Esculapio - Journal of Services Institute of Medical Sciences

Original Article

Recent Antimicrobial Susceptibility Patterns of Salmonella Isolates in A Tertiay Care Hospital Lahore

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Abstract

Objective: To determine the recent antimicrobial susceptibility patterns of salmonella isolates (typhi and paratyphi) in a tertiary care hospital of Lahore.

Methods: It is cross sectional retrospective study conducted out in King Edward Medical University(Pathology deptt)/Mayo Hospital Lahore.The study period is six months from May 2019 to October 2019(Peak months of Typhoid fever).During this six months study period, total of 4284 samples for blood culture were received that were inoculated on the macConkey and blood agar plates.The growths obtained were then processed through biochemical profiling and analytical profile index(API).The Kirby Bauer technique was used for antibiotic susceptibility testing and reporting was done on the basis of clinical laboratory standard institute(CLSI).

Results: During these six months, total 4284 blood samples were inoculated, out of which 433 growths were obtained. There were 84 strains of salmonella typhi isolated. Sensitivity pattern of different antibiotics showed that Azithromycin was sensitive to 70 (83.3%) isolates, imipenem in 72 (85.7%), ciprofloxacin to 56 (66.7%), gentamycin to 48 (57.1%), ceftriaxone to 45 (53.6%), cefepime to 20 (23.8%), chloramphenicol to 12 (14.3%) while ampicillin was least sensitive i.e. 8 (9.5%) isolates. There were 24 MDR(multidrug resistant) and 12 were XDR(extensive drug resistant) strains. We also found out that resistance to azithromycin drug is also emerging as 70 out of 84 strains were sensitive while remaining 14 were resistant.

Conclusion: According to recent antibiotic susceptibility against salmonella typhi, the most sensitive drugs are Carbapenems (imipenem or meropenem) these days. Second sensitive antibiotic is azithromycin.

Key Words: Antimicrobial susceptibility, Salmonella isolates, Carbapenems, Azithromycin.

How to cite: *Bukhari H., Komal T., Akhtar R., Mumtaz U.S., Waheed I., Recent Antimicrobial Susceptibility Patterns of Salmonella Isolates in A Tertiay Care Hospital of Lahore. Esculapio 2021;17(01):45-48*

DOI: ***https://doi.org/10.51273/esc21.251719***

Introduction

Typhoid fever is an acute and sometimes life-threatening infectious disease. It remains an enormous public health threat in many developing countries (including Pakistan) due to inadequate access to safe water, poor sanitation system and inappropriate use of antimicro-bial drugs.[1] An estimated 21 million infections and above 1.6 lac deaths occur by typhoid fever worldwide each year. It is prevalent in Pakistan, that mostly affects children and teenagers.[2]

Salmonella typhi is responsible for almost 30% of community acquired bacterial bloodstream infections in Asian population, whilst salmonella paratyphi A is an emerging pathogen that causes upto 35% of all enteric fever episodes. Notably, paratyphoid fever has almost common features as that of typhoid fever.[3]

Salmonella enterica (typhi and paratyphi isolates) is a facultative intracellular and human restricted pathogen, predominantly transmitted by feco-oral route. Salmonella typhi is a gram negative, rod shaped, flagellated bacterium. It has a polysaccharide capsule that increases its virulence by inhibiting phagocytosis. It is H2S producing motile organism.[4]

Blood culture, urine and stool examination, serology

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Submission Date: 03-02-2021
Acceptance Date: 27-02-2021

and PCR (polymerase chain reaction) is available for diagnosing typhoid fever. Out of all these tests, blood culture and PCR is considered as gold standard.[5]

The WHO currently recommends imipenem, ampicillin, sulphamethoxazole-trimethoprim, flouroquinolones, 3rd generation cephalosporins (ceftriaxone, cefixime) and azithromycin(AZM) for the treatment of typhoid fever.[6] Multiple drug resistant (MDR) typhoid fever is defined as resistance against three first line drugs including ampicillin, chloramphenicol and sulphamethoxazole-trimethoprim. In Pakistan it was reported to be 40%. After that flouroquinolones overtake as first line therapy but in early 2000, emerging resistance against flouroquinolones was increasingly being reported. In these circumstances, third generation cephalosporins become the treatment of choice for typhoid febrile illness in Pakistan.[8]

Currently sporadic cases of extensive drug resistant (XDR) typhoid are frequently being reported. XDR salmonella typhi is resistant to ampicillin, chloramphenicol, sulphamethoxazole-trimethoprim, flouroquinolones and ceftriaxone. For these cases, azithromycin and carbapenems are prescribed in XDR typhoid fevers. Recently it also has lost credibility due to emergence of resistance because of its overuse.[7,9]

We planned to conduct this study in order emphasize the alternating trends of salmonella typhi antibiotic susceptibility to antibiotics in past few years in Pakistan, As XDR salmonella typhi infections is an alarming situation that is causing increase in mortalities.

Methods

It was a retrospective cross sectional study conducted at department of pathology, King Edward Medical University Lahore for six months i.e. May 2019 to October 2019.After ethical approval, 4284 samples of blood cultures received from the inpatient and outpatient departments of Mayo Hospital Lahore. All the blood cultures recieved were inoculated on two plates i.e blood and macConkey agar. The growth obtained was then further processed through biochemical profiling and analytical profile index (API) 20E. The Kirby Bauer technique was used for antibiotic susceptibility testing and reporting was done on the basis of Clinical Laboratory Standard Institute (CLSI) 2019.

Results:

Out of 4284 blood cultures , 433 had growths and the remaining 3851 had no growths. There were 82 strains of salmonella typhi and 2 strains of salmonella paratyphi isolated from total 433 growths. The mean age of patients was 40.04±15.79 years. There were 56 (66.7%) patients of age 20-40 years, 18(21.4%) patients were of age 41-60 years and 10 (11.9%) patients were of age 61-80 years. There were 53 (63.1%) males and 31 (36.9%) females. Out of 84 cases, 82(97.6%) salmonella typhi while 2 (2.4%) had salmonella paratyphi. (Table 1)

In patients of age 20-40 years, salmonella typhi was present in 54 (96.4%) cases while salmonella paratyphi in 2 (3.6%) cases. In patients of age 41-60 years, salmonella typhi was present in 18 (100%) cases while salmonella paratyphi was not detected in this age group. In patients of age 61-80 years, salmonella typhi was present in 10 (100%) cases while salmonella paratyphi was not detected in this age group.

Sensitivity pattern of different antibiotics showed that Azithromycin was sensitive to 70 (83.3%) isolates, imipenem in 72 (85.7%), ciprofloxacin to 56 (66.7%), gentamycin to 48 (57.1%), ceftriaxone to 45 (53.6%), cefepime to 20 (23.8%), chloramphenicol to 12 (14.3%) while ampicillin was least sensitive i.e. 8 (9.5%) isolates. (Table 2)

Table 1: *Demographics of Patients*

n	84
Age (years)	40.04±15.79
20-40 years	56 (66.7%)
41-60 years	18 (21.4%)
61-80 years	10 (11.9%)
Gender	
Male	53 (63.1%)
Female	31 (36.9%)
Bacterium isolated	
Salmonella typhi	82 (97.6%)
Salmonella paratyphi	2 (2.4%)

Out of these 84 strains, 24 (28.57%) were multidrug resistant (MDR) and 12 (14.28%) were extensive drug resistant (XDR) strains of salmonella typhi.

In this study we also found that resistance to azithromycin drug is also evolving. As out of 84 strains of salmonella typhi, 14 were resistant to azithromycin and remaining 70 were sensitive.

Discussion

The findings of this study clearly shows that MDR and XDR salmonella infections are emerging fastly. Most of the strains were sensitive to carbapenems and secondly to azithromycin. So, meropenem/imipenem and azithromycin are good choices of drug treatment for typhoid fever at present.

There was peak of MDR salmonella typhi epidemic in south and southeast Asia in the early 1990s. In these cases flouroquinolones were recommended. After mutations of strains of salmonella typhi, flouroquinolones resistance developed that led to usage of parenteral ceftriaxone, that required hospitalization. Whereas antimicrobial resistance to these drugs is also increasing, such as recent emergence of XDR salmonella typhi organisms in Pakistan.[7]

Table 1: *Distribution of Sensitivity Palfern of Ortibotics in Solmonell Type*

		Isolated bacterium		Total	p-value
		Salmonella typhi	Salmonella paratyphi		
Azithromycin	Sensitive	70 (85.4%)	0 (0.0%)	70 (83.3%)	0.001
	Resistant	12 (14.6%)	2 (100%)	14 (16.7%)	
Imepenem	Sensitive	72 (87.8%)	0 (0.0%)	72 (85.7%)	0.000
	Resistant	10 (12.2%)	2 (100%)	12 (14.3%)	
Ciprofloxacin	Sensitive	54 (65.9%)	2 (100%)	56 (66.7%)	0.311
	Resistant	28 (34.1%)	0 (0.0%)	28 (33.3%)	
Gentamycin	Sensitive	46 (56.1%)	2 (100%)	48 (57.1%)	0.215
	Resistant	36 (43.9%)	0 (0.0%)	36 (42.9%)	
Ceftriaxone	Sensitive	43 (52.4%)	2 (100%)	45 (53.6%)	0.183
	Resistant	39 (47.6%)	0 (0.0%)	39 (46.4%)	
Cefepime	Sensitive	18 (22.0%)	2 (100%)	20 (23.8%)	0.010
	Resistant	64 (78.0%)	0 (0.0%)	64 (76.2%)	
Chloramphenicol	Sensitive	10 (12.2%)	2 (100%)	12 (14.3%)	0.000
	Resistant	72 (87.8%)	0 (0.0%)	72 (85.7%)	
Ampicillin	Sensitive	8 (9.8%)	0 (0.0%)	8 (9.5%)	0.642
	Resistant	74 (90.2%)	2 (100%)	76 (90.5%)	

The results obtained from blood cultures showed greater number of salmonella typhi isolates including extensive drug resistant strains that is a serious public health issue. Treatment of these extensive drug resistant salmonella infections is a big challenge for infectious diseases specialists. The only treatment options left are carbapenems and azithromycin antibiotics. Treatment plan of XDR typhoid includes intravenous meropenem (carbapenem) for one week followed by oral azithromycin.[8,10] Carbapenems are very important as well as effective antibiotic treatment for typhoid fever but the presence of carbapenemase producing enterobactereicae is also a serious issue.[9,11]

Small sample size, short duration study (6 months), antimicrobial pre-treatment and decreased sensitivity of blood cultures as compared to PCR are the main limitations of our study. Others include lack of minimum inhibitory concentration (MIC) and extended spectrum beta lactamases (ESBL) testing for different antibiotics.

Conclusion

It was concluded that carbapenems (meropenem or imipenem) and azithromycin are drugs of choice for XDR salmonella typhi infections now-a-days & antibiotic stewardship is required in order to prevent the prevailing resistance to different antibiotics.

In the background of rising MDR and XDR infections, healthy policy making, improved healthcare and institutional facilities and effective antibiotic stewardship is the need of hour to combat this problem.

Conflict of Interest: None

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