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Original Article (Pages: 18147-18156)

Shigella Antibiotic Resistance in Pediatric Shigellosis Infection: A Retrospective Study in Hormozgan, Iran

Aida Razavi [1], Zahra Tavassoli [2], Marjan Tariverdi [3], Mohammad Tamaddondar [4], Ali Rahnama Sisakht [5], Azin Tavasoli [6], * Mohammad Satarzadeh [7]

[1] Student Research Committee, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

[2] Ghaemieh health care center, Mazandaran University of Medical Sciences, Sari, Iran.

[3] Assistant Professor of Pediatric Infectious Disease, Department of Pediatrics, School of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

[4] Assistant Professor of Internal Diseases Training Department,Department of Nephrology, Hormozgan University of Medical Sciences, Bandar-Abbas, Iran

[5] Student Research Committee, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

[6] Department of Neuroscience, University of California San Diego, California, United State America.

[7] Student Research Committee, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

Abstract

Background: Shigella is a gram-negative, facultative anaerobic, nonperforming, nonmotile and rod-shaped bacterium that causes mucoid bloody diarrhea, known as dysentery or shigellosis. This study aimed to determine the prevalence of Shigella species and the antibiotic resistance pattern of Shigella species isolated from children with acute diarrhea in Bandar Abbas Pediatric Hospital, south of Iran.

Method: This descriptive and retrospective study was conducted based on the patients' information in their checklists, including age, gender, Shigella culture results, Shigella species, cessation of fever, city of residence, duration of symptoms before hospitalization, antibiotic use in the previous two weeks, degree of fever at the time of hospitalization, vomiting, convulsions, dehydration, death, frequency of diarrhea, and loss of blood in feces.

Results: Out of 162 patients, 82 (50.62%) were females, and 80 (49.38%) were males. Cultures of 46 patients (28.39%) were infected with Shigella flexneri species, 6 patients (3.72%) with Shigella boydii species, and 56 patients (34.58%) with Shigella sonnei species. Tetracycline had the highest rate of resistance (88.8%), and ciprofloxacin had the lowest resistance (7.41%).

Conclusion: The pattern of common Shigella species has changed from S. flexneri to S. sonnei in recent years. The pattern of antibiotic resistance among these species is also changing; so regular investigation of the prevalence of different species and their drug resistance pattern is necessary to make a correct decision about the appropriate treatment.

Key Words: Antimicrobial resistance, Dysentery, Shigella flexneri, Shigella sonnei, Treatment.

* Please cite this article as: Razavi A, Tavassoli Z, Tariverdi M, Tamaddondar M, Rahnama Sisakht A, Tavasoli A, Satarzadeh M. Shigella Antibiotic Resistance in Pediatric Shigellosis Infection: A Retrospective Study in Hormozgan, Iran. Int J Pediatr 2023; 11 (08):18147-18156. DOI: **10.22038/ijp.2023.74074.5341**

Corresponding Author:

Mohammad Satarzadeh, Student Research Committee, Hormozgan University of Medical Sciences, Bandar Abbas, Iran. Email: m.satarzadeh78@gmail.com

Received date: jul.31,2023; Accepted date: Aug.23,2023

1- INTRODUCTION

Shigellosis, caused by the invasion of the bacteria Shigella, results in a syndrome generally known as bloody diarrhea (1). Shigellosis is caused by four different strains of S. sonnei, flexneri, boydii, and dysenteriae; and is recognized as the main pathogen responsible for childhood diarrhea worldwide, resulting in 1.1 million deaths per year. Unfortunately, 61% of these deaths are children under the age of 5 (2, 3). This can be attributed to unwarranted use and self-administration of antibiotics which can also pose challenges to current treatments.

Initially, sulfonamides, tetracycline, streptomycin and chloramphenicol were prescribed for the treatment of Shigella infections (4, 5). Next, ampicillin and cotrimoxazole were used as alternatives. Currently, ciprofloxacin is recommended as a common prescription for the treatment of Shigella diarrhea (6, 7). In Iran, azithromycin is the most commonly prescribed antibiotic for children (8). The misuse of antibiotics affects routine treatment. Since antibiotic treatment plays an important role in reducing the prevalence and mortality rates of bacterial infections, preventing further complications, reducing diarrhea output and limiting stool disposal after the appearance of symptoms, the pattern of antibiotic resistance has been the focus of studies.

Recent studies have reported resistance to trimethoprim-sulfamethoxazole, tetracycline, chloramphenicol and streptomycin in Shigella infections (9, 10), but genetic and geographical differences have also been taken into account (11-13). Different strains prevalent in an area, along with genetic diversity and geographical differences, are considered in the resistance pattern of Shigella against routine antibiotic treatment, which can facilitate the management of treatment by recognizing these patterns in different regions. To address this issue, this study examined different strains of Shigella alongside antibiotic resistance in pediatrics with shigellosis in Hormozgan Province (a southern province in Iran). We aim to measure the pattern of antibiotic resistance among children and glance at the distribution of different Shigella strains in the pediatric population of Hormozgan province. Children from all parts of the province were examined for their antibiotic resistance patterns.

2- METHOD

A retrospective study was conducted in the city of Bandar Abbas, the center of Hormozgan Province in southern Iran. This study was at a single center and held in Bandar Abbas children's hospital. It was based on In vitro results of Shigella species resistance to antibiotics and retrospectively examined the files of patients referred to the emergency department.

2-1. Design and Population

We conducted our research by reviewing the records in Bandar Abbas children's hospital. A questionnaire was prepared by infectious disease specialists at the hospital, and based on this checklist, information from the medical records of children referred to the hospital between 2016 and 2022 were extracted.

All children aged one month to 15 years who were diagnosed with shigellosis during 2016-2022 and met the inclusion criteria were examined. The shigellosis was defined according to the International Classification of Diseases 11th (ICD-11) checklist, and the types of shigellosis were categorized based on this definition. Each case was checked with an infectious disease specialist and finally entered into the study. The exclusion criteria included insufficient information in the patient's file. Incomplete files were followed up after contacting the families of the individuals, and if there was no

cooperation in the next contact, they were ultimately removed from the study.

2-2. Data Collection

All necessary information, such as age, sex, Shigella culture results, Shigella type, fever cessation, city of residence, duration of symptoms before hospitalization, antibiotic use in the past two weeks, fever degree at admission, convulsive vomiting, dehydration, death, recurrent diarrhea, blood loss in stool, and extraction, were recorded in a checklist developed by the researcher under the supervision of pediatric infectious disease professors. We reviewed the files of the patients who were diagnosed with Shigella during 2016 to 2022; and the necessary information was extracted. If the demographic information was incomplete, we contacted the children's families. Hospital routine was accompanied by some limitations: From the time the samples were sent until the resistance and type of Shigella results were determined, ceftriaxone (50 milligrams\ kilograms, twice in 24 hours) was the treatment of choice for each child by injection. Also, azithromycin is only used for outpatients and laboratories have reported the resistance to the following antibiotics according to the requirements of the hospital.

a) Ampicillin

b) Tetracycline

c) Cotrimoxazol

d) Ceftriaxone

e) Gentamicin

f) Ciprofloxacin

g) Nalidixic acid

First, Patients' files were reviewed and demographic characteristics of the patients, including age and sex, were recorded. Then, based on the culture results, if the culture was positive and met the inclusion criteria (according to the relevant specialist's opinion) the case entered the study. The Shigella type was also mentioned. The antibiotic course was determined by reviewing the treatment period. Antibiotic resistance was also taken into account, if observed in the results.

Each child was given a stool exam container for sample collection and the sample containers were immediately sent to the laboratory. The laboratory introduced the cultivation method using a multiplex PCR panel. Shigella species resistance were set based on resistance standards by the Clinical and Laboratory Standards Institute (CSLI, https://clsi.org).

2-3. Data Analysis

All hospitalized children who were given a possible diagnosis of shigellosis in Bandar Abbas Children's Hospital, were included in this study. All samples were investigated by census. Statistical analyses were performed through descriptive methods including percentages of detection, species distribution, and resistance to tetracycline, cotrimoxazole, chloramphenicol, ampicillin, nalidixic acid, ceftriaxone, gentamicin, and ciprofloxacin (WHO recommended first- and second-line drugs). The percentage of species in each year was calculated from the total number of Shigella-positive isolates to assess the trend of species within the 5 years. For the strength of association (odds ratio) between Shigella-positive isolates and change in time (in a year), multiple logistic regression was performed where each of the species was an outcome variable and the period in years was treated as an exposure variable after adjusting for age and sex. The percentage of species was recorded in different graphs for different cities of Hormozgan province. In the graphical presentation, the equivalent of 5 years of antimicrobial resistance to each drug is plotted in 5-year periods for all Shigella species. Finally, the data were analyzed using SPSS software.

3- RESULTS

3-1. Population Outcomes

To determine antibiotic resistance and the prevalence of Shigella in Bandar Abbas, we conducted a study on 378 cases of symptomatic Shigella that caused diarrhea in children admitted to Bandar Abbas Children's Hospital over a period of 5 years. From among the 378 suspected cases, 162 were confirmed positive, with 82 (50.62%) being female and 80 (49.38%) being male. The study population consisted of 162 individuals, with 46 (28.39%) infected with Shigella flexneri, 6 (3.72%) with Shigella boydii, and 56 (34.57%) with Shigella sonnei based on culture results. In addition, 54 individuals (33.33%) tested positive for Shigella, but the species were not identified by the laboratory (**Table 1**).

Table-1: Demographic information including age and gender of the patients

Parameter		Number	Percentage
Age	≤1years old	42	6.1
	1-10 years old	111	81.6
	11-15 years old	42	12.3
gender	male	14	50.62
	female	12	66.5

3-2. Shigelosis History

From among the 162 individuals studied, 73 (45%) sought hospitalization and were admitted one day after the onset of symptoms, with 24 (14%) seeking medical attention during the initial hours of symptom onset. Additionally, 43 individuals (26%) had passed more than two days since their first symptoms, while the remaining individuals had passed more than two days since their first symptoms. 137 (84%) had a fever, while 25 (15%) did not (**Table 2**).

Among those admitted to the hospital, 20 (12%) had a temperature of 39 degrees Celsius at the time of admission, while 106 (65%) had a temperature ranging from 37.5 to 38 Celsius degrees. Fever was observed in three cases of boydii, 41 cases of flexneri, 42 cases of sonnei, and 51 cases of unknown origins (**Table 3**).

Table-2: Time interval between the parents' observance of the symptoms (fever, watery diarrhea and lethargy) and the patients' being visited by the emergency department of Bandar Abbas Children's Hospital

Parameter		Number	Percent
Duration of symptoms before hospitalization (days)	Less than 1	24	14.82
	1	73	45.06
	2	43	26.55
	3	11	6.79
	4	7	4.32
	5	4	2.46

Table-3: first temperature assessed in triage, before any treatment

Parameter		Number	Percent
Fever at the time of admission (Celsius)	Less than 37.5	36	22.22
	37.5-38.9	106	65.43
	39 and more	20	12.35

3-3. Antibiotic History

A quarter of the studied population had taken antibiotics in the last two weeks. In general, a large part of the population did not report the use of antibiotics in the last two weeks before the definitive diagnosis. Self-administration of antibiotics in the last two weeks finally showed resistance to antibiotics, with the highest statistics related to tetracycline. The highest resistance of Shigella bacteria isolated from the studied individuals was observed against tetracycline antibiotics in 144 individuals (88.8%). The lowest resistance was observed against the antibiotic ciprofloxacin in 12 individuals (7.4%). Considering that it is one of the common Shigella drugs in Iran, it seems to have continued its success in Asia. Apart from gentamicin, it can be said that other antibiotics that inhibit protein synthesis have the highest resistance statistics (tetracycline, chloramphenicol). **Table 4** shows the distribution of antibiotic resistance.

Table-4: Distribution of Shigella types and records of antibiotic use according to parents' declarations

Shigella Species		Number	Percentage
Flexneri		46	28.39
Boydii		6	3.72
Sonnei		56	34.78
Unknown		54	33.33
People who took antibiotic during 2 weeks ago	Yes	45	27.78
	No	117	72.22
* Antibiotic	Ampicillin	84	51.58
	Tetracycline	144	88.8
	Cotrimoxazol	105	64.81
	Ceftriaxone	26	16.05
	Gentamicin	21	12.96
	Ciprofloxacin	12	7.41
	Nalidixic acid	52	25.92
	Chloramphenicol	104	64.2

* The third part shows antibiotics that have been used during the treatment and children have shown resistance to them.

4- DISCUSSION

Abusing antibiotics can increase antibiotic resistance. Drug resistance in Shigella spp. can result from many mechanisms, such as a decrease in cellular permeability, extrusion of drugs by active efflux pumps, and overexpression of drug-modifying and inactivating enzymes or target modification by mutation (14, 15). Most antibiotics used in the treatment of

Shigella infection should be able to penetrate the cell membrane to reach intracellular accumulation and target sites (16, 17). Our results revealed that children who showed resistance to ampicillin and ceftriaxone were less than those who showed tetracycline resistance. Contrary to this finding, Rahbar observed that most strains were resistant to ampicillin and trimethoprim-sulfamethoxazole (88.5% and 98%, respectively), while resistance rates to chloramphenicol and ciprofloxacin, and were respectively 2.5% and 1%, in his study (18). Quinolone antibacterial agents, such as nalidixic acid, ofloxacin, and ciprofloxacin, interfere with DNA replication by inhibiting DNA topoisomerase IV and gyrase (19). Ciprofloxacin showed the lowest resistance statistics; perhaps it can be counted on to destroy the small subunit of the Shigella ribosome. Nalidixic acid did not show high rates either. Ayazi in Qazvin and Kurdi Darian in Isfahan also reported the prevalence of Shigella resistant to nalidixic acid as 2% and 4%, respectively (20, 21). In general, inhibiting DNA topoisomerase IV and gyrase can be considered a treatment path with low antibiotic resistance. Irregular use of antibiotics causes antibiotic resistance in bacteria, which makes the treatment of this infection long and complicated. To treat patients with acute Shigella infection, antibiotic therapy is the strategy of choice, which can reduce the symptoms and the number of disease vectors and prevent the spread of infection. Multidrug-Resistant Bacteria (MDR) are another important aspect, especially while resistance to the third generation of fluoroquinolones and cephalosporins and recently azithromycin is increasing over time (22, 23).

Irregular use of antibiotics causes antibiotic resistance in bacteria, which makes the treatment of this infection long and complicated. Beta-lactams, quinolones and macrolides are the first line of antibiotics (24), but currently, second-generation fluoroquinolones (ciprofloxacin) are recommended as the first choice for dysentery patients resistant to third-generation cephalosporins and nalidixic acid (25). In a study conducted by Majalan in Tehran on antibiotic resistance in different species of Shigella, the highest antibiotic resistance was observed compared to tetracycline, ampicillin and chloramphenicol antibiotics (26). In the study conducted by Hosseinpour, the highest antibiotic resistance against ampicillin was reported as 89.6%. In another study, most of the strains were resistant to ampicillin and trimethoprim-sulfamethoxazole (88.5% and 98%, respectively) (27), while resistance to chloramphenicol and ciprofloxacin was observed to be 2.5% and 1%, respectively. According to the results obtained from the above-mentioned studies and comparing them with the results we obtained from the antibiogram of the strains under investigation, it seems that the resistance of Shigella strains to antibiotics is increasing. Therefore, the use of antibiotics such as ampicillin, streptomycin, and sulfamethoxazole should practically be removed from the prescription of doctors, but ciprofloxacin and nalidixic acid can still be used in the treatment of shigellosis as antibiotics of choice. In a 10-year study on antibiotic resistance, it was shown that the resistance of Shigella strains is continuously increasing (28).

Shigella is a gram-negative, rod-shaped, immotile, and non-spore forming bacterium and a causative agent of acute diarrhea that may progress to bloody mucoid diarrhea (29, 30), also known as bacillary dysentery or shigellosis (31). Shigella sonnei causes a mild disease that may be limited to watery diarrhea, while Shigella flexneri and Shigella dysenteriae cause dysentery with bloody diarrhea (32). In our results, the sonnei species

accounted for most of the infected, so the share of the boydii species was the lowest. Flexneri, however, was not much different from the other two species, but the differences led to the situation that almost a third of the population was infected with an unknown species. The prevalence pattern of Shigella species is different between developing countries and undeveloped countries. Our results are similar to those of developing countries, and mostly sonnei strain is seen. In studies conducted in Iran, in Tehran, the most common species of Shagilla is S. sonnei (33), but in the southern and tropical regions, more species of S. Flexneri are seen (34).

In summary, the results of this study demonstrate that the pattern of antibiotic resistance among these species is also changing, so regular investigations on the prevalence of different species and their drug resistance pattern are necessary to make a correct decision about the appropriate treatment. In fact, increasing Shigella resistance to antibiotics is a serious warning that must be prevented by taking necessary measures. In Hormozgan province, flexneri and sonnei strains accounted for the largest population of affected children, which follows the pattern of developing and industrialized countries. Tetracycline was the most resistant antibiotic among the population, and tetracycline, cotrimoxazole, chloramphenicol, ampicillin, and nalidixic acid were among the antibiotics that were reported to be used by affected children. This pattern of antibiotic resistance in Hormozgan Province can be a turning point in the management of shigellosis and is also considered important in understanding the behavior of this bacterium due to geographical differences.

5- CONCLUSION

The prevalence of Shigella species has changed in Hormozgan. Abuse of antibiotics causes resistance in bacteria, which makes the treatment of this infection long and complicated. Knowledge of the pattern of antibiotic resistance in a specific geographical area is essential to properly prescribe antibiotic treatments with the aim of reducing the complications of the disease, the rate of bacterial elimination, and the treatment period. Since antibiotics are the treatment of choice to combat these pathogens, and due to the emergence of the antibiotic resistance Shigella strains, there is a need for regularly updated regional antibiotic sensitivity patterns of the pathogen to guide therapy.

6- ETHICAL CONSIDERATIONS

All procedures performed in this study involving human participants studies, were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors. The present study is part of a Doctor of Medicine (MD) dissertation (ethics code: IR.HUMS.REC.1400.350) in social work approved by the University of Hormozgan medical Science.

7- AVAILABILITY OF DATA

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

8- ACKNOWLEDGMENT

We are sincerely thankful to our counselors in the Clinical Research Development Center of Bandar Abbas Children’s Hospital.

9- REFERENCES

1. Respress E, Evener SL, Caruso E, Jacobson K, Bowen A, Kachur RE, Garcia-Williams AG, Wright ER. Preferences for Shigellosis-Related Health

Promotion Materials for Gay, Bisexual, and Other Men Who Have Sex With Men: Results From a Qualitative Assessment, Atlanta, GA. Sexually Transmitted Diseases. 2022; 49(4):304-9.

2. Williams P, Berkley J. Guidelines for the treatment of dysentery (shigellosis): a systematic review of the evidence. Pediatrics and international child health. 2018; 38 (sup1): S50–S65. Epub 2018/05/24. https://doi. org/10.1080/20469047.2017. 1409454 PMID: 29790845.

3. Behruznia P, Sadredinamin M, Hashemi A, Hajikhani B, Yousefi Nojookambari N, Behruznia M, Ghalavand Z. Decreased Susceptibility of Shigella Isolates to Azithromycin in Children in Tehran, Iran. Canadian Journal of Infectious Diseases and Medical Microbiology. 2022; 2022.

4. Zhang J, Jin H, Hu J, Yuan Z, Shi W, Yang X, Xu X, Meng J. Antimicrobial resistance of Shigella spp. from humans in Shanghai, China, 2004–2011. Diagnostic microbiology and infectious disease. 2014; 78(3):282-6.

5. Klontz KC, Singh N. Treatment of drug-resistant Shigella infections. Expert review of anti-infective therapy. 2015; 13(1):69-80.

6. Sah SK, Basnet S, Shrestha S, Ghale K, Tamang S, Mandal DK, Bahadur Pun S. Burden of Shigella spp and Vibrio spp, and their antibiotic sensitivity pattern in the patients with acute gastroenteritis in tertiary care hospital in Nepal. BMC Res Notes. 2019; 12(1):699.

7. Gebreegziabher G, Asrat D, Y WA, Hagos T. Isolation and Antimicrobial Susceptibility Profile of Shigella and Salmonella Species from Children with Acute Diarrhoea in Mekelle Hospital and Semen Health Center, Ethiopia. Ethiop J Health Sci. 2018; 28(2):197-206.

8. Farsiani H, Sasan MS. High rate of resistance to ceftriaxone and azithromycin among Shigella spp. isolates at three children's referral hospitals in Northeast Iran. Journal of Infection and Chemotherapy. 2020; 26(9):955-8.

9. O'Flanagan H, Siddiq M, Llewellyn C, Richardson D. Antimicrobial resistance in sexually transmitted Shigella in men who have sex with men: A systematic review. International journal of STD & AIDS. 2023; 34(6):374-84.

10. de Souza ZN, de Moura DF, de Almeida Campos LA, Córdula CR, Cavalcanti IMF. Antibiotic resistance profiles on pathogenic bacteria in the Brazilian environment. Archives of Microbiology. 2023; 205(5):185.

11. Pakbin B, Amani Z, Allahyari S, Mousavi S, Mahmoudi R, Brück WM, Peymani A. Genetic diversity and antibiotic resistance of Shigella spp. isolates from food products. Food Sci Nutr. 2021; 9(11):6362-71.

12. Vubil D, Balleste-Delpierre C, Mabunda R, Acácio S, Garrine M, Nhampossa T, Alonso P, Mandomando I, Vila J. Antibiotic resistance and molecular characterization of shigella isolates recovered from children aged less than 5 years in Manhiça, Southern Mozambique. Int J Antimicrob Agents. 2018; 51(6):881-7.

13. Khan SU, Aslam R, Ashraf M, Ali S, Saqib M, Khattak MA, Khattak US, Amanullah H, Wuryastuty H, Wasito R, Haryanto A, Ullah F, Ma M, Ali S. Prevalence of antibiotic resistance pattern in shigella isolates procured from pediatric patients at Faisalabad - Pakistan. Pak J Pharm Sci. 2022; 35(1):41-8.

14. Nuzhat S, Das R, Das S, Islam SB, Palit P, Haque MA, Chakraborty S, Hossain Khan S, Ahmed D, Alam B, Ahmed T, Jobayer Chisti M, A S G Faruque. Antimicrobial resistance in shigellosis: A surveillance study among urban and rural children over 20 years in

Bangladesh. Plos one. 2022; 17(11):e0277574.

15. Bian F, Yao M, Fu H, Yuan G, Wu S, Sun Y. Resistance characteristics of CTX-M type Shigella flexneri in China. Bioscience Reports. 2019; 39(9).

16. Terfassa A, Jida M. Prevalence and antibiotics susceptibility pattern of Salmonella and Shigella species among diarrheal patients attending Nekemte Referral Hospital, Oromia, Ethiopia. International journal of microbiology. 2018; 2018.

17. Tribble DR. Antibiotic therapy for acute watery diarrhea and dysentery. Military medicine. 2017; 182(suppl_2):17-25.

18. Rahbar M, Deldari M, Hajia M. Changing prevalence and antibiotic susceptibility patterns of different Shigella species in Tehran, Iran. The Internet J Microbiol. 2007; 3(2).

19. Chiou C-S, Izumiya H, Kawamura M, Liao Y-S, Su Y-S, Wu H-H, Chen W-C, Lo Y-C. The worldwide spread of ciprofloxacin-resistant Shigella sonnei among HIV-infected men who have sex with men, Taiwan. Clinical Microbiology and Infection. 2016; 22(4):383. e11-. e16.

20. Barari Skr, Ahmadpour Km. Prevalence of Shigella species and their antimicrobial resistance patterns at Amirkola children's hospital, North of Iran. 2007.

21. Pazhani GP, Niyogi SK, Singh AK, Sen B, Taneja N, Kundu M, Yamasaki S, Ramamurthy T. Molecular characterization of multidrug-resistant Shigella species isolated from epidemic and endemic cases of shigellosis in India. Journal of medical microbiology. 2008; 57(7):856-63.

22. Zayet S, Klopfenstein T, Pierron A, Royer P-Y, Toko L, Garnier P, Gendrin V. Shigella sonnei, an emerging multidrug-resistant sexually transmitted pathogen in Franche-Comté, France. Emerging Microbes & Infections. 2021; 10(1):1702-5.

23. Ma Q, Huang Y, Wang J, Xu X, Hawkey J, Yang C, Liang B, Hu X, Wu F, Yang X, Wang J, Li R, Li P, Xie J, Jia L, Wang L, Hao R, Tong Y, Holt KE, Qiu S, Sun Y, Song H. Multidrug-resistant Shigella sonnei carrying the plasmid-mediated mcr-1 gene in China. International journal of antimicrobial agents. 2018; 52(1):14-21.

24. Ap Seribelli A, Fraz MR, Medeiros MIC, Stehling EG, Falc JP. Molecular typing and occurrence of beta-lactam resistance genes of Shigella sonnei strains isolated from 1983 to 2014 in the S o Paulo state of Brazil. Microbiology and immunology. 2017; 61(12):547-53.

25. Gharpure R, Friedman CR, Fialkowski V, Collins JP, Strysko J, Marsh ZA, Chen JC, Meservey EH, Adediran AA, Schroeder MN, Wadhwa A, Fullerton KE, Watkins LF. Azithromycin and ciprofloxacin treatment outcomes during an outbreak of multidrug-resistant Shigella sonnei infections in a retirement community—Vermont, 2018. Clinical Infectious Diseases. 2022; 74(3):455-60.

26. Avakh Majalan P, Hajizade A, Nazarian S, Pourmand MR, Amiri Siyavoshani K. Investigating the Prevalence of Shigella Species and Their Antibiotic Resistance Pattern in Children With Acute Diarrhea Referred to Selected Hospitals in Tehran, Iran. Journal of Applied Biotechnology Reports. 2018; 5(2):70-4.

27. Ranjbar R. soltandallal MM, Talebi M, Pourshafie MR. Increased isolation and characterization of Shigellasonnei obtained from hospitalized children in Tehran. Iran J Health Popul Nutr. 2008; 26(4):426-30.

28. Gu B, Xu T, Kang H, Xu Y, Liu G, Pan S, Qian H, Ma P. A 10-year surveillance of antimicrobial susceptibility patterns in Shigella sonnei isolates circulating in Jiangsu Province, China. Journal of global antimicrobial resistance. 2017; 10:29-34.

29. Kaur G, Sathyabama S, Arora A, Verma S, Mubin N, Agrewala JN, Mayilraj S. Genome sequencing, annotation and comparative genomic analysis of Shigella dysenteriae strain SD1D. Gut Pathog. 2014; 6:28.

30. Qiu L, Wang H, Wang X. Conversion mechanism of heptachlor by a novel bacterial strain. RSC Adv. 2018; 8(11):5828-39.

31. Ranjbar R, Farahani A. Shigella: antibiotic-resistance mechanisms and new horizons for treatment. Infection and drug resistance. 2019:3137-67.

32. Shogbesan O, Rettew A, Shaikh B, Abdulkareem A, Donato A. Shigella sonnei Bacteremia Presenting with Profound Hepatic Dysfunction. Case Rep Gastrointest Med. 2017; 2017:7293281.

33. Eftekhari N, Bakhshi B, Pourshafie MR, Zarbakhsh B, Rahbar M, Hajia M, Ghazvini K. Genetic diversity of Shigella spp. and their integron content. Foodborne pathogens and disease. 2013; 10(3):237-42.

34. Ghaemi EO, Aslani MM, Moradi AV, Dadgar T, Livani S, Mansourian AR, Bakhshande Nosrat S, Ahmadi AR. Epidemiology of Shigella-associated diarrhea in Gorgan, north of Iran. Saudi Journal of Gastroenterology. 2007; 13(3):129-32.