Original Research Paper

Volume - 7 | Issue - 6 | June - 2017 | ISSN - 2249-555X | IF : 4.894 | IC Value : 79.96

Microbiology

Clinical characteristics and antibiotic sensitivity pattern in blood culture positive enteric fever in children

Dr Priyanka Pandit — MD (Microbiology), Assistant Professor, Department of Pathology, Command Hospital (EC), Kolkata, PIN 700027.

Dr Subhash Chandra Shaw — Associate Professor Department of Paediatrics, Command Hospital (EC), Kolkata, PIN 700027.

Dr Amit Devgan — Professor & HOD, Department of Paediatrics, Command Hospital (EC), Kolkata, PIN 700027.

ABSTRACT

Introduction: Despite availability of vaccination, children still form a large subset of Enteric disease population. Increasing antibiotic resistance is adding to the complexity of the disease. This study was undertaken to study the clinical characteristics and antibiotic susceptibility pattern of the isolates obtained in blood culture positive paediatric patients.

Material and Methods: Blood for culture and sensitivity was collected from paediatric cases of fever. Data of clinical characteristics and sensitivity pattern of Salmonellae to commonly used antibiotics was analyzed.

Results: A total of 34 children had culture proven enteric fever in the study period. There were 8 cases of *Salmonella Paratyphi A*, 2 cases of *Salmonella Paratyphi B* and rest all were *Salmonella Typhi*. Inj. Ceftriaxone was used empirically via Intravascular route in two divided doses and all the cases responded favourably.

Discussion: All children were found to be beyond 5 years of age. The clinical features of the disease observed in the children were much different from those of the adults. The antibiotic sensitivity pattern in our study revealed universal sensitivity to carbapenems, Tigecycline, Colistin and Ceftriaxone. However resistance to fluoroquinolones was almost 95%.

Conclusion: Sending blood culture in appropriate amount adhering to standard guidelines in any undiagnosed fever is necessary to diagnose enteric fever in children. The local sensitivity pattern should be relied while designing the hospital antibiotic policy on enteric fever and the indiscriminate use of antibiotics must be checked to prevent further drug resistance.

KEYWORDS : Enteric fever, Blood culture, Salmonellae, Antibiotic sensitivity testing, Anti-microbial resistance

INTRODUCTION

Enteric fever is one of the commonest causes of food-borne and water-borne illness affecting humans and is caused by *Salmonella enterica* serovars Typhi (*S. Typhi*), Paratyphi A, Paratyphi B and Paratyphi C.[1] With an overall case fatality of approximately 1% and increasing resistance to many antibiotics, the effective treatment is becoming more and more problematic.[2] A substantial burden of enteric fever is borne by children in spite of availability of vaccines.[3] Therefore we planned to study retrospectively, the clinical characteristics and antibiotic sensitivity pattern in blood culture positive enteric fever cases in children managed in a tertiary care teaching institute.

MATERIAL & METHODS

All cases with culture proven enteric fever admitted in the paediatric ward of a tertiary care teaching hospital of eastern India, between 01 Jan 2015 and 31 Mar 2017 formed the study subjects. The approval of the study was taken from the institutional ethics committee. Medical records of all the study subjects were retrieved retrospectively from the case files, computerised database and discharge papers. Data of clinical characteristics and sensitivity pattern of Salmonellae to commonly used antibiotics were entered from these records onto a Microsoft Excel database and further analysed. Descriptive statistics was used to describe the clinical characteristics and sensitivity pattern of Salmonellae.

Methodology followed for blood culture was as follows. Once a patient was suspected to be a case of enteric fever, a blood sample was drawn using the BacT/ALERT PF Pediatric Plus bottle (BIOMÉRIEUX, Marcy-l'ÉToile, France) having a capacity of 30ml. Keeping the ratio of 5-10%, for a 30ml BacT/ALERT bottle, 1ml-3ml of blood was drawn, in accordance with CDC guidelines for blood collection.[4] The inoculated bottle was then placed and incubated in the BacT/ALERT 3D™ 60 automated blood culture system by BIOMÉRIEUX (BIOMÉRIEUX, Marcy-l'ÉToile, France). The bottles flashed positive by the instrument were removed and a direct gram stain was done for provisional identification. Subculture was done on Blood, MacConkey and Chocolate agars. A Gram stain was done from the plates showing growth, and further identification and antibiotic susceptibility testing (ABST) was done using the Vitek 2 Compact (for automated identification and ABST) instrument by BIOMÉRIEUX(BIOMÉRIEUX, Marcy-l'ÉToile, France).

RESULTS

A total of 34 children had culture proven enteric fever in the study period. The age group affected were all between 6 to 10 years and there was a preponderance of male sex (67.6%) in the study subjects. The clinical characteristics are depicted in table 1 and the sensitivity pattern of Salmonellae (both Typhi and Paratyphi) are depicted in table 2. There were 8 cases of Salmonella Paratyphi A, 2 cases of Salmonella Paratyphi B and rest all were Salmonella Typhi. In all cases, Inj. Ceftriaxone was used empirically via Intravascular route at a dose of 100 mg/kg/day in two divided doses. There was no fatality or complications and the mean duration for fever to disappear after starting of antibiotics was 4 days.

DISCUSSION

Globally, it is estimated that there are about 26 million patients with blood culture positive enteric fever annually with majority of epidemiological data coming from adult population. In children, most data point towards lesser occurrence of disease in children less than 5 years of age except in higher incidence study sites where the magnitude of illness was same in 2-5 years as it is in 5-15 years.[5] We too found all children to be beyond 5 years of age and this is in agreement with the global data. The possible causes could be higher episodes of other nonspecific illnesses, difficulty in drawing blood for culture, excessive antibiotic usage, protective effects of breast feeding and vaccine for typhoid given at 2 years of age protecting for next 3 years. However, in relevant settings enteric must be actively ruled out in children less than 5 years as there is increased risk of mortality in them as compared to those affected in older age group.[6]

The clinical features universally found in our study population were fever, and lack of appetite. Fever often is the sole manifestation of enteric fever and often present as fever of unknown origin with inconclusive clinical and laboratory features. If untreated, it rises as a step ladder pattern and peaks at the second week of life. On the other hand hypothermia may be a manifestation in children in lower age group. The other common features in our population were vomiting, pain abdomen, hepatomegaly, splenomegaly and coated tongue. Features found less commonly in our study were cough, chills, diarrhoea, headache and body ache. We also did not find chills or relative bradycardia which is often found in adults with enteric fever. The findings are similar to global data of fever being almost universal

feature followed by coated tongue (71-85%). Other features described in more than half of children with enteric fever are hepatomegaly, cough, headache, abdominal pain and abdominal distension.[6] We did not encounter any case of abdominal distension or complications of enteric fever like shock, altered mental status, pneumonia, gastrointestinal bleeding or perforation, which are often described in literature mostly in those cases reporting late. Though the haematological investigations in our population were non-contributory, transient pancytopenia is described in literature due to seeding of salmonella to bone marrow as well as due to immunological injuries. Pancytopenia is more common in adults and in children often the leukocyte counts are normal or may be higher. Thrombocytopenia is often considered a sign of severe disease in typhoid fever with increased risk of complications.[7] Factors contributing to severe enteric fever are the inoculums size, immune status of patients, duration of illness before therapy, and the vaccination status.[8]The reasons why we did not encounter any case of complicated enteric fever, possibly are early reporting of children in hospitals, easy access to medical facilities, relatively better immunized population, and early use of ceftriaxone in presumptive enteric cases.

The antibiotic sensitivity pattern in our study revealed universal sensitivity to carbapenems, Tigecycline and Colistin and almost 95% sensitivity to Ceftriaxone. On this basis of our local antibiotic sensitivity pattern, all presumptive enteric cases receive Ceftriaxone and we are yet to encounter any in vivo resistance. However, alarmingly there was only 5.8% sensitivity to Nalidixic acid which is often considered a surrogate marker of sensitivity towards ciprofloxacin. The results are in agreement with reports from Shimla, India, where the overall resistance of Salmonella Typhi to Nalidixic acid was about 66% and resistance of Salmonella Paratyphi was about 75%.[9] Even a recent study from Pondicherry, India revealed antibiotic resistance of Salmonella Paratyphi A to Nalidixic acid to be almost universal.[10]

The presumptive treatment in form of appropriate antibiotics must start before the blood culture report is available and moreover the case fatality rate without appropriate antibiotics can be as high as 30%. Ideal antimicrobial drug should depend on local sensitivity pattern of Salmonellae. Multidrug resistance of salmonella namely to Chloramphenicol, Ampicillin and Co-trimoxazole is prevalent in Indian subcontinent since long.[11] The most preferred drug for severe typhoid fever in children by Dutta P et al, as described from eastern India[12] is too no more effective as evident from studies from India itself. Oral drugs like Cefixime is considered inferior to injectable Ceftriaxone and Azithromycin may be preferred in uncomplicated enteric. In view of extended spectrum β lactamases (ESBLs), resistance to third generation cephalosporins might limit therapeutic options in future leaving only carbapenems and Tigecycline as secondary antimicrobial drugs.[13]

CONCLUSIONS

The clinical presentation of enteric fever in children is often different from adults and sending blood culture in appropriate amount adhering to standard guidelines in any undiagnosed fever is necessary to diagnose enteric fever in children. The hospital antibiotic policy on enteric fever should rely on the local sensitivity pattern and the indiscriminate use of antibiotics must be checked to prevent further drug resistance.

Table 1. Clinical characteristics of culture proven enteric fever (N=34)

Clinical variables	Percentage
Fever	100
Lack of appetite	100
Cough	17.6
Chills	17.6
Diarrhoea	23.5
Pain abdomen	50
Vomiting	58.3
Headache	33.3
body ache	23.5
Rash	0
Dysuria	0
Hepatomegaly	91.1
Splenomegaly	52.9
Coated tongue	52.9

Table 2: Sensitivity pattern of Salmonellae causing enteric fever (N=34)

Antibiotic	Sensitivity (in percentage)	Resistance (in percentage)
Ampicillin	64.7	35.3
Amoxicillin/clavulanic acid	82.3	17.7
Piperacillin/Tazobactam	100	0
Cefuroxime	0	100
Cefuroxime axetil	0	100
Ceftriaxone	94.1	5.9
Cefoperazone sulbactam	97	3
Cefepime	100	0
Ertapenem	100	0
Imipenem	100	0
Meropenem	100	0
Amikacin	23.5	76.5
Gentamicin	26.4	73.6
Nalidixic acid	5.8	94.2
Ciprofloxacin	5.8	94.2
Tigecycline	100	0
Colistin	100	0
Trimethoprim/Sulfamethoxazole	94.1	5.9

REFERENCES

1. Harish BN, Menezes GA. Antimicrobial resistance in typhoidal salmonellae. Indian J Med Microbiol 2011; 29: 223-9.
2. Wain J, Hendriksen RS, Mikoleit ML, Keddy KH, Ochiai RL. Typhoid fever. The Lancet. Volume 385 , Issue 9973 , 1136-1145
3. Britto C, Pollard A J, Voysey M, Blohmke C J. An appraisal of the clinical features of paediatric enteric fever including a systematic review and meta-analysis of the age stratified disease occurence. Clin Infect Dis 2017 cix229. doi: 10.1093/cid/cix229
4. Clinician Guide for Collecting Cultures. Retrieved from https://www.cdc.gov> implementation
5. Ochiai R Leon, Acosta Camilo J, Danovaro-Holliday M Carolina, Baiqing Dong, Bhattacharya Sujit K, Agtini Magdarina D et al . A study of typhoid fever in five asian countries: disease burden and implications for controls. Bull World Health Organ [Internet]. 2008 Apr [cited 2017 May 02] ; 86(4): 260-268.
6. Azmatullah A, Qamar FN, Thaver D, Zaidi AK, Bhutta ZA. Systematic review of the global epidemiology, clinical and laboratory profile of enteric fever. J Glob Health 2015; Dec;5(2):020407. doi: 10.7189/jogh.05.020407
7. Reesi MA, Stephens G, McMullan B. Severe thrombocytopenia in a child with typhoid fever: a case report. Journal of Medical Case Reports (2016) 10:333 DOI 10.1186/s13256-016-1138-1136.
8. Yildirim I, Ceyhan M, Bayrakci B, Uysal M, Kuskonmaz B, Ozaltin F. A case report of thrombocytopenia-associated multiple organ failure secondary to Salmonella enterica serotype Typhi infection in a pediatric patient: successful treatment with plasma exchange. Ther Apher Dial. 2010;14(2):226-229.
9. Verma S, Thakur S, Kanga A, Singh G, Gupta P. Emerging salmonella paratyphi A enteric fever and changing trends in antimicrobial resistance of salmonella in Shimla. Indian Journal of Medical Microbiology. 2010; 28(1): 51-53
10. Menezes GA, Harish BN, Khan MA, Goessens W, Hays JP. Antimicrobial resistance trends in blood culture positive Salmonella Paratyphi A isolates from Pondicherry, India. Indian J Med Microbiol 2016; 34: 222-227.
11. Cooke FJ, Wain J. The emergence of antibiotic resistance in typhoid fever. Travel Med Infect Dis 2004;2:67-74
12. Dutta P, Rasaily R, Saha MR, Mitra U, Bhattacharya SK, Bhattacharya MK, Lahiri M. Ciprofloxacin for treatment of severe typhoid fever in children. Antimicrobial Agents and Chemotherapy. 1993; 37(5): 1197-1199.
13. Harish BN, Menezes GA. Antimicrobial resistance in typhoidal Salmonellae. Indian J Med Microbiol 2011;29:223-227.