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Changing Trends in Antibiotic Resistance Profile of *Salmonella enteritica species* in a Tertiary Care Hospital in Central Kerala

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Abstract
Background: *Infections due to salmonella is an important cause of significant morbidity and mortality in many developing countries. Salmonella Typhi being the major causative agent and affects roughly 21.6 million people each year.*
Objective: *A retrospective study was conducted to analyze the antibiotic sensitivity pattern of Salmonella enterica species isolated from clinical specimen from a tertiary care hospital.*
Materials and Methods: *A total of 39 Salmonella enterica species isolated from the blood and stool samples were analyzed from the period of 2011 January to 2017 June. Patients were in the age group of 2-63 years. Salmonella Typhi was the predominant isolate 74% (29). These isolates were tested for antimicrobial susceptibility according to the CLSI guidelines.*
Results: *No Multidrug resistant (MDR) strains were isolated where as sensitivity to Ciprofloxacin and Azithromycin decreased gradually since 2012.*
Conclusion: *Since 1987, when ciprofloxacin was approved for clinical use, fluoroquinolones (FQs) have been widely prescribed for a diverse range of infections, including bacterial enteritis and typhoid fever. A broad antibacterial spectrum, favorable safety profile, and excellent oral absorption have contributed to the popularity of these agents. However, marked increases in FQ resistance were observed within a decade of the introduction of these agents, and Salmonella infections have typified this trend. A careful consideration should be given before deciding the antibiotic for treatment in order to prevent the emergence of antibiotic resistance.*
Keywords: *Salmonella enterica, Flouroquinalone, Azithromycin , Multidrug resistance.*

Introduction

Infections due to salmonella is an important cause of significant morbidity and mortality in many developing countries. Salmonella Typhi is the major causative agent. This affects roughly 21.6 million people each year and kills 216000-600000 people each year of which62% of cases are in Asia[1]. Typhoid fever is prevalent in developing countries such as India and may be due to inadequate sanitation measures and lack of clean drinking water. Antibiotic resistance have been reported in Indian subcontinents since antibiotic treatment is the main form of treatment. Mortality is 30% in untreated cases but with proper antibiotic treatment it can be reduced to 0.5%.[2] Chloramphenicol has been the treatment of choice for typhoid fever from1948. Multi drug resistant is the term where the Salmonella isolates are resistant to Chloramphenicol, Co-trimoxazole and Ampicillin. It has been emerged soon following the rampant use of all the above antibiotics.

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Several studies have shown decreased susceptibility to Ciprofloxacin. Susceptibility to Azithromycin also decreasing due to rampant use of this drug for minor infections. It is worrying to note its varying drug susceptibility in different regions.

Materials and methods: A total of 39 Salmonella enterica species isolates from the blood and stool samples were analyzed from the period of 2011 January to 2017 June .Patients were in the age group of 2-63 years who were admitted with acute enteritis and or with fever who did not respond to the usual management, The study was conducted in a tertiary care hospital in Kerala. The organisms were isolated from blood by inoculating it in to Brain Heart infusion broth/BacT/Alert 3D system. Blood agar and MacConkey agar were used for isolating the organism. Stool culture was done in slective media and enrichment done by using Selenite F broth. Confirmation of the isloates was done by biochemical identification and using specific antisera. Antibiotic sensitivity testing were done according to the CLSI guidelines[3]. Minimum Inhibitory Concentration (MIC) of Ciprofloxacin and Azithromycin were done by Macro broth dilution method.

Results

Table No: 1 Total 39 *Salmonella enterica species isolates* during this period.

Isolates (n = 39)	Percentage
Salmonella Typhi	74.3 (n=29)
Salmonella Paratyphi A	17.9 (n=7)
Salmonella Paratyphi B	2.5 (n=1)
Salmonella Typhimurium*	2.5 (n=1)
Salmonella Newport*	2.5 (n=1)

**Salmonella Typhimurium, Salmonella Newport were identified from NICED Kolkatta.*

Out of the 39 patients 69% n= 27) were males, and 30.77% (n=12) were females. Patients were between the age group of 2-63 years.

Table No: 2 Age Distribution

Age in years	Percentage(n=39)
<15	23.07 (n= 9)
15-60	61.5 (n= 24)
>60	15.38 (n= 6)

Table no:3 clinical presentation

Symptom	Percentage (n=39)
High grade fever	82.05 (n=32)
Chills and rigors	41.02 (n=16)
Vomiting	38.4 (n=15)
Abdominal pain	20.5 (n=20.5)
Loose stools	66.66 (n=26)
Convulsions, coma, disorientation, weakness	5.12 (n=2)
Jaundice	2.56(n=1)
Organomegaly	20.5(n=8)

Table No:4 Sensitivity of Salmonella enteric species

Drugs	2011(n=7)	2012(n=4)	2013(n=1)	2014(n=1)	2015(n=5)	2016(n=13)	2017(n=8)
Ampicillin	14.2% (n=1)	75% (n=3)	100% (n=1)	100% (n=1)	80 % (n=4)	76.9% (n=10)	87.5% (n=7)
Ciprofloxacin	71.4% (n=5)	75% (n=3)	100% (n=1)	100% (n=1)	80% (n=4)	30.7% (n=4)	25% (n=2)
Ceftriaxone	100% (n=7)	75% (n=3)	100% (n=1)	100% (n=1)	100% (n=5)	92.3% (n=12)	100% (n=8)
Co-trimoxazole	100% (n=7)	100% (n=4)	100% (n=1)	100% (n=1)	100% (n=5)	100% (n=13)	100% (n=8)
Nalidixic acid	28.5% (n=2)	50% (n=2)	100% (n=1)	100% (n=1)	60% (n=3)	7.69% (n=1)	0% (n=0)
Azithromycin				100% (n=1)	100% (n=5)	69.2% (n=9)	75% (n=6)
Chloramphenicol	100% (n=7)	100% (n=4)	100% (n=1)	100% (n=1)	100% (n=5)	100% (n=13)	100% (n=8)

Table No:5 Sensitivity of *Salmonella Typhi*

Drugs	2011(n=5)	2012(n=2)	2013(n=1)	2014(n=1)	2015(n=5)	2016(n=9)	2017(n=6)
Ampicillin	0% (n=0)	100% (n=2)	100% (n=1)	100% (n=1)	80% (n=4)	88.88% (n=8)	83.33% (n=5)
Ciprofloxacin	60% (n=3)	100% (n=2)	100% (n=1)	100% (n=1)	80% (n=4)	33.33% (n=3)	33.33% (n=2)
Ceftriaxone	100% (n=5)	50% (n=1)	100% (n=1)	100% (n=1)	100% (n=5)	88.88% (n=8)	100% (n=6)
Co-trimoxazole	100% (n=5)	100% (n=2)	100% (n=1)	100% (n=1)	100% (n=5)	100% (n=9)	100% (n=6)
Nalidixic acid	40% (n=2)	50% (n=1)	0% (n=0)	0% (n=0)	60% (n=3)	0% (n=0)	16.66% (n=1)
Azithromycin				100% (n=1)	100% (n=5)	77.77% (n=7)	83.33% (n=5)
Chloramphenicol	100% (n=5)	100% (n=2)	100% (n=1)	100% (n=1)	100% (n=5)	100% (n=9)	100% (n=6)

Table No:6 Minimum inhibitory concentration (MIC)- Ciprofloxacin

Strains	MIC
S. Typhi(n=7)	4-64µg /ml
S. Paratyphi A(n=1)	32µg /ml
Nalidixic Acid resistant strains (n=3)	16-64µg /ml

SENSITIVE- <0.06 µg /ml RESISTANT- >1 µg /ml

Table No: 7 Minimum inhibitory concentration (MIC)- Azithromycin

Strains	MIC
S. Typhi(n=4)	32-64µg /ml
S. Paratyphi A(n=1)	64µg /ml

SENSITIVE- < 16 µg /ml RESISTANT- > 32 µg /ml

Discussion

Infections due to Salmonella species is an important public health problem in developing countries. In the present study Salmonella Typhi is the commonest isolate (74.3%) followed by Salmonella Paratyphi A (17.9%). Isolation of *S.* Typhi as the most common serotype is similar to the results from other Indian studies from Chennai, Shimla, Chandigarh and New Delhi.[4,5,6,7,8,9]. Resistance to commonly used antibiotics has been reported from different parts of India. In the present study Chloramphenicol and Cotrimoxazole showed 100% sensitivity where as Ciprofloxacin sensitivity seems to be decreasing over the time. Our observation of reemergence of susceptibility to chloramphenicol is comparable with studies by other Indian workers.[5,8,10,11.]There have been many reports of multidrug-resistant (MDR) *Salmonella(*resistant to ampicillin, trimethoprim–sulfamethoxazole and chloramphenicol)in the Indian subcontinent, but we did not isolate any MDR strains during our study. Yashawanth *et al* reported a sensitivity of 98.7% and 92.7% to ampicillin for *S.* Typhi and *S.* Paratyphi A in Mangalore[12]. However, as per Gupta *et al S.* Paratyphi A isolates were less susceptible to ampicillin (69.2%) in Chandigarh.[13] Prajapati *et al* reported a decreased susceptibility to ciprofloxacin, 86.6% for S. Typhi and 51.3% for S.Paratyphi A[14].In a separate study by Verma *et al*, sensitivity of *S.* Typhi & *S.* Paratyphi A was 67% and 71.5%respectively for ampicillin.In contrast, Tankhiwale *et al*, Nagpur, India, reported that 100%of the *S.* Paratyphi A isolates were sensitive to ciprofloxacin and Verma *et al* reported a sensitivity of 90.6% and 91.2% to *S.* Typhi and *S.* Paratyphi A respectively[9.5]. In the present study Azithromycin sensitivity showed a decreasing trend over the years. 100% in 2014 and only 83.33% in 2017. Similar results reported from other studies in South India [11]

Conclusion

Salmonella Typhi being the predominant isolate. Sensitivity to Chloramphenicol was 100% where as sensitivity to Ciprofloxacin and Azithromycin decreased gradually from 2012 to 2017. No MDR strains were isolated. Ciprofloxacin sensitivity

declined to33% from 100%..Due to decline in MDR strains, older drugs like Ampicillin, Chloramphenicol, and Cotrimoxazole still have an important role in management. In our opinion, the need for antibiotic protocols based on region wise susceptibility patterns is important. Azithromycin resistance is increasing, may be due to the rampant use of this drug for minor respiratory infections

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