ORIGINAL ARTICLE

Antimicrobial Sensitivity of Salmonella Species in Children - A Single-Centered Study

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ABSTRACT

Background: Salmonellae are gram-negative, facultative anaerobic bacteria. Typhoid fever has a non-specific and varied appearance in its early stages. A high-grade fever (>38°C) is the most common presenting sign. Salmonella pathogenicity is primarily determined bythe virulence components it possesses, such as Salmonella pathogenicity islands (SPIs), virulence plasmids, pili, and enterotoxins. The most common drug used was cefixime (66.6%), then ciprofloxacin, and according to a comparable study conducted in Pakistan (33.3%). Cefixime and ceftriaxone had a sensitivity of 60.9% and 65.8%, respectively. In 50.1% of S.typhi isolates, ciprofloxacin sensitivity was observed.

Aim: To determine the frequency of the most common salmonella specie and its drug sensitivity in children.

Methodology: This descriptive study was conducted in the Department of Pediatrics Bacha Khan Medical Complex Swabi from April 2022 to October 2022 in children with suspected enteric fever. Blood culture reports of suspected patients were sent to the laboratory and reports were followed, before reports arrived patients were started on antibiotics. The sensitivity of drugs was measured by calculating frequency and percentages.

Results: This study was conducted on 63 children having blood culture reports presented to us with suspected enteric fever including 25 females and 38 males with a mean age of 6.4±27 years. The most common organism in the blood culture of children presented with enteric fever was salmonella typhi (95.2%). Salmonella paratyphoid species shows 100% sensitivity to co-triaxle, co-trimoxazole and amikacin while 50.8% to azithromycin. Salmonella paratyphi A with 100% sensitivity to amikacin, ampicillin, azithromycin, cefepime, cefoperazone, cefotaxime, co-amoxiclav and colistin. While salmonella typhi were found to be 95.2% with drugs sensitivity amikacin, colistin, fosfomycin, co-trimoxazole, and ertapenem (100%) and ciprofloxacin (73%).

Practical implication: by knowing the most common organism and its drug's sensitivity and resistance, the resistance to antibiotics will be reduced, and targeted antibiotics will be used.

Conclusion: Salmonella typhiwas the most common pathogen detected in blood culture (95.2%) with 100%drug sensitivity to amikacin, colistin, fosfomycin, co-trimoxazole, and ertapenem.

Keywords: Salmonellatyphi, sensitivity, blood culture, children, enteric fever

INTRODUCTION

Salmonellae are facultatively anaerobic, gram-negative bacteria. The genus Salmonella, named after Dr. Daniel Salmon, was first described by Dr. Theobald Smith1 in 1866¹. Salmonella surface antigens are classified into three types: body (O) antigens, flagella (H) antigens, and capsule (VI) antigens. Salmonella serogroups can be classified based on their "O" antigens. Different serotypes can be further classified based on the "H" antigens. Salmonella has over 2600 serotypes divided into 42 serogroups^{2.3}.

The elevated risk of infection at this period may be due to weak immunity⁴.Enteric fever is a systemic disease caused by Salmonella entericaserovar Typhi (S.typhi) and Salmonella entericaserovar Paratyphi (S. paratyphi A, B, and C). Enteric Salmonella serovar Typhi (S.typhi)⁵. Typhoid fever has a non-specific and varied appearance in its early stages. A high-grade fever (>38oC) is the most common presenting sign. In endemic areas, outpatient clinics are used to treat acute non-specific febrile illnesses⁶. Salmonella pathogenicity is primarily determined by the virulence components it possesses, such as Salmonella pathogenicity islands (SPIs), virulence plasmids, pili, and enterotoxins⁷. Non-typhoidalsalmonella(NTS) serotypesmay lead to septicemia, acute gastroenteritis, chronic enteritis, and other illnesses. Young children are the population most susceptible to NTS, according to prior study^{8,9}.

S. typhi causes about 21 million cases of enteric fever each year, resulting in 700,000 fatalities, while S. para-typhi A causes over 5 million new infections^{10,11}. In the year 2000 alone, there were an estimated 21.5 million illnesses and 216,510 mortality globally, with the majority of recorded typhoid fever cases coming

Received on 14-11-2022 Accepted on 15-04-2023 from South and Southeast Asia, where the disease burden was highest, with over 10 million illnesses and 100,000 deaths¹⁰. Salmonella infections are associated to 93.8 million cases of gastroenteritis worldwide each year, according to the WHO, and Salmonella infections are responsible for 155,000 deaths¹². Typhoid fever continues to be a serious public health issue throughout the developing world, particularly in Asia¹³⁻¹⁵.

Doctors frequently third-generation prescribe cephalosporins, quinolones, and macrolides for human Salmonella infections¹⁶. A study reported that third-generation cephalosporins are not advised for usage in children because of the drug's adverse effects. Antibiotic abuse is one of the main causes of antibiotic resistance. Antibiotic resistance is particularly significant in severe systemic diseases because antibiotic treatment can save lives¹⁷.The most common drug used was cefixime (66.6%), then ciprofloxacin, according to a comparable study conducted in Pakistan (33.3%). Cefixime and ceftriaxone had a sensitivity of 60.9 percent and 65.8%, respectively. In 50.1% of S.typhi isolates, ciprofloxacin sensitivity was observed¹⁸. By knowing the most common organism and its drug's sensitivity and resistance, the resistance to antibiotics will be reduced, and targeted antibiotics will be used.

METHODOLOGY

This Descriptive study Department of Pediatrics Bacha Khan Medical Complex Swabi from April 2022 to October 2022 using a non-probability sampling technique. Children having fever with pain abdomen, white coated tongue, no urinary symptoms and no cough were included in this study while children having fever with MP slide positive, Measles, respiratory symptoms suggestive of Pneumonia, Tuberculosis and Culture proved UTI were excluded from this study. Blood culture reports of suspected patients were

RESULTS

Table-1: Type of organisms

Type of	organisms	Frequency	Percent		
Valid	Salmonella paratyphi	2	3.2		
	Salmonella paratyphi a	1	1.6		
	Salmonella typhi	60	95.2		
	Total	63	100.0		

Table-2: Salmonella Paratyphi drugs sensitivity

Drugs	Frequency	Percentages
Amikacin	63	100.0
Azithromycin	32	50.8
Co-trimaxole	63	100.0
Co-trimoxazole	63	100.0

Table-3:Salmonella Paratyphi A drugs sensitivity

Drugs	Frequency	Percentages
Amikacin	63	100.0
Ampicillin	63	100.0
Azithromycin	63	100.0
Cefipim	63	100.0
Cefeperazone	63	100.0
Cefotaxime	63	100.0
Co-amoxiclave	63	100.0
Colistin	63	100.0

Table-4: Salmonella Typhi drugs sensitivity

Drugs	Frequency	Percentages
Amikacin	63	100.0
Azithromycin	35	55.6
Cefipim	7	11.1
Ceferazone	14	22.2
Cefotaxime	5	7.9
Co-amoxiclav	11	17.5
Colistin	63	100.0
Amoxicillin	1	1.6
Fosfomycin	63	100.0
Ceftazidime	4	6.3
Chloramphenicol	3	4.8
Ciprofloxacin	46	73.0
Co-trimoxazole	63	100.0
Co-trimaxole	26	41.3
Ertapenem	63	100.0

This study was conducted on 63 children having blood culture reports presented to us with suspected enteric fever including 25 females and 38 males with a mean age of 6.4 ± 27 years. The most common organism in the blood culture of children presented with enteric fever was salmonella typhi (95.2%), salmonella paratyphi (3.2%) and salmonella paratyphi A(1.6%) (Table 1). Salmonella paratyphi species shows 100% sensitivity to co-triaxle, co-trimoxazole, and amikacin while 50.8% to azithromycin (table-2). Salmonella paratyphi A 100% sensitivity to amikacin, ampicillin, azithromycin, cefepime, cefoperazone, cefotaxime, co-amoxiclav and colistin (table-3). While salmonella typhi were found to be 95.2% with drugs sensitivity amikacin, colistin, fosfomycin, co-trimoxazole, and ertapenem(100%), ciprofloxacin(73.0%) and azithromycin 55.6% (Table 4).

DISCUSSION

A study conducted in Indonesia reported that typhoid fever accounted for 75% of the cases, while paratyphoid fever accounted for 25%. Typhoid and paratyphoid cases occurred at

rates of 1.4 and 0.5 per thousand people per year⁶, while in our study salmonella typhi was reported to be 95.2%.

A similar study conducted by Meina Yue et al⁷ reported that the most common organisms were *Salmonella* Typhimurium (34.43%) and *S.* Enteritidis(19.67%) with Ampicillin resistance the most common i.e., (63.93%) and cefotaxime (19.67%) while in our study salmonella, Paratyphi A were having 100% ampicillin sensitivity.

A similar study conducted in Vietnam¹³reported that after blood culture obtained after 3 days of fever were having salmonella typhi(8.5%) while in our study salmonella typewas 95.2%.

A study conducted in Karachi¹⁸ reported that blood culture having positive for salmonella typhi, antibioticsand their sensitivity assessed. The most resistant antibiotics were quinolones (85%), followed by ampicillin (83%) and trimethoprim-sulfamethoxazole (82%). Among the 72 patients, 48(66%) had prolonged drug resistance, 14 (19%) had multidrug resistance, and 11(15%) had typhoid, were sensitive while in our study salmonella typhi sensitivity were 100% to amikacin, colistin, fosfomycin, co-cotrimoxazole and ertapenem while cefepime, cefotaxime, co-amoxiclav, amoxicillin, ceftazidime and chloramphenicol were the most resistant drugs.

A similar study conducted by NiranjanPatilet al¹⁹ in India reported that the blood culture of 251 patients was taken and shown to have salmonella typhi(76.5%) and salmonella paratyphi (23.5%) with 100% sensitivity to cefixime, ceftriaxone, and azithromycin, chloramphenicol(94.4%) and only (3.6%) isolates were sensitive to ofloxacin, while in our study salmonella typhi were 95.2% with 100% drugs sensitivity to amikacin, colistin, fosfomycin, co-cotrimoxazole and ertapenem.

A study conducted in China²⁰ reported revealed salmonella typhimurium (79.2%) was the most prevalent serotype.The study analyzed NTS's medication resistance between 2009-2013 and between 2014-2018.Non-typhoidal salmonella had the highest rates of drug resistance to cefazolin, cefotaxime, ciprofloxacin, levofloxacin, and imipenem, according to our study. The drug resistance rates to compound sulfamethoxazole, ampicillin, ceftriaxone, cefepime, and chloramphenicol dropped significantly but remained high. Additionally, during the past 10 years, drug resistance to ceftazidime, piperacillin, and tazobactam has considerably decreased.Among 69 cases (13.7%) of 501 children with non-typhoidal salmonella infections, multi-drug resistant isolates were found.

A study conducted in southern Pakistan²¹ were having (81.1%) of children S. typhi while salmonella paratyphi were (18.9%). The drugs most commonly prescribed by the physician were cefixime (66.6%), followed by ciprofloxacin (33.3%). Cefixime and ceftriaxone showed 60.9% and 65.8% sensitivity, while Ciprofloxacin sensitivity was 50.1% in S. typhi isolated. While in our study salmonella typhiwas the most commonly occurring organism with 100% sensitivity to amikacin, colistin, fosfomycin, co-cotrimoxazole and ertapenem.

A similar study conducted in Tamil Nadu²² reported that nearly 100% of all the isolated salmonella species were sensitive to co-trimoxazole, ampicillin, chloramphenicol and third-generation cephalosporin resistance to azithromycin was 15%. There washigh resistance noted to nalidixic acid and quinolones. While in our study high sensitivity was noted to amikacin, colistin, fosfomycin, co-cotrimoxazole, and ertapenem.

A similar study conducted in Nepal²³ reported that Salmonella Typhi (68.8%) and Salmonella paratyphi A(31.1%) with higher drugs sensitivity to azithromycin, ciprofloxacin, cefixime, nalidixicacid, and ofloxacin while higher resisted were noted to fluoroquinolones.

A study conducted in Sokoto Nigeria²⁴ shows 5.9% of salmonella species were isolated among those were having 100% sensitivity to ofloxacin, ciprofloxacin and ceftriaxone while no sensitivity was noted towards ampicillin and augmentin.

CONCLUSION

Salmonella typhiwas the most common pathogen detected in blood culture (95.2%) with 100% drug sensitivity to amikacin, colistin,fosfomycin, co-trimoxazole and ertapenem. **Conflict of interest:** Nothing to declare

REFERENCES

- 1. Schultz M. Theobald smith. *Emerg Infect Dis.* 2008;**14**(12):1940–1942. doi:10.3201/eid1412.081188
- Desai PT, Porwollik S, Long F, et al. Evolutionary genomics of salmonella enterica subspecies. *MBIO*. 2013;4(2). doi:10.1128/mBio.00579-12
- Marzel A, Desai PT, Goren A, et al. Persistent infections by nontyphoidal salmonella in humans: epidemiology and genetics. *Clin Infect Dis.* 2016;62(7):879–886. doi:10.1093/cid/civ1221
- Fan Q, Yi M, Liu H, et al. The impact of age and pathogens type on the gut microbiota in infants with diarrhea in dalian, china. *Can J Infect Dis Med Microbiol.* 2020;2020:(8837156. doi:10.1155/2020/8837156
- Parry CM, Hien TT, Dougan G, White NJ, et al. (2002) Typhoid fever. N Eng J Med 347:1770-1782.doi: 10.1056/NEJMra020201.
- Vollaard AM, Ali S, Widjaja S, Asten HA, Visser LG, Surjadi C, van Dissel JT(2005) Identification of typhoid fever and paratyphoid fever cases at presentation in outpatient clinics in Jakarta, Indonesia. Trans R Soc Trop Med Hyg 99: 440-450.doi: 10.1016/j.trstmh.2004.09.012.
- Yue M, Li X, Liu D, Hu X. Serotypes, antibiotic resistance, and virulence genes of salmonella in children with diarrhea. J Clin Lab Anal. 2020;34(12):e23525. doi:10.1002/jcla.23525
- Wang P, Goggins WB, Chan E. Associations of salmonella hospitalizations with ambient temperature, humidity and rainfall in hongkong. *Environ* Int. 2018;**120**:(223–230. doi:10.1016/j.envint.2018.08.014
- Liang Z, Ke B, Deng X, et al. Serotypes, seasonal trends, and antibiotic resistance of non-typhoidal salmonella from human patients in Guangdong province, China, 2009–2012. BMC Infect Dis. 2015;15:(53. doi:10.1186/s12879-015-0784-4
- Crump JA, Luby S P, Mintz ED (2004) The global burden of typhoid fever. Bull World Health Organ 82:346-353.
- Karkey A, Arjyal A, Anders KL, Boni M.F, Dongol S et al. www.plosone.org Nov 2010;S(11) e 13988.doi.org/10.3126/jnps.v31i3.4382
- Majowicz SE, Musto J, Scallan E, et al. The global burden of nontyphoidal salmonella gastroenteritis. *Clin Infect Dis.* 2010;**50**(6):882–889. doi:10.1086/650733

- Lin FY, Vo AH, Phan VB, Nguyen T,Bryla D, Tran CT, Ha BK, Dang DT, Robbins JB(2000) The epidemiology of typhoid fever in the Dong Thap province, Mekong Delta Region of Vietnam. Am J Trop Med Hyg 62: 644-648.doi: 10.4269/ajtmh.2000.62.644.
- Siddiqui FJ, Rabbani F, Hasan R, Nizami SQ, Bhutta ZA (2006) Typhoid fever in children: some epidemiological considerations from Karachi, Pakistan. Int J Infect Dis 10: 215-222.doi: 10.1016/j.ijid.2005.03.010.
- Sinha A, Sazawal S, Kumar R, Sood S, Reddaiah VP, Singh B, Rao M, Naficy A, Clemens JD, Bhan MK (1999) Typhoid fever in children aged less than 5 years. Lancet 354: 734-737.doi: 10.1016/S0140-6736(98)09001-1.
- Wang X, Biswas S, Paudyal N, et al. Antibiotic resistance in salmonella typhimurium isolates recovered from the food chain through national antimicrobial resistance monitoring system between 1996 and 2016. Front Microbiol. 2019;10:(985. doi:10.3389/fmicb.2019.00985
- McDermott PF, Zhao S, Tate H. Antimicrobial resistance in nontyphoidal salmonella. *MicrobiolSpectr.* 2018;6(4). doi:10.1128/microbiolspec.ARBA-0014-2017.
- Laghari GS, Hussain Z, Hussain SZ, Kumar H, Uddin SM, Haq A. Antimicrobial susceptibility patterns of Salmonella species in Southern Pakistan. Cureus. 2019;11(4).doi: 10.7759/cureus.4379.
- Patil N, Mule P. Sensitivity pattern of salmonella typhi and paratyphia isolates to chloramphenicol and other anti-typhoid drugs: An in vitro study. Infection and drug resistance. 2019;12:3217.doi: 10.2147/IDR.S204618.
- Li-juan W, Luo Y, Guo-lu S, Zhong-yue L. Prevalence, Clinical Characteristics and Changes of Antibiotic Resistance in Children with Nontyphoidal Salmonella Infections from 2009–2018 in Chongqing, China. Infection and Drug Resistance. 2021;14:1403.doi: 10.2147/IDR.S301318.
- Laghari GS, Hussain Z, Hussain SZ, Kumar H, Uddin SM, Haq A. Antimicrobial susceptibility patterns of Salmonella species in Southern Pakistan. Cureus. 2019;11(4).doi: 10.7759/cureus.4379.
- Krishnasamy J, Srinivasan A. Sensitivity pattern of Salmonella isolates from blood culture in children in a tertiary care hospital in Western Tamil Nadu. Eastern Journal of Medical Sciences. 2020:8-10.
- Khadka P, Thapaliya J, Thapa S. Antimicrobial susceptibility pattern of Salmonella enterica, blood-stream isolates, among febrile children: a prospective study from Nepal.2019; 1-13. DOI: https://doi.org/10.21203/rs.2.14544/v1
- Najim Z, Kakako SL, Ochei J, Alkali BR, Mohammed K, Opaluwa SA. Prevalence and antibiotic susceptibility pattern of Escherichia coli and Salmonella spp isolated from diarrhoeic children in selected health centres in Sokoto, Nigeria. Asian Journal of Research in Infectious Diseases. 2019;12:1-8.