Original Article

Study on Isolation of Organism and Antibiotic Sensitivity Pattern in Blood Culture of Enteric Fever Patients in a Tertiary Care Hospital in Bangladesh

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ABSTRACT

A cross-sectional, observational study was conducted in the Department of Medicine, Mugda Medical College Hospital, Dhaka, Bangladesh, between March 2022 and September 2023, to observe the changing pattern of antibiotic sensitivity pattern among enteric pathogens causing enteric fever. A total of 50 blood culture and sensitivity reports were analyzed. Blood samples were derived from 50 patients included in this study, who were admitted into the medicine inpatient department of Mugda Medical College Hospital suffering from fever for at least 2 weeks and were confirmed having enteric fever. The predominant growth of two bacteria was observed in all (100%) samples. The most common organisms isolated were Salmonella typhi as typhoid fever pathogens and Salmonella paratyphi A as paratyphoid fever pathogens; these represented 88% and 12% of isolates respectively. Salmonella typhi organisms were found 100% sensitive to amoxycillin, trimethoprim-sulfamethoxazole, chloramphenicol, gentamicin, meropenem, cefepime, followed by imipenem (85%), ampicillin (81%), ceftriaxone (78%), levofloxacin (77%) and cefuroxime (77%). However, amoxicillin, trimethoprim-sulfamethoxazole, ceftazidime, cefotaxime, ceftriaxone and chloramphenicol were found 100% sensitive to paratyphoid pathogens. Very high rate of resistance was seen against nalidixic acid (88%), piperacillin-tazobactam (50%), azithromycin (47%), co-amoxiclav (40%) and doxycycline (40%) in salmonella typhi infections, while nalidixic acid and azithromycin were found 100% resistant to Salmonella paratyphi A infection.

Keywords: *Antibiotic sensitivity, antibiotic resistance, Salmonella typhi, Salmonella paratyphi*

Mugda Med Coll J. 2024; 7(2): 108-113
https://doi.org/10.3329/mumcj.v7i2.78776

INTRODUCTION

Enteric fever was a major cause of morbidity and mortality in the United States and Europe in the 19th century[1]. However, with the provision of clean water and good sewage systems, there has been a dramatic decrease in the incidence of typhoid in these regions. The disease remains a serious public health problem in developing countries[2]. It is classically caused by *Salmonella Typhi*, *S. Paratyphi* A, and rarely by *S. Paratyphi* B and C. Antimicrobial agents remain the mainstay of treatment for enteric fever; however, indiscriminate use of these drugs has led to the emergence of resistance in Salmonella spp. Reliable data from which to estimate the burden of disease in these areas is difficult to obtain. Many hospitals lack facilities for blood culture and up to 90% of patients with fever are treated as outpatients. Therefore, population-based estimates of blood culture confirmed typhoid cases are needed. Enteric fever is associated with an overall case–fatality rate of 2.5%, and it rises to 4.5% among hospitalized patients[3]. Prompt administration of appropriate antibiotic therapy prevents severe complications of enteric fever and reduces mortality to <1%[4]. The initial choice of antibiotics depends on the susceptibility of the *S. Typhi* and *S. Paratyphi* strains in the area of residence

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or travel. Although effective treatment with chloramphenicol was introduced in 1948[4], the emergence of resistance to chloramphenicol, ampicillin and cotrimoxazole has been of concern[5]. Currently, fluoroquinolones and third generation cephalosporins are drugs of choice for treatment of typhoid fever. However, recent reports of decreased susceptibility to these agents have led to the prospect of re-emergence of untreatable typhoid fever and an increasing global burden.

The global emergence of multidrug resistant strains and of strains with reduced susceptibility to fluoroquinolones are of great concerns[5]. Therefore, attempts to study the pathogen associated with typhoid fever and to elucidate prevalence pattern and drug resistance are vital to the future study of antimicrobial therapy. With this point of view, the present study was designed to observe the prevalence rate of typhoidal *Salmonella typhi* and *S. paratyphi* among the different age group patients and their antimicrobial sensitivity pattern by antibiogram.

METHODS

A cross-sectional, observational study was conducted based on a total of 50 blood culture and sensitivity reports of the enteric fever patients in Mugda Medical College Hospital, Dhaka, Bangladesh, a tertiary care hospital, from March 2022 to September 2023.

A total of 50 patients included in this study, who were admitted into the medicine inpatient department of Mugda Medical College Hospital suffering from fever for at least 2 weeks and were confirmed having enteric fever. Blood was taken aseptically in patients having strong clinical suspicion of enteric fever on basis of symptoms (fever, abdominal pain, headache, chills, cough, sweating, myalgias, malaise and arthralgia etc.) were inoculated on blood agar and MacConkey agar plates, which were incubated aerobically at 37^0C overnight for 72 hours. All *S. Typhi* and *S. Paratyphi* A isolates were identified using standard microbiological techniques and were confirmed by serotyping with specific antisera (based on O and H antigens). Antimicrobial susceptibility of the isolates was determined by the Kirby-Bauer disk diffusion test using Mueller-Hinton agar following the Clinical Laboratory Standards Institute (CLSI) guidelines. The antimicrobial agents tested were ampicillin (10µg), chloramphenicol (30µg), trimethoprim/sulfamethoxazole (1.25/23.75µg), nalidixic acid (30µg), ciprofloxacin (5µg), ceftriaxone (30µg), cefotaxime (30µg), and azithromycin (15µg). Interpretations as 'Sensitive' or 'Resistant' was done on the basis of diameters of zones of inhibition of bacterial growth as recommended by the disc manufacturer. Antibiotics against which sensitivity was tested in the present study included amoxicillin, amoxiclav, ciprofloxacin, amikacin, nitrofurantoin, gentamicin, ceftriaxone, meropenem and imipenem.

Descriptive statistics were used, data were presented as frequency and percentages. Results were presented through tables. The study was approved by the Institutional Review Board (IRB) of Mugda Medical College, Dhaka, Bangladesh.

RESULTS

A total of 50 blood culture and sensitivity reports were analyzed in this study with the following results. The highest susceptible age group of for enteric fever was 15-25 years (56%), followed by 26-36 years (20%), <15 years (16%), 37-47 years (4%) and e"48 years (4%) Among the patients, 36(72%) samples were from males and 14(28%) from females (Table-I); the prevalence of enteric fever were found more in males (Table-I). Among 50 samples, *Salmonella typhi* were found in 44 cases. The most useful antibiotics in this study were amoxycillin, trimethoprim-sulfamethoxazole, chloramphenicol, gentamicin, meropenem, and cefepime. Isolated organisms were found 100% of sensitive to those antibiotics, followed by imipenem (85%), ampicillin (81%), ceftriaxone (78%), levofloxacin (77%) and cefuroxime (77%). Very high rate of resistance was observed against nalidixic acid (88%), piperacillin-tazobactam (50%), azithromycin (47%), co-amoxiclav (40%) and doxycycline (40%) in *Salmonella typhi* infections (Table-I). Among 50 samples *Salmonella paratyphi A* were found in only 6 cases. The most useful antibiotics in this study were amoxycillin, trimethoprim-sulfamethoxazole, ceftriaxone, ceftazidime, cefotaxime and chloramphenicol, as isolated organism were found 100% sensitive to those antibiotics, followed by ampicillin (50%), ciprofloxacin (50%), and cefixime (50%). However, nalidixic acid and azithromycin were found 100% resistant to *Salmonella paratyphi* A infection (Table-III).

Table-I: *Age and sex distribution of the patients (n=50)*

Variables	Frequency	Percentage
Age group		
<15 years	8	16
15-25 years	28	56
26-36 years	10	20
37-47 years	2	4
≥48 years	2	4
Sex		
Male	36	72
Female	14	14

Table-II: *Antibiotic susceptibility pattern of Salmonella typhi*

Antibiotics	Number of isolates tested	Sensitive isolates(%)	Resistant isolates (%)
Amoxicillin	06	100	
Ampicillin	22	81.81	18.18
Trimethoprim-sulfamethoxazole	34	100	
Ciprofloxacin	38	68.42	31.57
Nalidixic acid	34	11.76	88.23
Cefixime	38	68.42	31.57
Ceftazidime	28	71.42	28.57
Cefotaxime	12	66.67	33.33
Azithromycin	38	52.63	47.36
Ceftriaxone	38	78.94	21.05
Chloramphenicol	08	100	
Gentamicin	16	100	
Amikacin	14	71.42	28.57
Co-amoxiclav	20	60	40
Cefuroxime	18	77.77	22.23
Meropenem	22	100	
Imipenem	14	85.71	14.29
Cefepime	14	100	
Piperacillin/ tazobactam	12	50	50
Levofloxacin	18	77.77	22.23
Doxycycline	10	60	40
Tetracycline	10	80	20
Colistin	08	50	50

Table-III: *Antibiotic susceptibility pattern of Salmonella paratyphi A*

Antibiotics	Number of isolates tested	Sensitive isolates(%)	Resistant isolates (%)
Amoxicillin	02	100	
Ampicillin	02	50	50
Trimethoprim-sulfamethoxazole	03	100	
Ciprofloxacin	02	50	50
Nalidixic acid	02		100
Cefixime	02	50	50
Ceftazidime	01	100	
Cefotaxime	01	100	
Azithromycin	02		100
Ceftriaxone	02	100	
Chloramphenicol	02	100	
Gentamicin			
Levofloxacin	01	100	
Tetracycline	01	100	

DISCUSSION

Enteric fever is a commonly found infectious disease in febrile patients encountered in practice of medicine these days. Enteric fever is one of the most important causes of morbidity even today in the developing countries like Bangladesh. This may be due to unhygienic food intake, unhealthy lifestyle of urban population of Dhaka city, due to abuse of chemotherapeutic agents and most importantly ignorance of people and little or no prevention measures. The present study investigated the causative organisms of enteric fever and their pattern of antimicrobial sensitivity as well as drug resistant.

Among total 50 blood samples, 36(72%) samples were from males and 14(28%) from females. Here, the prevalence of enteric fever is much higher in males. It was shown in several studies that males are at increased risk to develop enteric fever than females, as conducted in Bangladesh, Pakistan and Nepal[5]. However, another study from Ethiopia showed that females are more prevalent than males[6].

In present study we observe that the occurrence of enteric fever recorded among the enteric fever was higher among young patients (98%) compared to elderly groups (2%). In another study, done by Jamil et al. in Pakistan showed that most affected are young adults[7].

According to our study, the most common organisms isolated were *Salmonella typhi* and *Salmonella paratyphi*, which represented 88% and 12% respectively. *Salmonella typhi* organisms were found 100% sensitive to amoxycillin, trimethoprim-sulfamethoxazole, chloramphenicol, gentamicin, meropenem, cefepime, followed by imipenem (85%), ampicillin (81%), ceftriaxone (78%), levofloxacin (77%) and cefuroxime (77%). However, a study conducted in a provincial hospital in Philippines showed 100% sensitive to chloramphenicol, trimethoprim-sulfamethoxazole and ampicillin, which is not consistent with our study[8]. In another observational study, conducted in Pakistan showed that azithromycin and meropenem are the most effective antibiotics against isolates of Salmonella spp[9]. In our study, we also found amoxicillin, trimethoprim-sulfamethoxazole, ceftazidime, cefotaxime, ceftriaxone and chloramphenicol 100% sensitive to paratyphoid fever.

This study also revealed that a higher prevalence rate of resistance to the commonly prescribed antibiotic agent. Very high rate of resistance was seen against nalidixic acid (88%), piperacillin-tazobactam (50%), azithromycin (47%), co-amoxiclav and doxycycline (40%) in *Salmonella typhi* infections. Akter et al. showed in a study in Dhaka city 100% resistant to ampicillin, which is not consistent with our study result[10]. Malla et al. showed in a 2-year study done in Nepal on enteric pathogens that ampicillin, chloramphenicol and trimethoprim-sulfame thoxazole were found mostly resistant to salmonella infection[11]. In a similar study, done in Bangladesh also reported similar patterns of resistance as shown in our study[1]. Resistance to nalidixic acid has also been reported from India, China and Tunisia[2-4]. Our study revealed that nalidixic acid and azithromycin were 100% resistant to *Salmonella paratyphi* A infection. Same pattern was observed in a 1-year study done in USA[12].

Sajib et al. showed some difference from our study in 199-2001, out of 2,725 blood culture-confirmed paratyphoid cases, most of the isolates were susceptible to ampicillin, chloramphenicol, and cotrimoxazole; however, no isolate was resistant to those drugs[13]. No resistance to ceftriaxone was recorded, and >99% of the isolates were sensitive to azithromycin whereas >99% of the isolates exhibited decreased susceptibility to ciprofloxacin[13]. Nalidixic acid is of great importance and implies that these antibiotics cannot be used as empirical therapy for enteric fever infection particularly in the study area. Apart from these, 68% of *Salmonella typhi* infections and 50% of *Salmonella paratyphi* A isolates were found resistant against ciprofloxacin. The possible explanation behind the resistance showed to these antibiotics, may be because these agents have been in use for a long period are susceptible to misuse or abuse and consequently the specific organism has developed mechanisms to circumvent their mode of action to combat that specific antimicrobial drug[14,15]. Moreover, increased population can lead to increased dissemination of antibiotic-resistant bacteria and resistant genes[15,16]. As Bangladesh is a developing country with and increased population density and urbanization, those factors may facilitate the spread of resistant bacteria and genes, which was also observed in other countries[16]. Continuous use of antibiotics can be a reason for occurrence of resistance among adults in this study, which was also evident in Sri Lanka[17]. Inconclusive diagnosis and over dependent on broad-spectrum antibiotics in inpatient

and outpatient services in the hospital can be causes for antibiotic resistance[14,17].

Two alarming findings were revealed in our study: 1) substantial resistance shown to nalidixic acid and azithromycin by all isolates and some resistance to ciprofloxacin. According to our findings those agents cannot be a potential option for treatment in near future. However, patterns of resistance may also vary due to geographical distribution and demographic variance[14]. Physicians should be more cautious in prescribing similar antibiotics all over the country.

CONCLUSION

In conclusion, one can truly affirm that the choice of drugs in the treatment of enteric fever is quite narrow today due to the wide scale of resistance that common enteric pathogens show to different drugs, which have been used previously. Drugs like nalidixic acid, azithromycin and certain groups of cephalosporins, which were considered as effective against enteric pathogens, are hardly prescribed now as empirical therapy in areas where resistance rate to these antibiotics is high. However, it is clear that amoxycillin, trimethoprim-sulfamethoxazole, chloramphenicol, gentamicin, meropenem, cefepime are good choices for the treatment of indoor patients having enteric fever.

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