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Correlation of Bacteremia in Neonates with Bacterial Meningitis

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Abstract

Introduction: Meningitis is a critical condition involving most commonly neonates due to their immature immune system and greater permeability of blood brain barrier. Symptoms in neonatal meningitis are nonspecific and its long term complications could be deafness, blindness, cerebral palsy, seizures, hydrocephalus, or cognitive impairment. Therefore evaluation of the neonate should involve a high level of suspicion of meningitis to provide its early diagnosis and quick initiation of treatment.

Method: 244 neonates were enrolled whose blood and CSF samples were collected. CSF was cultured and incubated at 37 °C for 72 hours. Blood culture bottles were loaded in Automated Bact-alert 3D machine for maximum 5 days. Identification of microorganism by MALDI-TOF VITEK MS was done.

Results: Out of total 244 neonates enrolled, 153 cases were sterile on both CSF and Blood cultures. 56 CSF samples were found positive on culture, 30 were simultaneously positive for blood culture in which 26 had similar microorganism and 4 had different bacteria. Rest 26 blood cultures were sterile that indicates in 46.4 % of culture proven meningitis patients, there was no bacteremia.

Conclusion: There was a significant percentage of neonates reported with meningitis in whom blood culture was sterile. The signs and symptoms of meningitis are very subtle and vague in neonates. Therefore in neonates with symptoms of infection, one should always go for lumbar puncture for CSF culture along with other parameters. Meningitis, specially in neonates, should not solely be suspected in cases with positive blood culture as this could result in missing the diagnosis.

Meningitis, specially in neonates, should not be suspected only in cases with positive blood culture as this could result in missing the diagnosis.

Keywords: Neonatal meningitis; CSF culture; Blood culture; Bacteremia

Introduction

Neonatal meningitis is inflammation of the meninges during the first 28 days of life. Neonates are at high risk of meningitis and of resulting neurologic complications. Early recognition of neonates at risk of poor prognosis would be helpful in providing timely management. It is the most common and severe infection of the central nervous system (CNS), affecting the pia and arachnoid mater and subarachnoid space [1]. Bacterial meningitis is more common in the newborn period than at any other age, with a higher prevalence in pre-term and often hospitalised newborns [2]. It is widely thought that the formation of the blood-brain barrier (BBB) begins in late gestation and continues into the postnatal period. This period of greater permeability may make the developing brain more susceptible. Due to immature immune system and limited placental transfer of maternal antibodies, especially in preterm newborns, neonates

are the most susceptible of all age groups to develop infections [2]. In spite of the development of the rapid diagnosis of pathogens and new antibiotics, neonatal meningitis (NM) contributes to neonatal morbidity and mortality worldwide. Therefore bacterial meningitis can result in acute problems affecting the brain parenchymal vessels (vasculitis), ventriculitis, systemic complications (including pneumonia), and septic shock, all of which contribute to an unfavourable prognosis [3]. Approximately 25-50% of survivors suffer from neurological sequelae, such as deafness, blindness, cerebral palsy, seizures, hydrocephalus, or cognitive impairment [1, 4].

Meningitis is typically caused by the hematogenous spread of microorganisms into the central nervous system via the choroid plexus and cerebral microvasculature during sepsis [5]. Infrequently, it may develop as a result of the spread of infection from the scalp or skull or the contamination of an open neural tube defect, ventricular device or congenital sinus tract [6]. If there is delay in delivery, microbial infiltration of amniotic fluid may induce chorioamnionitis, an acute inflammation of the foetal membranes [5, 7]. In neonates signs and symptoms are vague and nonspecific thereby high level of clinical suspicion is required. Infants typically exhibit fever, lethargy, irritability, poor feeding, vomiting, diarrhoea, respiratory distress, convulsions, and a protruding fontanelle [8]. Standard diagnostic procedure for bacterial meningitis is cerebrospinal fluid (CSF) culture. Therefore, it is essential to do an LP as soon as possible, preferably prior to the use of antibiotics [9]. Meningitis is often more severe with gram-negative bacteria with a higher rate of mortality and morbidity.

Material and Methods

The study was conducted in the Department of Microbiology in collaboration with Department of Pediatrics of King George's Medical University (KGMU). It is a tertiary care centre in Lucknow, capital city of Uttar Pradesh.

Inclusion Criteria: Any neonate (28 days or less) who presented with symptoms suggestive of bacterial meningitis like fever/hypothermia with any of the following features like failure to suck /intolerance to feed, irritability/lethargy, hypotonia, vomiting, respiratory distress, apnea, bradycardia, hypotension, seizures and bulging anterior fontanelle or had fever (100.4 °F), undergoes septic screening. Septic screen includes a complete blood count (CBC) with differential count, blood culture, catheterized urine with culture, chest radiograph, and lumbar puncture.

Exclusion Criteria: Neonates with any anatomical malformation, structural abnormalities like neural tube defects, having any shunt example VP shunt, or those whose parents/guardian refused to give consent. We evaluated 401 neonates, from among these 142 were excluded as per the set criteria. Among these 259 neonates, simultaneous blood culture were obtained from 244 cases. We finally enrolled 244 neonates whose blood and CSF samples were collected and send to Department of Microbiology, King George's Medical University, Lucknow. CSF (1-3 ml) was collected by lumbar puncture with complete asepsis and transported to the laboratory within 2 hours of collection. Patient's name on all the labels and requisition forms were verified. Gross appearance of CSF was noted. Firstly culture was done on Chocolate agar, 5% Sheep Blood and MacConkey agar. Plates were then incubated in at 37 °C for 72 hours. Plates were read at 24, 48 and 72 hours. Secondly, Wet mount and Direct Gram stain were seen for pus cells and microorganisms. If White Blood Cell Count were increased more than 30 WBCs per mm^3, it was considered positive and ruled out contamination. Those samples that were culture positive, were further processed for identification of microorganism by MALDI-TOF VITEK MS, Biomeriux, France or by various Biochemical tests. A definitive diagnosis of meningitis was based on the growth of a pathogen from primary CSF culture and supportive clinical manifestation (seizures, thermal instability, and feeding intolerance, among others). Laboratory finding such as CSF analysis, blood, and CSF cultures were evaluated. Blood culture bottles were loaded in Automated Bact alert 3D machine. The blood culture bottles were incubated till they beep positive or a maximum for 5 days. Once beeped positive plating was done on 5% Sheep Blood and MacConkey agar followed by performing direct gram stain of the blood sample. Further identification of the microorganism was done as in Cerebrospinal fluid sample. If Blood culture bottle did not beep positive after 5 days of incubation it was noted as sterile.

Statistical Analysis Descriptive statistics was used for the comparison of data and appropriate statistical charts were used to present the data.

Results

In the study, total 244 neonates were enrolled who were suspected of meningitis and their blood and CSF samples were collected. Out of these, 153 cases were sterile on both CSF and Blood cultures. Total 56 CSF samples were found positive on culture in association with wet mount and direct gram stain. Five Coagulase Negative Staphylococcus (CONS) were isolated which were neither associated with increased WBC count nor there were pus cells and microorganisms seen in wet mount or direct gram stain; therefore were considered as contaminants and not included as culture positive. (Graph 1) shows various bacteria isolated from cerebrospinal fluid culture. Out of total 56 CSF positive cases, 30 were positive for blood culture in which 26 had growth of similar microorganism and four had different bacteria grown on culture. There were 26 blood samples that were sterile on culture even after 5 days of incubation at 37°C, from among 56 CSF culture proven cases of meningitis. [Table 1] . Bacterial isolates in CSF culture with concomitant sterile blood culture is shown in [Table 2].

Total no. of Samples (N=244)	***Total No. of isolates***
Same organism isolated as in CSF culture	26
2 different organism isolated from CSF and blood culture	4
Organism present in CSF Culture but sterile in Blood Culture	26
Both CSF & Blood Culture sterile	153
CSF Sterile, Microorganism in Blood Culture	35

Table 1: Correlation of CSF And Blood Culture Findings.

Microorganism in CSF	***Sterile Blood Culture***	***Percentage (%)***
Acinetobacter spp.	11	42.3
Chryseobacterium indologenes	2	7.7
Elizabethkingia anophelis	2	7.7
Enterobacter spp.	2	7.7
Enterococcus faecalis	3	11.5
Klebsiella pneumoniae	4	15.4
Pseudomonas aeruginosa	1	3.8
Staphylococcus haemolyticus	1	3.8
Total	26	46.4

Table 2: Bacterial Isolates in CSF Culture with Concomitant Sterile Blood Culture.

Discussion

Out of 244 neonates, similar findings of CSF and blood cultures were observed in 179/244 (26 plus 153 neonates) that makes 73.4 % of total neonates had concordance between CSF and blood cultures. 56 culture proven meningitis cases were reported, out of these 26 were sterile on blood culture that indicates in 46.4 % of meningitis patients there was no bacteremia. In 30 cases, microorganisms were isolated in both CSF and Blood cultures. 26 out of these 30 had similar bacteria isolated in both the samples whereas 4 had different bacteria. Among these 4, 3 were probable contaminant of blood culture (showed growth of Coagulase Negative Staphylococcus) with no microorganism seen on their direct gram stain and Coagulase Negative Staphylococcus being a normal commensal of human skin. One patient had *Acinetobacter baumanii* in CSF and *Klebsiella pneumoniae* in Blood culture. In a similar study, evaluated the first lumbar puncture of 9111 neonates from 150 NICUs [10]. CSF culture results were compared with results of blood cultures to establish its concordance in culture-proven meningitis. 92 of the 95 meningitis patients had a recorded blood culture. 35 (38%) of the 92 patients had a negative blood culture, while 57 (62%) of the patients had a concurrently positive blood culture. In 2 (3.5%) of 57

newborns who had both positive blood and CSF cultures, the isolated organisms were different.

Thereby a significant percentage of neonates were reported with meningitis in whom the blood cultures were sterile. Therefore in neonates with symptoms of infection, one should always go for lumbar puncture along with other investigations. CSF Culture is considered the gold standard for diagnosis of meningitis. Suspicion of meningitis should not be excluded if blood cultures are negative and CSF culture should always be performed in neonates presenting with any sign or symptoms of infections, to prevent missing the diagnosis. Lumbar puncture with CSF microscopy, biochemical, and microbiological analysis is the only means of accurately diagnosing meningitis in young infants. We aimed to independently identify simple indicators of meningitis that could be used as a practical screening tool to detect infants that warrant a LP and to evaluate the signs suggested by WHO [11, 12]. Previous studies showed a number of possible early markers of poor prognosis in neonatal meningitis [13]. Children with bacterial meningitis are at risk of developing neurological complications that include focal neurological deficits, subdural effusion, hearing loss, cognitive impairment, seizure disorder, and hydrocephalus. There is a need to optimize utilization of available vaccines and to develop vaccines for pathogens implicated in neonatal meningitis (GBS and *E. coli*). For children diagnosed with bacterial meningitis, starting antibiotic therapy without delay is critical for a good prognosis and to reduce the risk of developing neurological complications [14]. Bacterial meningitis is associated with high rates of mortality and morbidity is also studied in few other research work [15, 16]. Some researchers have found that antibiotic treatment prior to admission reduces CSF culture positivity rates by nearly 30% [17, 18]. Therefore more extensive research is required in this field so that this critical diagnosis is not missed.

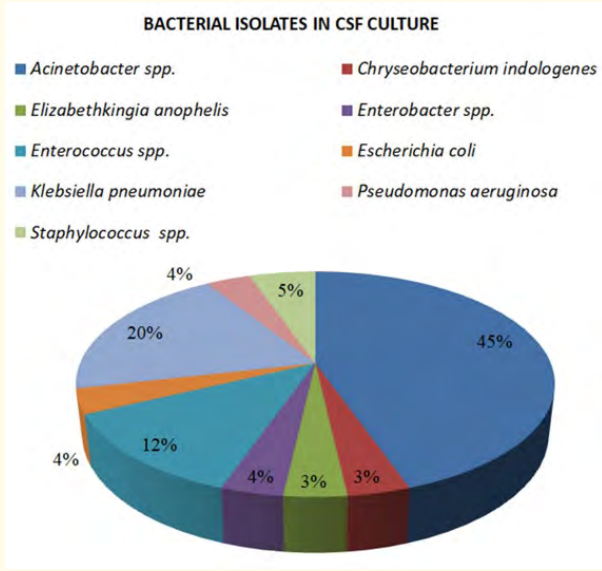

Figure Legend: Bacterial isolates in CSF culture.

Limitations

We did not perform LPs in infants with compromised respiratory or circulatory status and many infants died before LP was undertaken. It is therefore likely that we missed meningitis in some of these cases, especially on the first day of life and amongst those with very low birth weight (although all sick new-borns infants did receive appropriate intravenous broad-spectrum antibiotics for presumed sepsis as standard policy). We excluded these cases, but it may have reduced the predictive value of the signs we examined. Future studies should explore acceptability of post mortem LPs in resource poor nations, as this may aid in acquiring more robust data.

Conclusion

It is thereby concluded that bacterial meningitis which is an emergency with high level of mortality and morbidity, can easily be missed if we rely on blood cultures solely. It is a disaster for the neonates not to consider CSF culture and suspicion of meningitis at the first place.

Bacterial meningitis can occur in absence of bacteremia. Hence all neonates with signs and symptoms of infection should be evaluated with CSF and Blood cultures simultaneously. This practice would not only prevent from missing cases of meningitis but will save time for quicker diagnosis and thereby early initiation of treatment.

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