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Prognostic factors in children with purulent meningitis in Turkey.

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Abstract

In this study the clinical and laboratory findings of 48 children with purulent meningitis were examined, prospectively, to determine the prognostic factors in childhood meningitis in a developing country. Patients were examined for the following variables: history of antibiotic use; period between onset of symptoms and hospital admission; age at presentation; sex; fever; convulsion; level of consciousness; malnutrition; anemia; leukocyte and thrombocyte counts; erythrocyte sedimentation rate; serum C-reactive protein (CRP) level; and cerebrospinal fluid (CSF) including white blood cell count; glucose, protein, and CRP concentrations; antibiotic treatment; neurological sequelae; and fatality rate during the hospital stay. Most of these parameters were re-evaluated in all patients 36-48 h after admission. Patients were divided into 3 groups: surviving without sequelae, surviving with sequelae, and not surviving (deceased). A total of 48 children, 19 girls (39.5%) and 29 boys (60.5%), aged 2 months to 13 years, were included in the study. Of the 48 patients, 29 (60.5 %) survived without sequelae, 13 (27%) survived with sequelae and 6 (12.5%) died. In a comparison among groups, we found that absence of anemia, low ($<$ 1,000) CSF white blood cell (WBC) count, and high CRP level at admission were the indicative of poor prognosis. Thirty-six to 48 h after admission, the presence of fever, depressed level of consciousness, high ($>$ 1,000) CSF WBC count, and low CRP level were also poor prognostic factors. In addition, we observed that mortality rate was lower in the penicillin G + chloramphenicol group than in the ampicillin-sulbactam + cefotaxime group ($P < 0.05$). The mean period between onset of symptoms and hospital admission was longer in the surviving with sequelae and in the not surviving groups than in the surviving without sequelae group ($P < 0.05$).

KEYWORDS: purulent meningitis, prognosis, prospective study

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Original Article

Prognostic Factors in Children with Purulent Meningitis in Turkey

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In this study the clinical and laboratory findings of 48 children with purulent meningitis were examined, prospectively, to determine the prognostic factors in childhood meningitis in a developing country. Patients were examined for the following variables: history of antibiotic use; period between onset of symptoms and hospital admission; age at presentation; sex; fever; convulsion; level of consciousness; malnutrition; anemia; leukocyte and thrombocyte counts; erythrocyte sedimentation rate; serum C-reactive protein (CRP) level; and cerebrospinal fluid (CSF) including white blood cell count; glucose, protein, and CRP concentrations; antibiotic treatment; neurological sequelae; and fatality rate during the hospital stay. Most of these parameters were re-evaluated in all patients 36-48 h after admission. Patients were divided into 3 groups: surviving without sequelae, surviving with sequelae, and not surviving (deceased). A total of 48 children, 19 girls (39.5%) and 29 boys (60.5%), aged 2 months to 13 years, were included in the study. Of the 48 patients, 29 (60.5%) survived without sequelae, 13 (27%) survived with sequelae and 6 (12.5%) died. In a comparison among groups, we found that absence of anemia, low (< 1,000) CSF white blood cell (WBC) count, and high CRP level at admission were the indicative of poor prognosis. Thirty-six to 48 h after admission, the presence of fever, depressed level of consciousness, high (> 1,000) CSF WBC count, and low CRP level were also poor prognostic factors. In addition, we observed that mortality rate was lower in the penicillin G + chloramphenicol group than in the ampicillin-sulbactam + cefotaxime group ($P < 0.05$). The mean period between onset of symptoms and hospital admission was longer in the surviving with sequelae and in the not surviving groups than in the surviving without sequelae group ($P < 0.05$).

Key words: purulent meningitis, prognosis, prospective study

Bacterial meningitis accounts for a major group of hospital admissions in everyday pediatric practice, and remains a disease with significant morbidity and mortality [1, 2]. In particular, it is associated with a high case-fatality rate in developing countries [3-14]. A number of clinical and laboratory features including state of consciousness, age, seizures, duration of illness, and several laboratory factors such as total cerebrospinal fluid (CSF) white blood cell (WBC) count, concentration of glucose in CSF, leukopenia, anemia, and thrombocytopenia, have been correlated with the outcome of bacterial meningitis [15].

In this study the clinical and laboratory findings of 48 children with purulent meningitis in Turkey were

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examined, prospectively, to determine the prognostic factors in childhood meningitis in a developing country.

Material and Methods

This study includes 48 children with purulent meningitis who were followed at Yüzüncü Yıl University, Faculty of Medicine, Department of Pediatrics, between February 1999 and December 2000. Bacterial meningitis was diagnosed on the basis of clinical symptoms and signs, as well as on CSF findings including pleocytosis (more than 10 cells/mm^3) with predominance of polymorphonuclear leukocytes, and on the presence of bacteria as demonstrated by at least one of the following: (1) positive CSF Gram stain preparation, (2) positive CSF bacterial latex particle agglutination, or (3) positive CSF culture [16–18].

Meningitis caused by *Mycobacterium tuberculosis* was excluded. Patients with underlying immunodeficiencies, central nervous system structural defects, central nervous system shunts, or who had undergone recurrent central nervous system surgery were excluded. Cases of relapsing meningitis, defined as the reappearance of and laboratory signs of meningitis with identical bacterial etiology within 4 weeks of the first episode, were not included.

Patients were examined for the following variables: history of antibiotic use; period between onset of symptoms and hospital admission; age at presentation; sex; fever; convulsion; level of consciousness; malnutrition; anemia; leukocyte and thrombocyte counts; erythrocyte sedimentation rate (ESR); serum C-reactive protein (CRP) level; and CSF findings including WBC count, glucose, protein, and CRP concentrations; antibiotic treatment (either penicillin G + chloramphenicol or ampicillin-sulbactam + cefotaxime, which were randomized initially and changed as required during follow-up); neurological sequelae (as evaluated by clinical examination and cranial computerized tomography); and fatality rate during the hospital stay. Most of these parameters were re-evaluated in all patients 36–48 h after admission. Level of consciousness was determined based on the clinical status of the patient. Nutritional status of the children was assessed by the Gomez classification, using weight for age; weight that was 90%–110% of the Gomez values was accepted as normal, and weight less than 90% of the Gomez values were classified as malnourished [19].

In all patients, dexamethasone (0.6 mg/kg/day for 4 days) was given just before antibiotic therapy. Patients were divided into 3 groups: surviving without sequelae, surviving with sequelae, and not surviving.

The normal ranges of hemoglobin value and leukocyte count were 10–16 g/dl and 4,000–11,000/mm^3, respectively. The following values for CSF WBC count, protein, and glucose were accepted as normal: WBC count range of 0 to 7 WBC/mm^3; protein range of 5 to 40 mg/dl; and glucose $< 60\%$ of serum glucose level [20, 21].

Statistical analysis was performed using the Chi square test and variance analysis test (P value of less than 0.05 was considered statistically significant).

Results

A total of 48 children, 19 girls (39.5%) and 29 boys (60.5%), aged 2 months to 13 years, were included in the study. Most of these children were in the 3-month or the 3-year age group (Table 1). Of the 48 patients, 29 (60.5%) survived without sequelae, 13 (27%) survived with sequelae, and 6 (12.5%) died. Table 1 shows the effect of several clinical and laboratory features and antibiotic treatment on prognosis.

In a comparison among groups, we found that absence of anemia, low (< 1,000) CSF WBC count, and high CRP level at admission were indicative of poor prognosis. Thirty-six to 48 h after admission, the presence of fever, depressed level of consciousness, high (> 1,000) CSF WBC count, and low CRP level were also poor prognostic factors. Fever (> 38 °C) persisted approximately 7.5 days in all patients. While no difference in presence of fever at admission was observed among groups, fever was more frequent in the not surviving group at 36–48 h after hospitalization ($P < 0.05$).

The mean period between onset of symptoms and hospital admission was 3.79 ± 3.09 days in the surviving without sequelae group; it was 5.00 ± 4.39 days in the surviving with sequelae group and 9.83 ± 8.01 days in the not surviving group ($P < 0.05$).

Antibiotherapy was given for at least 10 days in all patients, and was continued in patients with complications for 4 weeks. We compared the groups in terms of initial antibotherapy, and observed that mortality rate was lower in the penicillin G + chloramphenicol group than in the ampicillin-sulbactam + cefotaxime group ($P < 0.05$) (Table 1).

The microorganisms isolated from CSF cultures were as follows: *Staphylococcus* in 3 (6.25%) infants, *Strepto-*

Table 1 The effect of several clinical and laboratory features and antibiotic treatment on prognosis

Pameters	Without Sequelae (n: 29) n (%)	With Sequelae (n: 13) n (%)	Not Surviving (n: 6) n (%)	X^2	*P*
History of antibiotic use	14 (48)	7 (54)	2 (33)	0.69	> 0.05
Age					
2–12 months	11 (38)	5 (38)	3 (50)		
13–36 months	7 (24)	3 (24)	1 (17)	0.34	> 0.05
> 36 months	11 (38)	5 (38)	2 (33)		
Sex					
Girl	9 (31)	7 (54)	3 (50)	2.26	> 0.05
Boy	20 (69)	6 (46)	3 (50)		
Fever at admission	12 (41)	3 (23)	3 (50)	1.74	> 0.05
Fever 36–48 h after admission	1 (4)	0 (0)	2 (33)	8.76	< 0.05
Convulsion at admission	14 (48)	6 (46)	2 (33)	0.44	> 0.05
Depressed level of consciousness at admission	24 (83)	10 (77)	5 (83)	0.22	> 0.05
Depressed level of consciousness 36–48 h after admission	10 (34)	9 (69)	5 (83)	7.38	< 0.05
Malnutrition	14 (48)	9 (69)	3 (50)	1.63	> 0.05
Anemia at admission	14 (48)	8 (61)	0 (0)	6.43	< 0.05
Anemia during 36–48 h after admission	12 (41)	9 (69)	0 (0)	8.16	< 0.05
Leukocyte count at admission					
Normal	8 (28)	6 (46)	2 (33)		
Leukopenia (< 4,000/mm^3)	3 (10)	1 (8)	0 (0)	7.9	> 0.05
Leukocytosis (> 11,000/mm^3)	18 (62)	6 (46)	4 (67)		
Leukocyte count 36–48 h after admission					
Normal	11 (38)	5 (38)	4 (67)		
Leukopenia (< 4,000/mm^3)	0 (0)	0 (0)	0 (0)	1.7	> 0.05
Leukocytosis (> 11,000/mm^3)	18 (62)	8 (62)	2 (33)		
Thrombocyte count at admission					
Normal (> 150,000/mm^3)	28 (96.5)	10 (77)	5 (83)	3.99	> 0.05
Low (< 150,000/mm^3)	1 (3.5)	3 (23)	1 (17)		
Thrombocyte count 36–48 h after admission					
Normal (> 150,000/mm^3)	23 (79)	11 (85)	4 (67)	0.80	> 0.05
Low (< 150,000/mm^3)	6 (21)	2 (15)	2 (33)		
ESR (mm/h) at admission					
Normal (≤ 20 mm/h)	6 (21)	1 (8)	2 (33)	1.95	> 0.05
High (> 20 mm/h)	23 (79)	12 (92)	4 (67)		
ESR (mm/h) 36–48 h after admission					
Normal (< 20 mm/h)	4 (14)	1 (8)	2 (33)	2.20	> 0.05
High (> 20 mm/h)	25 (86)	12 (92)	4 (67)		
Serum CRP level at admission					
Normal (> 6 mg/dl)	4 (14)	2 (15)	0 (0)	1.00	> 0.05
High (≥ 6 mg/dl)	25 (86)	11 (85)	6 (100)		
Serum CRP level 36–48 h after admission					
Normal (> 6 mg/dl)	6 (21)	1 (8)	0 (0)	2.38	> 0.05
High (≥ 6 mg/dl)	23 (79)	12 (92)	6 (100)		
CSF findings at admission					
WBC (/mm^3)					
< 1,000	14 (48)	12 (92)	3 (50)	7.58	< 0.05
> 1,000	15 (52)	1 (8)	3 (50)		

Protein (mg/dl)					
Normal	3 (10)	1 (8)	0 (0)	0.70	> 0.05
High	26 (90)	12 (92)	6 (100)		
Glucose (mg/dl)					
Normal	2 (7)	1 (8)	0 (0)	0.46	> 0.05
Low	27 (93)	12 (92)	6 (100)		
CRP level (mg/dl)					
Normal (≤ 6 mg/dl)	23 (79)	9 (69)	1 (17)	9.08	< 0.05
High (> 6 mg/dl)	6 (21)	4 (31)	5 (83)		
CSF findings 36–48 h after admission					
WBC (/mm^3)					
< 1,000	21 (72)	10 (77)	1 (17)	7.79	< 0.05
> 1,000	8 (28)	3 (23)	5 (83)		
Protein (mg/dl)					
Normal	6 (21)	4 (31)	1 (17)	0.66	> 0.05
High	23 (79)	9 (69)	5 (83)		
Glucose (mg/dl)					
Normal	5 (17)	1 (8)	0 (0)	1.72	> 0.05
Low	24 (83)	12 (92)	6 (100)		
CRP level (mg/dl)					
Normal (≤ 6 mg/dl)	28 (96.5)	10 (77)	4 (67)	5.88	= 0.05
High (> 6 mg/dl)	1 (3.5)	3 (23)	2 (33)		
Antibiotic treatment					
Penicillin G + Chloramphenicol	16 (55)	2 (16)	2 (33)	6.04	< 0.05
Ampicillin-Sulbactam + Cefotaxime	13 (45)	11 (84)	4 (67)		

ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; CSF, cerebrospinal fluid; WBC, white blood count.

coccus in 1 (2.0%) infant, Gram negative coccobacillus in 1 (2.0%) infant, Gram positive coccobacillus in 1 (2.0%) infant, and *Proteus mirabilis* in 1 (2.0%) infant. Bacteria were detected in the Gram stain of 17 (35%) patients, as follows: Gram positive coccus in 10 subjects, Gram positive bacillus in 2 subjects, Gram negative coccus in 3 subjects, and Gram negative bacillus in 2 subjects.

The following neurological deficits were detected in the surviving with sequelae group: hydrocephalus in 4 patients; hydrocephalus and choreoathetoic cerebral palsy in 1; hydrocephalus, peripheral facial palsy, and right hemiparesis in 1; hydrocephalus, subdural effusion, and brain abscess in 1; subdural empyema and inability to speak in 1; cerebral infarction, spastic cerebral palsy, and motor mental retardation in 1; brain abscess and inability to speak in 1; left hemiplegia in 1; peripheral facial palsy and strabismus in 1; and right abducence palsy in 1. Of 6 not surviving patients, 4 (67%) were diagnosed with hydrocephalus; 1 (16.5%) with subdural effusion; and 1 (16.5%) with mild dilatation in the lateral ventricle.

Discussion

The mortality rates in children with meningitis have been reported to range 1.4% and 47% in different series, and rates were found to be much higher in developing countries [1–14, 22–28]. In our study the mortality rate was 12.5%, which is lower than that reported in most other developing countries.

A number of studies have been performed to determine the prognostic factors in childhood purulent meningitis. In most studies, altered consciousness and convulsions on admission were found to be risk factors associated with death [3, 4, 6, 9, 11, 13, 14, 28–30]. Akpede *et al*. [31] found that age < or = 2 yrs, ill for > 7 days, antibiotic treatment, focal nerve deficits, abnormal posturing, and abnormal muscle tone were particularly associated with neurological sequelae, or with shock, coma, and death. Seizures were associated with either outcome [31]. Rothrock *et al*. [32] noted that there was no difference in incidence of focal neurologic signs and mortality between children who were pretreated and those who were not treated with antibiotics before the diagnosis of bacterial meningitis. In our series, we found that late

admission to hospital, the presence of fever, and depressed level of consciousness at 36–48 h after admission were poor prognostic factors. We also observed that the mortality rate was lower in the penicillin G + chloramphenicol group than in the ampicillin-sulbactam + cefotaxime group.

In many studies, it has been reported that low CSF leukocyte count is associated with high fatality rate [5, 6, 28]. In contrast, Javadekar *et al*. [14] reported that a CSF leukocyte count of more than 1,000 cells/mm^3 and CSF protein more than 500 mg/dl were statistically significant factors associated with higher mortality. They also noted that in cases of CSF glucose level below 20 mg/dl and CSF/blood glucose ratio below 0.2, the increase in mortality was highly significant [14]. Shaaban *et al*. [33] reported that a significant increase in the CSF protein concentration determined on admission was found in patients who died as compared with that found in those who survived. However, they noted that no difference was observed between the admission CSF leukocyte count in patients who died and that of those who survived [28]. In our series, we found that absence of anemia, low (< 1,000) CSF WBC count, and high CRP level at admission were indicative of poor prognosis. Thirty-six to 48 h after admission, high (> 1,000) CSF WBC count and low CRP level were also poor prognostic factors.

We can conclude that acute bacterial meningitis continues to be an important health problem in developing countries, and that public health measures will be necessary to minimize the impact of sequelae and reduce the mortality rate in infected children.

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