Prevalence, Serotyping and Antimicrobials Resistance of Salmonella

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Background: Salmonella is a food-borne enteropathogenic organism which causes illness with different clinical manifestations, commonly gastroenteritis, or enteric fever by typhoidal strain. It continues to be of public health concern in most developed and developing countries despite all efforts to control.

Objective: To evaluate the epidemiology and susceptibility pattern of salmonellosis in Bahrain.

Design: A Retrospective Study.

Setting: Salmaniya Medical Complex, Bahrain.

Method: Data of the incidence and epidemiological characteristics of salmonellosis in the Kingdom of Bahrain were retrieved from the Ministry of Health (MOH) website (2007 to 2017).

Detailed microbiological analysis of Salmonella ssp. isolates for the year 2017 were further studied after retrieving the data from Salmaniya Microbiology Laboratory.

Result: Significant reduction (61%) of salmonellosis incidence in Bahrain was observed over the study period, 39.6/100,000 in 2007 to 15.2/100,000 population in 2017. Cases of salmonellosis in Bahrain were mostly attributed to non-typhoidal isolates.

During the year 2017, 138 Salmonella spp. strains were identified from patients attending governmental health care facilities. One hundred two (74%) were Bahraini and 85 (62%) were males. The most predominant serotype was Enteritidis, while Salmonella typhi was the least identified isolate. There was uniform sensitivity to ceftriaxone and ciprofloxacin 6 (4.3%) among typhoidal isolates. Similar patterns of sensitivity were obtained among non-typhoidal salmonella with 99% susceptibility to ceftriaxone and 95% susceptibility to ciprofloxacin. On the other hand, our isolates showed extreme high rate of nalidixic acid resistance among typhi 6 (4.3%) but lower resistant profile among non-typhi 36 (26.1%).

Conclusion: There was a significant reduction in salmonellosis in Bahrain over the past 10 years. A high rate of nalidixic acid resistance among typhoidal isolates should preclude the use of ciprofloxacin as an empiric choice for treating typhoid fever among the population in Bahrain.

Bahrain Med Bull 2019; 41(4): 212 - 217

Salmonella is one of the most common causes of food-borne illness in humans. Its elimination is difficult due to high tolerance to environmental stress, widespread distribution, adaptability and antimicrobial resistance[1].

Typhoidal Salmonella, such as S. Typhi and S. paratyphi, only colonize humans and are usually acquired by the consumption of food or water contaminated with human fecal material. It is considered an important global public health problem and

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an economic burden in areas with poor sanitary conditions, crowding, and social chaos.

Other Salmonella serotypes are jointly termed non-typhoidal Salmonella, which naturally have an animal reservoir. A human typically acquires infections through ingestion of contaminated agricultural products such as poultry or eggs or, rarely, contaminated water. The clinical diseases of acquired infection vary from self-limiting gastroenteritis to life-threatening systemic sepsis[2].

Salmonella diarrhea is generally self-limiting, and antimicrobials are usually not required for treatment. However, it is critical to manage invasive infections and enteric fever. An antimicrobial resistance is a critical concern; it is usually secondary to the overuse of antimicrobial agents among animals and human, particularly ceftriaxone and ciprofloxacin, which are considered the drug of choice for treating salmonellosis among patients[3-5].

In the last two decades, MDR Salmonella has spread worldwide, thereby reducing the available therapeutic options, and the use of quinolone or third-generation cephalosporins as the first-line antimicrobial for the empiric treatment[6,7]. In addition, there is an increasing frequency of strains resistant to nalidixic acid and ciprofloxacin[8,9].

The antimicrobial resistance rates of S. Typhi to ciprofloxacin showed wide variability in different geographical locations. Some countries, such as Vietnam and Indonesia, showed low resistance rates; both showed uniform sensitivity to ciprofloxacin (0% resistance), Nepal showed 3.9% resistance to ciprofloxacin. Pakistan showed a high rate of ciprofloxacin resistance (88%)[10-13]. There was no previously published data about local antimicrobial susceptibility pattern of salmonellosis among the population in Bahrain.

The aim of this study is to evaluate the epidemiology and susceptibility pattern of salmonellosis in Bahrain.

METHOD

All data illustrated in this study were obtained from the official national surveillance data of communicable diseases published on the MOH website. The published incidence rate of Salmonellosis was available for 2007 to 2017, however, age distribution and incidence was only available for 2010-2016.

Further detailed microbiological data of Salmonella spp. isolates for the year 2017 were obtained through a retrospective cohort review of all blood and stool culture positive for Salmonella spp. isolates. All non-duplicate clinical isolates with positive growth of Salmonella spp from blood and/or stool during the study period of January 2017 to December 2017 were included in the study.

Isolates were identified using conventional biochemical tests. Salmonella spp. was confirmed with specific antisera and further classified into different serotypes[14].

Antimicrobial susceptibility patterns were determined using disc diffusion method to test the susceptibility pattern of Salmonella to 6 relevant antibiotics, which include ampicillin (10 µg), ceftriaxone (30 µg), chloramphenicol (30 µg), trimethoprim-sulfamethoxazole (25 µg), ciprofloxacin (5 µg) and nalidixic acid (30 µg). Interpretation was based on CLSI M100-S22 (Clinical and Laboratory Standards Institute, 2012)[15].

Extended Spectrum Beta-Lactamase (ESBL) production was analyzed by the double-disk diffusion test and was confirmed using Pheonix (BD Diagnostics, Sparks, MD, USA), automated microbial identification and antibiotic susceptibility testing system[16].

Resistance to nalidixic acid was used as a predictor of decreased susceptibility to ciprofloxacin. Multidrug resistance (MDR) of Salmonella isolates was defined as resistant to following traditional three first-line antimicrobial agents: ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole[17]. Age, sex and nationality of patients were documented.

RESULT

There was a significant reduction (61%) in the incidence of salmonellosis in Bahrain from 39.6/100,000 in 2007 to 15.2/100,000 in 2017. Salmonellosis cases in Bahrain were mostly caused by non-typhoidal isolates. The incidence of typhoidal illness in the Bahrain since 2007 was low with an incidence of 0.7 per 100,000 during 2007-2008, it peaked to 2.8/100,000 in 2009, then dropped again to 0.4/100,000 population in 2017, see figure 1.

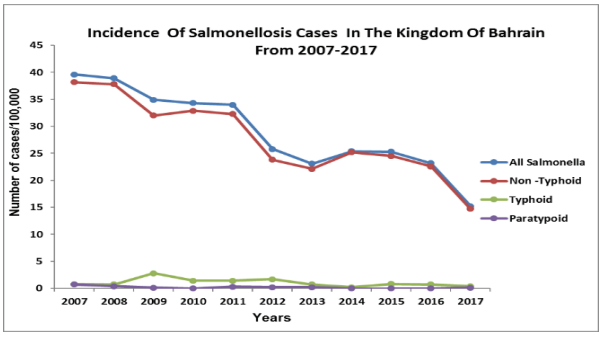

Figure 1: Incidence of Salmonellosis in Bahrain (2007-2017)

Salmonellosis incidence was higher among the pediatric age group <5 years, followed by the geriatric group >65 years. Salmonellosis trend revealed a significant reduction of salmonellosis among most age groups (with an average of 46.5% reduction from 2010 to 2016), see table 1 and figure 2. Among adolescents, there was a resurgence of incidence in 2016 (10% increase in the incidence in 2016 compared to 2010), and among children < 5 years where there was no significant reduction as other age groups (27% reduction from 2010 to 2016).

Table 1: Incidence of Salmonellosis by Age Group (2010 per 100,000 Population)

Incidence	2010	2011	2012	2013	2014	2015	2016	percentage of reduction (2010→2016)
0-4y	180.9	187	131.8	151.7	155.1	166.9	132.9	27%
5-14y	30.9	25	18.2	18.4	16.6	17.3	17.6	43%
`15-24y	15.7	15	11.5	5.2	10.0	11.8	17.2	-10%
25-34y	16.3	18	15.4	11.3	14.9	11.4	9.4	42%
35-44y	21.4	14	15.5	9.2	12.0	12.8	9.1	57%
45-54y	28.9	33	16.9	8.9	13.4	11.1	11.5	60%
55-64y	32.7	36	25.4	43.9	19.8	15.3	19.7	40%
65+y	72.4	56	74.8	34.4	37.2	35.7	41.0	43%

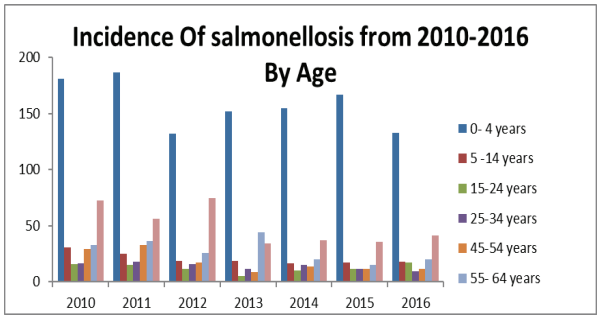

Figure 2: Incidence of Salmonellosis by age group (2010-2016)

In 2017, 138 Salmonella strains were identified from patients, isolated from stool in 113 (82%) patients and from blood among 25 (18%) patients. Six (4%) isolates were identified from both blood and stool. Those 6 cases were counted as blood isolates during further analysis of serotypes and antimicrobial susceptibility. One hundred two (74%) patients were Bahrainis. Non-Bahrainis are shown in figure 3; most were Bangladeshis, Indians and Pakistanis.

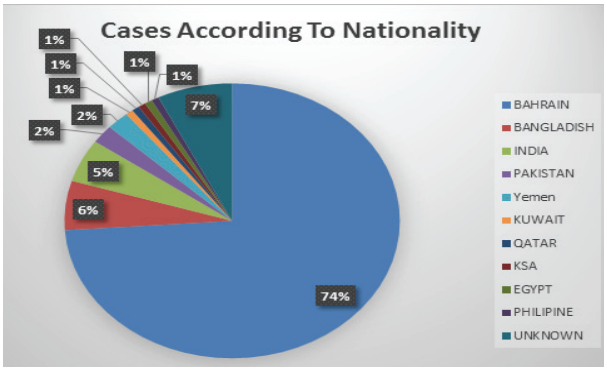

Figure 3: Cases Attending Governmental Health Care Facilities among Different Nationality (2017)

Fifteen (11%) cases were infants. Forty-seven (34%) were between 1-4 years, then decreased after the age of four and remained at a low level throughout adolescence and adulthood, see figure 4.

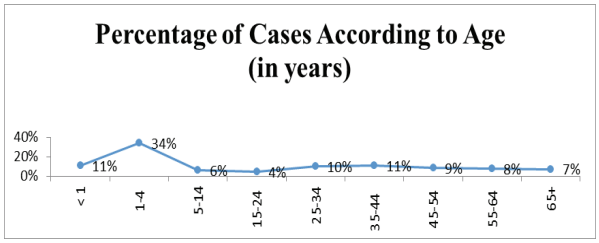

Figure 4: Distribution of Salmonella Cases Attending Governmental Health Care Facilities among Different Age Groups (2017)

Six (4%) were S. Typhi, 132 (96%) were non-typhoidal salmonellosis: 31 (22%) Salmonella Enteritidis, 29 (21%) Salmonella group C, 21 (15%) Salmonella typhimurium, and 18 (13%) Salmonella group B. Seven (5%) were Salmonella group D. Twenty-six (19%) isolates were non-serotype isolates. Table 3 shows stratification of the species by age group.

Table 2: Predominant Serotypes of Salmonella Isolates

Sources	Blood		Stool		TOTAL	
Serotype	N	%	N	%	N	%
S. group B	4	22%	14	78%	18	13%
S. group C	1	3%	28	97%	29	21%
S. group D	1	13%	6	86%	7	5%
S. enteritidis	11	32%	20	65%	31	22%
S. typhimurium	1	5%	20	95%	21	15%
S. typhi	6	86%	0	0%	6	4%
Others	1	4%	25	96%	26	19%
All	25	18%	113	82%	138	100%

Table 3: Salmonella Serotypes by Age Groups

Serotypes	Number of cases	Percentage
Infant <1 year (N=15)		
S. enteritidis	2	1.4%
S. Typhimurium	2	1.4%
S. group B	2	1.4%
S. group C	2	1.4%
Salmonella species	7	5%
Pediatrics 1-14 years (N=55)		
S. enteritidis	11	7.9%
S. group C	11	7.9%
S. Typhimurium	10	7.2%
S. group B	5	7.2%
S. group D	5	7.2%
S. Typhi	1	0.7%
Salmonella species	12	8.7%
Adolescent 15-18 years (N=1)		
S. enteritidis	1	0.7%
Adult 19-65 years (N=58)		
S. enteritidis	16	11.5%
S. group C	14	10%
S. group B	9	6.5%
S. Typhimurium	7	5%
S. Typhi	4	2.8%
S. group D	2	1.4%
Salmonella species	6	7.2%
Geriatric > 65 years (N=9)		
S. group B	3	2.2%
S. group C	2	15.9%
S. enteritidis	1	0.7%
S. group D	1	0.7%
S. typhimurium	1	0.7%
Salmonella species	1	0.7%

Antibiotics susceptibility revealed that Salmonella typhi strains, 6 (4%) were sensitive to ceftriaxone and ciprofloxacin but showed absolute resistance to nalidixic acid, see figure 5.

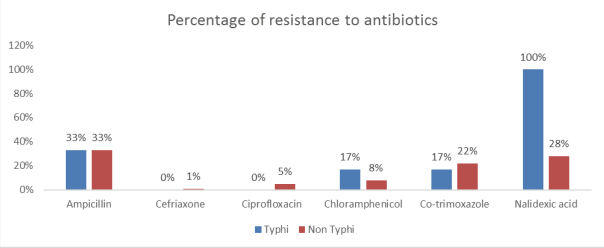

Figure 5: Percentage of Resistance of Salmonella ssp. Isolates

Susceptibility testing revealed 33% resistance to ampicillin and 17% resistance to both chloramphenicol and to co-trimoxazole. MDR (defined as resistant to chloramphenicol, co-trimoxazole and ampicillin) was detected in one isolate of Salmonella typhi. Most isolates of non-typhoidal Salmonella strains retained a high rate of susceptibility to ceftriaxone, 132 (96%). The only ceftriaxone resistant isolate was group D strains producing ESBL, which was isolated from a four-year-old Bahraini child.

Resistance to ciprofloxacin was identified among 7 (5%) non-typhoidal salmonellosis isolates and decrease susceptibility to ciprofloxacin was found among 37 (26.8%) isolates. Ampicillin susceptibility revealed a resistance rate of 33%, while chloramphenicol and co-trimoxazole both showed resistance of 8% and 22% respectively. MDR was found in 3 (2%) isolates and, two (1.4%) of them were group B, and C, while the third was non-serotype. Details of resistance among each of salmonella serotypes are displayed in table 4.

Table 4: Percentage of Non-Susceptibility (Resistant and Intermediate) among Different Salmonella Serotypes

Antibiotics	Group B n=18	Group C n=29	Group D n=7	Enteritidis n=31	Typhimurium n=21	Typhi n=6	S. species n=26
Ampicillin	9 (6.5%)	4 (2.9%)	5 (3.6%)	9 (6.5%)	11 (7.9%)	2 (1.4%)	6 (4.3%)
Cefriaxone	0%	0%	1 (0.7%)	0	0	0	0
Ciprofloxacin	3 (2.2%)	1 (0.7%)	0	2 (1.4%)	0	0	1 (0.7%)
Chloramphenicol	2 (1.4%)	5 (3.6%)	0	1 (0.7%)	2 (1.4%)	1 (0.7%)	1 (0.7%)
Co-trimoxazole	9 (6.5%)	5 (3.6%)	2 (1.4%)	1 (0.7%)	10 (7.2%)	1 (0.7%)	2 (1.4%)
Nalidexic acid	6 (4.3%)	7 (5%)	3 (2.2%)	17 (12%)	0	6 (4.3%)	3 (2.2%)

DISCUSSION

Salmonellosis continues to impose a significant health burden for both the developed and developing countries[18,19]. This study showed a great reduction in the incidence of salmonellosis in Bahrain over the past 10 years, a rate of 14.7 cases per 100,000 population, which is comparable with Canada (19.4 cases per 100,000 population), Poland (22.9 per 100,000 population), USA (16.42 per 100,000 population) and other European countries (20.7 cases per 100,000 population)[20-23]. This might be attributed to the 100% access to safe water and sanitation[24]. A similar reduction trend was observed among the population in the neighboring gulf countries such as Qatar, with reduction of salmonellosis incidence from 30.3 in 2004 to 18.1 per 100,000 populations in 2012[25].

The current study revealed that non-typhoidal illness contributes to the majority of salmonellosis cases; the incidence of typhoid fever was low (0.4 per 100,000population). In Egypt, a rate ranging between 14-60 per 100,000 populations was found. A high rate was reported in Iraq, Pakistan and Jordan[26]. The highest incidence of salmonellosis was mainly among children aged less than 5 years, as well as the geriatric age group; it is similar to other studies[22,27-30].

USA national data revealed that salmonellosis rate was 16.42 per 100,000, which is comparable to the 2017 rate in Bahrain (15.2 per 100,000 population)[22]. However, the rate among children below 5 years was 63.49 cases per 100,000 population in the USA which is almost half the rate in Bahrain (132.9 per 100,000 population).

Further detailed microbiological analysis of salmonella cases obtained during the year 2017 revealed that 77% of cases were Bahraini, which is different from other previously published studies in neighboring Gulf Council Countries[25,31,32].

The most common serotypes were S. Enteritidis followed by group C and S. Typhimurium, except among the geriatric age group, where salmonella group B was common followed by group C. A similar pattern of differential serotypes prevalence was revealed in previous studies reported from Saudi Arabia and the USA[22,30,33].

In this study, S. Typhi isolates showed uniform sensitivity towards most therapeutically relevant antibiotics (ceftriaxone and ciprofloxacin) with low resistance pattern to other first-line agents such as ampicillin (33%), cotrimoxazole and chloramphenicol (17%). All S. Typhi isolates (100%) were resistant to nalidixic acid and had higher resistance rate than observed in other studies[26]. Relatively low rates of nalidixic acid resistance among S. Typhi was observed in Lebanon, Cambodia, and some European countries[34-37]. High rates were observed in USA (67%) and Canada (80%)[34-37].

MDR rate in the present study was 16%, which is comparable to other studies[22]. Rahman et al found similar rates of MDR in Qatar (14%), Egypt (14%), Jordan (17%), Uzbekistan (15%). Much higher rates of MDR have been reported from countries with low sanitation standards such as Iraq (83%), India (60-70%) and Pakistan (50%)[26]. Previously published studies from other GCC countries, such as Kuwait and Saudi Arabia showed a comparable rate of MDR among S. Typhi (30% and 20% respectively)[31,38]. The sensitivity pattern of non-typhoidal salmonellosis was comparable to other studies[22,29,30,32]. Nalidixic acid resistance was documented among 28% of cases, while MDR rate was of 6%.

CONCLUSION

There was a reduction of salmonellosis in Bahrain over the past 10 years. Great effort is needed to target Bahraini children below 5 years and adolescent for the preventive measures by improving the hygienic measures of food chains and public education.

Our clinicians must be aware that ciprofloxacin is not an appropriate empirical therapeutic option in our community

considering our alarmingly high rate of nalidixic acid resistance and the consecutive risk of potential treatment failures. Hence, third generation cephalosporins, such as ceftriaxone should be used as an empiric antimicrobial till identification of antibiotics susceptibility.

Author Contribution: All authors share equal effort contribution towards (1) substantial contributions to conception and design, acquisition, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of the manuscript version to be published. Yes.

Potential Conflicts of Interest: None.

Competing Interest: None.

Sponsorship: None.

Acceptance Date: 17 August 2019.

Ethical Approval: Approved by the Medical Department, Salmaniya Medical Complex, Bahrain.

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