Short Communication

Group B streptococcal meningitis in children beyond the neonatal period in sub-Himalayan India

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Abstract

Objectives: To evaluate clinicolaboratory profile and the outcomes in children (1 to 59 months) diagnosed with Group B streptococcus (GBS) meningitis over a period of 1 year. **Materials and Methods:** Cerebrospinal fluid (CSF) samples of 250 pediatric patients (1 to 59 months) admitted with suspected acute bacterial meningitis(ABM)were subjected to cell count, biochemical profile, culture, latex particle agglutination (LPA) and polymerase chain reaction (PCR).They were also evaluated for complications and were followed-up till 6 months after discharge. **Results:** Forty patients (25 boys and 15 girls), 16% of total suspected cases of ABM were diagnosed with GBS by LPA method and 30 (75%) out of these were above 3 months of age. The median duration of hospital stay was 7 days (range 1 to 72 days). State of coma was observed in two (5%) and one (2.5%) died, while 20 (50%) patients recovered completely. **Conclusion:** GBS should be considered as an important cause of ABM in Indian children beyond the neonatal period and further studies are warranted to determine the actual problem of the disease in our country.

Key Words

Acute bacterial meningitis, group B streptococcus, latex particle agglutination, neonatal mortality

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Introduction

Acute bacterial meningitis (ABM) is one of the most serious infections in infants and younger children causing high mortality and morbidity. It remains a major cause of neurological sequelae worldwide. Group B Streptococcus (GBS, *Streptococcus agalactiae*) is a well-known cause of early (1st week of life) and late onset (7 to 90 days of age) invasive disease (LOD) in neonates and very young infants. It is one of the major cause of increased peripartum and neonatal morbidity and mortality in the West[1] and has been described as a cause of meningitis in the form of ultra-late onset disease (ULOD)in infants >3 months of age, children, and even adults.[2,3]

In the United States, the overall incidence of neonatal GBS infection was 1.7 cases per1,000 live births prior to the introduction of intrapartum prophylaxis, which thereafter declined dramatically to 0.34 to 0.37% cases per 1,000 live births in the recent years.[4] In India, the spectrum of GBS disease remains largely under recognized. Few studies that have been done reveal the maternal GBS colonization in range of 1.62 to 16%[5,6] and the colonization rates in infants born to asymptomatic maternal carriers of GBS are 53 to 56%, which are consistent with rates reported in other parts of the world. Only 12% of colonized infants develop the major disease.[5] The estimated incidence of neonatal GBS infection in India is approximately 1 per1,000 live births.[5,7] The importance of invasive GBS outside the perinatal setting is rarely reported in modern literature and very rarely has been reported as a causative agent of ABM in pediatric patients older than 3 months of age. Therefore, through this study we intend to lay emphasis on the clinico-laboratory profile and the changing pattern of invasive GBS disease in our setting.

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Materials and Methods

This prospective study was conducted over a period of 1 year from July 2012 through June 2013 on cerebrospinal fluid (CSF) samples of 250 pediatric patients (1 to 59 months) admitted with suspected ABM in the Department of Pediatrics in a tertiary care hospital at Shimla. The data collected was a subset from the project on surveillance for meningitis due to *Streptococcus pneumoniae, Hemophilus influenzae* b, and *Neisseria meningitidis* in children of age group 1 to 59 months. The criteria for suspected

ABM, included presence of fever with one or more than one of the following symptoms such as neck stiffness, bulging fontanel, altered or reduced level of consciousness, lethargy, convulsions in a child without a documented seizure disorder, and clinical suspicion of meningitis by the treating physician. The study was approved by the ethical committee of the institution and written informed consent was obtained from the parents. CSF samples were collected preferably prior to the start of antibiotics. Lumbar puncture was performed under aseptic precautions and the samples collected were subjected to laboratory examination including white cell count, biochemical analysis, Gram stain, bacteriological culture and latex particle agglutination (LPA). The CSF was centrifuged in sterile/conical centrifuge tube at 3,000 rpm for 30 min. The supernatant was transferred to a sterile cotton plugged glass tube. Gram stain was done by the modified Hucker's method. The remaining deposit was inoculated with the help of sterile nichrome loop on blood agar (BA), chocolate agar (CA), Mac Conkey agar (MA) and thioglycolate broth (TB). The BA and CA plates were incubated in CO_2incubator, with 5% carbon dioxide at 37°C for 48 h, while the MA and the TB were incubated aerobically at 37°C for 48 h and 7 days, respectively. Blood culture was also performed in all patients. Bacterial antigen detection in CSF was done by treating the supernatant with the BD Directigen™ Meningitis Combo Test Kit (Becton Dickinson and Company, USA).The sensitivity of LPA for GBS is 100% (95% confidence interval (CI): 95 to 100%), and the specificity is 90.5% (95% CI: 80 to 96%). Clinical and laboratory data of patients with a positive CSF agglutination for GBS was analyzed in our study. The clinical parameters included the age, duration of illness, clinical features, antimicrobial treatment used, out come at discharge, and follow-up which was done up to 6 months after the discharge. Further as a part of surveillance project, CSF samples were sent to CMC Vellore for confirmation of the pathogens by PCR. The PCR was done for *S. pneumoniae*, *N. meningitidis* ACW_{135}, *N. meningitidis* type b, and *H. influenzae* type b; but however was not available for GBS.

Results

Two hundred and fifty patients met the inclusion criteria for clinically suspected meningitis in the specified age group (1 to 59 months). LPA was performed on all CSF samples. Forty patients (25 boys and 15 girls), 16%of total suspected cases of ABM were diagnosed with GBS by LPA method. ULOD was documented in 30 (75%) children who presented with clinical features of fever (30;100%), convulsions (22;73.33%), altered or reduced level of consciousness (7;23.33%), and lethargy (14;46.66%). Bulging anterior fontanel and neck rigidity were observed in six (20%) and seven (23.33%) patients, respectively. Nine (30%) were born prematurely and 14 (46.66%) were underweight (<3 SD as per World Health Organization (WHO) standards).

LOD was seen in 10 (25%) infants who presented with fever (10;100%), convulsions (7;70%), and lethargy (4;40%). Bulging anterior fontanel was detected in one (10%) child, one (10%) was born prematurely, and one (10%) was underweight. In all 40 children, the duration of illness prior to the presentation was less than 7 days. As per the national programme of immunization, all children were completely immunized for their age, but none had received immunization for *H. influenzae* b, *S. pneumoniae*, and *N. meningitidis*. Before being referred to the tertiary care hospital, 37 (92.50%) had received prior antibiotic treatment from some peripheral institutions. These included third generation cephalosporins (ceftriaxone), aminoglycosides (amikacin and gentamicin) and macrolides (azithromycin). All patients (37;100%) received a third generation cephalosporin antibiotic(either ceftriaxone or cefotaxime). Fifteen (37.50%) patients received amikacin along with the cephalosporin. The CSF leukocyte count ranged from 0 to 20 cells/mm^3 with neutrophilic predominance. The CSF sugar levels ranged from 24 to 119 mg/dl and proteins from 10 to 150 mg/dl. Gram staining and culture reports were negative in all the cases. None of the samples were reported to be positive on PCR for *H. influenzae* b, *S. pneumoniae*, and *N. meningitides*. Among the ULOD cases, four (13.33%) developed seizures during hospitalization and the intracranial pressure got raised in one (3.33%) patient. Ventilatory support was required in one (3.33%) child. State of coma was observed in two (6.66%) and one (3.33%) died; while, one (3.33%) patient left the hospital against medical advice. In LOD cases, two (20%) developed seizures, intracranial pressure got raised in one (10%), and ventilatory support was required in one (10%) child. Follow-up till 6 months after discharge could be done in 13 (43.33%) ULOD cases and out of these three (23.07%) developed seizures, one (7.69%) monoparesis, and one (7.69%) sixth and seventh cranial nerve palsies with hydrocephalous. In LOD group, three (30%) cases were followed-up among whom one (33.33%) developed seizures. Twenty (50%) patients recovered completely. No significant differences were found between two groups regarding clinical features, complications, and outcome on follow-up except for prematurity and low birth weight which appeared to be more associated with ULOD.

Discussion

GBS is a major pathogen of pregnant or postpartum mothers, neonates, and immunocompromised adults. Various etiological agents causing ABM in neonatal period include mainly GBS, *Escherichia coli*, Klebsiella species, and *Listeria monocytogenes*. Though the common pathogens in children 1 month to 12 years are mainly *S. pneumoniae*, *H. influenzae* b, and *N. meningitidis*; however, the etiological agents in neonatal and postneonatal patients may overlap during first 3 months of life, in which GBS may also be a causative agent.[8] Information regarding the onset of meningitis due to GBS beyond 3 months of age is sparse even in the western literature. In the present study, LPA detected 40 cases (16%) to be positive for GBS and out of these, 30 (75%) were above 3 months of age. Our results correlate with the study done by some other Indian authors, who reported 27 (15.97%) of 169 CSF samples of age group 118 months to be positive for GBS by LPA, with 16 (59%) children being above 3months of age.[9] Previous studies have reported low sensitivity of culture when performed after the initiation of antibiotic treatment. Various authors have advocated the usefulness of bacterial antigen detection test for the diagnosis, especially in situations where patient has received prior antibiotics.[10] The results of the present study demonstrate the same. A retrospective 10-year analysis of 402 CSF samples from Korea, identified 99 (24.6%) children with GBS. In this study, 8.1% of *S. agalactiae* meningitis patients presented within the first 6 days of life in contrast to the previous report which revealed, 54.4 and 59.6% in the United States and European

countries, respectively. The remaining cases presented between 7 days and 5 months.[11] Florindo *et al* reported GBS as the causative agent of 60 meningitis episodes in children aged 3 months to 12 years from Angola during a study conducted from 2004 to 2005.[12] Previously, various case reports have also described GBS as a cause of meningitis in children beyond the neonatal period.[13,14]

Clinical manifestations of invasive GBS infection beyond early infancy have been enumerated as meningitis, septic arthritis, endocarditis, sepsis, central venous catheter, and ventriculostomy infections. Apart from the colonization of mothers, hospitalization and medical interventions may also be an important risk factor for the development of ultra-late onset sepsis.[15,16] In present study, prematurity and low birth weight were observed more in the ULOD as compared to the LOD group. Various authors have also postulated preterm birth as a risk factor for GBS infection.[1] Therefore in the present study, various predisposing factors which might have been responsible for GBS meningitis (ULOD and LOD group) were high number of preterm births (25%), low birth weight (37.5%), and possibly high maternal colonization rates, though the data of which is still lacking from this region.

Conclusion

This study emphasizes that GBS should be considered as an important pathogen causing invasive infections beyond the neonatal period and prematurity, appears to be significantly associated with ULOD. Hence, continued surveillance with more detailed studies are warranted to know the actual magnitude of problem and the spectrum of diseases caused by this pathogen in our setting.

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