Detection of Acute Childhood Meningitis using PCR in a group of Children at Childs Central Teaching Hospital/Baghdad

Rana Fahmi Shitran,[1] Warqaa Y. Khudur [1], Mohammed E. Atallah[2]

[1] Lecturer, Department of pediatrics , University of Anbar/ Iraq, [2]Specialist, Alramadi Teaching Hospital for Maternity and Childhood /Iraq

Abstract

Bacterial meningitis is an important cause of death in both developed and developing world.

The study was done on 116 patients admitted to child central teaching hospital in Baghdad ,and diagnosed with meningitis depending on CSF findings and PCR results while determination of type of microorganism depend on PCR result . In this study we aimed to assess the patients regarding their numbers ,clinical manifestations , complications and type of bacteria causing the disease .Regarding the results of PCR, streptococcus meningitis at the top of the list for the bacterial causes while no any reported cases with Hemophillus influenza and this could be referred to the program of vaccination applied in Iraq which included the vaccines against both types of bacteria. Results :of 116 patient involved in this study, majority (44%) were below 1 year ,with male predominance (57.8 %).most of the patients symptoms between 1-3 days (56%).all patients presented with fever. The diagnosis depend on the PCR results (57.8%) were negative and (37.9%) showed streptococcal infection .All blood culture were surprisingly negative because majority of included patients received antibiotics in outpatient visits before admission and diagnosis.

Patients admitted and followed up to one year for development of complications. Sixteen cases developed complications, (3.4%) of them with subdural effusion and most of complication occur in streptococcal positive PCR results .

***Keywords**: PCR; Childs central teaching; childhood; Baghdad*

Introduction

Meningitis in generic is defined as membranes of the inflammation that surround the spinal cord and brain . the causes Microbiological include, utilizer the routine pneumococcal vaccine conjugate , meningitis bacterial effected about 6000 people all the year in the United States; the children at 18 years old or less happen the half case [1].

In infants and young children, Streptococcus pneumoniae, Neisseria meningitides, and Haemophilus influenzae type b are the commonest causes of bacterial meningitis worldwide.while among children older than 5 years of age and adolescents, S. pneumoniae and N. meningitidis are the main causes of bacterial meningitis [1,2].

The incidence of meningitis caused by Hib has decreased predominantly in areas of the world where Hib conjugate vaccines are used routinely [3].

In 1995, before global fortification versus Streptococcus pneumoniae, the happen of meningitis pneumococcal was most than 20 cases per 100,000 US population in younger children less two years old [1]. The seven more common types that cause meningitis in the United States are 4, 6B, 9V,14, 19, 18C, and 23 [4]. These types are involved in the heptavalent pneumococcal conjugate vaccine, The incidence of disease invasive, containing meningitis bacterial, make happen via S. pneumoniae has been markedly reduced via near 90% after the introduction of this vaccine beginning in

Corresponding author:
Rana Fahmi Shitran
Email: rana.fahmi85@yahoo.com

infancy.[5]

Typical result of CSF in meningitis bacterial contain pleocytosis commonly with a WBC count major, than 1000 cells/mm3 and dominance of polymorphonuclear leukocytes. the WBC count can be normal in some cases, especially when performed early in the course of the disease, [6], and there could be a lymphocyte predominance. It is common for the polymorphonuclear leukocyte count to increase after 48 hr. of diagnosis and then reduced gradually after that [7]. usually concentration of Glucose is decreased with a CSF-to-serum ratio glucose at 0.6 or low in neonates and 0.4 or low in children less 2 months of age, while concentration of protein is increased [8].

Exception of meningitis happen via gram-negative bacilli enteric , the benefit of bacterial CSF cultures ordinarily decreases soon after antibiotic therapy started [9-10]. Polymerase testing chain reaction of CSF is most sensitive than CSF culture, especially in patients who previous received therapy antimicrobial [11]

Wide-range polymerase chain reaction have appear a sensitivity Of at 86% and specificity of 97% in detecting organisms multiple together compared with the results culture [12]. The reaction of polymerase chain techniques sensitive comparative with o clinical setting [13]. The focal neurologic signs, instability cardiovascular , makes the doubt of increased pressure intracranial most like. In that cases, imaging brain should be done prior to a lumbar puncture to possible avoid the herniation [14].

Patient and Method

A retrospective study was conducted on patients admitted to child's Central teaching hospital in Baghdad from the first of January 2018 till first of July 2018. This hospital is a tertiary care center for pediatrics and receive many referred cases from periphery of Baghdad and other governorates.

Data were collected , according to preformed questionnaire designed by the researchers , the information regarding , Age , sex , clinical presentations , laboratory tests including CSF findings and PCR results, lines of treatment , and acute complications were recorded .

The studied sample include 116 patients admitted to infectious ward at child's central teaching hospital. The inclusion criteria include clinical manifestations of meningitis including (fever ,seizure ,refuse to eat ,vomiting, headache ,bulging fontanel and positive meningeal signs)[15] plus either a culture positive from CSF or culture negative with a positive CSF antigen study or gram stain in conjunction with CSF leukocyte concentration of > 10/mm3 , blood positive culture with CSF. WBC. > 100/mm3 ; in ambiguity of isolates bacterial ; CSF WBC > 4000/mm3.[16] CSF samples collected on admission were subjected to laboratory investigations including cells count and their differentiation ,glucose and protein level ,and CSF culture and CSF samples for PCR results also had been sent to Central public health laboratory. Because PCR of CSF is more sensitive than CSF culture in patients previously treated with antibiotics [11] ; and as soon as most of the included patients were treated with antibiotics prior to admission , so we depend on PCR of CSF results while CSF culture results was non informative. All patients underwent full neurological examination on admission to assess any neurological deficit at time of diagnosis ,during the period of treatment and up to 1 year follow up visits.

Management usually started with empirical antibiotics with intravenous dexamethasone and supportives then the antibiotics can be changed depending on CSF culture and PCR results then the patient was followed for response to treatment and for acute complications during the period of hospitalization.

Any recorded cases with missed information regarding clinical manifestations ,CSF findings ,PCR results and complications was omitted Patients with chronic disease , congenital cranial or spinal cord malformations, prosthetic valve on CNS, cerebral palsy and previous episodes of bacterial meningitis where all excluded from the study.

All included patients were vaccinated according to Iraqi schedule of vaccination, those who were not complete their vaccination and immigrants who are missing many doses of vaccination were all excluded from the study.

All admitted patients were followed during the period of admission for development of acute neurological complications (subdural effusion, hydrocephalus, abscess, stroke, cortical atrophy, diminished consciousness, persistent seizure, spasticity ,hypotonia). Those with acute neurological deficit at time of admission were also registered.

Brain imaging was done for patients with focal neurologic signs, cardiovascular instability, or papilledema prior to a lumbar puncture to avoid possible herniation [14].Imaging study also done for those with new onset neurological deficit and suspected complications.

Results

The mean age of patients was 2.58 ± 3.36 years; 57.8% were males and 42.2% were females and 90.5% were from Baghdad. Fever was presented in all patients followed by seizure which was found in 64.7% as shown in table and figure (1). Subdural effusion was found in 3.4% of cases as shown in table (2).

Table 1: Distribution of study patients by general characteristics

Variable	No. (n=116)	Percentage (%)
Age (Years)		
< 1	51	44.0
1 - 5	48	41.4
6 - 10	11	9.5
> 10	6	5.2
Gender		
Male	67	57.8
Female	49	42.2
Residence		
Baghdad	105	90.5
Outside Baghdad	11	9.5
Duration of symptoms before admission		
< 24 hrs.	13	11.2
1 – 3	65	56.0
> 3	38	32.8

Figure 1 shows the results of PCR. We noticed that 57.8% of cases showed negative results, while 37.9% showed streptococcal infection.

Figure 2: Results of PCR

Table 2: Distribution of study patients by complication

complication	No. (n=116)	Percentage (%)
Subdural effusion	4	3.4
Hydrocephalus	1	0.9
Abscess	1	0.9
Stroke	2	1.7
Diminished Consciousness	2	1.7
Persistent Seizure	1	0.9
Spasticity	3	2.6
Hypotonia	2	1.7

According to CT scan finding that showed in table (3), brain lesion was detected in 11.2% of cases (6% of them was in the right side), brain edema in 6.9% and bleeding in 2.6% of cases.

Table 3: CT scan finding

CT Finding		No. (n=116)	Percentage (%)
Lesion	Right	7	6.0
	Left	2	1.7
	Bilateral	3	2.6
	Cortex	1	0.9
Brain Edema		8	6.9
Bleeding		3	2.6

Regarding outcome, all study patients were discharged well.

Discussion

regardless of the advance in medicine, meningitis

bacterial causes essential morbidity and death-rate in children in both developing and developed countries. loss of the hearing Sensorineural , hydrocephalus and mental retardation , seizures, motor disabilities , as well as most delicate outcomes such as academic and cognitive, and problems the behavioral are discover in post-meningitis children [17]

Bacterial meningitis is an important cause of morbidity and mortality worldwide so early diagnosis is an important step to decrease it's complications and this must be start from high index of suspicion regarding any symptom that may present bacterial meningitis and at the top of the list the fever which was seen in all patients in our study and this differs from a study done by HFM farag [18] who found that fever was the presenting feature in 92.1% of the patients and this may be explained by the time lag between the onset of symptoms and presentation at hospital as majority of patients in current study delayed in seeking medical attention and hospitalization. Regarding the age distribution of the patients , the infants in current study were more liable for bacterial meningitis than other age groups (44%) of the total cases and this result agree with Rehana Basri et al's [19] study where (54%) of the patients were below one year .

The male patients was the predominat in current study (57.8%) and this result agree with H Choudhury etal and Kirimi E etal [20] where male patient accounting for 58,6% .

The most important point in our study is the type of microorganism that causing meningitis. we depend on PCR result rather than CSF culture although it's more expensive than CSF culture and sensitivity but it's more precise and it is not affected by prior use of antibiotics [11] ,as soon as most of participated patients in our study were given oral antibotics before diagnosis of meningitis and prior to blood sampling so majority of the results of CSF culture involved in our study were negative.

In current study PCR results showed that streptococcal pneumonia is the most common causative organisms (37.9%) followed by Neisseria meningitis (4.3%) and this result agree with Erleena nur H etal who found that streptococcal pneumonia also the commonest organisms and account for (23%) and Neisseria meningitis (4%) [21]

In current study there is no H. influenza microorganisms and this differs from Hussain IH et al who found that Homophiles influenza kind b (Hib) were the utmost common aetiological agent [22] and this may be explained by the vaccination program in Iraq which include H.influenza vaccine since 2012 and all included patient in this study were vaccinated according to Iraqi schedule of vaccination

As a part of our study we look for the development of complications and this depends on the early and late follow up of the patients during admission and after discharge from the hospital , and its relationship to causative agent . subdural effusion was at the top of the list (3.4%)of the total complications followed by spasticity(2.6%) , then stroke ,hypotonia , disturbed level of consciousness (1.7%) finally the hydrocephalus ,persistent seizure and abscess(0.9 %) . These results compared with Sadie Namani (1) where subdural effusion founded in 28.6% , recurrent seizure 7. 8% and hydrocephalus (2.6%) [17] and this is explained as the insufficient drainage of CSF through the arachnoid villi which is more occurred in children which favor the development of subdural effusion.

Conclusion

Infectious meningitis is a big health problem. Though the introduction of vaccination program in Iraq had changed the frequency of the causative agents ;and eliminate H. Influenza from the list. Streptococcus pneumonia remains on the top ;We hope ,in the next years with recent introduction of pneumococcal vaccine to Iraqi schedule of vaccination ,to reduce or minimize the number of infected patients and in turn reduce complications and suffering children..

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both MOH and MOHESR in Iraq

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References

[1] Schuchat A, Robinson K, Wenger JD, et al. Bacterial meningitis in the United States in 1995.Active Surveillance Team. N Engl J Med 1997;337:970– 6.

[2] Dawson KG, Emerson JC, Burns JL. Fifteen years of experience with bacterial meningitis. Pediatr Infect Dis J 1999;18:816– 22.

[3] Martin M, Casellas JM, Madhi SA, et al. Impact of Haemophilus influenzae type b conjugate vaccine in South Africa and Argentina. Pediatr Infect Dis J 2004;23:842– 7.

[4] Feikin DR, Klugman KP. Historical changes in pneumococcal serogroup distribution: implications for the era of pneumococcal conjugate vaccines. Clin Infect Dis 2002;35:547–55.

[5] Black S, Shinefield H, Baxter R, et al. Postlicensure surveillance for pneumococcal invasive disease after use of heptavalent pneumococcal conjugate vaccine in Northern California Kaiser Permanente. Pediatr Infect Dis J 2004;23:485–9.

[6] Freedman SB, Marrocco A, Pirie J, Dick PT. Predictors of bacterial meningitis in the era after Haemophilus influenzae. Arch Pediatr Adolesc Med 2001;155:1301 – 6.

[7] Straussberg R, Harel L, Nussinovitch M, Amir J. Absolute neutrophil count in aseptic and bacterial meningitis related to time of lumbar puncture. Pediatr Neurol 2003;28:365– 9.

[8] Saez-Llorens XM. Acute bacterial meningitis beyond the neonatal period. In: Long SS, editor. Principles and practice of pediatric infectious diseases. 2nd ed. Philadelphia7 Churchill Livingstone; 2003. p. 264– 71.

[9] Kanegaye JT, Soliemanzadeh P, Bradley JS. Lumbar puncture in pediatric bacterial meningitis: defining the time interval for recovery of cerebrospinal fluid pathogens after parenteral antibiotic pretreatment. Pediatrics 2001;108:1169–74.

[10] Nigrovic LE, Kuppermann N, McAdam AJ, Malley R. Cerebrospinal latex agglutination fails to contribute to the microbiologic diagnosis of pretreated children with meningitis. Pediatr Infect Dis J 2004;23:786–8.

[11] Chiba N, Murayama SY, Morozumi M, et al. Rapid detection of eight causative pathogens for the diagnosis of bacterial meningitis by real-time PCR. J Infect Chemother. 2009;15(2):92-98.

[12] Schuurman T, de Boer RF, Kooistra-Smid AM, van Zwet AA. Prospective study of use of PCR amplification and sequencing of 16S ribosomal DNA from cerebrospinal fluid for diagnosis of bacterial meningitis in a clinical setting. J Clin Microbiol 2004;42:734– 40.

[13] Bryant PA, Li HY, Zaia A, et al. Prospective study of a real-time PCR that is highly sensitive, specific, and clinically useful for diagnosis of meningococcal disease in children. J Clin Microbiol 2004;42:2919– 25.

[14] Shetty AK, Desselle BC, Craver RD, Steele RW. Fatal cerebral herniation after lumbar puncture in a patient with a normal computed tomography scan. Pediatrics 1999;103:1284 –7.

[15] Wolf SM. Laboratory evaluation of the child with a febrile convulsion. Pediatrics 1978; 62:1074-6

[16] Berkley JA. Mwangi I ,Ngetsd CJ, etal. Diagnosis of acute bacterial meningitis at a distant hospital in sub-saharan Africa. Lancet 2001:357:1753-7

[17] Namani S, Milenkovi´c Z, Koci B. A prospective study of risk factors for neurological complications in childhood bacterial meningitis. J Pediatr (Rio J). 2013;89:256---62.

[18] Farag HFM,MM abdel-fatah ,AM Youssri. Epidemiological ,clinical and prognostic profile of acute bacrerial meningitis among children in Alexandria Egypt . indian journal of medicine microbiology ,2005;23(2);95-101

[19] Rehana Basri.Burden of bacterial meningitis :A retrospective review on laboratory parameters and factors associated with death in meningitis,Kelantan Malaysia. Nagoya J. Med. Sci,2015: 77. 59 ~ 68,

[20] H Choudhury, M Ashrafuz Zaman, M Jahangir Hossain, et al. Outcome and prognostic factors of acute meningoencephalitis in children of Southern Bangladesh Sri Lanka Journal of Child Health, 2012; 41(1): 27-32

[21] Erleena Nur H, Jamaiah I, Rohela M, Nissapatorn V. Bacterial meningitis: A five year (2001–2005) retrospective study at university malaya medical center (UMMC), kuala lumpur, Malaysia. Southeast Asian J Trop Med Public Health, 2008; 39: 73–77.

[22] Hussain IH, Sofiah A, Ong LC, Choo KE, Musa MN, Teh KH, Ng HP. Haemophilus influenzae meningitis in Malaysia. Pediatr Infect Dis J, 1998; 17 (9 suppl): 189–190.