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**Antimicrobial Susceptibility Patterns of Salmonella Typhi From Kigali, Rwanda.**

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**Abstract.**

Background: Salmonellosis is a major health problem, especially in developing countries like Rwanda. Salmonella typhi infects only human and human transmission occur through feacal-oral route. Moreover, species are becoming resistant to the commonly used antibiotics.

Objective: The aim of the present study is to know antimicrobial susceptibility patterns with special reference to multidrug resistance Salmonella enterica serovar Typhi and reduced susceptibility to nalidixic acid.

Materials: A total 69 S.typhi isolated of King Faisal hospital, Kigali, Rwanda from stool and blood specimens were included in the study. Antimicrobial susceptibility was done by using Kirby-Bauer disc diffusion method.

Results: There was decreased susceptibility was observed in Chloramphenicol, Ampicillin, Amoxicillin/Clavulanic acid, Tetracycline, Cotrimoxazole and Nalidixic acid. These were significant increase in the multidrug resistant salmonella typhi (MRST) from 9.1% to 25% respectively between 2007 and 2008. All the isolates were 100% sensitive to Ceftriaxone, Levofloxacin and Ciprofloxacin.

Conclusion: Typhoid fever has been endemic in Kigali. Decreased susceptibility towards nalidixic is observed which gives us alarm for treatment failure towards fluoroquinolones. The antibiotic sensitivity pattern is changing and resistant cases are emerging due to inappropriate use of antibiotics.

**Keywords: Antimicrobial susceptibility, Salmonella Typhi, Rwanda.**

## **Introduction:**

Typhoid fever is a systemic disease contracted by ingestion of contaminated food or water. It is caused by the bacterium *Salmonella enterica* serovar Typhi, which is a pathogen only of humans. The illness may be mild or severe. These conditions are sometimes referred to collectively as enteric fever. It is encountered worldwide but is primarily found in developing countries where sanitary conditions are poor.<sup>(1)</sup> The World Health Organization (WHO) estimates that 16 to 33 million cases of typhoid fever occur each year, with 500,000 to 600,000 deaths (a case fatality rate of between 1.5 and 3.8%).<sup>(2)</sup> The majority of typhoid occurs in Asia, Africa, and Latin America where frequent outbreaks are reported.

In 1948 chloramphenicol was introduced to treat the disease. Drug resistant salmonella typhi has been reported as early as 1972 in Mexico and been observed in other countries like Bangladesh, Thailand, Vietnam, Korea, Peru and India.<sup>(3)</sup> Ampicillin and cotrimoxazole were effective alternative drugs till the end of 1990's when strains resistant to all the first line anti-salmonella drugs used at that time, were reported.<sup>(4)</sup>

Multidrug-resistant *S.typhi* (MDRST) is epidemiologically defined as strains resistant to any two antimicrobials in vitro even if the antimicrobials tested are known to be clinically ineffective. A more useful definition of MDRST is reserved for strains resistant to all three first-line antityphoidal antimicrobial agents, namely Ampicillin, Chloramphenicol and Cotrimoxazole.<sup>(5)</sup> Typhoid fever, caused by MDRST, has become a significant cause of morbidity and mortality over recent

years. The incidence of MDRST is reported to be as high as 60%, although there are some reports noting its decline. The present study was, therefore, undertaken to determine the antimicrobial susceptibility patterns of local isolates of *S.typhi* with special reference to their multidrug resistance and reduced susceptibility to nalidixic acid.

## **Materials and Methods:**

A retrospective study was conducted by utilizing the records of 2007 & 2008 of Microbiology unit, Laboratory services, King Faisal Hospital, Kigali, Rwanda. A total of 69 salmonella typhi isolates from blood and stool specimens were included in the study and did not include multiple isolates from the same patient. All the isolates were identified by using API 20 E (BIOMERIEUX) and were confirmed by serological test by using salmonella typhi "O" and "H" specific antisera. All the isolates were tested for their susceptibility to Ampicillin (10µg), Chloramphenicol (30µg), Amoxicillin/Clavulanic acid (20µg+10µg), Cotrimoxazole (1.25µg+23.75µg), Tetracycline (30µg), Nalidixic acid (30µg), Ciprofloxacin (5µg), Ceftriaxone (30µg) and Levofloxacin (5µg) from Oxoid. Antimicrobial susceptibility testing was carried out by using Kirby-Bauer disc diffusion method on Muller-Hinton agar media. Statistical analysis was performed by using Epi Info software (version 3.5.1 august 2008) which was downloaded from CDC website.

## **Result:**

The antibiogram of salmonella typhi is shown in the table1, there is a significant decreased sensitivity were absorbed towards Ampicillin, Amoxycillin/Calvvlanic acid, Chloramphenicol, Cotrimoxazole, Tetracycline and Nalidixic acid between the two years. All the isolates were sensi-

tivity to Ciprofloxacin, Ceftriaxone and Levofloxacin. There was an increase in MDRST in 2008, which were resistant to all three first-line antityphoidal antimicrobial agents, namely Ampicillin, Chloramphenicol and Cotrimoxazole which is shown in the table: 2.

**Table: 1** ANTIBIOTIC SENSITIVITY PATTERNS OF SALMONELLA TYPHI

ANTIBIOTICS	2007 (n=33)		2008 (n=36)		2007 & 2008 (n=69)		P-VALUE
	% of Sensitivity	% of Resistant	% of Sensitivity	% of Resistant	% of Sensitivity	% of Resistant	
Ampicillin	81.8	18.2	47.2	52.8	63.7	36.3	0.006
Amoxycillin/Calvvlanic acid	91	9.1	66.6	33.4	78.2	11.8	0.03
Chloramphenicol	81.8	18.2	75	25	78.2	21.8	NS*
Cotrimoxazole	81.8	18.2	50	50	65.2	34.8	0.01
Nalidixic acid	97	3	80.5	19.5	88.4	39	0.05
Tetracycline	91	9	66.6	33.4	78.2	56	0.03
Ciprofloxacin	100	0	100	0	100	0	NS*
Ceftriaxone	100	0	100	0	100	0	NS*
Levofloxacin	100	0	100	0	100	0	NS*

\* NS = non significant

**Table: 2** Multi drug resistant (MDR) Salmonella typhi

Year	No of isolates	No of MDR salmonella typhi	% of MDR salmonella typhi	P -value
2007	33	3	9.1	0.083
2008	36	9	25.0	

## Discussion

This study was conducted to know the antibiotic sensitivity patterns of salmonella typhi, though the sample size was limited and typing was not done, this study reveals some relevant changing pattern in antibiotic response of Salmonella isolates.

All the salmonella isolates showed a significant decrease in susceptibility to Ampicillin, Amoxycillin/calvvlanic acid, Chloramphenicol, Cotrimoxazole and Tetracycline which are used as first line antimicrobial agents against salmonella typhi. The rate of resistance observed in this study is consistent with incidences of increased antibiotic resistance reported among Gram-negative bacilli such as

Klebsiella, Enterobacter, Citrobacter, Acinetobacter and Pseudomonas aeruginosa in other parts of the world.<sup>(6)</sup>

There is a significant increase in the MDRST were observed from 9.1% in 2007 and 25% in 2008. Ackers et al reported that 16% of isolates were MDRST, while Nadeem et al reported 69% of the isolates which were MDRST.

Quinolones are highly effective against salmonellae in vitro. Ciprofloxacin is considered the drug of choice for the treatment of multidrug resistant typhoid, replacing Chloramphenicol. In the present study all the salmonella isolates were sensitive to ciprofloxacin which is in agreement with Ackers et al, Themina et al.<sup>(7, 8)</sup> Notable decreased susceptibility to Nalidixic acid was 92% in 2007 and 82.6% in 2008. Nalidixic acid resistance is a marker for predicting low-level resistance to ciprofloxacin among S.typhi and also an indicator of treatment failure to ciprofloxacin. It gives alarm that there is decrease susceptibility towards nalidixic acid which leads to the treatment failure in typhoid fever caused salmonella typhi in Kigali. Hence, it is suggested that all S.typhi isolates should be screened for nalidixic acid resistance along with ciprofloxacin. All patients with nalidixic acid resistant strains should be treated with higher doses of ciprofloxacin or ofloxacin. In the recent years, cephalosporins have gained importance for the treatment of enteric infections. First and second line generation cephalosporins are ineffective and should not be used to treat typhoid fever. In the present study all the isolates are sensitive to cefotaxime and Ceftriaxone and were also observed by Lakshmi et al from India.<sup>(4)</sup>

## Conclusions:

The findings of the present study indicate that MDRST strains were increased in Kigali. Salmonella typhi isolates were sensitive to ciprofloxacin but decreased susceptibility to nalidixic acid. Fluoroquinolones should no longer be used for therapy, if the prevalence of nalidixic acid resistant salmonella typhi is high. Resistance of nalidixic acid as a screening test for detecting reduced susceptibility to quinolones. This simple disc-diffusion test can predict probable treatment failures to quinolones. Probably further determine the exact minimum inhibitor concentration (MIC) of all isolates to quinolones is useful not only to detect exact MIC but also to conform the less susceptibility among the local isolates. This laboratory-based study highlights the patterns of S. typhi in a hospital set up. Most of the typhoid fever patients are treated on an outpatient basis, detailed information is required and response to therapy could not be obtained. Therefore further surveillance on typhoid fever, its clinical and epidemiological correlation with the resistant and susceptible strain is recommended.

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