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Research Article

Monitoring of Antibiotics Resistance in *Salmonella Typhi*, *S. Typhimurium* and *S. Enteritidis* in Dakar/Senegal

NGOM Babacar[1]*, Diagne R[2], Dia ML[3], Sarr A[3], Sow R[3], Samb A[1] and Sow AII[3]

[1]Private Institute of Training and Medicals Researches of Dakar, Senegal

[2]National Public Health Laboratory, Faculty of Health of the University of Thiès, Senegal

[3]Laboratory of Bacteriology and Virology, Cheikh Anta Diop University, Senegal

***Corresponding author:** NGOM Babacar, Laboratory of Bacteriology of the Institute of Training and Medical Research of Dakar (IPFORMED), 181 Sacre Coeur 3 VDN, Dakar, Senegal

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Abstract

Introduction: In recent years there has been a greater increase in antibiotic-resistant bacteria. It therefore appears that more urgent for bacteriology laboratories to perform very frequently monitoring of antibiotic resistance of the isolated bacterial strains and it is in this context that our study.

Materials and Methods: A total of 111 strains including 35 *Salmonella Typhi*, *S. Typhimurium* 31 and 45 *S. Enteritidis* was isolated in the laboratory of Bacteriology-Virology CHNU Fann. The identification of strains was done from biochemical characteristics (Analytical Profile Index 20E, BioMerieux) and antigen. Antibiotic susceptibility was studied by the agar diffusion technique (with recommendations Committee for Antibiotic Susceptibility Testing of the French Society of Microbiology).

Results: Following this work, it appears that 5.9% of *Salmonella Typhi* produce ESBL, 94.4% are wild phenotypes, 94.75% are susceptible to cephalosporins, 97% are susceptible to fluoroquinolones (pefloxacin, norfloxacin, ciprofloxacin) well that nalidixic acid and cotrimoxazole, and finally, they are sensitive to chloramphenicol 100%.

Conclusion: Chloramphenicol remains a very active antibiotic against typhoid fever. This is also the case for cephalosporins, fluoroquinolones, tetracyclines, cotrimoxazole and amoxicillin. The production of Extended Spectrum Beta-Lactamases is well established in some strains of *Salmonella* and therefore the surveillance must be more rigorous in order to avoid their dissemination.

In addition, molecular biology work should also be undertaken to better understand the types of ESBL produced.

Keywords: *Salmonella*; Antibiotics; ESBL

Introduction

In humans, *salmonella* is responsible for typhoid, paratyphoid fever and the most common and widespread foodborne illness. Typhoid fever is a strictly human disease with sometimes serious complications in malnourished or immunocompromised individuals whose causative organism is *Salmonella Typhi* or Eberth's bacillus. It is common in countries with a low level of hygiene (more than ten million cases a year). *Salmonella* causing food poisoning that can cause diarrhea, vomiting, moderate fever are due to serovars other than that involved in typhoid fever and among the most frequently implicated serotypes are *Salmonella Typhimurium* and *S. Enteritidis* [1,2]. These germs were naturally sensitive to most antibiotics active on gram-negative bacilli [3]. However, with the frequent occurrence of multidrug-resistant strains (most often producing beta-lactamases), it was necessary to conduct antibiotic resistance surveillance studies of isolated strains. It was in this context that our work was focused on 111 *Salmonella* strains (*S. Typhi*, *S. Typhimurium* and *S. Enteritidis*) isolated in the Bacteriology laboratory of Fann of Dakar.

Materials and Methods

The study involved 35 strains of *Salmonella Typhi*, 31 *S. Typhimurium* and 45 *S. Enteritidis* collected in pathogenic situations (Table 1). The samples were taken from hospitalized patients in the various departments of CHNU Fann Dakar of Senegal and patients seen in external consultation.

The biological diagnosis of these strains was made directly by stool culture and blood culture [2-4]. They were identified according to their biochemical culture traits (API 20 E) and antigenic (anti-*Salmonella* agglutinating sera) [5-7]. The antibiogram was performed according to the agar diffusion method (and according to the recommendations of the Antibiogram Committee of the French Microbiology Society).

The antibiotics tested were as follows: Amoxicillin (AMX; 25µg), Amoxicillin/Clavulanic Acid (AMC; 20/10µg), Ticarcillin (TIC; 75µg), Piperacillin (PIP; 75µg), Cephalothin (CEP; 30µg), Cefoxitin (FOX; 30µg), Ceftriaxone (CRO; 30µg), Cefotaxime (CTX; 30µg), Ceftazidime (CAZ; 30µg), Cefepime (FEP; 30µg), Cefixime (CFM; 10µg), Aztreonam (ATM; 30µg), Imipenem (IMP;10µg), Chloramphenicol (CHL; 30µg), Tetracycline (TCY; 30µg), kanamycin (K; 30µg), Tobramycine (TOB; 30µg), Gentamicin (GM; 10µg), amikacin (AN; 30µg), Netilmicin (NET; 30µg), colistin (CS; 10µg)

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Table 1: Distribution of serotypes according to biological products.

Serotypes	Biological products	
	Blood	Stools
S. Typhi	22	13
S. Typhimurium	15	16
S. Enteritidis	24	21

Trimethoprime/Sulfamethoxazole (SXT; 1,25/23,75µg), nalidixic acid (NAL; 30µg), Pefloxacin (PEF; 5µg), Norfloxacin (NOR; 5µg), Ciprofloxacin (CIP; 5µg), Nitroxoline (NI; 20µg).

The ESBL search was performed by the synergy test between third generation cephalosporins and the amoxicillin + clavulanic acid disc.

Results

The study showed that *Salmonella Typhi* remained highly susceptible to antibiotics in the beta-lactams, tetracyclines, phenicolates and quinolones family.

In fact, the strains tested were 96.8% sensitive to amoxicillin, 94.3% to ticarcillin and 97.1% to piperacillin. Cephalosporins also remained very active on *Salmonella Typhi*. It is sensitive to 94.1% to cefalotine, 88.9% to cefotaxime, 94.4% to ceftriaxone, 95.7% to ceftazidime and 100% cefixime.

Carbapenems in this case imipenem was 100% active on *Salmonella Typhi*.

The strains tested were also very sensitive to phenicolates, tetracyclines, cotrimoxazoles, as well as nalidixic acid and fluoroquinolones. In fact, they had a sensitivity of 100% to chloramphenicol, 100% to tetracycline, 97% to cotrimoxazole, 100% to Pefloxacin, 95.5% to norfloxacin and 95.7% to ciprofloxacin (Table 2).

Of the 35 strains of *S. Typhi* studied, 2 are broad spectrum beta-lactamase producers and the rest are wild-phenotype.

Salmonella Typhimurium exhibited high resistance to some antibiotics such as amoxicillin, ticarcillin, piperacillin, chloramphenicol, tetracyclines, and cotrimoxazole. However, the strains encountered were 100% sensitive to cephalosporins (cefalotin, cefoxitin, cefotaxime, ceftriaxone, ceftazidime), quinolones, colistin, imipenem, aztreonam, and 98.34% to aminoglycosides (kanamycin , tobramycin, gentamicin, amikacin, netilmicin). High resistance to chloramphenicol, tetracycline, and cotrimoxazol was noted with respectively 34.8%, 33.3% and 40.9%.

Salmonella Enteritidis had a mean sensitivity of 91.64% to cephalosporins (cefalotin, cefoxitin, cefotaxime, ceftriaxone, ceftazidime), 96.8% to chloramphenicol, 100% to aminoglycosides (kanamycin, tobramycin, gentamicin, amikacin, netilmicin) and 100% to fluoroquinolones (pefloxacin, norfloxacin, ciprofloxacin). Reading Table 2 reported the sometimes high resistance of several antibiotics such as amoxicillin, ticarcillin, tetracycline. However, the most striking phenomenon was the average 28.9% resistance to nalidixic acid.

Discussion

The study revealed that *S. Typhi* strains had very low levels of resistance (not more than 7%) to the antibiotics tested in the Fann Bacteriology laboratory. Indeed, 94% of the strains are wild-type, only 6% (ie 2 strains) produce a broad-spectrum beta-lactamase contrary to what is observed in other parts of the world (Mexico, Vietnam, Tajikistan) where the Isolated ESBL secretory *S. Typhi* is very important [8].

Table 2: Resistance profiles of *Salmonella Typhi*, *S.Typhimurium* and *S. Enteritidis* strains.

Antibiotics tested	R (%) de *S. Typhi*	R (%) de *S. Typhimurium*	R (%) de *S. Enteritidis*
Amoxicilline	3,2	45,8	37,8
Amoxicilline/Acide clavulanique	5,7	12	12,8
Ticarcilline	2,9	48	38,5
Piperacilline	4,5	13,3	12,5
Céfalothine	5,9	0	7,7
Céfoxitine	3,1	0	2,6
Céfotaxime	7,4	0	4,3
Ceftriaxone	5,6	0	4,3
Ceftazidime	4,3	0	8,3
Aztréonam	4,8	0	8,7
Imipenem	0	0	0
Chloramphenicol	0	34,8	3,2
Tetracycline	0	33,3	13,3
Kanamycine	4,8	0	0
Tobramycine	3,3	4,3	0
Gentamicine	2,9	4	0
Amikacine	0	0	0
Netilmicine	0	0	0
Trimethoprime/ Sulfamethoxazole	3	40,9	27
Colistine	0	0	3,2
Acide nalidixique	3	0	28,9
Pefloxacine	0	0	0
Norfloxacine	4,5	0	0
Ciprofloxacine	4,3	0	0
Nitroxoline	0	0	0
Cefépime	0	0	0
Cefixime	0	0	0

R (%) = Percentage of Resistance

Similarly, all strains of *S. Typhi* were sensitive to chloramphenicol despite the existence of strains of *Salmonella* resistant to this antibiotic in many other developing countries such as Congo [9] or not [10]. The latter remained therefore very active for the treatment of typhoid fever. However, it is feared for its toxicity because it is no longer used in France and where it is replaced by thiamphenicol.

According to a study conducted by Wang J et al. [11] published in 2017, we found that our *S. Typhimurium* strains were far more sensitive to cephalosporins and quinolones. Indeed, where our strains were 100% sensitive to these two major families of antibiotics, the work of Wang J and al. [11] showed that 20% of its strains were resistant to ceftriaxone, 5% to cefoxitin, 3.6% to ciprofloxacin and

79.2% to nalidixic acid. In addition, its strains also had significantly higher resistance than ours, as is the case for tetracycline (83.7% *vs.* 33.3%), chloramphenicol (54.9% *vs.* 34.8%), cotrimoxazole (47.4% *vs.* 40.9%) and gentamycin (37% *vs.* 0%).

This same study by Wang J and al. [11] highlighted the presence of ESBL genes of CTX, TEM, OXA and SHV types. However our strains being 100% sensitive to cephalosporins do not carry ESBL genes. In *S. Enteritidis* the study shows a high resistance rate against nalidixic acid 28.9%. However, a study conducted in Korea showed much more worrying results with 81% resistance to nalidixic acid [12].

Conclusion

To treat typhoid fever, chloramphenicol remains the antibiotic of choice because of the intracellular location of *salmonella*. Indeed, this antibiotic is concentrated in the mesenteric lymph nodes during absorption by the digestive tract and easily penetrates the infected cells. In adults, the starting dose is 0.75g/day, then this dose is increased very gradually from 0.50g/day to 2.5 to 3g/day, divided into 4 doses to avoid a too brutal release of endotoxins into the blood. In addition, amoxicillin, cotrimoxazole, tetracyclines, some third-generation cephalosporins and fluoroquinolones are also very effective against *Salmonella Typhi*.

He production of extended-spectrum beta lactamases is well established in some strains of *Salmonella* (*S. Typhi* and *S. Typhimurium*) and therefore the surveillance must be more rigorous in order to avoid their dissemination.

The resistance to nalidixic acid of *S. Enteritidis* is of alarming proportions. This phenomenon should be followed very closely to prevent this from spreading to fluoroquinolones.

In addition, molecular biology work should also be undertaken to better understand the types of broad-spectrum beta-lactamases produced as well as the plasmid media that mediate these resistances in *S. Typhi*.

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