Assessment of the Prognostic Factors for Abnormal Neurodevelopmental Outcomes in Children with Acute Bacterial Meningitis by Using RNDA Tool

Abstract

This observational follow up study was carried in the Department of Paediatrics, Institute of Child and Mother Health (ICMH), Matuail, Dhaka, during November 2016 to December 2017, to determine the prognostic factors for assessment of the prognostic factors for abnormal neurodevelopmental outcomes in children with acute bacterial meningitis by using RNDA tool. A total of 56 children with acute bacterial meningitis of age > 1month - 15 years admitted in the inpatient department were enrolled in this study. Most 34 (60.7%) of the children belonged to age <12 months and male to female ratio was almost 2:1.More than half (58.9%) children admitted >48hrs after onset of illness, 11(19.6%) children received previous treatment with antibiotics and most (85.7%) of the children had occurrence of seizures prior to admission. More than one third (39.3%) children had >100 cell count in their CSF. CSF glucose/ serum glucose ratio was found <0.2 in case of 8(14.3%) children. More than three fourth (78.6%) children had high protein in their CSF. Abnormal developmental outcome assessed by RNDA on follow ups. It was observed that gross motor development was mildly impaired in 6(12.0%), 8(16.3%) and 5 (11.6%) cases on 1^{st}, 2^{nd} and 3^{rd} follow up respectively. Gross motor was moderately impaired in 4 (8.0%), 3 (6.1%) and 3 (7.0%) cases on 1^{st}, 2^{nd} and 3^{rd} follow up respectively. Accordingly, fine motor was mild impaired in 5 (10.0%), 4 (8.2%) and 5 (11.6%) cases and moderately impaired in 2 (4.0%), 3 (6.1%) and 2 (4.7%) cases on 1^{st}, 2^{nd} and 3^{rd} follow up respectively. Cognition was mild impaired in 11 (22.0%), 12 (24.5%) and 11 (25.6%) cases and moderately impaired in 4 (8.0%), 4 (8.2%) and 3 (7.0%) cases on 1^{st}, 2^{nd} and 3^{rd} follow up respectively. Children found with any selective neurological complication or abnormal developmental outcome in at least one follow up was considered to be abnormal. Hypertonic muscle tone and exaggerated jerk was found in 2(3.8%) children. 5(9.6%) children had developmental regression on follow up. 3(5.8%) children had squint, 2 (3.8%) children had subdural effusion, 2 (3.8%) children had visual deficit, 6 (11.5%) children had hearing deficit and 4 (7.7%) children had afebrile seizures on follow up. One (11.1%) child with focal seizure and 6 (60.0%) children with hazy CSF colour had significantly ($p<0.05$) developed abnormal developmental outcome. Children under 12 months of age, children who received previous treatment with antibiotics, seizures prior to admission, high WBC count, hazy CSF colour and CSF glucose/ serum glucose ratio below 0.2 were significantly ($p<0.05$) associated with acute complications

during hospital stay. Children with focal seizure and children with hazy CSF colour were significantly ($p<0.05$) associated to abnormal developmental outcome. Multivariate regression analysis showed no significant ($p>0.05$) association between acute complications and prognostic factors. Age under 12 months in adjusted OR 0.970 with 95.0% C.I 0.943 to 0.997, CSF leukocytosis in adjusted OR 0.99 with 95.0% C.I. 0.99 to 1.00) and CSF glucose/serum glucose ratio<0.2 in adjusted OR 15.23 with 95.0% C.I. 1.28 to 100.0 were significantly associated with abnormal developmental outcome in multivariate regression analysis.

Keywords: Prognostic Factors, Abnormal Neurodevelopmental, Outcomes RNDA, Bacterial Meningitis.

Introduction

Acute Bacterial meningitis (BM) is a severe infection responsible for high mortality and disabling sequelae in children. Early identification of patients at high risk of these outcomes is necessary to prevent their occurrence by adequate treatment as much as possible. For this reason, several prognostic models have been developed. [1] studied etioclinical profile and outcome of acute bacterial meningitis in post neo natal U-5 children. The neurological complications resulting from bacterial meningitis include subdural effusions or empyemas, cerebral abscesses, focal neurological deficits (e.g., hearing loss, cranial nerve palsies, hemiparesis, or quadriparesis), hydrocephalus, cerebrovascular abnormalities, altered mental status, and seizures [2,3]. More subtle outcomes like cognitive, academic and behavioral problems are also observed in post-meningitis children [4,5]. WL Lin et al [6] enrolled CSF culture-proven bacterial meningitis patients aged from 1 month to 18 years in a medical center. The patients were divided into “normal” and “abnormal” groups for each laboratory result and in combination.Mortality and morbidity rates are high among children with acute bacterial meningitis, especially in young ages. Namani et al [7] determined the most common neurologic complications during the acute phase of childhood bacterial meningitis and long term sequelae. A total of 277 children (aged 0-16years) were evaluated for acute neurologic complications following bacterial meningitis. In addition, antibiotic treatment and good care facilities decreased the occurrence of complications substantially in developed countries but ABM continues to be an important cause of morbidity and mortality in children in developing world [8,9]. National data regarding ABM is extremely limited in Bangladesh. Age <12 months and severity of clinical presentation at admission were identified as the strongest predictors of neurological complications and may be of value in selecting patients

for more intensive care and treatment. Bacterial meningitis is associated with a high rate of morbidity and mortality. The risk of death or development of complications is related to age, underlying conditions, causal agent, disease severity and duration during the acute phase, and, occasionally, delay in starting effective antimicrobial therapy [10]. Early identification of patients at high risk of unfavorable outcomes is necessary to prevent their occurrence by adequate treatment as much as possible. Although several prognostic factors for prediction of mortality or sequelae have been identified, the exact predictive value of these factors remains uncertain [11]. Purpose of this study was also to identify the risk factors for acute neurological complications and poor developmental outcome, so that clinicians are alert while treating patients who may be easily missed but are actually at a high risk of mortality and morbidity. Early prediction of poor developmental outcome may help the physician in selecting children who may require extensive follow-up and whose parents need to be counseled.

Materials And Methods

This observational follow up study was carried in the Department of Paediatrics, Institute of Child and Mother Health (ICMH), Matuail, Dhaka, during November 2016 to December 2017, to determine the prognostic factors for acute neurological complications neurodevelopmental outcome in children with acute bacterial meningitis. A total of 56 children with acute bacterial meningitis of age > 1month - 15 years admitted in the inpatient department were enrolled in this study.

Inclusion criteria:

1. Bacterial meningitis cases were included according to World Health Organization definition [12].

a. Presence of clinical findings such as fever, headache, meningeal irritation findings in accordance with cerebrospinal fluid (CSF) examination showing at least one of the following:

- turbid appearance;
- leukocytosis (>100 cells/mm3);
- leukocytosis (10 - >100 cells/mm3) and either an elevated protein (>100 mg/dL) or decreased glucose (<40 mg/dL)

b. With or withoutLaboratory-confirming by

- growing (culture) or

- identifying (by Gram stain or antigen detection methods) a bacteria pathogen in the CSF or from the blood in a child with clinical syndrome consistent with bacterial meningitis.

2. Age: >01 month to 15 years.

Exclusion criteria:

- Previous neurological deficit, e.g. Cerebral palsy, Epilepsy.
- Neural tube defect such as spina bifida.
- Hydrocephalus with shunt

Study Procedure: All admitted children aged from >1 month to 15 years, satisfying the case definition, was enrolled in the study. Written consent from parents was obtained for each case after explaining the purpose of the study. On admission, the investigator took a detailed history, examined the patient thoroughly and complete the clinical questionnaire. Thereafter, lumbar puncture was performed in each patient except when contraindicated and cerebrospinal fluid (CSF) was sent to the laboratory within hours for cytology and biochemistry. In the microbiology laboratory, CSF was examined by Gram stain and CSF culture was done to detect S pneumoniae, N meningitides and H influenzae. Blood sample was collected at the same time. Apart from routine investigations in all patients, USG and neuro-imaging of brain was performed according to clinical necessity. Treatment of the cases was started without delay after macroscopic view of CSF, pending the laboratory report. A follow up schedule was maintained. All the enrolled children attended the Child neurology follow up clinic in OPD of ICMH. Total 3 follow ups were taken. 1st follow up was done after 1 month. 2nd and 3rd follow up was done after 3 and 6 months respectively. In each follow up each child was assessed for specific neurological complications and neurodevelopmental outcome. Neurodevelopmental outcome was assessed and recorded using Rapid Neurodevelopmental Assessment (RNDA) tools.

Neurodevelopmental Assessment: Rapid Neurodevelopmental Assessment (RNDA) was used for evaluation for developmental status and behavioural problems. The subject's performance against the regular age was evaluated in eight items (gross motor, fine motor, vision, hearing, speech, cognition, behavior, and seizures). Successful completion of an item was considered to be "age appropriate," whereas non completion was recorded by decreasing levels of competence as "mild," "moderate," or "severe" impairment.

Data analysis: Data was checked and cleaned before incorporating into statistical software (SPSS-Version12). Categorical data was compared using chi square test and odds ratio and

95% confidence intervals was calculated.Multiple regression analysis was done to find out the risk or prognostic factors for development of acute neurological complication and developmental outcome. p value below 0.05 was considered as significant.

Results

Table I: Distribution of study subjects by socio-demographic characteristics (n=56)

Demographic characteristics	Number of patients	Percentage
Age group		
< 12 months	34	60.7
12 months up to 5 year	16	28.6
More than 5 year	6	10.7
Sex		
Male	38	67.9
Female	18	32.1
Father's occupation		
Farmer	5	8.9
Self employed	18	25
Service	25	44.6
Business	8	14.3
Mother's occupation		
Housewife	54	96.4
Service	1	1.8
Others	1	1.8
Father's education		
No formal education	4	7.1
Primary not completed	7	12.5
Primary completed (up to S.S.C)	16	28.6
S.S.C completed and above	29	51.8
Mother's education		
No formal education	2	3.6
Primary not completed	13	23.2
Primary completed (up to S.S.C)	15	26.8

S.S.C completed and above	26	46.4
Socioeconomic Status (Average monthly family income in taka)		
Low income group (Up to 10,000)	9	16.1
Middle income group (10,001 to 20,000)	39	69.6
Upper income group (20,000 +)	8	14.3

Table I showssocio demographic characteristics of study children, it was observed that 34 (60.7%) children belonged to age <12 month. More than two third (67.9%) children were male. Al-most half (44.6%) of the children's fathers were service holders and maximum (96.4%) children's mothers were housewives. More than half (51.8%) of the children's fathers and almost half (46.4%) of the children's mothers completed S.S.C. About two-third (69.6%)children's average monthly family income was in between TK 10,001 to 20,000.

Table II: Distribution of the study subjects by laboratory investigations (n= 56)

Investigation	Number of patients	Percentage
Total WBC count		
Normal	37	66.1
High	19	33.9
Serum Sodium level		
Normal	24	42.9
Low	32	57.1
CSF Colour		
Clear	35	62.5
Hazy	15	26.8
Blood Stained	6	10.7
CSF Cell count (number of cell/cmm)		
Normal (0 to 5)	2	3.6
>5 to 100	32	57.1
>100	22	39.3
CSF glucose /serum glucose ratio		
>0.2	48	85.7

<0.2	8	14.3
CSF protein		
Normal	12	21.4
High	44	78.6

Table II shows status of laboratory investigations of the study children. It was observed that 19(33.9%) children had high WBC count. 32(57.1%) children had low serum sodium level. CSF colour was hazy in case of 15(26.8%) children. More than one third (39.3%) children had >100 cell count in their CSF. CSF glucose/ serum glucose ratio was found <0.2 in case of 8(14.3%) children. More than three fourth (78.6%) children had high protein in their CSF.

Table III: Distribution of the study subjects by Acute complications (n=53)

Acute complications	**Number of patients**	**Percentage**
Hypertonic/ increased Muscle Tone	3	5.7
Exaggerated Jerks	3	5.7
Squint	3	5.7
Subdural effusion	1	1.9
Developmental regression	3	5.7
Hemiparesis	1	1.9
Hearing deficit	2	3.8
Visual deficit	2	3.8

Table III shows presence of acute complications among the study children, it was observed that 3(5.7%) children had hypertonic muscle tone, number of children had exaggerated jerks and squint were same (3, 5.7%) during discharge. 2(3.8%) children had hearing deficit and same number of children had visual deficit during discharge. One (1.9%) child developed subdural effusion and hemiparesis during hospital stay.

Table IV: Distribution of the study subjects by developmental outcome assessed by RNDA on follow up.

Developmental outcome assessed by RNDA	**1st follow up (n=50)**	**2nd follow up (n=49)**	**3rd follow up (n=43)**

	n(%)	n(%)	n(%)
Gross motor			
Normal	40(80.0)	38(77.6)	35(81.4)
Mild impairment	6(12.0)	8(16.3)	5(11.6)
Moderate impairment	4(8.0)	3(6.1)	3(7.0)
Fine motor			
Normal	43(86.0)	42(85.7)	36(83.7)
Mild impairment	5(10.0)	4(8.2)	5(11.6)
Moderate impairment	2(4.0)	3(6.1)	2(4.7)
Cognition			
Normal	38(76.0)	33(67.3)	29(67.4)
Mild impairment	11(22.0)	12(24.5)	11(25.6)
Moderate impairment	4(8.0)	4(8.2)	3(7.0)
Vision			
Normal	48(96.0)	47(95.9)	41(95.3)
Moderate impairment	2(4.0)	2(4.1)	2(4.7)
Hearing			
Normal	44(88.0)	47(95.9)	42(97.7)
Mild impairment	6(12.0)	2(4.1)	1(2.3)
Seizure			
Absent	49(98.0)	44(89.8)	38 (88.4)
Present	0(0.0)	4(8.2)	4(9.3)

Table V shows presence of abnormal developmental outcome assessed by RNDA on follow ups. It was observed that gross motor development was mildly impaired in 6(12.0%), 8(16.3%) and 5 (11.6%) cases on 1st, 2nd and 3rd follow up respectively. Gross motor was moderately impaired in 4 (8.0%), 3 (6.1%) and 3 (7.0%) cases on 1st, 2nd and 3rd follow up respectively. Accordingly, fine motor was mild impaired in 5 (10.0%), 4 (8.2%) and 5 (11.6%) cases and moderately impaired in 2 (4.0%), 3 (6.1%) and 2 (4.7%) cases on 1st,

2nd and 3rd follow up respectively. Cognition was mild impaired in 11 (22.0%), 12 (24.5%) and 11 (25.6%) cases and moderately impaired in 4 (8.0%), 4 (8.2%) and 3 (7.0%) cases on 1st, 2nd and 3rd follow up respectively. Vision was found moderate impaired in 2 (4.0%, 4.1% and 4.7% respectively) cases on each follow up. Accordingly, hearing was found mild impaired in 6 (12.0%), 2 (4.1%) and 1 (2.3%) cases on 1st, 2nd and 3rd follow up respectively. On follow up, 4 cases (8.2% and 9.3% respectively) complained of afebrile seizures on 2nd and 3rd follow-up.

Table V: Overall distribution of children with selected neurological complications and abnormal developmental outcome (found in at least one follow up) (n=52)

Developmental outcome	Number of patients	Percentage
Muscle Tone		
Normal	50	96.2
Hypertonic	2	3.8
Jerks		
Normal	50	96.2
Exaggerated	2	3.8
Squint		
Absent	49	94.2
Present	3	5.8
Subdural effusion		
No	50	96.2
Yes	2	3.8
Developmental regression		
No	47	90.4
Yes	5	9.6
Visual deficit		
Absent	50	96.2
Present	2	3.8
Hearing deficit		
Absent	46	88.5
Present	6	11.5
Seizure		
Absent	48	92.3

Present	4	7.7

Table V shows overall distribution of children with selected neurological complications and abnormal developmental outcome. Children found with any selective neurological complication or abnormal developmental outcome in at least one follow up was considered to be abnormal. Hypertonic muscle tone and exaggerated jerk was found in 2(3.8%) children. 5(9.6%) children had developmental regression on follow up. 3 (5.8%) children had squint, 2 (3.8%) children had subdural effusion, 2 (3.8%) children had visual deficit, 6 (11.5%) children had hearing deficit and 4 (7.7%) children had afebrile seizures on follow up.

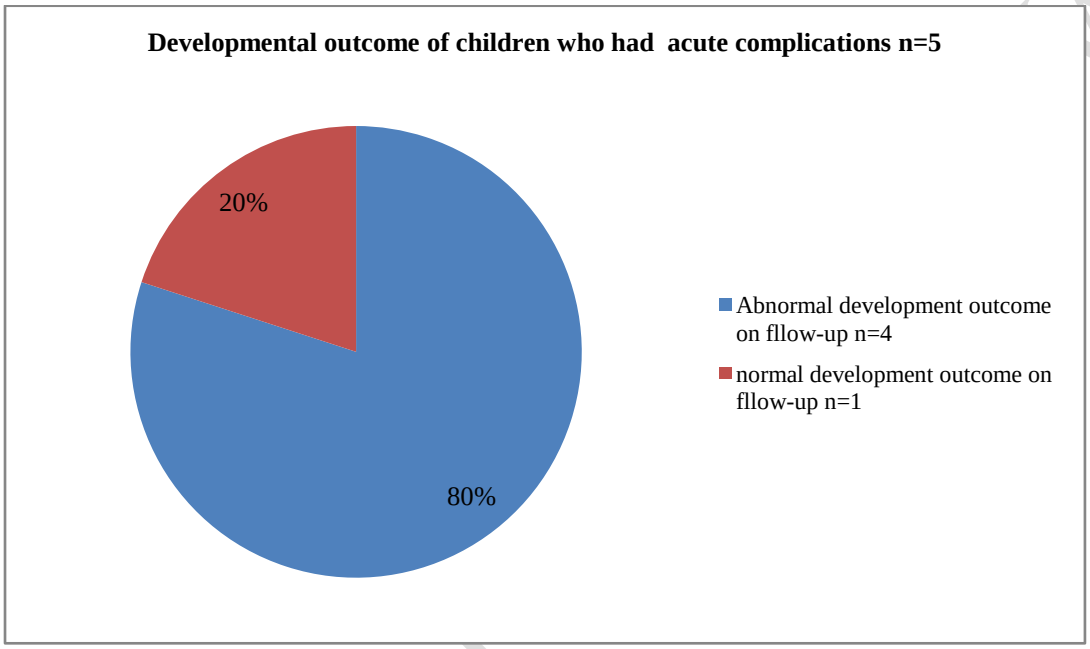

Fig-1: Developmental outcome on follow-up of children who had acute complications.

Fig-1 depicts that 4 (80%) of total 5 children who had acute complications developed abnormal developmental outcome.

Table VI: Association of acute complication with prognostic factors (n=56)

Prognostic factors	**Acute complication**		**P-value**
	Present (n=8) n	**Absent (n=48) %**	
Age group			
< 12 months	5(62.5)	27(56.25)	
>12 months up to 5 year	0(0.0)	18(37.5)	0.011
More than 5 year	3(37.5)	3(6.25)	
Sex			

Male	6(75.0)	32(66.7)	0.640
Female	2(25.0)	16(33.3)	
Duration of the (>48hrs) illness prior to admission			
<48hrs	1(12.5)	22(45.8)	0.076
>48hrs	7(87.5)	26(54.2)	
Previous treatment with antibiotics			
Yes	5(62.5)	7(14.6)	0.012
No	3(37.5)	41(85.4)	
Occurrence of Seizures prior to admission			
Yes	4(50.0)	43(91.5)	0.002
No	4(50.0)	4(8.5)	
Duration of 1st attack of convulsion			
<15 minutes	3(60)	33(75.0)	0.471
>15 minutes	2(40)	11(24.9)	
Type of seizure			
Focal	0(0.0)	1(2.4)	0.755
Generalized	4(100.0)	41(97.6)	
Total WBC count			
Normal	3(37.5)	34(70.8)	0.047
High	5(62.5)	14(29.2)	
Serum sodium level			
Normal	1(16.7)	20(41.7)	0.258
Low	5(83.4)	28(58.3)	
CSF Colour			
Clear	1(14.3)	32(68.1)	0.014
Hazy	5(71.4)	10(21.3)	
Blood Stained	1(14.3)	5(10.6)	
CSF leukocytosis (>100)			
Absent	2(28.6)	32(66.7)	0.446
Present	5(71.5)	16(33.3)	

CSF protein (>200mg/dl)			
Absent	2(25.0)	8(16.8)	0.568
Present	6(75.0)	40(83.7)	
CSF glucose /serum glucose ratio			
>0.2	5(62.5)	43(89.6)	0.042
<0.2	3(37.5)	5(10.4)	

***** Values expressed as numbers (n) and percentages (%) in parenthesis. P value 0.05 was considered as level of significance. P value was obtained by chi-square test.

Table VI shows association of acute complication with prognostic factors of the study children, it was observed that 5(56.25%) children <12 months of age, 5(62.5%) children with previous treatment with antibiotics, 4(50.0%) children with seizures prior to admission, 5 (62.5%) children with high WBC count, 5(71.4%) children with hazy CSF colour and 3(37.5%) children with CSF glucose/ serum glucose ratio below 0.2 developed acute complication during hospital stay. In all these cases the difference was statistically significant (P<0.05) between two groups.

Table VII: Association of abnormal developmental outcome with prognostic factors (n=53)

Prognostic factors	**Abnormal developmental outcome**		**P-value**
	Present (n=11) n(%)	**Absent (n=42) n(%)**	
Age group			
< 12 months	8(72.8)	26(57.6)	
12 months up to 5 year	3(27.3)	13(28.6)	0.110
More than 5 year	0(0.0)	6(13.2)	
Sex			
Male	9(81.8)	29(64.4)	0.268
Female	2(18.2)	16(35.6)	
Duration of the (>48hrs) illness prior to admission			
<48hrs	5(45.5)	18(40.0)	0.741
>48hrs	6(54.5)	27(60.0)	

Previous treatment with antibiotics			
Yes	2(18.2)	9(20.5)	0.866
No	9(81.8)	35(79.5)	
Occurrence of Seizures prior to admission			
Yes	9(81.8)	38(86.4)	0.702
No	2(18.2)	6(13.6)	
Duration of 1st attack of convulsion			
<15 minutes	7(77.7)	29(72.5)	0.745
>15 minutes	2(22.3)	11(27.5)	
Type of seizure			
Focal	1(11.1)	0(0.0)	0.037
Generalized	8(88.9)	38(100.0)	
Total WBC count			
Normal	6(54.5)	30(66.7)	0.166
High	5(45.5)	15(33.3)	
Serum Sodium level			
Normal	5(55.5)	15(34.4)	0.226
Low	4(44.4)	29(66.4)	
CSF Colour			
Clear	3(30)	30(68.2)	0.037
Hazy	6(60)	9(20.5)	
Blood Stained	1(10.0)	5(11.4)	
CSF leukocytosis (>100)			
Absent	5(45.5)	18(39.9)	0.741
Present	6(54.5)	27(59.6)	
CSF protein >200ml/dl			
Absent	2(20.0)	6(13.2)	0.259
Present	8(80.0)	39(86.4)	
CSF glucose /serum glucose ratio			
>0.2	9(81.8)	39(86.7)	0.680
<0.2	2(18.2)	6(13.3)	

***** Values expressed as numbers (n) and percentages (%) in parenthesis. P value 0.05 was considered as level of significance. P value was obtained by chi-square test.

Table VII shows Association of abnormal developmental outcome with prognostic factors of the study subjects, it was observed that 1(11.1%) child with focal seizure and 6 (60.0%) children with hazy CSF colour developed abnormal developmental outcome. In both cases, the difference were statistically significant (P<0.05) between two groups.

Table VIII: Risk factor analysis for acute complications associated with prognostic factors in multivariate logistic regression model (n=56)

prognostic factors	**Crude OR**	**95.0% C.I. for EXP(B)**		**Adjust OR**	**95.0% C.I. for EXP(B)**	
		Lower	**Upper**		**Lower**	**Upper**
Age < 12 months	1.30	0.23	7.87	1.080	0.972	1.200
Male sex	1.50	0.23	12.21	2.361	0.387	14.406
Duration of the illness > 48 hrs prior to admission	0.17	0.01	1.58	0.907	0.078	10.575
Previous treatment with antibiotics	9.76	1.52	70.08	0.611	0.001	0.001
Occurrence of Seizures prior to admission	0.09	0.01	0.68	1.481	0.272	8.064
Duration of 1st attack of convulsion >15 minutes	0.50	0.06	5.01	1.028	0.904	1.170
Focal seizure	0.00	0.00	233.7	0.761	0.001	0.001
Leukocytosis	0.25	0.04	1.43	0.880	0.701	1.106
Low Sodium level	0.28	0.01	2.85	0.953	0.811	1.120
CSF colour hazy	0.08	0.00	0.77	0.383	0.129	1.136
CSF leukocytosis	0.20	0.02	1.37	1.001	0.999	1.003
CSF high protein	1.67	0.19	12.21	0.996	0.989	1.003
CSF glucose/serum glucose raito<0.2	0.19	0.03	1.42	1.967	0.229	16.890

*** indicates significant association**

Multiple logistic regression was performed

Multivariate logistic regression for acute complications associated with prognostic factors was statistically not significant.

Table IX: Risk factor analysis for abnormal developmental outcome associated with prognostic factors in multivariate logistic regression model (n=56)

prognostic factors	**Crude OR**	**95.0% C.I. for EXP(B)**		**Adjust OR**	**95.0% C.I. for EXP(B)**	
		Lower	**Upper**		**Lower**	**Upper**
Age < 12 months *	1.95	0.39	10.81	0.970	0.943	0.997
Male sex	2.48	0.41	19.01	3.297	0.352	30.86
Duration of the illness > 48 hrs prior to admission	1.25	0.27	5.64	7.467	0.552	100.0
Previous treatment with antibiotics	0.86	0.11	5.63	0.001	0.001	0.001
Occurrence of Seizures prior to admission	0.71	0.10	6.10	1.073	0.059	19.52
Duration of 1st attack of convulsion >15 minutes	1.33	0.20	10.95	1.012	0.851	1.202
Focal seizure	4.63	0.0	100.0	0.001	0.001	0.001
Leukocytosis	0.60	0.13	2.76	1.005	0.760	1.32
Low Sodium level	2.42	0.46	13.01	1.013	0.946	1.08
CSF colour hazy	0.20	0.03	1.06	0.399	0.058	2.76
CSF leukocytosis*	1.25	0.27	5.64	0.999	0.998	1.00
CSF high protein	1.63	0.19	11.92	1.006	0.988	1.02
CSF glucose/serum glucose raito<0.2*	0.69	0.10	5.94	15.231	1.28	100.0

*** indicates significant association**

Multiple logistic regression was performed.

Age < 12 months with adjusted OR 0.970 (95.0% C.I 0.943 to 0.997), CSF leukocytosis with adjusted OR 0.99 (95.0% C.I. 0.99 to 1.00) and CSF glucose/serum glucose raito<0.2 with

adjusted OR 15.23 (95.0% C.I. 1.28 to 100.59) were significantly associated with abnormal developmental outcome.

Discussion

The present study findings were discussed and compared with previously published relevant studies. In this study, it was observed that 67.9% children were male and male to female ratio was 2.1:1. Similar findings also observed by George et al [12]. More than half (58.9%) children admitted >48hrs after onset of illness, 11(19.6%) children received previous treatment with antibiotics and most (85.7%) of the children had occurrence of seizures prior to admission. The characteristics of convulsion showed that, 7(14.6%) children had >2 episodes before admission, 7(14.6%) underwent 1st attack of convulsion lasting for >15 minutes and only 1(2.1%) had focal convulsion. Out of 53 survived, 52(98.1%) children were available for at least one follow-up. 50(94.3%) children came during 1st follow up, 49(92.4%) during 2nd follow up, 43(81.1%) during 3rd follow up and 1(1.9%) children did not came for a single follow up. Total 11(21.1%) children were found to develop selective neurological complications or poor developmental outcome in at least one follow up. The study children were examined for the following variables during discharge and follow up: age, gender, duration of the illness prior to admission, < or > 48 hours, previous treatment with antibiotics; occurrence of seizures prior to admission, duration of 1st attack of convulsion occurred prior to admission, type of seizure occurred prior to admission, nutritional status, total leukocyte count, serum sodium level, CSF Colour, CSF cytology, CSF protein and CSF glucose /serum glucose ratio. Children under 12 months of age, children who received previous treatment with antibiotics, children having occurrence of seizures prior to admission, with high WBC count, with hazy CSF colour and with CSF glucose/ serum glucose ratio below 0.2 were significantly ($p<0.05$) associated with acute complications during hospital stay. Children with focal seizure and children with hazy CSF colour were significantly ($p<0.05$) associated to have impaired developmental outcome. Young age (indicated as younger than two years old), is considered an important prognostic factor for adverse outcome of children with bacterial meningitis [13, 14]. In a large multicenter study, Turel et al [115]evaluated clinical features and sequela in children with acute bacterial meningitis (ABM). Presence of focal neurologic signs at presentation and turbid cerebrospinal fluid appearanceincreased sequelae significantly. De Jonge et al [13] in a systematic review of prognostic studies, found high WBC count as a statistically significant prognostic factor predicting death or sequelae due to BM in children 0-18 years of age. Low CSF/blood glucose ratio (<0.2) found to be an

important prognostic factor for poor outcome in several studies [16,17]. In the current study, 62.5% children with high WBC count, 71.4% children with hazy CSF colour and 37.5% children with CSF glucose/ serum glucose ratio below 0.2 developed acute complication during hospital stay. In all these parameters the difference was statistically significant ($P<0.05$) and is consistence with previous studies. In this study, it was observed that 11.1% children with focal seizure and 60.0% children with hazy CSF colour developed abnormal developmental outcome. In both cases, the difference were statistically significant ($P<0.05$) between two groups. Namani et al [18] reported that Children who manifested focal neurological deficit at admission had a significantly higher incidence of neurological complications. There are some other studies in which it was found that presence of focal neurologic signs at presentation increased sequelae significantly in children with acute bacterial meningitis [15, 19] which supports this study.Acute complications were not significantly ($p<0.05$) associated with prognostic factors in multivariate logistic regression analysis. Age < 12 months with adjusted OR 0.970 (95.0% C.I 0.943 to 0.997), CSF leukocytosis with adjusted OR 0.99 (95.0% C.I. 0.99 to 1.00) and CSF glucose/serum glucose raito<0.2 with adjusted OR 15.23 (95.0% C.I. 1.28 to 100.0) were significantly associated with impaired developmental outcome in multivariate logistic regression analysis. These findings are similar to multiple previous studies shown earlier[16,18,20]. High CSF WBC count was indicative of poor prognosis in a study by Kirimi et al [21] and is consistent with our finding.

Conclusion

Majority of the children were age less than 12 months and male were predominant. Four (80.0%) out of 5 children having acute complications developed abnormal developmental outcome. Children under 12 months of age, children who received previous treatment with antibiotics, seizures prior to admission, high WBC count, hazy CSF colour and CSF glucose/ serum glucose ratio below 0.2 were significantly ($p<0.05$) associated with acute complications during hospital stay. Children with focal seizure and children with hazy CSF colour were significantly ($p<0.05$) associated to abnormal developmental outcome.

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