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Research Article

Aetiology of Meningitis in Paediatric Age Group at a Tertiary Care Centre in Hyderabad, India - A Cross Sectional Study

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Abstract

Background: Meningitis continues to be a serious public health problem that requires early prompt diagnosis and treatment. There is a need for a periodic review of meningitis since the pathogens responsible for the infection vary with time, geography, and patient age. The aim of this study is to identify the aetiological agents in suspected paediatric meningitis cases attending tertiary care hospital.

Methods: This cross- sectional study was conducted for a period of one year (August 2018-2019) in the Department of Clinical Microbiology, Niloufer hospital for Women and Children, Hyderabad after obtaining clearance from institutional ethical committee. Out of 135 suspected meningitis cases, 79 were enrolled into the study based on inclusion criteria. CSF samples collected by Lumbar Puncture and were processed immediately by standard conventional techniques for identification of bacteria, fungi, parasites and ELISA for IgM antibodies against viral antigens of HSV 2, VZV, EV 71. The demographic data and associated laboratory findings were analysed in detail.

Results: Out of 79 samples, 32 (40.5%) were confirmed as meningitis of bacteria and viral aetiology. No fungal and parasitic agents were identified. Prevalence of viral meningitis (32.9%) was found to be more than bacterial meningitis (7.5%). The most common viral agent was HSV2 (61.5%) followed by VZV (38.4%). Among bacterial pathogens, Gram negative organisms (66.6%) were more than Gram positive organisms (33.3%). Infants and neonates were most commonly affected. Out of 15 districts covered, maximum number of viral meningitis cases were reported in and around Hyderabad during spring and winter seasons.

Conclusion: To conclude, Viruses played a predominant role as compared to bacteria in paediatric meningitis and this was dictated by factors like endemicity, geography and season. There is a need for more studies to identify the emerging aetiologies of paediatric meningitis.

Keywords: Paediatrics; Viral Meningitis; HSV2; VZV; Bacterial Meningitis

Introduction

Meningitis is defined as inflammation of the meninges, a thin membranous coverings of the brain and the spinal cord [1]. Meningitis is a serious public health problem that requires early diagnosis, treatment, and preventive measures [2]. It is a notifiable disease with significant morbidity and mortality. Neonates are more prone to meningitis due to immature immune system and increased permeability of blood-brain barrier (BBB) [3]. The incidence of meningitis shows regional and seasonal variation. Latest estimated global burden is 2.82 million (2016). The incidence of meningitis in neonates and children under 5yrs age group is 56% with a mortality of 46% [3,4]. In the Indian scenario, bacterial ae-

tiology accounts for 55.3% of cases in below 1yr age group [4,5]. There is insufficient published data regarding viral meningitis [5,6]. However, few record based Indian studies reported 43.3% viral meningitis cases in paediatric age group [6,7]. *S. pneumoniae, N. meningitidis, H. influenzae*, *L. monocytogenes,* and *S. aureus* are important bacterial pathogens of acute bacterial meningitis in the west but the relative incidence of these is less in South East Asia where *P. aeruginosa, E. coli, and K. pneumoniae* are important pathogens [8]. The most common viral meningitis pathogens are non-polio enteroviruses, herpes simplex viruses, mumps measles and influenza viruses. Among fungal pathogens, *Cryptococcus neoformans* is most common in children with immunodeficiencies. Parasitic meningitis is due to causes like *N. fowleri, A. cantonensis, B. procyonis, G. spinigerum* (CDC 2019) [9,10]. The main objectives of the present study is identification of aetiological agents in suspected paediatric meningitis patients and analysis of demographic, clinical and laboratory data.

Materials and Methods

The Present study was conducted for a period of 1 year (August 2018-2019) at the Department of Clinical Microbiology, Niloufer hospital for Women and Children, Osmania Medical College, Hyderabad. Clearance from institutional ethical committee [Osmania medical college-ECR/300/Inst/AP/2013/RR-16] was obtained. Out of 135 suspected meningitis cases, 79 were enrolled into the study based on inclusion criteria. Inclusion criteria was neonates, infants and children upto 12yrs attending to the hospital with clinical history suggestive of meningitis. Exclusion criteria was all cases with tubercular meningitis, iatrogenic meningitis, non-infectious meningitis and age above 12yrs. Informed consent was obtained from parents/guardians after explaining in detail the objectives of the study. The details of all patients including demographic data, clinical history, clinical examination notes, prior investigations done and treatment history was documented and analysed. CSF samples from all cases in study group were collected in sterile containers by Lumbar Puncture using standard techniques under aseptic conditions by clinicians. The CSF sample was divided into 2 parts. One part was sent for culture and microscopy to identify bacterial and fungal aetiologies. Second part was preserved at -20°c and sent for serological diagnosis of viral aetiology by IgM ELISA antibody test for HSV 2, VZV, EV-71 antigens. Samples were processed without any delay. The samples were centrifuged at 1000 x g for 10-15 minutes. The sediment of centrifuged sample was subjected for culture and microscopic examination for bacterial and fungal processing by standard microbiological conventional methods. Culture isolates were identified based on biochemical reactions and further subjected to Antimicrobial susceptibility testing as per CLSI guidelines. Fungal cultures were observed for growth at 48hrs, 72hrs and weekly upto 4wks. For detection of parasites, wet mounts were examined microscopically for trophozoites of *N. fowlerii* and larvae of helminthic parasites like *A. cantonensis, B. procyonis, G. spinigerum.*

Serological test (ELISA) for viral agents: The 2nd sample which was preserved at -20°c was subjected to Quantitative IgM ELISA as per manufacturer's literature protocol for HSV 2, VZV, EV71 viruses using HSV IgM (Cat no: E13652595), VZV IgM (Cat no: E13651838), EV71 IgM (Cat no: E13652113) ELISA Kits of Sincere Biotech. Ltd company, Beijing, China. Purified Human HSV 2/VZV/EV 71 antigen coated microtiter plate wells were used to detect specific IgM antibodies in CSF samples. The ELISA results were analysed within the detection range of 61.35 pg/ml - 5000 pg/ml by considering Standard 4 as cut off value.

Results, Discussion and Conclusion

Out of 79 CSF samples processed, 32 (40.5%) were confirmed as meningitis by bacteria and viruses. No fungal and parasitic aetiology were found. The prevalence of viral meningitis (n = 26;32.9%) was found more than bacterial meningitis (n = 6;7.5%). Among the tested viral aetiological agents, the most common was HSV2 (61.5%) followed by VZV (38.4%) (Table 1). 50% neonates showed bacterial aetiologies whereas 38.4% infants showed viral aetiologies with decreasing trend as the age advances. The most common clinical presentation of study group was convulsions followed by fever. Non-specific symptoms like rash, vesicles, loose stools, vomitings, upper respiratory tract symptoms were more associated with viral meningitis. Radio-imaging studies showed Normal CT/MRI Brain scans in 69.6% (n = 55) indicating meningitis in the study group. Geographical distribution among 15 districts covered in

Type	Organism	Positive cases (%)
Bacteria (n = 6)	*S. aureus*	2 (33.3%)
	E.coli	2 (33.3%)
	K. pneumoniae	2 (33.3%)
Viruses (n = 26)	HSV2	16 (61.5%)
	VZV	10 (38.4%)
	EV71	Nil
Fungi	Nil	Nil
Parasites	Nil	Nil

Table 1: Aetiological agents identified in meningitis cases.

this study showed maximum viral meningitis cases in and around Hyderabad district and bacterial meningitis cases were equally distributed in Rangareddy, Kamareddy, Mahbubnagar, Nalgonda, Sangareddy, Vikarabad districts. Seasonal distribution showed gradual increase in no. of viral meningitis cases in January, February then peak was observed in March followed by fall in number of cases and nil cases in May, June, July and again gradual increase in number of cases in August, September with shorter peak in October followed by fall in November and nil cases in December (Table 2).

Characteristic			BM (n = 6)	VM (n = 26)
Gender	Males		50% (n = 3)	46.2% (n = 12)
	Females		50% (n = 3)	53.8% (n = 14)
Age	Neonates (Day 0 to Day 30)		50% (n = 3)	34.6% (n = 9)
	Infants (Day 31- 12 months)		33.3% (n = 2)	38.4% (n = 10)
	Children (1 year-12 years)		16.7% (n = 1)	27% (n = 7)
Geography	Hyderabad District		Nil	34.6% (n = 9)
Season			Spring, Winter	Winter
Clinical Features	Specific		66.7% (n = 4)	73% (n = 19)
	Non-specific			57.6% (n = 15)
Duration of illness	Acute (<72 hrs)		50% (n = 3)	61.5% (n = 16)
	Sub acute (>72 hrs)		50% (n = 3)	38.4% (n = 10)
Laboratory analysis	Serum CRP (>10 mg/l)		100% (n = 6)	26.9% (n = 7)
	Blood WBC (Newborns:9,000-30,000 <2yrs: 6,200-17,000 >2yrs:5,000-10,000)	Raised	66.7% (n = 4)	-
		Low		23.1% (n = 6)
		Normal	33.3% (n = 2)	76.9% (n = 20)
	CSF Glucose (60-80 mg/dl)	Low	100% (n = 6)	26.9% (n = 7)
		Normal		73.1% (n = 19)
	CSF Proteins (Newborn: 40-120; <1 month: 20-80; >1 month:15-40mg/dl)	Raised	33.3% (n = 2)	80.8% (n = 21)
		Normal	66.7% (n = 4)	19.2% (n = 5)
	CSF cell count (Pleocytosis: Neonates: >10 white cells/mm^3 Others: >5 white cells/mm^3)	Neutrophils High	100 % (n = 6)	-
		Lymphocytes High	-	100 % (n = 26)
Radio-imaging CT/MRI brain scans	Normal		83.3% (n = 5)	73.1% (n = 19)
	Abnormal (Prominent ventricles, Hypodensity of basal ganglia/cerebellar region/parietal lobes/Rt. cerebral cortex/Superior sagittal sinus/Thickened cortex, Rt. thalamus infarct/Brainstem ischemia)		16.7% (n = 1)	26.9% (n = 7)
Outcome	Recovered		83.3% (n = 5)	88.5% (n = 23)
	Neurological sequele		-	7.7% (n = 2)
	Deaths		16.7% (n = 1)	3.8% (n = 1)

Table 2: Demographic, Clinical, Laboratory data of confirmed cases.

BM: Bacterial meningitis; VM: Viral meningitis.

In the present study, Hyderabad showed high preponderance for paediatric meningitis during spring and winter seasons which is a point of concern. The suspected meningitis cases in study group were mainly of neonates and infants accounting for 77.2%. It was observed that paediatric age group was highly affected with viral meningitis (32.9%) which is in consistent with Borade., *et al*. study (43.29%) [7]. In the present study, HSV2 accounted for 61.5% and VZV for 38.4% whereas Pormohammad., *et al*. [11] study reported 9.8% VZV and 1.4% HSV ½. Even though Enteroviruses causes 70-95% of aseptic meningitis [10], but the present study showed nil cases of IgM antibody against EV71. According to another study in Turkey including children and adults, herpesviruses, were observed more than enteroviruses [12]. The reason for higher herpesviruses in our study can be due to history of maternal antenatal TORCH infections and contagious transmission of infections from infected siblings/family members. In the present study, we have adopted quantitative IgM ELISA test for detection of viral aetiologies. This is in consistent with explanation by Stiernstedt., *et al*. [13] that measurement of CSF antibodies was a more sensitive and specific method than measurement of serum antibodies by either IFA or ELISA. Even Rashmi., *et al*. [6] states that since IgM cannot cross blood brain barrier, CSF IgM specific to a virus is highly suggestive of brain invasion by pathogen and this provides early, quick and accurate diagnosis.

The prevalence of bacterial meningitis (7.5%) in the present study is in consistent with studies conducted by Sasan MS., *et al*. in Shiraz-Iran (12.3%) and Hosseininasab A., *et al*. in Mashhad-Iran (16.3%) [14].On contrary, a higher prevalence of bacterial meningitis was reported in Indian studies conducted in Kolkata by S. Joardar., *et al*. (34.66%) [15] and in Tamil Nadu by Minz S., *et al*. (18.56%) [16]. The low rate of bacterial meningitis in this study can be due to immunization, prior admission in different hospitals, administration of empirical antibiotics prior to lumbar puncture. Our study is in consistent with the explanation by Bareja R., *et al*. [8] that regional variations in aetiology is seen even in close geographical locales and races. Among bacterial agents, *S. aureus*, *E. coli, K. pneumoniae* were most common which is similar to other studies [8,17].

In the present study, it was observed that bacterial meningitis was more in neonates (50%) whereas viral meningitis is observed to be more in infants (38.4%) this is in consistent with Wang YJ., *et al*. study [18]. Bacterial meningitis cases showed specific features like fever, convulsions and meningeal signs which is in consistent with Sonavane AE., *et al*. study [19]. Viral meningitis showed fever, convulsions, altered sensorium and irritability, non-specific features and meningeal signs which is in consistent with Wang YJ., *et al*. [18] study. In the present study, pleocytosis was defined as >10 white cells/mm3 for neonate and >5 white cells/mm3 for others and findings of biochemical and cytological analysis were in consistent with other studies [6,18,20]. It was observed 100% raised serum CRP in bacterial meningitis which is in accordance with P L Prasad., *et al*. study who reported raised Serum CRP in 29 cases of bacterial and zero in all cases of viral meningitis [21]. According to Schwarz S., *et al*. although CSF lactate and serum procalcitonin have been reported to be useful to distinguish bacterial meningitis from aseptic meningitis [22], they were not routinely checked in our department due to high cost. Majority of Normal CT/MRI brain scans suggesting of meningitis is in consistent with Nagra I., *et al*. study [23]. In this study, it was observed that 83.6% recovered with early intervention and management in meningitis cases. Early identification for specific cause will decrease the disease burden and prevent unnecessary use of antibiotics in viral meningitis cases.

Limitations

To establish the aetiologies of meningitis, sensitive strategies for the diagnosis of organism need to be explored. CSF cultures were negative for bacterial aetiologies because of administration of empirical antibiotics prior to hospitalization. Although many viruses cause viral meningitis, only 3 viruses were studied in this study because these were most common causative agents, cost restrain to study all viruses, unavailability of comparable published data in our region. As cost remains a significant barrier for molecular diagnostics, So we have adopted CSF ELISA in correlation with other available tests in our settings. For detection of parasitic agents, direct wet mount of specimen which is a low sensitive test was adopted due to unavailability of resources for specific diagnosis in the present settings.

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Volume 4 Issue 12 December 2021