

<http://www.pjbs.org>

PJBS

ISSN 1028-8880

**Pakistan
Journal of Biological Sciences**

ANSI*net*

Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

Increasing Antimicrobial Resistance among *Shigella* Isolates in the Bushehr, Iran

¹O. Gharibi, ²S. Zangene, ²N. Mohammadi, ³K. Mirzaei, ¹A. Karimi, ¹A. Gharibi and ¹A. Khajehiean
¹Public Health Center, Bushehr Medical University of Science, Bushehr, Iran
²Laboratory of Fatemeh Zahra Hospital, Bushehr Medical University of Science, Bushehr, Iran
³Faculty of Medicine, Bushehr Medical University of Science, Bushehr, Iran

Abstract: Antibiotics are drugs used for treatment of infections caused by bacteria. Misuse and overuse of these drugs have contributed to phenomena known as antibiotic resistance. In this research, the antimicrobial resistance of the *Shigella* has been determined. This descriptive research analyzed registered laboratory data of patients referred to Fatemeh Zahra Hospital of the Bushehr, Iran. *Shigella* was isolated from their cultured sample from the year 2002-2008. In this study, the total of 121 registered *Shigella* collected from 2002-2008 were analyzed. There were 62 cases of *S. sonnei*, 46 cases of *S. flexneri*, eight cases of *S. boydii* and five cases of *S. dysenteriae* among them. Furthermore, two cases of *Shigella sonnei* were collected from the blood and the rest from the watery stools of the infected patients. The following is the resistance pattern of these organisms; to ciprofloxacin, 4.25%; ceftizoxime, 8.62%; nalidixic acid, 12.12%; co-trimoxazole, 86.13% and to tetracycline, 93.02%. Results of antibiogram showed that highest rate of drug resistance belongs to tetracycline and Co-trimoxazole and the lowest belongs to ciprofloxacin and ceftizoxime. One of the important issue for clinicians, now a day is drug resistance of microorganisms. This phenomenon is increasing due to some factors such as improper use of antibiotics and irrational prescribing. These factors lead to development of new drug resistant species.

Key words: Antimicrobial resistance, *Shigella*, tetracycline, co-trimoxazole, ciprofloxacin

INTRODUCTION

Shigella is one of the most important causes of bloody diarrhea in the developing and under developing countries. *Shigella* can cause gastrointestinal tract infections in all age groups, especially child and newborns (Erqou *et al.*, 2007). All serotypes of *Shigella* can cause infection out of the intestinal tract but it is rare. These infections such as bacteremia (Hawkins *et al.*, 2007; Dronda *et al.*, 1988), septicemia (Spiers, 1974), keratitis (Muytjens *et al.*, 2006), osteomyelitis (Kligler and Hoepflich, 1984), urinary tract infection (Anatoliotaki *et al.*, 2003) and perinephric abscess (Al-Soub *et al.*, 2005), were reported in literatures. Tetracycline was broadly used against *Shigella* for the treatment of related infections in human and animals. The first observed resistance to tetracycline was belonging to *S. dysenteriae* in 1953 (Chopra and Robert, 2001) and first resistance to sulfonamides was observed in Japan, Also resistance to ampicillin which was internationally used as drug of choice in the first decade of early 1980s was worldly increased and covered the Asia and Africa continents. co-trimoxazole was used for treatment of shigellosis but resistance to this antibiotic occurred middle of the 1980s (Niyogi, 2007). At present nalidixic

acid is used in endemic cases in developing countries as a first drug of choice in the treatment of infant shigellosis, but newly there is some report about the resistance to this medicine from different parts of the world and all species of *Shigella* are no longer sensitive to this drug. Results of the researchers from all over the world shows resistant to antibiotics are widely increased. Therefore, conducting research about this matter is seen to be important. This study aimed to determine the resistance pattern of *Shigella* sp. isolates collected from Fatemeh Zahra Hospital of Bushehr, Iran from 2002-2008.

MATERIALS AND METHODS

This research was conducted in the Fatemeh Zahra Hospital of Bushehr, Iran in the period of 2002-2008. All the cases of isolates of *Shigella* was studied without considering the age of patients whom the sample was collected. Stool samples of the patients were collected in the closed plastic container and was sent to microbiological laboratory for examination. Stool samples were cultured in the xylose-lysine-deoxycholate agar (XLD) and were incubated during 24 h in 37°C. The colorless (non-fermentation) colonies were chosen for identifying of enteropathogenic bacteria such as *Shigella*

sp. Some special tests for distinguishing *Shigella* sp. from other enteric pathogens was conducted as follows: gram negative rods, non motile, non lactose ferment, oxidase, lysine decarboxylase, Simmon's citrate, Voges Proust, urease were negative, mannitol and sucrose fermentation, ONPG test, ornithine decarboxylase test and indole were variable positive and Triple Sugar Iron Agar were alkaline/acid with no production of Hydrogen Sulfur and finally the identified *Shigella* sp. using special *Shigella* antiserum was confirmed and their types was identified (Gharibi *et al.*, 2010). It was antibiogramed by Kirby-bauer disk diffusion method and using Mueller-Hinton medium. For sensitivity test, the following disc was used 5 µg ciprofloxacin, 30 µg nalidixic acid, 30 µg ceftizoxime, 23.75 µg co-trimoxazole and 30 µg tetracycline.

RESULTS

In this research, the number of 121 samples of *Shigella* collected from the year 2002-2008 was studied. The total number of 62 cases were *Shigella sonnei*, 46 were *S. flexneri*, 8 were *S. boydii* and 5 were

S. dysenteriae. Furthermore, two cases of *Shigella sonnei* were from blood and the rest from stool.

The resistance pattern of the organisms was determined using five antibiotics such as ciprofloxacin, nalidixic acid, ceftizoxime, co-trimoxazole and tetracycline (Table 1). Results of the antibiogram isolates of *Shigella* showed most resistance rate is belong to Tetracycline with 93.2% and co-trimoxazole 86.13% and the lowest is belong to Ciprofloxacin with 4.25% and Ceftizoxime, 8.62% and Nalidixic acid, 12.12% (Table 1-3).

DISCUSSION

High rate of resistance of *Shigella* sp. to tetracycline and co-trimoxazole in the period of 2002-2008 shows low efficacy of these drugs against these organisms and improper use of these drugs by patients and irrational prescribing of clinicians for treatment of different infectious diseases such as diarrhea (Table 1). Resistance of *Shigella* sp. to ciprofloxacin and ceftizoxime was not observed in year 2003 while during the period of three-year resistance to ciprofloxacin and ceftizoxime reached to 11.5 and 13.5 %, respectively. Ciprofloxacin is the drug of choice in Western countries (Haukka and Siitonen, 2008) but resistance to it were increased worldwide (Wong *et al.*, 2010; Folster *et al.*, 2011; Wilson *et al.*, 2006). Nalidixic acid is the drug of choice for the treatment of shigellosis in the developing countries. Nalidixic acid is the drug for the treatment of shigellosis in the children and its resistance is increasing. Resistance rate of 7.8% in 2003 and 30% in 2007 to this antibiotic is considerable. Among the isolated species of *Shigella*, *S. sonnei* and secondly *S. flexneri* have the highest rate of prevalence but antibacterial resistance of *S. flexneri* was more than *S. sonnei* (Table 1).

The results of research in different cities of Iran and other countries as well shows resistance of *Shigella* sp. to these antibiotics conform to the results of this study. For instance, the results of a study conducted in Tehran, Iran in 2003-2005 the resistance of these bacteria to co-trimoxazole was 98% and to nalidixic acid 11.5% (Rahbar *et al.*, 2007). In other studies done in Shiraz, Iran in 2003, the rate of resistance of these organisms to co-trimoxazole was reported 90.2% and to nalidixic acid 9.8% but all species were sensitive to ciprofloxacin (Farshad *et al.*, 2006). In addition, in a study conducted in Nepal in 2002-2004, rate of resistance of *Shigella* sp. reported as follows: to tetracycline, 74.4%; to co-trimoxazole, 80.7%; to nalidixic acid, 31.3% and to ciprofloxacin, 2.4% (Wilson *et al.*, 2006). In another study has done in Ethiopia between 2001-2005, the rate of resistance to tetracycline, co-trimoxazole and

Table 1: Sensitivity pattern of isolated *Shigella* collected from patients of Fatemeh Zahra Hospital from 2002-2008

Antimicrobials	<i>Shigella</i> sp.				Total
	<i>sonnei</i>	<i>flexneri</i>	2003	2007	
Ciprofloxacin	3.8	7.6	0.0	11.5	4.25
Ceftizoxime	9.6	16.6	0.0	13.6	8.62
Nalidixic acid	6.8	17.2	7.8	30.0	12.12
Co-trimoxazole	87.2	89.6	82.0	91.0	86.13
Tetracycline	83.3	100.0	95.0	93.0	93.02

Table 2: Sensitivity pattern of isolated *Shigella flexneri* collected from patients of Fatemeh Zahra Hospital from 2002-2008

Antimicrobials	<i>Shigella flexneri</i>			
	Resistant		Sensitive	
	No.	%	No.	%
Tetracycline	22	100.0	0	0.0
Co-trimoxazole	26	89.6	2	6.8
Ciprofloxacin	2	7.6	23	88.4
Ceftizoxime	3	16.6	14	77.7
Nalidixic acid	5	17.2	22	75.8

Table 3: Sensitivity pattern of isolated *Shigella sonnei* collected from patients of Fatemeh Zahra Hospital from 2002-2008

Antimicrobials	<i>Shigella sonnei</i>			
	Resistant		Sensitive	
	No.	%	No.	%
Tetracycline	15	83.3	3	16.6
Co-trimoxazol	41	87.2	5	10.6
Ciprofloxacin	2	3.8	48	92.3
Ceftizoxime	3	9.6	32	90.3
Nalidixic acid	3	6.8	15	72.7

ciprofloxacin were reported 86, 73.4 and 8.9%, respectively (Yismaw *et al.*, 2008). Also in Phnom Pen Hospital of Cambodia all the *Shigella* isolates were resistant to co-trimoxazole (Meng *et al.*, 2011). In a study in Dares Salam, Tanzania between 2005-2006, the rate of resistance of *Shigella* sp. to tetracycline and co-trimoxazole was 100 and 93.3%, respectively (Moyo *et al.*, 2011).

Furthermore most important matter is propagation of new strains of the *Shigella* sp. which are resistant to several antibiotics which make the treatment for bacteremia and septicemia more difficult.

Recently, many of the isolated *Shigella* are resistant to several drugs such as sulfonamides, tetracycline and co-trimoxazole (Rahman *et al.*, 2007; Vrints *et al.*, 2009; Hosseini *et al.*, 2007) and there is low resistance to the new drugs of choice such as nalidixic acid and ciprofloxacin. Stopping self medication and irrational uses of antibiotics prevents propagation of recent resistant species; also multiple antibiotic therapy to eradicate the organism is recommended.

CONCLUSION

Antibiotic resistance is one of the most important issues which are increasing very fast. High resistance rate of *Shigella* sp. to antibiotics such as co-trimoxazole and tetracycline makes the treatments so hard. Nalidixic acid is the drug of choice for the treatment of dysentery caused by bacilli in the underdeveloped countries that its rate of resistance is increasing too and for improper treatment it will be increased with higher rate in such a way that its treatment in near future will be more difficult.

REFERENCES

- Al-Soub, H., M. Al-Maslmani, J. Al-Khuwaiter, Y. El-Deeb and S.S. El-Shafie, 2005. *Shigella flexneri* Perinephric abscess and bacteremia. Ann. Saudi Med., 25: 419-421.
- Anatoliotaki, M., E. Galanakis, T. Tsekoura, A. Schinaki, S. Stefanaki and A. Tsilimigaki, 2003. Urinary tract infection caused by *Shigella sonnei*. Scand J. Infect. Dis., 35: 431-433.
- Chopra, I. and M. Robert, 2001. Tetracycline antibiotics: Mode of action, applications, molecular biology and epidemiology of bacterial resistance. Microbiol. Mol. Biol. Rev., 65: 232-260.
- Drona, F., F. Parras, J.L. Martinez and F. Baquero, 1988. *Shigella sonnei* bacteremia in an elderly diabetic patient. Eur. J. Clin. Microbiol. Infect. Dis., 7: 404-405.
- Erqou, S.A., E. Teferra, A. Mulu and A. Kassu, 2007. A case of shigellosis with intractable septic shock and convulsions. Jpn. J. Infect. Dis., 60: 314-316.
- Farshad, S., R. Sheikhi, A. Japoni, E. Basiri and A. Alborzi, 2006. Characterization of *Shigella* strains in Iran by plasmid profile analysis and PCR amplification of *ipa* genes. J. Clin. Microbiol., 44: 2879-2883.
- Folster, J.P., G. Pecic, A. Bowen, R. Rickert, A. Carattoli and J.M. Whichard, 2011. Decreased susceptibility to ciprofloxacin among *Shigella* isolates in the United States, 2006 to 2009. Antimicrob. Agents Chemother., 55: 1758-1760.
- Gharibi, O., K. Mirzaei, A. Karimi and H. Darabi, 2010. Mixed infections of *Vibrio cholerae* O₁ Ogawa EL Tor with *Shigella dysenteriae*. Pak. J. Biol. Sci., 13: 1110-1112.
- Haukka, K and A. Siitonen, 2008. Emerging resistance to newer antimicrobial agents among *Shigella* isolated from Finnish foreign travellers. Epidemiol. Infect., 136: 476-482.
- Hawkins, C., B. Taiwo, M. Bolon, K. Julka, A. Adewole and V. Stosor, 2007. *Shigella sonnei* Bacteremia: Two adult cases and review of the literature. Scand J. Infect. Dis., 39: 170-173.
- Hosseini, M.J., R. Ranjbar, H. Ghasemi and H.R. Jalalian, 2007. The prevalence and antibiotic resistance of *Shigella* sp. recovered from patients admitted to Bouali hospital, Tehran, Iran During 1999-2001. Pak. J. Biol. Sci., 10: 2778-2780.
- Kligler, R.M. and P.D. Hoepflich, 1984. Shigellemia. West J. Med., 141: 375-378.
- Meng, C.Y., B.L. Smith, L. Bodhidatta, S.A. Richard and K. Vansith *et al.*, 2011. Etiology of diarrhea in young children and patterns of antibiotic resistance in Cambodia. Pediatr. Infect. Dis. J., 30: 331-335.
- Moyo, S.J., N. Gro, M.I. Matee, J Kitundu and H. Mymel *et al.*, 2011. Age specific aetiological agents of diarrhoea in hospitalized children aged less than five years in Dares Salaam, Tanzania. BMC Pediatr., 23: 11-19.
- Muytjens, H.L., C.A. Eggink, F.C. Dijkman, J.M. Bakkens and W.J. Melchers, 2006. Keratitis due to *Shigella flexneri*. J. Clin. Microbiol., 44: 2291-2294.
- Niyogi, S.K., 2007. Increasing antimicrobial resistance: An emerging problem in the treatment of shigellosis. Clin. Microbiol. Infect., 13: 1141-1143.
- Rahbar, M., M. Deldari and M. Hajia, 2007. Changing prevalence and antibiotic susceptibility patterns of different *Shigella* species in Tehran, Iran. Internet J. Microbiol., 3.

- Rahman, M., S. Shoma, H. Rashid, S. El Arifeen and A.H. Baqui *et al.*, 2007. Increasing spectrum in antimicrobial resistance of *Shigella* isolates in Bangladesh: Resistance to azithromycin and ceftriaxone and decreased susceptibility to ciprofloxacin. *J. Health Popul. Nutr.*, 25: 158-167.
- Spiers, A.S., 1974. *Shigella sonnei* septicaemia in a child with acute monocytic leukaemia. *Br. Med. J.*, 1: 456-456.
- Vrints, M., E. Mairiaux, E.V. Meerverne, J.M. Collard and S. Bertrand, 2009. Surveillance of antibiotic susceptibility patterns among *Shigella sonnei* strains isolated in Belgium during the 18-year period 1990 to 2007. *J. Clin. Microbiol.*, 47: 1379-1385.
- Wilson, G., J.M. Easow, C. Mukhopadhyay and P.G. Shivananda, 2006. Isolation and antimicrobial susceptibility of *Shigella* from patients with acute gastroenteritis in western Nepal. *Indian J. Med. Res.*, 123: 145-150.
- Wong, M.R., V. Reddy, H. Hanson, K.M. Johnson and B. Tsoi *et al.*, 2010. Antimicrobial resistance trends of *Shigella* serotypes in New York City, 2006-2009. *Microb. Drug Resist.*, 16: 155-161.
- Yismaw, G., C. Negeri and A. Kassu, 2008. A five-year antimicrobial resistance pattern of *Shigella* isolated from stools in the Gondar University hospital, northwest Ethiopia. *Trop. Doct.*, 38: 43-45.