



## Case Report

## Extended-Spectrum Beta-Lactamase Secreting *Shigella* Spp Strains Isolated From a Senegalese Child with Trisomy 21

*Shigella* spp productrice de bêta-lactamases à spectre élargi chez un enfant sénégalais porteur de trisomie 21

Mba Elhadji Bambo Diakhaby<sup>1</sup>, Abou Ba<sup>1,2</sup>, Omar Gueye<sup>1</sup>, Daouda Ndour<sup>1</sup>, Saliou Diouf<sup>1,2</sup>, Coumba Toure-Kane<sup>1,2</sup>

1. Dalal Jamm National Health Center
2. Cheikh Anta Diop University of Dakar
- 3.

**Corresponding author:** Dr Diakhaby

Email: [diakhaby57@gmail.com](mailto:diakhaby57@gmail.com)

**Keys words:** *Shigella* spp, ESBL, resistant strain, Trisomy 21

### ABSTRACT

*Shigella* spp is a Gram-negative bacillus belonging to the *Enterobacteriaceae* family. It is most often responsible for diarrhoea in children under 5 years of age and also in adults. The uncontrolled use of antibiotics has led to the development of resistant strains that pose a threat to public health. This resistance of strains associated with genetic diseases such as trisomy 21 can cause huge management problems. This report relates the first case of shigellosis in Senegal with multi-resistant *Shigella* spp in a child with trisomy 21.

### RÉSUMÉ

*Shigella* spp est un bacille gram négatif de la famille des entérobactéries. Il provoque le plus souvent des diarrhées chez l'enfant de moins de cinq ans et chez les adultes. L'usage incontrôlé des antibiotiques est à l'origine du développement de souches résistantes qui posent déjà un problème santé publique. Ces souches résistantes posent encore plus de problèmes de prise en charge chez les sujets avec des troubles g anomalies génétiques ou chromosomiques. Nous reportons le premier cas de shigelose spp multirésistante chez un enfant sénégalais trisomique.

### INTRODUCTION

Shigellosis is one of the most common diarrhoeal diseases in developing countries, particularly in flood-prone countries. The agent responsible for this disease is *Shigella* spp. This micro-organism is one of the most common enteropathogens responsible for childhood diarrhea. It is endemic throughout the year in developing countries, with outbreaks in certain seasons or during humanitarian disasters (1). Because *Shigella* can survive gastric acidity and is an intracellular pathogen, it is difficult to treat. In addition, the uncontrolled use of antibiotics has led to the development of resistant strains that pose a threat to public health (2). Shigellosis kills several hundred thousand people worldwide each year, mainly children under 5 years of age. They are highly infectious, as 10 to 100 bacilli are sufficient to cause the disease (1).

Mutiresistant Sighelle infections associated with genetic diseases such as trisomy 21 can cause problems in care. Trisomy 21 is the most common chromosomal abnormality in live-born children, with an incidence of one in 600 to one in 900 in the United States (3, 4).

Respiratory tract infections, particularly otitis media, have been identified as one of the most important health problems in children with this abnormality (5). This increased susceptibility to infections is related to abnormal immune system parameters (6, 7).

In the context of a COVID 19 pandemic and underdevelopment marked by problems of insalubrity, particularly in the suburbs, Senegal is not to be outdone with the emergence of multi-resistant strains: a case of shigellosis with *Shighella* spp secreting an extended-spectrum CTXM1 type beta-lactamase was observed in the pediatric ward of the Dalal Jamm National Hospital Centre in Guediawaye in a child with trisomy 21.

### CASE REPORT

It was a 9-month-old male infant born to a 39-year-old mother, 8 gestures, 6 pares. Delivery was at term by transverse low caesarean section on scarred uterus with resuscitation at birth. The birth weight was 2460 g for a height of 43 cm. He was exclusively breastfed until 6 months with a well conducted dietary diversification. The immunization status was up to date according to Senegal's Expanded Program of Immunization. He was

admitted to the pediatric ward at Dalal Jamm Hospital for bloody diarrhoea associated with vomiting and fever. The examination found a dysmorphic facies suggestive of trisomy 21, moderate dehydration and low weight at 5895 gr. The blood ionogram was normal with a natraemia of 135.5 mmol/l and a kalaemia of 3.72 mmol/l. Renal function is normal with urea at 0.2 g/l and creatinine at 5.2 mg/l.

A stool sample was sent to the Bacteriology Virology Laboratory for stool culture. Macroscopically, the stool was greenish mucous. Fresh microscopic examination revealed leukocytes at a rate of 5/microscopic field and rare presence of red blood cells. Examination after Gram staining showed a monomorphic flora essentially consisting of Gram negative bacillus. A culture at 37°C was made on Hektoen, Salmonella-Shigella and selenite broth. The selenite broth had been transplanted on a second Hektoen and SS after just 4H incubation.

After 18 to 24 hours of incubation, a monomorphic growth was observed on all culture dishes with no lactose fermentation. This suspect culture was identified with the compact Vitek 2 of the Biomerieux platform. A strain of *Shigella Spp* was identified by the latter. The antibiogram was performed using the agar diffusion method while respecting the recommendations of the committee of the antibiogram of the french society of microbiology. The interpretative reading of the antibiogram showed that the strain was a ESBL secreter. It was resistant to all beta-lactam antibiotics except cefoxitin and imipenem. It was also resistant to aminoglycosides (amikacin, gentamicin) and has decreased sensitivity to quinolones. The only antibiotics tested that were effective in vitro were carbapenems and ciprofloxacin (Table 1). The interpretive reading showed a higher activity of ceftazidime than cefotaxime (lower MIC ceftazidime than cefotaxime) thus pointing to a CTX-M ESBL.

**Table 1 : Antibiogram results**

Antibiotics	Résultats
Ampicillin	Résistant
Ticarcillin	Résistant
Amoxicillin/Clavulanic acid	Résistant
Cephalotin	Résistant
Cefotaxime	Résistant
Cefoxitin	Susceptible
Ertapenem	Susceptible
Imipenem	Susceptible
Amikacine	Résistant
Gentamicine	Résistant
Tobramycine	Résistant
Nalidixic acid	Résistant
Ciprofloxacin	Susceptible
Ofloxacin	Résistant

Thus, the search for CTXM in groups 1 and 9 was performed by PCR (Table 2). PCR revealed the CTXM gene of group 1.

Genes	Primer sequences	size	Annealing temperature
blaCTXM1	F GGTAAAAAATCACTGCGTC	800	55°C
	R TTGGTGACGATTTTAGCCGC	800	

The patient was then put on ciprofloxacin and metronidazole. The evolution was favourable with a disappearance of the diarrhoea. The control coproculture carried out after treatment showed an absence of pathogenic germs.

## DISCUSSION

Diarrhea in childhood is very frequent (two episodes/year/children less of 5 years), rarely fatale (mostly mild) and not requiring additional exploration. But it can justify a hospitalization in case of dehydration (delay of care) or risk of dehydration (8).

Globally, acute gastrointestinal infections, including diarrhoea, are among the leading causes of morbidity and mortality in children, particularly in underdeveloped countries (9). Poor access to safe drinking water, inadequate sanitation, low literacy rates and unavailability of health facilities in remote areas are the main factors predisposing to diarrhoeal diseases in these countries (10, 11). It is mainly of viral origin (rotavirus ++++) and it has for main complication dehydration. Also in our case, the poor hygiene could be associated with *Shigella* spp infection (8).

Trisomy 21 is a predisposing factor to infections. This can be explained by the fact that this chromosomal abnormality leads to immunosuppression (5, 6).

In the case of this report, the general symptoms of bacillary dysentery, including abdominal discomfort, dehydration and passage of blood-stained stools containing mucus, helped us to make a rapid clinical diagnosis. The findings on leukocyte microscopy and the presence of numerous non-lactose-fermenting colonies on Hektoen culture medium led to the suspicion of *Shigella* spp-associated dysentery. Similar cases of *Shigella* spp-associated invagination have been reported from India (12) and the United States (13, 14).

This report represents a case of *Shigella* strain producing CTXM-type ESBL. *Shigella* is a germ that is naturally sensitive to beta-lactam antibiotics. Cases of ESBL-producing shigella have been described in several developing countries (15, 16, 17).

CTXMs are non-TEM non-SHV ESBLs. They were first described in Germany in strains of *E. coli*. These enzymes are characterized by their preferential activity for cefotaxime rather than ceftazidim (18). Shortly after being described, CTXM spread worldwide until it became predominant in enterobacteria (19). Some authors even report that these CTX-M genes are endemic in most European, Asian and South American countries, with high prevalence rates ranging from 30 to 90% for *E. coli* (20). CTXM-like ESBLs in shigelles have been reported in several studies (21, 22) in Asia. In Senegal, a

study conducted by the Pasteur Institute between 2001 and 2010 showed the presence of CTXM in strains of *Shigella flexneri*.

## CONCLUSION

The emergence of BLSE-secreting strains of *Shigella* spp. will limit the therapeutic options for acute dysentery. Resistance genes can be transferred to wild strains resulting in rapid spread. Barrier measures must be established to address this problem.

## RÉFÉRENCES

- <https://www.pasteur.fr/fr/centre-medical/fiches-maladies/shigellose> (consulted at May, 11<sup>th</sup> 2020)
- Kazi A, Hisyam Ismail CMK, Anthony AA, Chuah C, Leow CH, Lim BH, Leow CY.** (2020). Conception et évaluation d'un vaccin recombinant chimérique ciblant les anticorps codant pour les antigènes de la membrane externe de *Shigella flexneri*. *Infection, génétique et évolution*, 80, 104176. doi: 10.1016 / j.meegid.2020.104176
- Yang Q, Rasmussen SA, Friedman JM.** Mortality associated with Down's syndrome in the USA from 1983 to 1997: a population-based study. *Lancet* 2002; 359:1019–25.
- Canfield MA, Honein MA, Yuskiv N, Xing J, Mai CT, Collins JS.** National estimates and race/ethnic-specific variation of selected birth defects in the United States, 1990–2001. *Birth Defects Res A Clin Mol Teratol* 2006; 76:747–56.
- Turner S, Sloper P, Cunningham C, Knussen C.** Health problems in children with Down's syndrome. *Child Care Health Dev* 1990;16:83–97
- Burgio GR, Ugazio AG, Nespoli L, Marcioni AF, Bottelli AM, Pasquali F.** Derangements of immunoglobulin levels, phytohemagglutinin responsiveness and T and B cell markers in Down's syndrome at different ages. *Eur J Immunol* 1975; 5:600–3.
- Burgio GR, Lanzavecchia A, Maccario R, Vitiello A, Plebani A, Ugazio AG.** Immunodeficiency in Down's syndrome: T lymphocyte subset imbalance in trisomic children. *Clin Exp Immunol* 1978; 33:298–301
- Trieu TV, Pontual LD.** Conduite à tenir devant une diarrhée aiguë chez l'enfant. *La presse médicale* ; 2013, (42), 60-65. <https://doi.org/10.1016/j.lpm.2012.10.012>.
- Centers for Disease Control and Prevention** ; 2016 . <http://www.cdc.gov/shigella/general-information.html>
- Niyogi SK.** Shigellosis. *Journal of Microbiology* . 2005; 43 (2): 133-143.
- Sangeetha AV, Parija SC, Mandal J., Krishnamurthy S.** Profils cliniques et microbiologiques de la shigellose chez les enfants. *Journal of Health, Population and Nutrition* . 2014; 32 (4): 580-586.
- Sreenivasan S, Kali A, Pradeep J.** Infection à *Shigella flexneri* multirésistante simulant une invagination intestinale. *Journal of Laboratory Physicians* . 2016; 8 (1): 55-57. doi: 10.4103 / 0974-2727.176225.
- Nylund CM, Denson LA, Noel JM.** Entérite bactérienne comme facteur de risque pour l'invagination infantile: une étude de cohorte rétrospective. *Journal of Pediatrics* . 2010; 156 (5): 761–765. doi: 10.1016 / j.jpeds.2009.11.026.
- Lett DW, Marsh TD.** Shigellosis in a newborn. *American Journal of Perinatology*. 1993; 10 (1): 58–59. doi: 10.1055 / s-2007-994703.
- Ghosh S, Pazhani GP, Chowdhury G.** Genetic characteristics and changing antimicrobial resistance among *Shigella* spp. isolated from hospitalized diarrhoeal patients in Kolkata, India. *Journal of Medical Microbiology*. 2011;60(10):1460–1466. doi: 10.1099/jmm.0.032920-0.
- Sattar AS, Abbasi SA, Usman J, Faqir F, Kaleem F, Hanif F.** Extended-spectrum  $\beta$ -lactamase production in *Shigella flexneri*. *Journal of the College of Physicians and Surgeons Pakistan*. 2010;20(11):768–769.
- Acikgoz ZC, Gulay Z, Bicmen M, Gocer S, Gamberzade S.** CTX-M-3 extended-spectrum  $\beta$ -lactamase in a *Shigella sonnei* clinical isolate: first report from Turkey. *Scandinavian Journal of Infectious Diseases*. 2003;35(8):503–505. doi: 10.1080/00365540310013270.
- Poirel L, Naas T, Nordmann P.** Genetic support of extended-spectrum-lactamases. *Clin Microbiol Infect* 2008; 14:75–81.
- Decousser JW, Poirel L, Nordmann P.** Characterization of a chromosomally encoded extended-spectrum class A -lactamase from *Kluyvera cryocrescens*. *Antimicrob Agents Chemother* 2001; 45:3595–8.
- Livermore DM, Canton R, Gniadkowski M, Nordmann P, Rossolini GM, Arlet G, et al.** CTX-M: changing the face of ESBLs in Europe. *J Antimicrob Chemother* 2007; 59:165–74.
- Parajuli NP, Joshi G, Pardhe BD, Shakya J, Bhetwal A., Shakya S, Khanal, PR.** Shigellosis Caused by CTX-M Type ESBL Producing *Shigella flexneri* in Two Siblings of Rural Nepal: First Case Report from the Country. *Case Reports in Infectious Diseases* ; 2017, 1–5. doi: 10.1155 / 2017/1862320.
- Williams E, Lew TE, Fuller A, Spelman, DW, Jenney AW.** Un cas de cholécystite aiguë et de gastro-entérite à *Shigella sonnei* produisant des BLSE multi-résistants chez un voyageur de retour. *Journal of Travel Medicine* ; (2018) ; 25 (1). doi: 10.1093 / jtm / tay029.