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RESEARCH ARTICLE

CLINICAL ANALYSIS ON 129 HOSPITALIZED CHILDREN WITH PURULENT BACTERIAL MENINGITIS

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ABSTRACT

Objective: The present study aimed to explore etiology, clinical features and treatment of children with purulent bacterial meningitis.

Methodology: Hospital based retrospective cross sectional study, we reviewed cases of purulent bacterial meningitis occurring at Qilu hospital from January 2011 through September 2016. Records of all patients, comprising data on clinical presentations, laboratory findings and treatment were obtained and analyzed.

Results: 129 children met criteria and were analyzed. Male to female ratio was 1.8:1, 82(63.6%) males and 47(36.4%) female. Cases were classified into five age groups: 1month-1 year76%, 1-2 years 4.7%, 2-5 years 8.5%, 5-12 years 8.5% and 12-15 years 2.3% (mean age is 2.93 months). Confirmed cases were 48(37%), the main bacteria cultured were *Staphylococcal species* 21%, *Streptococcus pneumoniae* 19%, *group B Streptococcus (GBS)* 15% and *Escherichia coli* 13%. Less detected bacteria were *Enterococcus fecalis, Enterococcus fecium* and *Klebsiella pneumoniae*. *Staphylococcal species* showed resistance to penicillin G by 100%, Oxacillin 62%, Amoxicillin 50%, Ampicillin sulbactam 38% and Ceftriaxone 38%. Gram positive bacterial were sensitive to vancomycin, chloramphenicol, Meropenem and linezolid whereas Gram negative bacteria were sensitive to Meropenem, amikacin and linezolid.

Conclusion: *Staphylococcal species, Streptococcal pneumoniae, Group B streptococcal* and *Escherichia coli* were the predominant pathogens responsible for purulent bacterial meningitis over the past 5¾ years. Rate of bacteria detection is still low and emergence of antimicrobial resistance together are of great concern, Therefore more intervention are needed to be address so as to reduce burden of Purulent bacterial meningitis and its neurological sequalae to the survivors.

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INTRODUCTION

Purulent bacterial meningitis (PBM) is the devastating infection of central nervous system, in which leptomeninges (pia-arachnoid) become inflamed by pyogenic bacteria (Daroff *et al*., 2015). *Neisseria meningitides, Streptococcus pneumonia (S.pneumonia), and Haemophilusinfluenzae (H.influenzae)*are the commonest etiologies of acute bacterial meningitis in children of more than 1 month (Namani *et al*., 2012). The incidence of PBM is estimated to be 1–2 million cases every year worldwide, ranked fourth cause of acquired disability (Castelblanco *et al*., 2014).

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McIntyre *et al* reported that about 180,000 deaths occur every year worldwide due to PBM among children aged 1–59 months (McIntyre *et al*., 2012). The incidence of bacterial meningitis in United States of America (U.S.A) was 1.38 cases per 100 000 population from 2006–2007 (Thigpen *et al*., 2011). Where as the annual incidence in China was higher ranged between 6.95 to 22.30/100000 in children under 5 years. This was reported in a population-based surveillance for bacterial meningitis in China conducted from September 2006 to December 2009. The commonest etiologies found in China population were *H.influenzae* and *S.pneumonia* (Li *et al*., 2014). Cerebral spinal fluid (CSF) culture is the "gold standard" for diagnosis of PBM, it's crucial to obtain the causative microorganism for rationalization of treatment

(Schuchat and Messonnier, 2007). However, there is little information about the etiology of bacterial diseases of infants and children in China and many countries worldwide. About 1/3 of patients misuse antiobitics prior to hospital visit in China, this contributes to negative results of blood or CSF culture (Yang *et al*., 1993). Inpatients with Negative CSF culture other investigations can be used support diagnosis like detecting bacterial components by polymerize chain reaction (PCR), CSF analysis of glucose, protein, Lactate,C reactive protein (CRP), serum procalcitonin (Mekitarian Filho *et al*., 2014; Liu *et al*., 2008; Franco-Paredes *et al*., 2008). CSF lactatehas been found to be useful in differentiate between bacterial and aseptic meningitis in children with CSF pleocytosis (Weisfelt *et al*., 2006). Despite advancement in medicine, 20% survivors of bacterial meningitis do experience developmental disorders and neuropsychological impairment (Edmond *et al*., 2010; Wang *et al*., 2015). The issue of global emergence multidrug-resistant bacteria have brought challenges in the management of PBM, moreover many cases of PBM, etiologies have not been isolated in both CSF and blood culture due to antibiotics use before lumbar puncture (Li *et al*., 2014; Yang *et al*., 1993). In this hospital based retrospective study we aimed to determine the clinical profile at commonest etiologies and treatment of bacterial meningitis on children admitted to the pediatric ward in QiluHospital of Shandong University.

MATERIALS AND METHODS

Study design and Study population

The hospital-based retrospective cross-sectional study involving a review of children aged 1month to 15 years with PBM, admitted to a pediatric ward atQilu hospital from January 2011 to September 2016. Qilu hospital is the tertiary hospital in Shandong Province, Pediatric wards have 240 beds and treats more than 9600 hospitalized patients every year. The records of all patients with PBM during this 5¾ years period were obtained; demographic data, clinical features, laboratory findings and treatment.

Diagnosis of PBM

Inclusion criteria

- Children with a history of fever >38.5^{o}C, headache, neck stiffness, limb weakness, vomiting, bulging anterior fontanelle, altered consciousness were considered a suspected case of PBM.
- A suspected case with a CSF examination showing at least one of the following; was considered a 'probable' case: turbid CSF appearance, leukocytosis >100/mm^3
- Leukocytosis of 10–100 /mm^3 with elevated protein level (>41mg/dl or 0.41g/l) or decreased glucose level (<2.5 mmol/l).
- Laboratory-confirmed, with the identification of a bacterial pathogen (*H.influenza*, *S.pneumoniae*, *meningococcus*, or others) in the cerebrospinal fluid (CSF) was considered 'confirmed' case
- Blood culture positive with clinical symptoms consistent with bacterial meningitis, was considered 'confirmed' case.

Exclusion criteria

- Cases not fulfilling any of the above criteria and/or those with evidence suggesting othercentral nervous system CNS disorders.
- Age below 1month and above 15 years were excluded. The criteria used above are consistent with the World Health Organization (WHO) case definition (Guo *et al*., 2016).

Data collection procedure

The sampling method used in this study is a convenience sampling method. 129 cases of PBM met inclusion criteria, their data from computerized files of Qilu Pediatric wards were collected. Patient's information was stored in Chinese language and translation to English was done by special translating devices and by help of student who understands English and Chinese language. The information was gathered by using data collection form (attached file no 1), the form includes socio-demographic profiles, clinical signs and symptoms, laboratory, radiological findings, antibiotics used and complications observed during hospital stay.

Data Management and Statistical Analysis

Descriptive analysis was analyzed as mean ±SD, one wayANOVA used to compare two means, Chi-square test ($\chi 2$) or Fisher's exact test was used to analyze data for continuous and categorical variables as appropriate. Data collected was analyzed by using statistical software, Statistical Package for Social Science (SPSS) version 17. P value less than 0.05 was regarded as statistically significant.

Ethical consideration and approval

Ethical clearance was obtained from Qilu hospital ethical committee, after review and approval of the study. We used the data from computerized clinical records, hence it had no direct impact on patients, all measures to protect privacy and confidentiality was observed. Hospital Registration numbers were used instead of patient's names. The study was done under supervision.

RESULTS

Demographic data

A total of 129 children (aged 1 month to 15 years) with Purulent bacterial meningitis (PBM) were studied, 82(63.6%) male and 47(36.4%) female, giving male to female ratio of 1.8:1. We classified patients into five age groups: 1month to 1year 98 cases (76%), 1-2 years 6 cases (4.6%), 2-5 years 11 cases (8.5%), 5-12 years 11 cases (8.5%) and 12-15 years 3 cases (2.3%) (figure.1) and their mean age was 2.93months.78 cases (60.5%) came from rural areas whereas51 cases (39.5%)were from urban areas.Summer was the season of the highest incidence of PBM (44%) followed with winter (27%), spring (16%) and autumn had the lowest incidence (13%). The mean length of hospital stay was 3 weeks and 2 days, 1 week was minimum and 8 weeks was maximum hospital stay. The proven (confirmed) cases were 48 (37%). About 103 (79%) of patients were on antibiotics before admission to our hospital.98 cases (76%) presented with early complications of PBM.

Clinical symptoms, signs and laboratory findings

All patients 129(100%) had fever of more than 38.5^{o}C, alteration of mental statuswas present in 85 cases (65.5%), convulsions 53 cases (43.4%), vomiting 48 cases (37.2%),

neck stiffness38 cases (29.5%), limb weakness 36 cases (28%), bulging anterior fontanelle 23 cases (17.8%) and the least symptom was headache 20 cases (15.5%).

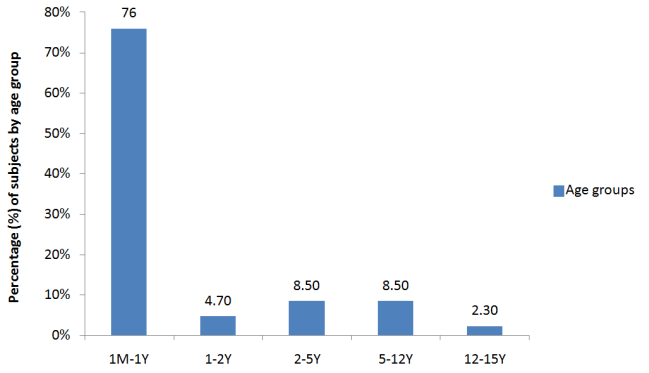

Figure 1. Distribution of subjects according to the age groups: 1 month to 12 months (1M-1Y), 13 to 24 months (1-2Y), 25 months to 59 months (2-5Y), 60 months to 144 months (5-12 Y) and 145 months to 180 months (12-15Y)

We found 12(14.3%) of 85 subjects with mental alteration had positive blood culture (P =0.008).

Table 1. Clinical symptoms and signs

Clinical manifestations	Cases	Percentage
	N=129	%
Fever	129	100
Limb weakness	36	28
Headache	20	15.5
Altered Mental state	85	65.9
Convulsions	53	43.4
Neck stiffness	38	29.5
Bulging anterior fontanelle	23	17.8
Vomiting	48	37.2

Cerebral Spinal fluid examination results of129 cases with PBM were obtained, presented in Table 2.The CSF WBC count more than 1000/mm^3 was seen in41(31.8%) cases, 501-1000/mm3 in 21(16.3%), 101-500/mm^3 in 46(35.6%) cases and 11-100/mm3 in 21(16.3%).CSF Neutrophils levels >50% seen in 62 cases (48.9%) and < 50% in 65(51.1%) cases. CSF Glucose<2.5mmol/l in 81(63%) cases and >2.5 mmol/l seen in 48(37%). CSF protein levels more than 0.41g/l in 103(79.8%) cases. 66(59%) cases had raised CSF lactate > 2.1 mmol/l, we found 24(36.4%) of 66 subjects with raised levels of CSF lactate have positive CSF culture (P =0.02).

Table 2. CSF Laboratory findings

CSF results	values	Cases (n)	Percentage %
CSF WBC	11-100 /mm^3	21	16.3
	101-500 /mm3	46	35.6
	501-1000 /mm^3	21	16.3
	>1001 /mm^3	41	31.8
CSF Neutrophils	>50%	62	48.9
	<50%	65	51.1
CSF Protein	>0.41g/l	103	79.8
	<0.41 g/l	26	20.2
CSF Glucose	<2.5 mmo/l	81	63
	>2.5 mmol/l	48	37
CSF Lactate	>2.1 mmol/l	66	59
	<2.1 mmo/l	45	41

WBC White blood cell and CSF Cerebral spinal fluid

Blood routine results (see table 3). We found 117 cases (91.5%) with WBC count of >9.5 X 10^9/L, 9 cases (7%) had normal level of WBC and 3 cases (1.5%) had WBC < 3.5X10^9 /L. Hemoglobin levels between 60-90g/l were found in 44 cases (34.7%), 90-110g/l in 61 cases (51.7%) and >110g/l in 16 cases (13.6%). CRP levels more than 70mg/l in 60 cases (50%) and between 8-69 mg/l in 40 cases (34%). We found 63.7% of patients with subdural effusion had CRP >70mg/l (P=0.012), likewise 56.2% of patients with hydrocephalus had CRP >70 mg/l, (P=0.048).

Erythrocyte segmentation rate (ESR) levels >20 mm/hour was found in 92 cases (76%). Lactate dehydrogenase (LDH) levels of more than 230 U/L was seen in 87 cases (85.5%). Serum Sodium less than 135mmol/l was found in 28 cases (24%), minimum sodium levels was 124mmol/l. 25 cases (20.7%) had Creatinine Kinase (CK) levels >140 U/L, CK MB levels of more than 4ng/ml were seen in 48 cases (39.7%). There was slightly elevation of Alanine aminotransferase (ALT) > 40U/L, Aspartate aminotransferase (AST) >40U/L and GGT >45U/L in 21%, 30.5% and 49.2% cases respectively.

Table 3. Blood routine results

BLOOD TEST	values	Cases	Percentage%
ESR	>20 mm/hour	92	76
CRP	>70 mg/l	60	50
	8-69 mg/l	40	34
CK	>140 U/L	25	20.7
CK MB	>4 ng/ml	48	39.7
Sodium (Na)	<135 mmol/l	28	24
ALT	>40 U/L	26	21
AST	>40 U/L	37	30.5
GGT	>45 U/L	61	49.2
Hemoglobin	>110 g/l	16	13.6
	90-110 g/l	61	51.7
	60-90g/l	44	34.7
White blood cell	>9.5 X 109 /L	117	91.5
	3.5-9.5 /L	9	7
	< 3.5X109 /L	3	1.5
LDH	>230 U/L	87	85.5
BUN	>7.8 mmol/l	5	4

CRP C- reactive protein, ESR Erythrocyte segmentation rate, CK creatinine kinase, AST Aspartate aminotransferase, ALT Alanine aminotransferase, GGT gamma glutamyltranspeptidase, LDH Lactate dehydrogenase and BUN blood urea nitrogen

Bacteria isolates and antimicrobial susceptibility pattern

CSF and Blood culture positive were found in 48(37%) cases, whereas 36 cases from CSF culture and 12 cases from Blood culture, which make the number of confirmed cases to be 48(37%). Positive pathogens were calculated on the basis of the positive result obtained in the CSF or blood culture. The most frequently detected pathogens were *Staphylococcal species* (n=10, 21%) followed by *S.pneumoniae* (n = 9, 19%), group B Streptococcus (GBS) (n = 7, 15%) and E.coli 13% other pathogens detected were *E.fecalis, E.fecium,* and *Klebsiellapneumoniae* see Figure 2.

About 107(79%) patients were given antibiotics in other hospitals before admission to Qilu hospital. Highly prescribed antibiotics in other hospitals were third generation Cephalosporin (Ceftriaxone) 50.4% and penicillins (Flucloxacillin, Ampicillin, Piperacillin-Tazobactam) 34.1%, meropenem 33.3% and vancomycin in 17%. The combination of two antibiotics was used in 48% of cases in other hospitals whereas in our hospital we found about 86% of patients were

on combined antibiotics, Most of the patients responded on combination dosage of Meropenem and vancomycin.

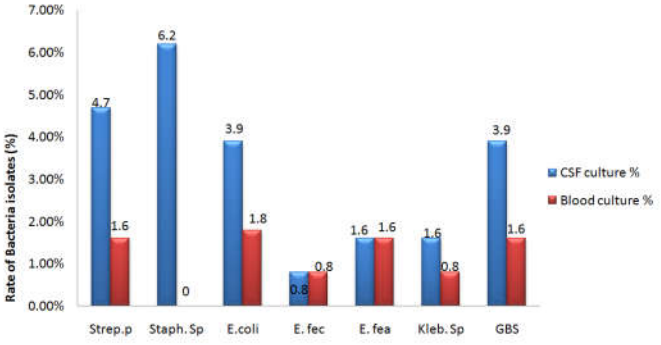

Figure 2. Distribution of bacteria isolates from Cerebrospinal fluid and blood culture: Streptococcal pneumoniae (strep.p), Staphylococcal species (Staph.sp), Escherchiae coli (E.coli), Enterococcus fecalis (E.fec), Enterococcus fecium (E.fec), Klebsiellaspicies (Kleb.sp) and Group B streptococcus (GBS)

Information on antimicrobial sensitivity and resistance was obtained in 41% cases only. *Staphylococcal species* isolates (n=9) were resistant to Penicillin G, Erythromycin and Sulfamethoxazole/triomephoprim by 100%, Oxacillin 62%, Amoxicillin 50%, Ampicillin sulbactam 38% and Ceftriaxone 38%. All *Staphylococcalspecies* isolateswere sensitive to Vancomycin, Mofloxacin and Linezolid by 100%. All *Streptococcal pneumoniae* isolates (n=7) had 100% resistance to Erythromycin and sulfamethoxazole/triomephoprim, 67 % resistance rate to Penicillin G and amoxicillin, 33% resistance to Oxacillin, Ampicillin sulbactam and Ceftriaxone while all isolates were sensitive to Meropenem, Chloromphenical and Linezolid. *E.coli* (n=3) had relatively high resistance (100%) to Erythromycin, 67% resistance rate to Ceftriaxone and Ampicillin sulbactam. All E.coli isolates were sensitive to Amikacin, Meropenem and Ceftazidime.

DISCUSSION

Purulent bacterial meningitis has been found to have a high prevalence in younger children especially male in many studies, with a decreasing occurrence in older age group (Guo *et al*., 2016; He *et al*., 2016). We obtained similar findings in this study whereby most children were under 1 year of age 76% and male 63.6%, this findings suggest younger age, being male arethe risk factors of developing PBM (de Jonge *et al*., 2010). In China PBM incidence is higher (6.95 to 22.3 cases/100 000 children < 5 years of age) compared to U.S.A (1.38 cases per 100 000 population) (Thigpen *et al*., 2011; Li *et al*., 2014). Dramatic decrease of PBM cases in U.S.A has been achieved following the availability of immunization programs for *H.influenza*, *N. meningitides*, and *S. pneumoniae*, these vaccines are available in China but some of them are not in National immunization program, so parents have to pay (Thigpen *et al*., 2011; Tunkel *et al*., 2004). In our study high number of PBM cases (60.5%) came from rural areas while 39.5% of patients were from urban areas, the reason being poor coverage of vaccination programs in some rural areas (Liu *et al*., 2010). Brouwer MC and Huttunen P*et al* have reported that CSF cultures are projected to be positive in 70%–85% of patients with bacterial meningitis who had no prior antimicrobial therapy (Tunkel *et al*., 2004; Huttunen *et al*., 2009; Scarborough *et al*., 2007). In our study confirmed cases were 48 (37%) only, about 79% of patients we studied had been already on antibiotics before admission to our hospital, and this contributed to low detection of pathogens. Tendency of antibiotics use before lumbar puncture or even without Clinician prescription has been reported in different studies and this makes detection of bacterial meningitis etiologies to be challenge globally (Li *et al*., 2009; Yang *et al*., 1993). Guo *et al* and Zhui *et al* both found *S.pneumoniae* as the leading pathogen in PBM (Guo *et al*., 2016; He *et al*., 2016). However we found *Staphylococcal species* as the most frequent bacteria, followed with *Streptococcal pneumoniae*. Mengistu *et al* reported *Staphylococcal species* were common in all age group (Mengistu *et al*., 2013). African countries, the majority of meningitis cases are caused by *S.pneumoniae*, and has been associated with high mortality rate when occurred in patients with human immunodeficiency virus (HIV) (Scarborough and Thwaites, 2008; Cohen *et al*., 2010). Invasive pneumococcal disease (including meningitis) in Developing countries is a leading cause of morbidity and mortality, with about 0.7 to 1.0 million deaths annually, affecting children < 5 years of age (Okike *et al*., 2014).

WHO has recommended the inclusion of the heptavalent pneumococcal conjugate vaccine in national immunization programs, only 26 of 193 WHO members states have introduced this vaccine into their national immunization programs for children (Okike *et al*., 2014). However it has been reported the emergence of pneumococcal serotypes which is not covered by the pneumo-vaccines and there's increasing resistance of *S. pneumoniae* to conventional antibiotics, this contributesto high rate of pneumococcal meningitis in many regions worldwide (Huttunen *et al*., 2009). *E.coli* and *GBS* were seen mainly on < 1 year infants as reported in Beijing study (Guo *et al*., 2016). Like wise in United Kingdom high incidence of *GBS* was found on infants less than 3 month (Verani *et al*., 2010), here we found *GBS* and *E.coli* as third and fourth leading etiology of PBM. An intervention like Intrapartum antibiotics administration to pregnant women with the premature rapture of the membrane has taken place to reduce *GBS* infections, but this has prevented only early-onset *GBS* infection (Patras *et al*., 2015; Zhang *et al*., 2007), for that reason better strategy for preventing *GBS* infection is still needed. Prospective study done in Italy from 2009-2013 found *N. meningitides* to be the commonest etiology of PBM accounting for 34.1% of total cases and *Staphylococcus species* was least etiology with 2.4% (degli Atti *et al*., 2014). Whereas in our study *N.meningitides* was not isolated, these findings can be supported with low incidence of meningococcal disease in China 0.18–0.2/100 000 population due to wide spread of meningococcal vaccine programs (CAO *et al*., 2012). We observed that different regions or countries have different patterns of bacterial meningitisetiologies, also etiologies trend do change over a period of time (Thigpen *et al*., 2011; Guo *et al*., 2016). The antimicrobial sensitivity and resistance resultswas obtained in 41%cases of positive CSF and blood culture, other 59% they tested negative at our hospital but had positive culture results from other hospitals, this was contributed with use of antibiotics before admission to our hospital (Yang *et al*., 1993). *Staphylococcal species* (n=9) we observed resistance rate of 100% to Penicillin G, Oxacillin 62%, Amoxicillin 50%, Ampicillin sulbactam 38% and Ceftriaxone 38%. All *Staphylococcal species* were sensitive to Vancomycin, Mofloxacin and Linezolid by 100%. Our study resultsclosely related to the study done in Namibia on antimicrobial sensitivity pattern of CSF whereby they foundthe resistance rate of *Staphylococcal species* to amoxicillin, penicillin and Sulfamethoxazole/ triomephoprim were 78.6%,

73.5% and 62.1% respectively, All *Staphylococcalspecies* were sensitive to Vancomycin and Amikacin (Mengistu *et al*., 2013). All *S.pneumoniae* isolates had 100% resistance to Erythromycin and sulfamethoxazole/triomephoprim, Penicillin, amoxicillin 67%, Ceftriaxone 33%, whereas all *S.pneumoniae* they were sensitive to Meropenem, Chloromphenical and Linezolid. However lower resistance to penicillins were observed in developed countries compared to our findings, resistance rate to penicillins in Canada 3.9% (Le Saux, 2014), Europe 24.4% (Torné *et al*., 2014), and U.S.A 38.9–42.7% (Mendes *et al*., 2014), Hackel *et al* reported increasing rate of penicillin resistance worldwide (Hackel *et al*., 2013). *E.coli* had relatively high resistance (100%) to Erythromycin, 67% resistance rate to Ceftriaxone and Ampicillin sulbactam. All *E.coli* isolates were sensitive to Amikacin, Meropenem and Ceftazidime. Similar results were reported in Beijing 2016 and Australia 2010 studies whereby Gram-positive bacteriawere sensitive to vancomycin and linezolid, Gram-negative bacteria were sensitive to Meropenem (Guo *et al*., 2016; Visintin *et al*., 2010). Vancomycin and the third-generation cephalosporin (IV Cefotaxime, Ceftazidime) have been suggested as an empirical treatment in Countries with the prevalence of antimicrobial-resistant isolates also in children who had prolonged exposure to antibiotics (Snedeker *et al*., 1990). Same way here patients were given Meropenem 84.9%, Vancomycin 57.4% and, few cases were given Teicloplanin 14%, Chloramphenicol 8.5% and Linezolid 4.7%. Our hospital is tertiary hospital in Shandong province we frequently admitsevere cases of PBM who have been on several antimicrobial treatment with out improvement. Therefore patients in our setup often respond to the strong antibiotics.

Clinical presentation of childhood bacterial meningitis has remained the same for years despite the changing epidemiology of the common causative bacteria (Yang *et al*., 1993; He *et al*., 2016). Infants may experience non specific signs and symptoms such as fever, poor feeding, vomiting, lethargy, and irritability (He *et al*., 2016; Scarborough *et al*., 2007). While for older children are more likely to experience fever, headache, photophobia, irritability, lethargy, convulsions, signs of meningeal irritation (neck stiffness, positive kerning sign and brudzinski sign) and rarely confusion and coma (Yang *et al*., 1993; Huy *et al*., 2010). Main clinical features found in this study were fever > 38.5 ^{0}C, alteration of mental status, convulsions, vomiting, neck stiffness, limb weakness, bulging anterior fontanelle and headache, these findings are similar to what have been found in previous studies (de Jonge *et al*., 2010; El Bashir *et al*., 2003). In the CSF analysis we observed substantial increase in CSF WBC count >500 mm^3 in 48.1% cases, CSF neutrophils >50% in 62(48.9%) cases, lower glucose level <2.2mmol/l on 81(63%) cases, 103(79.8%) cases with high protein levels >0.41 g/l similar findings has been obtained in several studies (Guo *et al*., 2016; de Jonge *et al*., 2010; Sakushima *et al*., 2011). The systematic review found the proportion of neutrophils, high CSF lactate, and low CSF glucose, as well as high serum procalcitonin (PCT), are the independent factors most predictive of bacterial meningitis (Sakushima *et al*., 2011). We observed increased CRP levels >70mg/l in 50% cases, 8-69mg/l in 34% cases, likewise Guo *et al* reported that CRP >70mg/l can be used to differentiate PBM and aseptic meningitis (Guo *et al*., 2016). Sakushima *et al* found raised CSF lactate, CSF CRP and serum CRP to be highly associated with bacterial meningitis we also obtained raised levels of LDH (85%),CRP (84%) and CSF lactate (59%) (Sakushima *et al*., 2011). Elevated CSF lactate greatly suggesting bacterial meningitis and can be used to distinguish between bacterial and aseptic meningitis in children with raised CSF WBC count (pleocytosis) (Van de Beek *et al*., 2004). We found the high level of lactate >2.1 mmol/l associated with the positive CSF culture test (P=0.02), this finding together with previous studies emphasize the role of CSF lactate in bacterial meningitis diagnosis (Schuchat and Messonnier, 2007; Mekitarian Filho *et al*., 2014; Siddiqui and Yohoshuva, 2016). Hyponatremia <135mmol/l found in 28 cases (24%), this finding correlates with that of Zhihui He *et al* who observed low blood sodium <135 mmol/l in 98 cases (22.8%) (He *et al*., 2016), this findings signify the importance of checking serum electrolytes in PBM cases. Anemia can occurs with all forms of bacterial meningitis and severe form seen more in *H.influenza* (Kaplan and Oski, 1980). In the present study we found low hemoglobin of 60-90g/l in 34.7% cases and 90-110g/l in 51.7% cases. This results implies the need of observing hemoglobin levels to PBM patients. It's crucial for the patients with negative CSF culture results to do the comprehensive analysis of CSF and blood, together with clinical symptoms and signs of meningitis to avoid misdiagnosis and mismanagement (He *et al*., 2016).

Conclusion

The common organisms isolated from CSF were *Staphylococcal species, S.pneumoniae, GBS* and *E. coli*. Confirmed cases were 48(37%), low detection of etiologies has been contributed with higher rate of antibiotics use before admission. We observed the role of supportive investigations like Lactate, CRP, LDH and MRI etc. in making diagnosis. All common organisms isolated from CSF showed high sensitivity to Ceftazidime, meropenem, vancomycin and linezolid. High rate of resistance was seen on Penicillins and Ceftriaoxone. Different regions or countries have different patterns of bacterial meningitis etiologies, also etiologies trend mostly change over a period of time. Therefore it is important to conduct clinical laboratory surveillance regularly for better understanding of causative microorganism, antimicrobial sensitivity, and resistance patterns, to ensure good coverage of vaccination programs, lumbar puncture before antibiotics administration to every suspect of meningitis these are fundamental strategies in reduction of morbidity and mortality of PBM.

Limitations

This study has got several limitations because it was hospital based retrospective cross sectional study, which madeus to rely on the quality and quantity of information that had already been gathered in files. Some data were missing such as vaccination status, information of antimicrobial sensitivity and resistance were incomplete.Future longitudinal, prospective and multicenter surveillance for detection pathogens, long-term outcome of bacterial meningitis should be conducted.

Conflicts of interest: The authors declare that there is no conflict of interest.

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