Distribution of Serogroup and Antibiotic Resistance Patterns of *Shigella* Species in Iran, 1984-2018: A systematic Review

İran'da Shigella Türlerinin Serogrup ve Antibiyotik Direnç Modellerinin Dağılımı, 1984-2018: Sistematik bir derleme

Hamid Reza Nouri [1], Majid Validi[2], Jalal Mardaneh[3], Korosh Ashrafi –Dehkordi [4]

[1] Cellular and Molecular Biology Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran.
[2] Department of Medical Laboratory Sciences, School of Allied Medical Sciences, Shahrekord University of Medical Sciences, Shahrekord, Iran
[3] Department of Microbiology, School of Medicine, and Infectious Diseases Research Center, Gonabad University of Medical Sciences, Gonabad, Iran.
[4] Department of Molecular Medicine, School of Advanced Technologies, Shahrekord University of Medical Sciences, Shahrekord, Iran.

ABSTRACT

Background: Shigellosis is recognized as a global concern by the WHO. *Shigella* genus includes 4 species of *Shigella dysenteria*e, *Shigella flexneri, Shigella boydii* and *Shigella sonnei*. Geographic distribution and antimicrobial susceptibility patterns of *Shigella* species are different.
Methods: We searched published studies in Science Direct, PubMed, PubMed Central (PMC), Scopus, Google Scholar, and ISI Web of Science, Medlib, Magiran, Iranian Scientific Information Database (SID) and 'IranMedex between 1984 and 2018.
Results: Many studies in Iran and elsewhere in the world emphasize the emergence of *Shigella* resistant species. Most of them have shown high resistance to TMP/STX, tetracycline, ampicillin and streptomycin , and some have resistance to antibiotics such as ciprofloxacin, azithromycin, and tetracyclines have reported.
Conclusions: The frequency of *Shigella* species is very different in different countries. The distribution and prevalence of *Shigella* species in different countries may depend on the level of economic development, age, and environmental factors.

Keywords: *Shigella* species; Serogroup; Antibiotic resistance; Iran

Received: 08.13.2021 **Accepted**: 05.27.2022

ÖZET

Arka plan: Şigelloz, WHO tarafından küresel bir endişe kaynağı olarak kabul edilmektedir. Shigella cinsi 4 tür Shigella dysenteriae, Shigella flexneri, Shigella boydii ve Shigella sonnei içerir. Shigella türlerinin coğrafi dağılımı ve antimikrobiyal duyarlılık kalıpları farklıdır.
Yöntemler: Bu araştırmada, 1984 ve 2018 yılları arasında Science Direct, PubMed, PubMed Central (PMC), Scopus, Google Scholar ve ISI Web of Science, Medlib, Magiran, Iran Scientific Information Database (SID) ve 'IranMedex'te yayınlanmış çalışmaları araştırdık.
Sonuçlar: İran'da ve dünyanın başka yerlerinde yapılan birçok çalışma Shigella'ya dirençli türlerin ortaya çıktığını vurgulamaktadır. Çoğunun TMP/STX, tetrasiklin, ampisilin ve streptomisine yüksek direnç gösterdiği ve bazılarının siprofloksasin, azitromisin ve tetrasiklinler gibi antibiyotiklere direnç gösterdiği bildirilmiştir.
Sonuç: Shigella türlerinin sıklığı farklı ülkelerde çok farklıdır. Shigella türlerinin farklı ülkelerdeki dağılımı ve yaygınlığı, ekonomik gelişme düzeyine, yaşa ve çevresel faktörlere bağlı olabilir.

Anahtar Sözcükler: Shigella türleri; serogrup; Antibiyotik direnci; İran

Geliş Tarihi: 13.08.2021 **Kabul Tarihi:** 27.05.2022

ORCID IDs.H.R.N.0000-0001-6521-0875,M.V.0000-0001-8023-0620,J.M.0000-0001-9010-2518,K.A.D.0000-0001-7105-731X

Address for Correspondence / Yazışma Adresi: Majid Validi, PhD, Department of Medical Laboratory Sciences, School of Allied Medical Sciences, Shahrekord University of Medical Sciences, Shahrekord, Iran. P.O. Box 8813833435, Telephone: +983833346720. Fax: +9833349113. E-mail: validi543@gmail.com

doi:http://dx.doi.org/10.12996/gmj.2022.69

INTRODUCTION

Shigella is a gram-negative, spores-free, non-motile, non-motile, non-capsular, intracellular pathogen, belonging to the *Enterobacteriaceae* family. The bacterium was introduced in the 1890s as an etiologic agent of the dysentery of bacillary shigellosis. The bacterium was discovered about 100 years ago by Japanese microbiologist Shiga. *Shigella* was introduced as a gender in the 1950s. *Shigella* genus includes 4 species of *Shigella dysenteriae*, *Shigella flexneri, Shigella boydii* and *Shigella sonnei*. These four species are also known as group A, B, C, and D, respectively. Group A has 15 serotypes, Group B has 8 serotypes, Group C has 19 serotypes and group D has 1 serotype. These serotypes differ in terms of biochemical and antigenic properties. Human is the natural reservoir of this bacterium.

Geographic distribution and antimicrobial susceptibility patterns of *Shigella* species are different. Previous studies have shown that patterns of antimicrobial resistance of *Shigella* species vary between countries and even within a country. Shigellosis transmission usually occurs through contaminated food and water, or person-to-person contact. Since the infectivity dose (ID) of this bacterium is low, only 10 dysentery bacilli may cause clinical illness, while 100-200 bacilli are required for *S. Sonnei* or *S. flexneri* infection. *Shigella*, as an important pathogen in the *Enterobacteriaceae* family, provides suppressing the host immune system, hygiene conditions and colonization in the intestine.

In 2013, the average annual shigellosis in the United States (US) was 482 per 100,000 people. Most of the reported cases were in the summer months. In recent studies of the Centers for Disease Control and Prevention (CDC), approximately 78% of all *Shigella* isolates belonged to *S.sonnei* and the rest were related to *S. flexneri* and *S. boydii*.

Eighteen percent of *Shigella* infections in the US are related to *S. flexneri*. *S. dysenteriae* is rarely found in the US. A total of 50 cases of 7746 *Shigella* infections were reported in 2012. The highest incidence of *Shigella* infection was in Borducca (13.2%), New Jersey (7.6%) and Minnesota (7.1%). The highest prevalence was in the case of shigellosis (27.77 cases) in 100,000 people among children less than age of 5 years.

An estimated 450,000 cases of Shigellosis occur annually in the United States, according to the CDC estimate. In 2012, the overall incidence of *Shigella* infection was 2.5 cases per 100,000 populations. In the past 10 years (between 2002 and 2011), the majority of *Shigella* infections was reported in January-March. The latest outbreak reported in February 2010 was due to *Shigella sonnei*.

Globally, the prevalence of shigellosis is estimated at approximately 164.7 million cases a year, of which 163.2 million were from developing countries and 1.1 million were dead. About 60% of all episodes and 61% of all deaths due to shigellosis in the children less than age of 5 years. Shigellosis incidence in developing countries may be 20 times higher than in developed countries. Although the relative importance of Shigella serotypes is not known, it is estimated that about 30% of these infections are due to *S. dysenteriae*.

The prevalence of mortality from *S. dysenteriae* infections may reach 30%. Malnutrition patients are at risk of death.Although the mortality rate from shigellosis in developed countries is low compared to developing countries, the infection due to *S. dysenteriae* is associated with a significant mortality rate in the developing world. The overall mortality rate of *Shigella* infection in developed countries is less than 1%. Although the mortality rate due to *S. dysenteriae* infections in the Far East and the Middle East may range from 20 to 25 percent.

The mortality rate among *S. dysenteriae* type 1 patients that requiring hospital admission is 15%, which increases due to delay in treatment and improper antibiotic treatment. Infants, non-infant children, measles children, children with malnutrition and adults over 50 years of age are at increased risk of more severe disease and death.

According to a recent CDC report, 28% of cases of intestinal bacterial infections are related to *Shigella* infection. Considering that children less than 5 years of age account for 7% of all reported cases, this is indicative of the importance of treating *Shigella* infection in this population .*S. dysenteriae* serotype 1 is one of the mortality factors in the epidemic, *S. boydii* is limited to the Indian subcontinent, and *S. flexneri* and *S. sonnei* are common in developed and developing countries. *S. flexneri* is responsible for the development of endemic in the world.

S. flexneri is the most commonly isolated species in developing countries and is the most common cause of death. The prevalence of *S. flexneri*, *S. sonnei*, *S. boydii* and *S. dysenteriae* in developed countries was 16, 77, 2 and 1%, and in developing countries it was 60, 15, 6, and 6%, respectively (1).

METHODS

Data Extraction

A literature search was performed to identify published studies between 1984 and 2018. Published studies were identified using an initial search of the Science Direct, PubMed, PubMed Central (PMC), Scopus, Google Scholar, and ISI Web of Science. In addition to articles published in English, including Medlib, Magiran, Iranian Scientific Information Database (SID) and 'IranMedex' were searched as well for relevant articles.

RESULTS

In the study of Shahsavan et al in Tehran in 2012, out of the 70 isolates of *Shigella* spp, *S. sonnei* was dominant. In this study, the antibiotic susceptibility pattern showed a high prevalence of resistance to streptomycin, trimethoprim-sulfamethoxazole (TMP/STX), and tetracycline. All isolates were susceptible to quinolones, including norfluxacin, levofloxacin and ciprofloxacin. Most isolates were resistant to seven antibiotics and became known as multi-drug resistant (MDR) strains. The majority of isolates were (MDR). resistant rate to streptomycin, tetracycline and trimethoprim were 100, 96 and 98%, respectively (2).

In a study by Azam Fatahii et al. In 2012 in Isfahan, out of a total of 58 isolates suspected of being *Shigella, S. sonnei* was dominant. Antibiotic susceptibility pattern showed a high rate of resistance to cotrimoxazole (100%), ceftriaxone (88.9%), cefaxime (85.2%) and Azithromycin (70.4%) and the main resistance to nalidixic acid (29.6%), furazolidone (33.3%), ciprofloxacin (14.8%) and ofloxacin (25.9%). In this study, 88.3% of *S. sonnei* isolates and one *S. flexneri* isolates were resistant to three antibiotics and became known as MDR strains (3).

In Talebreza et al study., in 2013 in Tehran, out of 36 isolates of *Shigella*, *Shigella sonnei* were dominant. Antibiotic susceptibility showed that most of the isolates were resistant to amoxicillin (86.1%) and cotrimoxazole (83.3%), and all isolates were susceptible to ciprofloxacin and imipenem (4).

In the Ghavam et al study in 2013 in Tehran, out of the 507 *Shigella* isolates, *S. sonnei* was dominant. All of *Shigella* isolates were susceptible to cefotaxime (66.2%) and nalidixic acid (60.2%), while isolates were mainly co-trimoxazole (94.4%) and ampicillin (68.1%). The antibiotic susceptibility pattern of *Shigella sonnei* and *Shigella flexneri* species showed that *Shigella sonnei* was susceptible to cefotaxime (66.34%), nalidixic acid (9.64%) and ampicillin (52.4%) and resistant to cotrimoxazole (97.3%). *Shigella flexneri*. It was mainly susceptible to cefotaxime (61.9%), nalidixic acid (56.1%), and the highest resistance to ampicillin (96.75%) and co-trimoxazole (92.1%) (5).

In a study by Shahsavan et al. in Tehran in 2017, the detection of *tetA*, *tetB*, *tetC* and *tetD* genes by polymerase chain reaction (PCR) and real time PCR and efflux pump was investigated for tetracycline resistant *Shigella* isolates. All isolates were MDR and were resistant to three antibiotic classes. Resistance to tetracycline and doxycycline was reported in 96 and 94% of cases, respectively. All isolates were susceptible to levofloxacin and norfloxacin and were resistant to streptomycin. *tetA* and *tetB* were detected by PCR in 66 and 12% isolates and by real time PCR in 90% and 18% isolates, respectively. *tetC*, *tetD*, not detected in any isolate (6).

In Taghi Akhi et al., in 2015, in Tabriz the results of antibiotic susceptibility testing showed that 100% of isolates were ampicillin-resistant and 100% of isolates were sensitive to ceftazidime, cefepime (7).In a study by Jafari et al. in 2003 in Tehran, of the 50 *Shigella* isolates *S. sonnei* was dominant. *Shigella* isolates showed the highest resistance to tetracycline (95%) and trimethoprim sulfamethoxazole (91.7%), and more than 90% of *Shigella* isolates were sensitive to cefexim, ceftriaxone, cetfazidim, nalidixic acid, gentamicin, and ciprofloxacin (8).In the Eftekhari et al. a study in 2003 in Khorasan Razavi, *S. flexneri* isolates were dominant species. 45% of the isolates were the MDR. The highest levels of resistance were reported for TMP/STX (93.7%) and tetracycline (87.5%) (9).In Mirnejad et al., study in 2013, in Tehran, out of the 34 Shigella isolates, *S. flexneri* was dominant. All isolates were resistant to tetracycline, ampicillin, streptomycin and TMP/STX.

Ninety- four percent of *Shigella* isolates were sensitive to gentamicin and ceftazidime, 91% to ceftriaxone and ticaricillin and 88% to cephalothin (10).In Talebreza study and et al, in 2013 in Tehran, from 36 *shigella* species, *S. sonnei* was the dominant species. In this study, the highest resistance was to amoxicillin (86.1%) and cotrimoxazole (83.3%). None of the isolates were resistant to ciprofloxacin or imipenem (11).In Ranjbar et al., study in 2003 in Tehran, out of the 302 *Shigella* isolates, *S. sonnei* was dominant. In this study, more than 94% of *S. sonnei* isolates were resistant to co-trimoxazole and less than 6% resistant to nalidixic acid, ampicillin, chloramphenicol, cefixime, and kanamycin. None of these isolates were resistant to ceftizoxime, ceftazidime, gentamicin, ciprofloxacin, amikacin, furazolidone, cephalothin, cefotaxime, cephalexin, and nitrofurantoin (12).In the study of Katouli et al. in 1986, in Sanandaj and Tehran among the 59 isolates of Shigella, *S. sonnei* isolates were dominant . Thirteen (72%) isolates from Sanandaj and 33 (80%) isolates from Tehran were resistant to 1 or more antibiotics. Also, 9 (50%) strains from Sanandaj and 26 (63%) strains from Tehran were resistant to 3 or more antibiotics (13).In the Haghi Ashtiani et al study conducted in 2005 in Tehran, in 1329 *Shigella* isolates, resistance to antimicrobial agents increased over the years 2001-2005. Resistance to kanamycin, ceftazidime, nalidixic acid, and ciprofloxacin has increased, and the sensitivity to chloramphenicol , gentamicin and TMP/STX were stable from 1996 to 2005 (14).A Hosseini et al study in 1991 in Tehran, of the 90 isolates of *Shigella*, *S. sonnei* was dominant. The highest resistance was to ampicillin (97%), TMP/STX and tetracycline (81%). None of the isolates were resistant to ciprofloxacin and ceftriaxone (15).

In a study by MoezArdalan et al. In 2001 in Karaj, *S. flexneri* was the dominant species among 123 *Shigella* isolate. In this study, the most common resistance was observed in *Shigella* isolates with tetracycline (73.5%), TMP/STX (70.4%) and amoxicillin-clavulanic acid (50%). Also, 87.8% of isolates were MDR (16).In Farshad et al., In 2003, in Shiraz, *S. sonnei* was the dominant species among 82 *Shigella* isolate. multiple drug resistance was observed to nalidixic acid, co-trimoxazole, cephalothin in 1/21% isolates and multiple drug resistance to nalidixic acid, co-trimoxazole, amikacin in 3.65% isolates (17).In the study of Hosseini MJ, et al. in 2007, in Tehran, among all *Shigella* isolates, *S. flexneri* serotype 3a was a dominant species. In this study, the results of the antibiotic susceptibility pattern of isolates showed that isolates were susceptible to amikacin, ciprofloxacin, gentamicin, ceftizoxime, ceftriaxone, ceftazidime, cephalothin, tobramycin, chloramphenicol, nalidixic acid and kanamycin, and all isolates were resistant to tetracycline, ampicillin, TMP/STX, and streptomycin (18). In Ranjbar et al., in 2003, in Tehran out of 89 isolates of *Shigella*, *S. sonnei* was dominant. More than 90% of the *shigella sonnei* isolates were resistant to TMP/STX, tetracycline, and streptomycin. The most susceptible was observed to cephalothin, ticarcillin, cefotaxime ceftriaxone, amikacin, ceftazidime, kanamycin, and gentamicin. Most of the isolates had a MDR pattern (19) .In Alizadeh-Hesar et al., in 2012 in Tehran, out of the 70 isolates of *Shigella*, *S. flexneri* was the dominant species. 98.5% of the isolates were MDR and no resistance was observed to ciprofloxacin. In this study, the results of the antibiotic susceptibility pattern of isolates showed that streptomycin 98%, tetracycline (97.14%), tetracycline (94.3%), and resistance to minocycline (93%) were resistance., while less resistance to gentamicin (2.85%) and nalidixic acid (8.5%) were shown (20).In the study of Hosseini Nave et al. in 2013 in Kerman, among 56 isolates of *Shigella*, *S. flexneri* was the dominant species. The highest resistance was observed to ampicillin, TMP/STX and tetracycline (92.9%). Shigella isolates were resistant to third generation cephalosporins and susceptible to ciprofloxacin (21).In the study of Dibaj et al. in 2006 in Isfahan , among the 13 *Shigella* isolates, *S. sonnei* was dominant. The highest resistance was observed to amoxicillin-clavulanic acid (69.23%), chloramphenicol (53.84%), tetracycline (61.53%), and TMP/STX (76.92%) (22).A study in 2011 in Abadan by Jomezadeh et al., out of the 36 isolates of *Shigella*, *S. flexneri* was the dominant species. All *Shigella* isolates were sensitive to ciprofloxacin and ceftriaxone. Among isolates, 47.2% were resistant to two or more antibiotics, with multiple resistance to TMP/STX, ampicillin and tetracycline (23).In the study of Esmaeili Dooki et al. in 2009 *S. sonnei* had a higher resistance to antibiotics than other species in this study, the results of the antibiotic susceptibility pattern of isolates showed that *Shigella* in among the seven *Shigella* isolates, *S. sonnei* was dominant in Kerman. All bacteria isolated were resistant to erythromycin and cefixime and susceptible to amikacin and cefotaxime (24).In the study of Mamishi et al. in 2001 in Tehran, 322 *Shigella* isolates, *S. sonnei* isolates were dominant. The sensitivity of *Shigella* isolates to nalidixic acid was higher in 2001-2003 than in the years 2004-2006 (25).

In a study by Ranjbar et al. in Tehran in 2008, out of 322 *Shigella* isolates, *S. sonnei* was dominant. In this study, 31.5% of isolates were resistant to nalidixic acid (26).In Mahmoudi et al., study *in* 2013 in Tehran, among the 85 *Shigella* isolates, *S. sonnei* was dominant. In this study, the results of the antibiotic susceptibility pattern of isolates showed that the highest and lowest resistance was observed for TMP/STX and nalidixic acid, respectively. Except for *S. sonnei* and *S. flexneri* isolates, all isolates were resistant to ampicillin, and TMP/STX (27).In the study of Zahedi Bialvaeia et al., in 2012 in Tehran, 52 *Shigella* isolates were tested. 7.69% of isolates were MDR. 15.4% of isolates were positive-Extended Spectrum Beta Lactamases (ESBL) with the phenotypic method and the CTX-M gene was detected in 47.6% of resistant isolates (28).In the study of Mostafavi et al. in 2010 in Isfahan, out of the 44 *Shigella* isolates, *Shigella sonnei* was dominant. Ninety four and nine tenths of a percent and 43.8%, were sensitive to ciprofloxacin and cefotaxime, respectively, and sensitivity to ceftriaxone ampicillin, TMP/STX and cefixime was less than 30% (29).In a study by Barari Savadkoohi et al. In 2010 in Babol, among the 260 *Shigella* isolates, *S. flexneri* was a dominant species. In this study, the results of antibiotic susceptibility showed that most isolates were MDR (30).In the study of Tajbakhsh et al. in Tehran in 2008, out of the 44 *Shigella* isolates, *S. sonnei* was dominant. In all *Shigella* isolates, multidrug resistance was observed in at least to three antibiotic classes. Resistance was to apramycin, carbapenems (imipenem and meropenem), colistin, and florfenicol (31).In Qureishi et al., in 2003 in Zahedan, among the 147 *Shigella* isolates, *S. flexneri* was a dominant species. 57.9% of the *Shigella* species were resistant to more than 4 antibiotics. More than 90% of isolates were sensitive to cefixime, ceftriaxone, ceftazidime, nalidixic acid, gentamicin ciprofloxacin and ampicillin-sulbactam, and all isolates were sensitive to ciprofloxacin. Resistance to more than 4 antibiotics in 58% of *S. sonnei* isolates, resistance to six antibiotics in 16.6% of *S. flexneri* isolates, and resistance to six antibiotics in *S. boydii* isolates were observed. All *S. dysentery* isolates were resistant to tetracycline (32).In a study by Ranjbar et al. in 2003 in Tehran, among the 302 *Shigella* isolates, *S. sonnei* was the dominant species. In this study, resistance to the ceftizoxime, ceftazidime, gentamicin, ciprofloxacin, amikacin, furazolidin, cephalothin, cefotaxime, cephalexin and nitrofurantoin were not detected in any one. Only 6.2% of isolates were resistant to 3 or more antibiotics. More than 94% of isolates were resistant to co-trimoxazole (33).In a study by Ranjbar et al., in 2005, in Tehran, 83 isolates of *Shigella* were conducted. All strains were resistant to streptomycin, co-trimoxazole and tetracycline. None of these isolates were resistant to ceftriaxone, ceftizoxime, ceftazidime, ciprofloxacin, cephalothin, and cefotaxime (34).

In a study by Ranjbar et al. in 2008 in Tehran, 55 isolates of *Shigella* were conducted. 92.7% were sensitive to cephalosporins of the 3rd generation (3 GC). Three *S. sonnei* isolates and a *S. flexneri* isolate resistant to third-generation cephalosporins were ESBL-Positive. CTX-M-15, TEM-1 and CMY-59 genes were also identified in these isolates (35).In Rahbar et al., from 2003 to 2005 in Tehran, among the 220 isolates of *Shigella*, *S. sonnei* was dominant. 88.5%, 98%, 11.5%, 5.5% of isolates were resistant to ceftriaxone, nalidixic acid, TMP/STX and ampicillin, respectively (36).In a study by najafi et al . in 2004 in Mazandaran, among 103 *Shigella* isolates, *S. flexneri* isolates were dominant. 59.2% of isolates were resistant to TMP/STX. 100% sensitivity to any of the antibiotic classes studied was not observed. Ninety four and six tenths of a percent of the isolates were resistant to two and more than antibiotics (37).In a study by Hamedi et al. in 2004 in Mashhad, among the 90 *Shigella* isolates, *S. flexneri* was the dominant species. The most sensitive was to nalidixic acid, ciprofloxacin, cefixime (97%), and gentamicin (81%), and the highest resistance was to tetracycline (93%) and cotrimoxazole (88%) (38).

In the study of Mardaneh et al. in 2010, in Shiraz, among the 90 *Shigella* isolates, *S. sonnei* was the dominant species. The highest resistance was reported to co-trimoxazole (92.2%), ampicillin (65.6%) and tetracycline (65.6%). The most sensitive was to imipenem, ciprofloxacin, ceftazidime, and ceftizoxime (39).In the study of Khorshidi et al. in 2002 in Kashan, among 56 *Shigella* isolates, *S. fexneri* was the dominant species. All isolates were susceptible to ciprofloxacin, gentamicin, and ceftizoxime, and 58.9% of isolates were resistant to the SXT and 78.6% of isolates to cephalothin. 62.21% of isolates were resistant to two antibiotics SXT and cephalothin, 62.21% to three antibiotics (cephalothin, SXT and ampicillin) , 7.1% to four antibiotics cephalothin, SXT, ampicillin, and chloramphenicol (40).

In a study by Yousefi Mashouf et al. in Hamadan from January 2001 to December 2004, among 166 *Shigella* isolates, *S. flexneri* was the dominant species. *S. dysenteriae* 100%, *S. flexneri* 90%, *S. sonnei* 80%, and *S. boydii* 60% and in total, 82.5% of the isolates were resistant to one or more antibiotics. 90% to chloramphenicol, 89% to ampicillin, 84% to cotrimoxazole, 83% to tetracycline and 51% to nalidixic acid. The resistance to nalidixic acid and ceftriaxone was different in the four species of *Shigella*. *S. dysenteriae* isolates were more resistant to nalidixic acid and ceftriaxone than *S. flexneri*, *S. sonnei*, and *S. boydii* isolates. 78% of *Shigella* isolates were resistant to at least two antibiotics and were resistant to several antibiotics (41).In a study by Dahifar et al. in 2005 in Tehran, 6 *Shigella* isolates were investigated. 33.3%, 50% and 100% isolate, were resistant to nalidixic acid, ampicillin, and TMP/STX, respectively. All isolates were also sensitive to amikacin (42).In a study by Yaghoubi et al in 2015 in Tehran, *S. sonnei* was the dominant species among Shigella isolate. This study was conducted to identify the virulence genes of *ipaBCD*, *VirA*, *sen*, *set1A*, *set1B*, *ial*, *ipaH, stx* and *sat* by multiplex polymerase chain reaction (multiplex PCR) (43).In a study by Ahangarzadeh rezaee et al in 2013 in Tabariz, of the 177 *Shigella* isolates*, S. flexneri* was the dominant species. In this study, the antibiotic susceptibility pattern showed that in 139 strains isolated between 1995 and 1999 and 38 strains isolated between 2009 and 2013 the antibiotic resistant was lower during the first time than the second time, and the results showed a significant increase in resistance to chloramphenicol, ceftizoxime, and amikacin. Also, more than 50% of isolates were resistant to more than seven antibiotic types (44).In a study by Ghaemi et al. in 2013 in Gorgan, the prevalence of *Shigella* and various species isolated from diarrhea was studied and out of the 56 isolates of *Shigella*, *Shigella sonnei* was dominant (45).In the Shahsavan et al study in 2012 in Tehran, out of the 50 *Shigella* isolates, *Shigella sonnei* was dominant. All isolates were susceptible to quinolones, including norfluxacin, levofloxacin and ciprofloxacin. The majority of isolates were (MDR). resistant rate to streptomycin, tetracycline and trimethoprim were 100, 96 and 98%, respectively (2).In the study of Sadeghabadi et al. in 2013 in Isfahan, out of the 58 *Shigella* isolates, *S. sonnei* was dominant. *Shigella* isolates were resistant to azithromycin (70.4%), ceftriaxone (88.9%) and cefiferase (85.2%), respectively. About 88.3% of *S. sonnei* isolates, one *S. flexneri* isolate, were resistant to at least three classes of antibiotics (MDR) (46).In the study of Velayati et al. in 1986 in Isfahan, five isolates of *Shigella* were investigated. The purpose of this study was to isolate and determine the EPEC, *salmonella*, and *shigella* serotypes and their antibiotic resistance patterns (47).In a study by Asadi et al. in Tehran in 2006, out of 100 isolates of *Shigella*, *Shigella sonnei* was dominant. In this study, the importance of identifying *ipaB* gene in the rapid diagnosis of Isolated *Shigella* species was studied. The highest resistance in *S. dysentery*, *S. flexneri*, *S. sonnei* and *S. boydii* was reported to co-trimoxazole. The results of this study showed that approximately, 50% of the strains were resistant to tetracycline and co-trimoxazole (48)In a study by Movahedi et al. in 2012 in Qom, 312 *Shigella* isolates were studied. In this study, the prevalence of neurological complications caused by shigellosis and its effective factors was investigated (49).In the study of Salmanzadeh-Ahrabi et al. in 2003 in Tehran, out of *Shigella* isolates, *S. sonnei* was dominant. All isolates were sensitive to ceftriaxone and ciprofloxacin. Resistance to ampicillin (81.4%), TMP/STX (93.6%), chloramphenicol (28.2%) and tetracycline (98.7%), cefixime (5.1%) and nalidixic acid (2.6%) were reported. Antibacterial susceptibility patterns of *Shigella* species were determined using the standard disc diffusion method. Total isolation of *Shigella* species. was found 11.5%. *S. sonnei* was the most common species (55.1%), followed by *S. flexneri* (% 30.8), *S. boydii* (% 9.6) and *S. dysenteria* (4.5%). Resistance to ampicillin (81.4%), TMP/STX (93.6%), chloramphenicol (28.2%) and tetracycline (98.7%) were high, while low resistance was to ceflexime (5.1%) and nalidixic acid (2.6%) . All isolates were sensitive to ceftriaxone and ciprofloxacin. This data may help doctors to select the appropriate empirical chemotherapy, although performing of an antibacterial sensitivity test is always recommended (50).In a study by Nahid et al., in 1981, in Shiraz, 206 isolates of *Shigella* were investigated. In this study, were investigated the production of E colicins and its types and the production of non-E colicin from 1000 *Shigella*, *Salmonell*a and *Escherichia coli* strains isolated from clinical specimens (51).In the study of Dabbagh moghaddam et al. in 2005 in 25 provinces of Iran, 1710 isolates of *Shigella* were investigated. In this study, during a 7-year period (2005-2011), 1710 cases of Shigellosis from 25 provinces of Iran were reported among military personnel. The prevalence rate in Hormozgan, Guilan and Khuzestan provinces were reported 2 per 1,000 people and in Isfahan and Golestan provinces was less than 0.2 per 1000 people. About 30% of reported cases (485 cases) were from Hormozgan province. About 70% (1196 cases) were reported from five provinces of Hormozgan, Khuzestan, Sistan-Baluchestan, Bushehr, and Guilan. The prevalence of Shigellosis in the spring, summer, autumn and winter seasons was 55, 21, 15, and 9 percent, respectively (52).In a study by Barak et al. in 2014 in Ardabil, out of the 33 *Shigella* isolates, *S. flexneri* was the dominant species. In this study, the antibiotic susceptibility pattern showed that resistance to amikacin in *S. dysentery*, resistance to cefixime and ceftriaxone in *S. flexneri*, was more compared with other species. All *S. boydii* isolates were resistant to ceftazidime and all *S. sonnei* isolates were susceptible to ceftazidime, gentamicin and imipenem, and resistant to co-trimoxazole. All *Shigella dysentery* isolates are susceptible to ciprofloxacin, gentamicin and ofloxacin, and resistance to co-trimoxazole and azithromycin. All *S. boydii* isolates were resistant to ceftazidime, co-trimoxazole and azithromycin, and susceptible to ofloxacin, gentamicin and ciprofloxacin (53).In a study by Hassanzadeh et al. in 2004 in Shiraz, out of 11 *Shigella* isolates was studied. In this study, the prevalence of *Campylobacter jejuni* and *Campylobacter coli* among other bacterial agents causing acute diarrhea was evaluated (54).In a study by Afshari Abarghan et al. in 2012 in Tehran, 106 isolates of *Shigella* were investigated. This study was conducted with the aim of identifying *Shigella sonnei* species using PCR with specific *wbzg* gene and serologic method (55).In a study by Ataei-Pirkooh et al in 2009 in Tehran, four of *Shigella* isolates were studied. In this study, the rate of infection of rotavirus and coinfection with some other enteropathogenic agents in children less than 6 years of age with acute gastroenteritis was investigated (56).In a study by Nikfar et al. from June 2013 to May 2014, 193 strains of *Shigella* were isolated from children. *S. flexneri* was a dominant species. In this study, 125, 63, 4 and 1 isolates of *S. flexneri*, *S. sonnei*, *S. boydii* and *S. dysenteriae* were identified, %, respectively. Resistance to co-trimoxazole and ampicillin was reported 77% and 89%, respectively. The highest resistance to co-trimoxazole was observed in *S. flexneri* isolates and the highest resistance to nalidixic acid was observed in *S. sonnei* isolates (57).In the study of Soltan Dallal et al in Tehran from January to December 2015, from 310 stool samples were identified 16 *Shigel*la isolates (9 *S. flexneri* and 7 *S. sonnei*). All isolates were resistant to streptomycin. *S. flexneri* isolates had a high resistance to streptomycin (100%), tetracycline (85.7%), ampicillin (85.7%), and chloramphenicol (71.4%). All isolates of *S. sonnei* were completely susceptible to gentamicin and ciprofloxacin. While *S. flexneri* isolates had low resistance to gentamicin and ciprofloxacin. In isolates of *S. flexneri*, three isolates had class 2 integron and three isolates had class 1 and 2 integrons. One isolate also lacked the class 1 and 2 integron. Class 3 integron was not detected in any of the *S. flexner* isolates. In isolates of *S. sonnei*, 2 isolates had class 2 integron, one isolate with class 1 integron , and 5 isolates had class 1, 2 integrons. One isolate also lacked the class 1 and 2 integrons. The class 3 integron was not identified in any of the *S. sonnei* isolates (58).

In the Zamanlou study between 14 May 2014 and May 2015, 142 isolates of *Shigella* were studied for antibiotic resistance patterns, Identifying class 1 and 2 integrons and genotyping by enterobacterial repetitive intergenic consensus (ERIC)- (PCR) method. High resistance to TMP/STX, ampicillin, streptomycin and tetracycline was observed in isolates. Out of the 73 isolates of *S. flexneri*, 10, 31, 10 and 22 isolates were isolated from Ardabil, Kerman, Urmia and Tabriz, respectively, from 16 isolates of *S. boydii*. 4, 4, 5, and 3 isolates were isolated from Ardabil, Kerman, Urmia and Tabriz, respectively. Of 47 isolates *S. sonnei*, Four, 13, 24, and 6 isolates were isolated from Ardabil, Kerman, Urmia and Tabriz, respectively, 6 isolates of *S. dysentery* 1, 2, and 3 isolates were isolated from Kerman, Urumia and Tabriz, respectively. Of the 142 isolates, 79 (55.6%) had -class 1 integron and 114 (80.3%) isolates had classes 2 integron. Results of ERIC (PCR) showed that *S. flexneri* had 6 genotypes and *S. dysentery* had 3 genotypes (59).

DISCUSSION

Shigellosis is recognized as a global concern by the World Health Organization (WHO). One of the treatment problems is the emergence of strains that are resistant to several antibiotics at the same time. Antibiotic resistance in these bacteria was first observed in Japan in 1955 and then quickly spread to different areas. But the severity of this expansion depends on factors such as geographical, health and economic conditions. However, due to the increase in the isolation of the sonic species in some countries and the high resistance of this species to nalidixic acid, the continuous evaluation of the drug resistance pattern of *Shigella* species seems to be necessary. Many studies in Iran and elsewhere in the world emphasize the emergence of *Shigella* resistant species.

Most of them have shown high resistance to TMP/STX, tetracycline, ampicillin and streptomycin , and some have resistance to antibiotics such as ciprofloxacin, azithromycin, and tetracyclines have reported. The frequency of *Shigella* species is very different in different countries. The distribution and prevalence of *Shigella* species in different countries may depend on the level of economic development, age, and environmental factors such as the public water supply system and the health of the country.

In certain parts of Iran, such as the capital city of Iran, Tehran, despite the fact that public health in this city is favorable and high, there is a significant reduction in the prevalence of *S. flexneri* compared to *S. sonnei*. *S. flexneri* has been reported as a common species in Iran in 1984-1985 and 2001-2002. Similar results have been reported in some Asian countries such as Saudi Arabia, Pakistan, and Jordan, Bangladesh, Taiwan, Vietnam, India, Thailand and Kuwait, *S. sonnei* is the predominant species of *Shigella* in other regions of Iran such as Tehran , Shiraz, Bushehr, Gorgan, Isfahan, Babol. *S. flexneri* is the predominant species of *Shigella* in other regions of Iran such as Ardabil, Tehran, Zahedan, Mazandaran (Quaemshahr), Mashhad, Kashan, Hamadan, Kerman, Karaj, Tabriz. In a study by Kahsay et al. on the Sero-diversity of *Shigella* spp antibiotic resistance variables between 2001-2014 in Asia, Africa, and South America. Of the three studies in Africa, five studies in Asia and one in South America, *Shigella* species were highly resistant to ampicillin. While all strains were susceptible to ciprofloxacin (60).

Shigella sonnei was prevalent, but in recent years, *S. flexneri* has become widespread. The reason for these changes seems to be the improvement of sanitary and epidemiological conditions. The easy transfer of *S. flexneri* is comparable to *S. sonnei*.

The *S. flexneri* and *S. sonnei* ratio of a geographical region indicates the standard health status of that area. When the overall level of personal and environmental health rises, the rate *S. flexneri* decreases while incidence ratio *S. sonnei* goes up. This change in the *Shigella* serogroup probably is the result of increasing the level of health in the country and according to the pattern which is observed in advanced countries. Choosing a drug for the treatment of patients with acute diarrhea depends on the physician's knowledge of the regional antibiotic susceptibility of the *shigella* species.Factors such as systematic regional and periodic monitoring and detemiaring of serotyping and antibiotic susceptibility patterns of *Shigella* isolates are important for Shigellosis treatment and control. Epidemiology and antibiotic susceptibility of species are constantly changing. In developed countries, the is *S. sonnei* is the dominant species, but recent changes in developing countries have been the dominant change, in which *S. flexneri* serotypes have been replaced instead of *S. sonnei*.Fluoroquinolones (the most effective of them are norfloxacin and ciprofloxacin) and third-generation cephalosporins are recommended by WHO as the first line treatment for patients with shigellosis.Antibiotic treatment eliminates the dysentery syndrome and reduces the duration of the disease and excretes bacteria from the feces and ultimately prevents them from spreading. Resistance to widely used antibiotics such as ampicillin, TMP/STX, nalidixic acid and tetracycline are increasing in different parts of the world, which has raised concern and importance over the world.

CONCLUSION

Shigella sonnei was prevalent, but in recent years, *S. flexneri* has become widespread. The reason for these changes seems to be the improvement of sanitary and epidemiological conditions. The easy transfer of *S. flexneri* is comparable to *S. sonnei*.

Conflict of interest

No conflict of interest was declared by the authors**.**

REFERRENCES

1. Jaya Sureshbabu. Shigella Infection. (Available at https://emedicine.medscape.com/article/968773-overview). 2018

2. Shahsavan S, Nobakht M, Rastegar-Lari A, Owlia P, Bakhshi B. Multi-locus sequence type analysis of *Shigellas* pp. isolates from Tehran, Iran. *Iran J Microbiol*. 2016;8(5):298–306.

3. Fatahi A, Ajami A, Bozorgzad M, Nekoeian S, Khazeni A. A Comparison between Culture and Multiplex PCR for Detection and Identification of Shigella Species in Patients with Shigellosis from Isfahan Province in 2014-2015. Journal of Medical Microbiology and Infectious Diseases. 2015 Jan 15;3(1):23-8.

4. Talebreza A, Memariani M, Memariani H, Shirazi MH, Shamsabad PE, Bakhtiari M. Prevalence and Antibiotic Susceptibility of Shigella Species Isolated From Pediatric Patients in Tehran. Archives of Pediatric Infectious Diseases. 2016;4(1).

5. Ghavam P, Monajemzadeh M, Ashtiani MT, Mamishi S, Farahani NN, Tanzifi P. Shigellosis and Changes of Antimicrobial Susceptibility During Six Years. Iranian Journal of Pediatrics. 2017 Jun 1;27(3).

6. Shahsavan S, Owlia P, Rastegar Lari A, Bakhshi B, Nobakht M. Investigation of Efflux-Mediated Tetracycline Resistance in Shigella Isolates Using the Inhibitor and Real Time Polymerase Chain Reaction Method. Iranian Journal of Pathology. 2017 Jan 1;12(1):53-61.

7. Akhi MT, Bialvaei AZ, Ghotaslou R, Asgharzadeh M, Naghili B, Pirzadeh T, Kafil HS, Gholizadeh P. Faecal carriage of ESBL and plasmid-mediated AmpC β-lactamase genes in Klebsiella spp. and Shigella spp. isolated from inpatient and outpatient carriers in Tabriz, Iran. Journal of Fundamental and Applied Sciences. 2016;8(3):16-29.

8. Jafari F, Hamidian M, Rezadehbashi M, Doyle M, Salmanzadeh-ahrabi S, Derakhshan F, Reza Zali M. Prevalence and antimicrobial resistance of diarrheagenic Escherichia coli and Shigella species associated with acute diarrhea in Tehran, Iran. Canadian journal of infectious diseases and medical microbiology. 2009;20(3):e56-62.

9. 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 Mar 1;10(3):237-42.

10. Mirnejad R, Vahdati AR, Rashidiani J, Erfani M, Piranfar V. The antimicrobial effect of lactobacillus casei culture supernatant against multiple drug resistant clinical isolates of Shigella sonnei and Shigella flexneri in vitro. Iranian Red Crescent medical journal. 2013 Feb;15(2):122.

11. Talebreza A, Memariani M, Memariani H, Shirazi MH, Shamsabad PE, Bakhtiari M. Prevalence and Antibiotic Susceptibility of Shigella Species Isolated From Pediatric Patients in Tehran. Archives of Pediatric Infectious Diseases. 2016;4(1).

12. Ranjbar R, Aleo A, Giammanco GM, Dionisi AM, Sadeghifard N, Mammina C. Genetic relatedness among isolates of Shigella sonnei carrying class 2 integrons in Tehran, Iran, 2002–2003. BMC infectious diseases. 2007 Jun 22;7(1):62.

13. Katouli M, Pachenary A, Jaafari A, Moghaddam AA, Dehaghi NH, Mirfattah ZA, Najafi Y, Shafyi E. The role of Shigella spp. in childhood diarrhoea in Iran and their antibiotic resistance. Scandinavian journal of infectious diseases. 1989 Jan 1;21(4):415-9.

14. Ashtiani MT, Monajemzadeh M, Kashi L. Trends in antimicrobial resistance of fecal Shigella and Salmonella isolates in Tehran, Iran. Indian Journal of Pathology and Microbiology. 2009 Jan 1;52(1):52.

15. Hosseini MJ, Ranjbar R, Ghasemi H, Jalalian HR. The prevalence and antibiotic resistance of Shigella sp. recovered from patients admitted to Bouali Hospital, Tehran, Iran during 1999-2001. Pakistan Journal of Biological Sciences. 2007 Aug 15;10(16):2778-80.

16. MoezArdalan K, Zali MR, Dallal MM, Hemami MR, Salmanzadeh-Ahrabi S. Prevalence and pattern of antimicrobial resistance of Shigella species among patients with acute diarrhoea in Karaj, Tehran, Iran. Journal of Health, Population and Nutrition. 2003 Jun 1:96-102.

17. Farshad S, Ranjbar R, Hosseini M. Molecular genotyping of Shigella sonnei strains isolated from children with bloody diarrhea using pulsed field gel electrophoresis on the total genome and PCR-RFLP of IpaH and IpaBCD genes. Jundishapur journal of microbiology. 2015 Jan;8(1).

18. Ranjbar R., Hosseini M.J., Kaffashian A.R., Farshad S. An outbreak of shigellosis due to Shigella flexneri serotype 3a in a prison in Iran. Arch. Iran Med. 2010;13(5):413–416

19. Ranjbar R, Afshar D, Tavana AM, Najafi A, Pourali F, Safiri Z, Zanjani RS, Jafari NJ. Development of multiplex PCR for simultaneous detection of three pathogenic Shigella species. Iranian journal of public health. 2014 Dec;43(12):1657.

20. Alizadeh-Hesar M, Bakhshi B, Najar-Peerayeh S. Clonal dissemination of a single Shigella sonnei strain among Iranian children during Fall 2012 in Tehran, IR Iran. Infection, Genetics and Evolution. 2015 Aug 1;34:260-6.

21. Nave HH, Mansouri S, Emaneini M, Moradi M. Distribution of genes encoding virulence factors and molecular analysis of Shigella spp. isolated from patients with diarrhea in Kerman, Iran. Microbial pathogenesis. 2016 Mar 31;92:68-71.

22. Dibaj R, Aslani MM, Heidarieh P, Hashemi A, Ataei B, Daei-Naser A, et al. Conventional and molecular investigation of Shigella isolates in relation to an outbreak in the area of Isfahan, Iran. Iran J Microbiol 2013;5(4):339-44.
23. Jomezadeh N, Babamoradi S, Kalantar E, et al. Isolation and antibiotic susceptibility of Shigella species from stool samples among hospitalized children in Abadan, Iran. Gastroenterol Hepatol Bed Bench. 2014;7:218–23
24. Esmaeili Dooki MR, Rajabnia R, Barari Sawadkohi R, Mosaiebnia Gatab Z, Poornasrollah M, Mirzapour M. Bacterial entropathogens and antimicrobial susceptibility in children with acute diarrhea in Babol, Iran. Caspian J Intern Med. 2014 Winter; 5(1): 30–34.
25. Mamishi S, Mashoori N, Mahboobi N, Pour Akbari B. Increasing resistance to nalidixic acid in Shigella subgroups in a comparative study between 2001–2003 and. Singapore Med J. 2009;50(8):791-3.
27. Mahmoudi S, Pourakbari B, Moradzadeh M, Eshaghi H, Ramezani A, Ashtiani MT, Valian SK, Mamishi S. Prevalence and antimicrobial susceptibility of Salmonella and Shigella spp. among children with gastroenteritis in an Iranian referral hospital. Microbial Pathogenesis. 2017 Aug 31;109:45-8
28. Zahedi Bialvaei A, Samadi Kafi Hl, Asgharzadeh M, , Yousefi M. CTX-M extended-spectrum β-lactamase-producing Klebsiella spp, Salmonella spp, Shigella spp and Escherichia coli isolates in Iranian hospitals. Braz J Microbiol 2016;47:706-11.
29. Mostafavi N, Bighamian M, Mobasherizade S, Kelishadi R. Resistance of Shigella strains to extended-spectrum cephalosporins in Isfahan province. Medical journal of the Islamic Republic of Iran. 2016;30:428.
30. Savadkoohi RB, Ahmadpour-Kacho M. Prevalence of Shigella species and their antimicrobial resistance patterns at Amirkola children hospital, North of Iran. Iranian Journal of Pediatrics. 2007;17(2):118-22.
31. Tajbakhsh M, García Migura L, Rahbar M, Svendsen CA, Mohammadzadeh M, Zali MR, Aarestrup FM, Hendriksen RS. Antimicrobial-resistant Shigella infections from Iran: an overlooked problem?. Journal of antimicrobial chemotherapy. 2012 Feb 17;67(5):1128-33
32. Qureishi M, Borji A, Bokaeian M, Roudbari M, Shahraki S, Niazi A, Zangiabadi M. Antimicrobial resistance of Shigella spp. isolated from diarrheal patients in Zahedan. Acta Medica Iranica. 2008;46(5):413-6.
33. Ranjbar R, Dallal MM, Talebi M, Pourshafie MR. Increased isolation and characterization of Shigella sonnei obtained from hospitalized children in Tehran, Iran. Journal of health, population, and nutrition. 2008 Dec;26(4):426.
34. Ranjbar R, Bolandian M, Behzadi P. Virulotyping of Shigella spp. isolated from pediatric patients in Tehran, Iran. Acta microbiologica et immunologica Hungarica. 2017 Feb 16;64(1):71-80.
35. 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).
37. Najafi N, Ghasemian R, Shariatzadeh M, Alian S. Antimicrobial Resistance of Shigella from Patients with Acute Diarrhea. Quaemshahr, Mazandaran, Iran. Research Journal of Biological Sciences. 2008;3(3):332-6.
38. Hamedi A. Antibiotic resistance in children with bloody diarrhea. Acta Medica Iranica. 2009;47(2):121-4
39. Mardaneh J, Poor SA, Afrugh P. Prevalence of Shigella species and antimicrobial resistance patterns of isolated strains from infected pediatrics in Tehran. Int J Entric Pathog. 2013;1(1):28-31.
40. Khorshidi A, Akbari H. Emergence of Multidrug-Resistant Shigella in Iran. Journal of Infectious Diseases and Antimicrobial Agents. 2006 Apr;23(1):15-9.
41. Yousefi Mashouf R, Moshtaghi A A, Hashemi S H. Epidemiology of Shigella species isolated from diarrheal children and drawing their antibiotic resistance pattern. Iranian Journal of Clinical Infectious Disease 2006;1(3):149-155.
42. Dahifar H, Ghorbani A, Ghods M. Isolated and non-isolated enteric pathogens in children with diarrhea and related laboratory characteristics. Medical Journal of The Islamic Republic of Iran (MJIRI). 2008 May 15;22(1):40-6.
43. Yaghoubi S, Ranjbar R, Dallal MM, Fard SY, Shirazi MH, Mahmoudi M. Profiling of Virulence-associated Factors in Shigella Species Isolated from Acute Pediatric Diarrheal Samples in Tehran, Iran. Osong public health and research perspectives. 2017 Jun;8(3):220.
44. Rezaee MA, Abdinia B, Abri R, Kafil HS. Comparison of the antibiotic resistance patterns among Shigella species isolated from pediatric hospital between 1995-1999 and 2009-2013 in North-West of Iran.
45. Ghaemi EO, Aslani MM, Moradi AV, Dadgar T, Livani S, Mansourian AR, Nosrat SB, Ahmadi AR. Epidemiology of Shigella-associated diarrhea in Gorgan, north of Iran. Saudi Journal of Gastroenterology. 2007 Jul 1;13(3):129.
46. Sadeghabadi AF, Ajami A, Fadaei R, Zandieh M, Heidari E, Sadeghi M, Ataei B, Hoseini SG. Widespread antibiotic resistance of diarrheagenic Escherichia coli and Shigella species. Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences. 2014 Mar;19(Suppl 1):S51
47. Velayati Aa, Ghazi Saldl Ki, Taravati M. A study of Salmonella, Shigella and enteropathogenic Escherichia coli serotypes in acute gastroenteritis children under the age of five. Medical Journal of The Islamic Republic of Iran (MJIRI). 1987 Nov 15;1(1):22-31.
48. Asadi M, Ghafouri I. Identifying IpaB Gene in Shigella Bacteria and Determining the Antibiotic Sensitivity of Shigella strain. Advances in Bioresearch. 2015 Nov 1;6(6).
49. Movahedi Z, Sadeghimoghadam P, Akhavansepahi M, Akhlaghdoost M, Shokrollahi MR, Heydari H, et al. Prevalence of Neurological Complications Caused by Shigellosis in Children Hospitalized at Qom Children Hospital. International Research Journal of Applied and Basic Sciences 2015; 9 (9): 1614-17.
50. Salmanzadeh-Ahrabi S, Habibi E, Jaafari F, Zali MR. Molecular epidemiology of Escherichia coli diarrhoea in children in Tehran. Annals of tropical paediatrics. 2005 Mar 1;25(1):35-9.
51. WALEH, NAHID S. "SHORT COMMUNICATION Distribution of Group E Colicin Types in Shiraz, Iran." *Microbiology* 127.1 (1981): 219-222.
52. Dabbagh-Moghddam A, Tabibian E, Noorifard M, Hosseini-Shokouh S J, Rahimi-Dehgolan S, Tootoonchian M. Epidemiologic profile of shigellosis among Iranian military personnel: a retrospective study in the Army. Ann Mil Health Sci Res. 2014; 12 (2) :91-94
53. Barak M, Arzanlou M, Babapour B, Ghorbani L. Antibiotic resistance pattern of bacterial enteritis among hospitalized children in Ardabil: a single center experience. Int J Adv Med. 2016 Nov;3(4):989-993
54. Hassanzadeh P, Motamedifar M. Occurrence of Campylobacter jejuni in Shiraz, southwest Iran. Medical Principles and Practice. 2007;16(1):59-62.
55. Abarghan NA, Bakhshi B. Molecular Diagnosis of Shigella Sonnei Isolates with Wbzg Gene in Stool Sample of Children with Diarrhea in Tehran. Iranian Journal of Public Health. 2014 Jan 1;43(2):176.
56. Ataei-Pirkooh A, Shamsi-Shahrabadi M, Haghi-Ashtiani MT. Incidence of coinfection between rotavirus and some enteropathigenic agents in children referred to children medical center hospital, Tehran 2009. Iran J Vir. 2011;5:23-7.
57. Nikfar R, Shamsizadeh A, Darbor M, Khaghani S, Moghaddam M. A Study of prevalence of Shigella species and antimicrobial resistance patterns in paediatric medical center, Ahvaz, Iran. Iranian journal of microbiology. 2017 Oct;9(5):277.
58. Dallal MM, Omidi S, Douraghi M, Ashtiani MT, Yazdi MK, Okazi A. Molecular analysis of integrons and antimicrobial resistance profile in Shigella spp. isolated from acute pediatric diarrhea patients. GMS Hygiene and Infection Control. 2018;13.
59. Zamanlou S, Rezaee MA, Aghazadeh M, Ghotaslou R, Nave HH, Khalili Y. Genotypic Diversity of Multidrug Resistant Shigella species from Iran. Infection & chemotherapy. 2018 Mar 1;50(1):29-37.
60. Kahsay AG, Muthupandian S. A review on Sero diversity and antimicrobial resistance patterns of Shigella species in Africa, Asia and South America, 2001-2014. *BMC Res Notes*. 2016;9(1):422.