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STUDY OF PREDICTIVE VALUE OF CLINICAL FEATURES IN THE DIAGNOSIS OF MENINGITIS IN INFANTS AND CHILDREN

Pediatrics

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ABSTRACT

The present study "Study of predictive value of clinical features in the diagnosis of meningitis in infants and children" was done in Department of Pediatrics, Darbhanga Medical College and Hospital, Laheriasarai.A standardized questionnaire, which documented symptoms and signs and the results of laboratory investigations was completed prospectively for each child. The history of illness was initially obtained from complaints volunteered by parents. This was then complemented by specific questions from the investigator. The physical examination of child documented the general status of child sign of meningeal irritation and other vital measurement. Lumbar puncture was performed, CSF was collected in sterile vials directly from the needle.Of the total 132 patients studied 42 had meningitis, and 90 did not have meningitis. Although lumbar puncture were performed due to suspicion of meningitis.Almost all the clinical features present in both groups. Even sign of meningeal irritation (brudzinski's sign, kernig's sign and neck rigidity) also present in nonmeningitic group. Hence on the basis of clinical features only, meningitis could not be diagnosed. All the suspicious case of meningitis should be confirmed by cerebrospinal fluid examination.

KEYWORDS

INTRODUCTION

Meningitis is most devastating infections in children associated with a high rate of acute complication, mortality and risk of chronic morbidity. In India community incidence of meningitis in India is not known, 95% of cases occur under 5 years of age. The risk of infection is greatest among infants specially in preterm baby.

Inflammation of the meninges (brain and spinal cord) is called meningitis that results in occurrence of meningeal symptoms eg, headache, nuchal rigidity, photophobia, refusal of feeds, altered sensorium, seizures etc. Most of these manifestations are non-specific and often indistinguishable from those of other febrile illnesses. In order to improve prognosis of the infection, early diagnosis and prompt treatment are crucial to prevent mortality and incidence of neurological sequele, but published data suggest that fewer than half of cases of childhood meningitis (30%) are identified at first assessment in hospital.

An meningitis is serious disease because of the severe nature of the disease, lumbar puncture-the most valuable procedure to establish the diagnosis of meningitis. is performed. Whenever the disease is even minimally suspected. For primary care worker with limited training and facilities, World Health Organization Integrated Management of Childhood Illness (IMCI) guidelines advice referral of all children with general danger sings as potential meningitis cases.

In practice, a simplified set of IMCI signs (Lethargy, unconsciousness, seizures or neck stiffneck) are reported to be 98% sensitive and 72% specific for meningitis at the outpatient level. This is relevant in outpatient departments and private clinics specially when the physician has to take decision whether to tap or not to tap.

It may be possible to observed a pattern which would differentiate a meningitic child from a non-meningitic one. For all practical purposes the objective measure of the presence or absence of meningitis on the basis of clinical features can be validated against cerebrospinal fluid (CSF) fining. Thus it is proposed to study clinical features in children undergoing lumbar puncture for the suspicion of meningitis to delineate which signs and symptoms are most indicative of the diagnosis as meningitis at different ages and also to study the accuracy of these clinical features for making a diagnosis of meningitis. Many observational scales for identifying serious illness in young children have been devised. It is also proposed to assess the accuracy of such a scale (Modified Yale's Score) in the diagnosis of meningitis.

AIMS AND OBJECTIVES

1. To comparative study of the clinical features among children with meningitis and without meningitis who have undergone CSF analysis on suspicion of meningitis.
2. To study the accuracy of various clinical features which are predictive of diagnosis of meningitis.

MATERIAL AND METHODS

The present study "Study of predictive value of clinical features in the diagnosis of meningitis in infants and children" was done in Department of Pediatrics, Darbhanga Medical College and Hospital, Laheriasarai.

Selection of Patients :

Patients between one month to twelve years of age were selected from in patient Department of Pediatrics DMCH, Laheriasarai, for the study. A standardized questionnaire, which documented symptoms and signs and the results of laboratory investigations was completed prospectively for each child. The history of illness was initially obtained from complaints volunteered by parents. This was then complemented by specific questions from the investigator. The physical examination of child documented the general status of child sign of meningeal irritation and other vital measurement. Lumbar puncture was performed, CSF was collected in sterile vials directly from the needle. CSF was examined for cells (using Neubour Chamber

after adding Turk's fluid to dissolve red blood cell), protein and sugar by another observer and sent for bacterial culture.

On Examination :Weight, Body temperature as measured, Pete chiae / rash, Modified Glasgow Coma Scale (GCS). Trauner& James (1985), Capillary refill time, Photophobia, Nuchal rigidity, Kernig's sign, Brudzinski's sign, Vincent's sign (recorded in posture 3 as described by vincent. Thomas and Matheus 1993), Anterior fontanelle (when open) for bulging/tense, Fudus Examination, Tone, Focal neurological deficit, Deep tendon reflexes, Plantar responses, Ankle clonus, Presence of associated illness.

All the study items entered were coded on a 2-3 paint scale on a questionnaire (appendix).

In children 2 years of age or less, special note was also made of the following :
1. Quality of cry
2. Hydration
3. Consolability
4. color
5. Response to overtures

These five features were recorded as components as a modified Yale's score (modified from McCarthy et al, 1982) and 3 paint scale (0,1,2,) the individual score were added to give a modified yale score ranging from 0-10.

In addition total and differential leukocyte count in blood (TLC and DLC) was done by standard methods.

Outcome Factor:
Presence or absence of CSF pleocytosis (i.e, cell > 10/cu mm). The diagnosis of meningitis was made if cerebrospinal fluid pleocytosis defined as > 10 cells /cumm was found on CSF examination.

Statistical methods :
Clinical features were compared between meningitis and non meningitis children. Data was entered on a dbase file and univariate analysis done using Epi-info package on computer. Sensitivity, specificity and predictive value of various clinical finding were calculated by constructing 2x2 table. In addition, different age groups of patients (>24 months, < 24 Months, 12 months and 6 monthes) were analyzed separately, as were children with fever and convulsion. Sensitivity specificity and predictive value of various combinations of clinical features were also calculated.

RESULTS

Table – 1 Comparative Study Of Symptoms In Patients With And Without Meningitis.

Symptoms	Meningitis (n=42)		No meningitis (n=90)		OR (95% CI)	P value*
	No.	%	No.	%		
Fever	34	81	76	88.6	0.67(0.2-2.1)	0.616
Fever grade						
Low	2	5.9	7	9.2		
Moderate	10	29.4	18	23.7		
High	22	64.7	51	67.1	-	0.870
Fever onset						
Insidious	1	3	4	5.3		
Subacute	4	11.7	7	9.2		
Acute	29	84.3	65	85.5	-	0.866
Convulsion	20	47.6	63	70	0.42(0.1-4.5)	0.057
Convulsion type						
Generalised	18	90	56	85.5		
Focal	2	10	7	11.1	0.67(0.1-4.5)	0.955
Convulsion frequency						
1-3/day	14	70	44	69.8		
4-6/day	4	20	16	25.4		
>6/day	2	10	3	4.8	--	0.870
Headache (presence or absence recorded in 47 patients)	14/20	70	11/32	34.3	4.80(1.1-21.6)	0.019**
Refusal to feed	41	97.6	82	91.1	3.1(.4-69.4)	0.547
Altered sensorium	28	66.7	50	55.6	1.51(0.6-3.7)	0.434
Vomiting	19	45.2	40	44.4	1.07(0.5-2.6)	0.971
Weakness	9	21.4	9	10	2.83(0.4-2.2)	0.990
Ear Discharge	6	14.3	7	7.8	2.17(0.5-8.9)	0.379
Irritability	16	38.1	35	38.9	0.91(0.4-2.2)	0.990

* x^2 test with yates correction/ fisher's exact test.
** Significant

Table – 2 Comparative Study Of Clinical Sign In Patients With And Without Meningitis.

Symptoms	Meningitis (n=42)		No meningitis (n=90)		OR (95% CI)	P value*
	No.	%	No.	%		
Temperature on admission						0.923
<100^{0}F	13	31.0	30	33.3		
100^0-102^{0}F	9	21.4	20	22.3		
>102^{0}F	20	47.6	40	44.4	--	
Rash/Petechiae	4	9.5	3	3.3	-	0.254
Capillary refill time						0.281
< 3 sec	36	85.7	78	86.7		
3-5 sec	6	14.3	8	8.9		
> 5sec	0	0	4	4.4	--	
Modified GCS						0.432
> 10	24	57.1	50	55.6		
7-10	6	14.3	18	20.0		
<7	12	28.6	22	24.4	--	
Photophobia	1	2.4	4	2.4	1.21 (0-18.1)	0.652

Brudzinski's sign	4	9.5	1	1.1	7.78(0.1-205.1)	0.075
Kernig's sign	7	16.7	5	5.6	3.27(0.79-13.8)	0.062
Neck rigidity	19	45.2	10	11.1	6.23 (2.2-17.9)	0.0001***
Vincent's sign (examied in 39pts)	11/14	78.6	4/28	14.2	18.33(2.7-152.1)	0.0001**
Ant. Fontanelle tense/bulgins (open in 61pts)	8/17	47.1	11/50	22.0	3.15(0.8-12.9)	0.034**
Fundus change	7	16.7	15	16.7	1.03(0.3-3.3)	0.837
Increased tone	15	35.7	30	33.3	1.15(0.4-2.8)	0.920
Focal deficit	11	26.2	7	7.8	4.5(1.3-16.0)	0.012**
Abnormal deep reflexes	14	35.7	39	43.3	0.74(0.29-1.9)	0.622
Plantar extensor (examied in 67pts)	9/22	40.9	17/50	34.0	1.29(0.4-4.8)	0.851
Clonus	4	9.5	2	2.3	3.84(0.5-35.3)	0.301
Associated illness	5	11.9	28	31.1	0.29(0.1-1.0)	0.045**
Blood TLC Mean SD	8926.561763.2		10156.849952		-	0.405
Blood polymorphs % Mean SD	68.38 13.12		57.54 13.58		-	0.002**

* X^2 test with yates correction/fisher exact test used for discrete variable student 't' test used for continuous variable.
** Significant.

DISCUSSION

Meningitis is a great burden for patients family and medical staff, even epidemiology has changed a lot after novel immunization and infection prevention strategies. Most diagnostic approaches have aimed at maximizing its sensitivity. The diagnosis of meningitis is based on clinical feature confirmed by cerebrospinal fluid (CSF) examination. Lumber puncture has been performed whenever meningitis is included in the differential diagnosis.

In my study all the patients in the meningitis group had CSF polymorphs more than 30/cumm. ShileBhave et al (2002) reported all meningitis patients CSF have >40 leukocye/mm^3. In patients without meningitis CSF pleocytosis was less than 10 cell/mm^3 with was predominantly lymphocytes. 35 of our 42 patients with abnormal CSF had polymorphonuclear cells of 70% or more. Thus, we can conclude that the most of these patients had acute bacterial meningitis. A small percentage may have had viral meningitis, encephalitis or even tubercular meningitis.

In our study only 5 patients had positive CSF culture whereas in western studies it goes upto 70%. The reason behind low yield of culture is use of antibiotic prior to admission and may include poor quality of culture media.

In our study 1-6 month 19%, 6-12 month – 23.8%, 42.8% of patients below age < 1yr. In T.A. Ogunlesi (2005) & Sheila Bhave et al (2002) study infants comprises 38.7% and 78% respectively.

In our study fever is one of the most common symptoms in i.e. in patients of meningitis (81%) as well as those without meningitis (88.6%). Thus fever alone is a highly nonspecific symptom for the diagnosis of meningitis in all age groups. In patients aged more than 2 years, almost all patients of meningitis were febrile while in patients below < 2year only 65% were febrile. This implies that meningitis rarely occurs in the absence of fever in children aged > 2 yr, but is not uncommon without fever in infancy. James A. Berkly (2004) reported fever in 85% case as meningitis and have formulated an indicator for absence of meningitis which includes

(I) absence of history of fever
(ii) H/o Diarrhea
(iii) Positive malaria slides,

In our study altered consciousness (GCS<10) was present in 66.7% of patients of meningitis and 55.6% in patients without meningitis. As this is common in both groups, this symptom has got little significance regarding the prediction of meningitis. ShilaBhave et al (2002) observed altered sensorium in 98% of patients in meningitis. M. W. Weber et al (2002) observed impaired sensorium in 84% in meningitis and 50% in non meningitis group with 84% sensitivity and 76% specificity in predicting meningitis. J. A. Berkley (2004) reported adjusted likelihood ratio (ALR>1.5) for impaired consciousness making it a significant predictor of meningitis in comparison to normal consciousness (ALR <0 .74). Srivastava et al (1968) and Udani et al (1983) observed altered sensorium in 12% of their meningitis patients.

Clinical Prediction model for bacteremia/bacterial meningitis :

	Sensitivity%	Specificity%
(1) Clinical appearance + abnormal wbc count	83.9	54.0
(2) Clinical appearance + abnormal wbc count + urine analysis	87.1	50.7
(3) Temperature + appearance + lab investigation	93.6	27.3%

The most common final diagnosis in non meningitic group (90) in our study were acute encephalitis, febrile seizure, acute gastroenteritis with electrolyte imbalance, and pneumonia. Levy, Wong, Fried (1990) observed that the diseases most suggestive of meningitis were gastroenteritis, pneumonia, otitis, tonsillitis and urinary tract infection in their series.

Comparison of the clinical features and white blood cell counts of patients in our study we found many variables which were significant on univariate analysis (P<0.05). Variable with P value <0.25 on univariate analysis were entered into a multiple logistic regression analysis. These included convulsions, headache, neck rigidity,Brudzinski's sign Kernig's sign, photophobia, Vincents sign, tense/bulging anterior fontanelle, focal neurological deficit, associated illness and peripheral polymorphs percentage. This is a form of stratified analysis used to select those variables with a significant independent relation with the dichotomous outcome variable in this case the presence or absence of meningitis. In this way the effect of interaction between study variables is eliminated.

In our study, only 2 variables namely neck rigidity and blood polymorphs % were significant independent predictors of meningitis. Presence of one or both of signs were present in 24 patients each with and without meningitis giving a sensitivity of 68.5% and specificity of 71.4%. Both of them were present in 10 patients with meningitis and none of the patients without meningitis, giving a sensitivity of 28.5% and specificity of 100%. So in a given patient who is undergoing lumbar puncture for the diagnosis of meningitis, we can judge the chance of having meningitis by looking at these 2 clinicolaboratory features only. M.W. Weber et al (2002) conducted a similar study, in which regression analysis was performed for the groups of variables to identify independent predictors. For meningitis Independent predictors were vomiting, convulsion, bulging fontanelle, reduced feeding, irritability, sick appearance, arousal, restlessness and stiff neck. On examination Wheeze and Cough heard are significant negative predictors of meningitis. On combination model WHO-IMCI algorithm (Unconsciousness, inability to feed, convulsions lethargic or stiff neck) has sensitivity, specificity, PPV, NPV are 98%, 70%, 8% & 100% respectively. For combination of lethargic & stiff neck sensitivity & specificity, NPV are 96%, 74% and 100% respectively. Of particular interest is the negative predictive value of 100% in all the above combination models. Another study conducted by J.A. Berkley (2004) in which variables with adjusted likelihood rate (ALR) of 1.5 were regarded as potentially useful independent clinical indicators. They found bulging fontanell, neck stiffness, cynosis impaired consciousness partial seizures, and seizures outside the febrile convulsion age range as independent indicators of meningitis. Above mentioned predictors have sensitivity 79% and specificity 80%.

After calculating sensitivities and specificities of clinical features we observe uncertainty in almost every thing we deal - the patients history,

clinical examination, the laboratory test, prognosis and response to treatment. Different physicians have different opinion that may very significantly. However we understand clearly that such a prediction rule would be useful for clinicians when considering the probability of meningitis in hospitalised children in India.

CONCLUSIONS

Almost all the clinical features present in both groups. Even sign of meningeal irritation (brudzinski's sign, kernig's sign and neck rigidity) also present in nonmeningitic group. Hence on the basis of clinical features only, meningitis could not be diagnosed. All the suspicious case of meningitis should be confirmed by cerebrospinal fluid examination.

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