptococcus pneumonia, Neisseria meningitides, 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 or 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, Brudziniski sign. [15]
3) Increased ICP: is suggested by headache, vomiting, bulging fontanels, widening of the sutures, oculomotor or abducent nerve palsy, hypertension with bradycardia, apnea. [16]

Diagnosis: Early diagnosis and prompt management arc 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 hrs. duration, in the absence of increased ICP, should receive antibiotics as soon as possible after 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 CT scan. [19, 20]

PATIENTS AND METHODS:

Study design: This is a prospective descriptive study conducted for the period from 1st September 2007 to 1st March 2008 in Children Welfare Teaching Hospital to assess the different patterns, clinical presentations and early complications of meningitis in children aged 1 month-l5 years.

Study sample: Out of one hundred- forty children admitted to the children Welfare Teaching Hospital with a clinical suspicion of meningitis, only one hundred of them were included as they match the inclusion criteria.

Inclusion criteria: Children (1 month-l5 yean) presented with signs and symptoms suggestive of meningitis admitted to the Children Welfare Teaching Hospital during the period of the study in whom lumbar puncture was done and it was not traumatic and CSF contained >5 WBC/mm^3.

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

1. Age < 30 days, because the clinical presentation and the laboratory profiles of CSF are different in this age group from older children.
2. If lumbar puncture not done for any reason.
3. If CSF- WBC ≤ 5/mm^3.
4. If lumbar puncture 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/mm^3.
3. Positive blood culture in conjunction with CSF- WBC of > 100/mm^3.
4. In the absence of bacterial isolate, CSF WBC of > 4000/mm^3.

Partially treated bacterial meningitis was considered if there is a history of use antibiotic before LP, negative CSF culture, negative gram stain and CSF pleocytosis (CSF WBC > 5/nm3) with neutrophil predominance. [22]

Viral meningitis was considered when there is no history of use of antibiotic before LP, CSF pleocytosis (CSF WBC > 5/mm^3) mainly of lymphocytes and negative csf culture for a known bacterial pathogen. [22]

- CSF glucose was considered low when it was <40mg/dl, CSF protein was considered high when it was >l00mg /dl, CSF cell (neutrophil or lymphocyte) predominance was considered when it was >50% of total WBC
- Count in CSF. [23,24]

Data collection:

The following data were obtained from all the cases:

1. Name, age, sex, date of admission, address.
2. History of antibiotic use and its duration.
3. Signs, symptoms suggestive of meningitis (fever, headache, vomiting, decreased appetite, convulsion, type and duration of convulsion, irritability, lethargy, photophobia, neck stiffness, kernig sign, Brudziniski sign, bulging fontanel,

neurological deficit and its type, loss of consciousness).

4. Duration of signs and symptoms before admission.
5. Investigations:
   a. Blood for (Hb, WBC, platelet, CRP).
   b. CSF for (color, glucose, protein level, total WBC count and differential, CRP, gram stain, culture).

Serum and CSF CRP was detected by latex agglutination method using latex particle coated with goat IgG antihuman CRP which show agglutination in the presence of CRP. This qualitative test performed by mixing a drop (50 µl) of specimen with a drop (50 µl) of latex reagent on a disposable slide. Both were mixed gently. The test was considered positive if clear agglutination was visible macroscopically within 2 min. Absence of agglutination within 2 minutes indicate negative sample. Positive test occurred when serum or CSF-CRP level $\geq$ 6 mg/L. The type of CRP kit used in this study is CRP-latex (SPINREACT).

Brain CT scan was done only for 23 patients who had a suspicion of complications.

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. (Table.1).

Twelve (40%) of patients with bacterial meningitis were under 1 year, eighteen (60%) were above 1 year. Seventeen (50%) of the patients with viral meningitis were under 1 year, and seventeen were above 1 year. Fourteen (39%) of the patients with partially treated meningitis were under 1year, twenty two (61%) were above 1 year. P.value=0.595. (Table.2).

Males affected more than females in bacterial and partially treated bacterial meningitis, but Females affected more in viral meningitis. P.value = 0.6. (Table.3).

The overall clinical features of meningitis were as following:

Fever (94%), poor feeding (65%), vomiting (64%), convulsion (47%), neck stiffness (40%), lethargy (33%), bulging fontanel (23%), headache (21%), diarrhea (20%), positive kernig sign (19%), coma (7%), positive Brudziniski sign (5%), photophobia (4%).

The type of convulsion in meningitis was generalized in 32 cases and focal in 15 cases.

The major clinical features in all types of meningitis were fever, vomiting, and poor feeding.(Table.4).

In those under 1 year, the major symptoms were: fever in 40 (93%), vomiting in 27 (62%), the major signs were: irritability in 22 (51%), lethargy in 20 (46%), bulging fontanel in 17 (39%).

In those above 1 year, the major symptoms were: fever in 54 (94%), vomiting in 37 (64%), the major signs were: neck stiffness in 34 (59%), positive Kernig sign in 16(28%). (Table. 5).

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 7 cases (23%), and positive CSF pleocytosis (WBC >4000/mm) with neutrophil predominance in 5 cases (17%).

CSF was turbid in only 8 cases; all of them had bacterial meningitis.

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 ±27.88mg/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 ±62.36mg/dl (minimal was 4 mg/dl, maximal was 471 mg/dl). CSF pleocytosis (CSF-WBC >5/mm^3) with neutrophil predominance (neutrophil > 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 and the results were as follows: gram positive cocci in 3 cases (17%) , gram negative diplococci in 5 cases (28%), gram negative coccobacilli in 10 (55%).

CSF- gram stain was negative in all cases of partially treated bacterial meningitis.

CSF- culture was negative in all cases of partially treated bacterial meningitis. 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].

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]. (Table .6).

Positive CSF- culture and CSF-CRP were appeared mainly in those aged under 1 year, while positive CSF- gram stain, low CSF glucose (<40 mg/dl), positive serum CRP, and high CSF protein (>100 mg/dl) appeared mainly in those above 1 year. Low hemoglobin level (<10g/dl), and leucopenia (WBC <4000/mm^3) appeared mainly in those below 1 year. (Table. 7).

Positive CSF-CRP, serum CRP, and CSF- gram stain were mainly occurred in those had positive CSF culture. P.value=<0.0001. (Table .8).

Sensitivity, specificity, positive and negative predictive values of CSF-CRP, CSF- Gram stain, CSF -culture, and serum –CRP were revealed in (Table .9).

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
Coma	5	(17)	2	(59)	0	(0)	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
Lethargy	14	(47)	11	(32)	7	(19)	35
Photophopia	2	(7)	2	(6)	0	(0)	4
Positive Kernig sign	10	(33)	6	(18)	3	(8)	19
Poor feeding	23	(77)	28	(82)	14	(47)	65
Positive Brudzinski sign	3	(10)	1	(2)	1	(2)	5

Table 5 : Clinical features of meningitis according to the age group.

Clinical features	Age				Total
	1mo-1yr		> 1yr-15 yr		
	No.	(%)	No.	(%)	
Convulsion	25	(58)	22	(38)	47
Fever	40	(93)	54	(94)	94
Coma	2	(4)	5	(8)	7
Neck stiffness	6	(13)	34	(59)	40
Bulging fontanel	17	(39)	6	(10)	23
Vomiting	27	(62)	37	(64)	64
Headache	0	0	21	(37)	21
Irritability	22	(51)	11	(19)	33
Lethargy	20	(46)	15	(26)	35
Photophobia	0	0	4	(6)	4
Positive kernig sign	3	(6)	16	(28)	19
Positive Brudzinski sign	2	(4)	3	(5)	5

Table 6: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)

Table 7:The laboratory findings in meningitis according to the age group.

CSF findings		Age				Total
		1mo-1yr		>1yr-15yr		
		No.	(%)	No.	(%)	
CSF culture	+	14	(32)	8	(14)	22
	-	29	(68)	49	(86)	78
CSF pleocytosis	Lymphocyte predominant	23	(53)	13	(23)	35
	PMN predominant	20	(47)	44	(77)	65
CSF CRP	+	15	(34)	13	(22)	28
	-	28	(66)	44	(78)	72
Gram stain	+	7	(16)	11	(19)	18
	-	36	(84)	46	(81)	82
CSF glucose	≤ 40 mg/dl	13	(30)	20	(35)	33
	>40 mg/dl	30	(70)	37	(65)	67
CSF protein	<100 mg/dl	19	(44)	30	(53)	49
	≥100mg/dl	24	(56)	27	(47)	51
	>11,000/mm	5	(11)	17	(29)	22

Table 8:The results of CSF-CRP, Serum-CRP, and CSF- Gram stain according to the results of CSF culture.

Laboratory parameters		Positive CSF Culture (n=22)	Negative CSF culture (n=78)	Total	p.value
CSF-CRP	+	19	9	28	<0.0001
	-	3	69	72	
Serum-CRP	+	16	15	31	<0.0001
	-	6	63	69	
CSF-Gram stain	+	15	3	18	<0.0001
	-	7	75	82	

Table 9: Sensitivity, Specificity, positive and negative predictive value of CSF-CRP, serum –CRP, CSF culture, and CSF- Gram stain in bacterial meningitis.

Laboratory parameters	Sensitivity %	Specificity %	Positive predictive value %	Negative predictive value %
CSF –CRP	77	93	82	90
Serum-CRP	53	78	52	80
CSF culture	73	100	100	90
CSF- Gram stain	60	100	100	85

DISCUSSION:

This study showed that the mean age of children with meningitis was 2.84+3.47 years (range: 1 month-l5 years), approximate the result (mean age 3 years) found by Husain EH, et al. [25]

Males were affected more likely 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 is 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, 92% of partially treated bacterial meningitis. Franco, et al [27] revealed fever in 92% in children with bacterial meningitis.

The most common presenting signs in children aged less than one year with meningitis were irritability in 5l% and bulging fontanel 39%. Franco C, et al reported bulging fontanel in 27%, irritability it 54% it those under 6 months with bacterial meningitis.

The most common presenting signs in those older than one year with meningitis were neck stiffness (59%), seizure in 51%, and positive Kernig sign in 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 the mean CSF glucose was 52 mg/dl and the mean CSF protein was 180 mg/dl in children with bacterial meningitis.

In this study, CSF gram stain was positive in 18 (60%) oases 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 l00%, negative predictive value 90%. CSF culture was positive in 30% in Wisam E. [31] study, in 35% in Sahai S, et al [32] study and 79% in Berkley J, et al [33] study.

In our study, CSF-CRP 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% viral meningitis. John M, et al[35]. showed that CSF-CRP vas 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.

CONCLUSION:

1. Meningitis is one of the most serious infections in children, causing high rate of morbidity and mortality.
2. Males affected more likely 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 with bacterial meningitis and may be a useful supplement for rapid diagnosis of bacterial meningitis.

REFERENCES:

1. Probe. CG. Centlal Nervous System Infections. In Behrman RE, Kliegman RM, Jenson HB, editors. Nelson Textbook of pediatrics. 20 th ed. Philadelphia, pa: WB Saunders co; 2020:2936-48.
2. Chavcs-Bueno S, McCracken GH. Bacterial meningitis in children. Pediatr clin N Am. 2005;25: 795-810.
3. Dubos F, Lamotte B, Bibi-Triki F, et al. Clinical decision rules to distinguish between bacterial and aseptic meningitis. Arch Dis Child. 2006;91:647-50.
4. Martha Lmuller, Russell Wsteele. Pediatric Bacterial Meningitis.emedicine2019, Medscape.com/article/961497-overview.
5. Abdulwahed zainel, Hana Mitchell. Bacterial menigitis in children , neurological complication, associatrd risk factors , prevention .National Library of medicine .2021;9:535.
6. Shima Javadinia , Mohsen Tabasi .C-reactive protein of CSF , as sensitive approach for diagnosis of meningitis .National Library of medicine .2019;9:2372-77.
7. Nicole Wengem, Joshna Rhein.Baseline serum CRP level predicts mortality in cryptococcal meningitis. open forum infectious disease , 2020; 7 Issue 12.
8. Pollard AJ. Global epidemiology of meningococcal disease and vaccine efficacy-Pediatr Infect Dis J. 2004, 23: S 274-79.
9. Bridy-Pappas AE, Margolis MB, Center KJ. Streptococcus pneumoniae: description of the pathogen, disease epidemiology, treatment and prevention. Pharmacotherapy. 2005;25:1193-2012.
10. Yoger & Guzman-Cottrill J. Bacterial meningitis in children: Critical review of current concept. Drugs. 2005;65:1097 -120.
11. Strawser D. Pediatric bacterial meningitis in the emergency department. J emergency Nursing. 1997; 23:310-15.
12. Bonthius DJ, Karacay B. Meningitis and encephalitis in children an update. Neurol Clin N Am. 2002;20:1013-38.
13. Meli DN, Christen S, LEIB SL, Tauber MG. Current concepts in the pathogenesis of meningitis caused by streptococcus pneumonia. Cur Opin Infect Dis 2002;15:253-57.
14. Smith AL. Bacterial meningitis. Pediatric in Review 1993;14:11-18.
15. Spach DH, Jckson LA. Bacterial meningitis. Neurol Clin N Am. 1999;17:7ll-35.
16. Ostenbrink R, Moons KG, Theunissen CC. Signs of meningeal irritation at the emergency department: How often bacterial meningitis? Pediatr Emerg care. 2001;17:161- 164.
17. Kacica MA, Lepow ML. Meningitis: clinical presentation and work up. Pediatric annals. 1994;23: 69-75.
18. Pong A, Bradley JS. Bacterial meningitis and the newborn infant. Infect dis Clin North Am. 1999;13:711-23.
19. El Bashir H, Laundry M, Booy R Diagnosis and treatment of bacterial meningitis. Arch Dis Child. 2003;88:615-20.
20. Taylor MR, Keane CT, Periappuram M. Skin scraping is a useful investigation in

meningococcal disease. BMJ. 1997;314: 831-32.
21. Kanegayo J, Solicmanzadeh P, Bradley J. Lumbar puncture in Pediatric Bacterial Meningitis: Defining the Time Interval for Recovery of Cerebrospinal Fluid Pathogens After parenteral Antibiotic pretreatment. Pediatrics. 2001;108:1169- 74.
22. Farag HM, Abdel-Fattah MM, Youssri AM. Epidemiological, clinical, and prognostic profile of acute Bacterial Meningitis among Children in Alexandria, Egypt. Indian J Med Microbiol. 2005; 23: 95-101.
23. Oostenbrink R, Moons KG, Twijnstra MJ. Children with & meningeal signs. Arch Pediatr Adolesc Med. 2002;156:l189-94.
24. Vincent J, Thomas K, Mathew O. An improved clinical method for detecting meningeal irritation. Arch Dis Child. 1993;68:215-18.
25. Husain EH, Al-Shawaf F, Bahbahani E. Epidemiology of childhood meningitis in Kuwait. Med Sci Monit 2007;13:220-23.
26. Nashwao NJ. Acute Bacterial meningeal in children beyond the Neonatal period. Athesis submitted to the Iraqi Commision of Specialties of Pediatrics, 2000.
27. Franco C, L. mnoglia L, Hemandez I .Epidemiology and outcomes of bacterial meningitis in Mexican children: l0 year experience (1993 -2003). International J of infectious disease. 2007: 162: l-7.
28. Tunkel AR, Scheld WM: Acute bacterial meningitis, Lancet. 1995;346:1675-79.
29. Sormnunen P, Kallio MJ, Kilpi T. C-reactive protein is useful in distinguishing Gram stain negative bacterial meningitis from viral meningitis in children, J Pediatr. 1999;134:725-29.
30. Chinchankar N, Mane M, Bhave S. Diagnosis and outcome of bacterial meningitis in early childhood. Indian Pediatr. 2002;39:914-21.
31. Wisam E. Acute bacterial msnin8itis in children. A thesis submitted to the Iraqi Commision of Specialties of Pediatrics. 2006.
32. Sahai S, Mahdevan S, Srinivasan. Childhood bacterial meningitis in Pondicherry, South India. Indian J Pediali. 200l;68:839-41.
33. Berkley J, Mwangi I, Ngesta C. Diagnosis of acute meningeal in children at adistric hospital in sub-saharan Africa. Lancet. 2001;351:1753-57.
34. Pemde HK, Harish K, Thawrani YP. C-reactive protein in childhood meningitis. Indian J Pediatr. 1996;63: 73-77.
35. John M, Raj 15, Macaden R, Raghuveer TS. Cerebrospinal fluid C-reactive protein measurement, abedside test in the rapid diagnosis of meningeal. J Trop Pediatr. 1990;36:213-17.
36. Abramson JS, Hampton, KD, Babu S. The use of C-reactive protein from cerebrospinal fluid for differentiating meningitis from other central nervous system diseases. J Infect Dis. 1985;l5l:854-58.
37. Tankhiwale S. Bacteriological study of pyogenic meningitis with special reference to C-reactive protein. Indian J of medical microbiology. 2001;19:159-60.