

## A retrospective study of community-acquired *Salmonella* infections in patients attending public hospitals in Lagos, Nigeria

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### Abstract

**Introduction:** A retrospective cohort study on *Salmonella*-associated diseases (SADs) was conducted in 14 public hospitals across Lagos State, Nigeria, between 1999 and 2008.

**Methodology:** Medical records of clinically diagnosed patients with confirmed *Salmonella* infections were reviewed for the 10-year period. Laboratory diagnosis of typhoid fever cases in all the hospitals were first based on Widal agglutination tests then followed by culture, while non-typhoidal *Salmonella* infections were based on culture technique.

**Results:** A total of 85,187 confirmed cases of SADs were found, of which 880 deaths were recorded (case-fatality rate = 1.03% / 10 years). The mean incidence of SADs in Lagos State for the 10-year period was estimated at 45 cases per 100,000 persons/year, while that of typhoid fever alone was 16 cases per 100,000 persons/year. During the studied period, the number of deaths due to typhoid fever was significantly ( $P < 0.05$ ) higher than deaths due to gastroenteritis except in 2003 and 2004. Risk associated with typhoidal deaths was 4 to 11 times greater when compared to gastroenteritis deaths between 2000 and 2002. *Salmonella*-associated diseases were most prevalent in adults 21 –to30 years of age (49.49%). Cases of patients with invasive *Salmonella*-associated gastroenteritis were observed mainly in children under five years of age.

**Conclusion:** The current surveillance data indicated high incidence of SADs in areas exposed to environmental contaminations. This study revealed that infections caused by *Salmonella enterica* serovars are endemic in our environment thus poses a serious threat to public health. Constant public health education is essential to avert undue epidemics.

**Key words:** *Salmonella*; diseases; retrospective; typhoid fever; gastroenteritis; medical records

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### Introduction

The true incidence of *Salmonella*-associated diseases (SADs) in humans is difficult to evaluate because of lack of an epidemiological surveillance systems, especially in developing countries. Each year, there are 12 to 33million cases of typhoid fever worldwide [1]. In the United States and most European countries, epidemic typhoid is predominantly a disease of travelers returning to their home countries from endemic areas [2]. There are 1.4 million cases of nontyphoidal salmonellosis annually, resulting in 168,000 visits to physicians, 15,000 hospitalizations and 580 deaths [3] and 500 cases of typhoid fever in the USA [1]. Typhoid fever is endemic throughout Africa and Asia and persists in the Middle East, a few Southern and Eastern European countries and Central and South America [4]. In Nigeria, typhoid fever is among the major

widespread diseases affecting both young children and young adults as a result of many interrelated factors such as inadequate facilities for processing human wastes and indiscriminate use of antibiotics [5,6]. Morbidity associated with illness due to *Salmonella* continues to be on the increase, in some cases resulting in death [5]. It is difficult to evaluate SADs burden because of the very limited scope of studies the lack of coordinated epidemiological surveillance systems at all levels of government (federal, state and local), and the presence of other diseases considered to be of higher priority. These situations have undermined reported cases of waterborne infections, particularly typhoid fever. Sporadic outbreaks of typhoid fever often cause widespread enteritis among urban and rural communities [7]. Over the years reliable epidemiological data from which to estimate the

burden of SADs in Lagos State has become obscured, because most of the public hospitals in the state found it difficult to make data available, where it existed, to appropriate agencies for proper documentation, planning and interventions. This study was initiated with a view to generate information through a coordinated epidemiological surveillance study from which SADs burden in Lagos could be assessed. To our knowledge this is the first report of a large population-based retrospective cohort study on laboratory-confirmed *Salmonella* infections in recent years in Lagos Nigeria.

## Methodology

### *Ethical approval*

Ethical approval was through the ethical committee of the Institution and permission from Lagos State Ministry of Health

### *Study design*

A 10-year retrospective cohort study on SADs was conducted in Lagos State, Nigeria, between 1999 and 2008. Fourteen prominent public hospitals across the state were used as study areas and are as follows: Ikeja General Hospital (IGH), Badagry General Hospital (BGH), Apapa General Hospital (AGH), Isolo General Hospital (IGH), Surulere General Hospital (SGH), Ikorodu General Hospital (KDGH), Ebute-Metta General Hospital (EBGH), Orile-Agege General Hospital (OAGH), Lagos-Island General Hospital (LGH), Gbagada General Hospital (GGH), Mainland (Yaba) General Hospital (MGH), Ajeromi General Hospital (AJGH), Agbowo General Hospital (AWGH) and Epe General Hospital (EGH). These hospitals served as referral centres for both in-patients and out-patients in all the local government council areas of the state. Medical records of clinically diagnosed patients with confirmed *Salmonella* infections were reviewed for the 10-year period.

### *Case definition and data collection*

The medical records of these hospitals categorized *Salmonella*-associated diseases as typhoid fever, gastroenteritis, food poisoning, septicemia and psychosis. Typhoid fever cases were diagnosed by clinicians as having pyrexia for up to five days or more with one or more of the following symptoms: diarrhoea, vomiting, loss of appetite, persistent headache, and malaise. Gastroenteritis cases were diagnosed by the physician as having intestinal disorder and/or frequent passing of stool.

Some patients were also observed with complications such as psychosis and septicemia. Demographic data such as age, sex, underlying conditions of the patients, number of death cases, and vaccination status were recorded. Nationality of the patients and countries visited during the month before onset of infection (travel-associated cases) could not be derived.

### *Procedures used to process samples collected from patients throughout the 10-year period in all the hospitals*

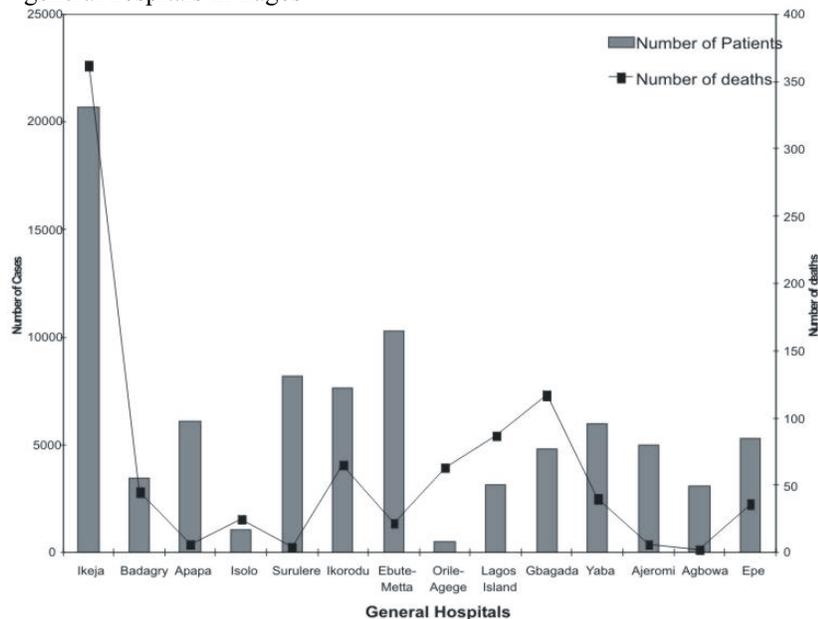
Several attempts were made at source identification to ensure compliance with the standard procedures in each of these hospitals. Laboratory diagnosis for typhoid cases in all the hospitals were first based on Widal agglutination tests and confirmation by bacteriological analysis of blood, bone marrow, and stool and/or urine samples of the patients. The Widal test was performed with standardized *Salmonella enterica* serovar Typhi O and H antigens and values more than the cutoff titre value (1:160 for O and H agglutinins) were regarded as positive. Blood samples were inoculated into brain-heart infusion broth in a ratio of 1:9 and incubated at 37°C. Subculture was made on the following media: blood agar (Oxoid, London,UK) MacConkey's agar (Oxoid) and *Salmonella*-*Shigella* agar (Oxoid). Stool samples from cases of gastroenteritis were cultured directly on solid media. All culture plates were incubated aerobically at 37°C for 24 hours. Colonies were first Gram stained and then subjected to biochemical tests as described by Cowan and Steel [8]. None of the hospitals performed serotyping of the *Salmonella* isolates.

### *Statistical analysis*

F-statistics calculating analysis of variance using the SPSS 11.0 Statistical Package (IBM, Chicago, USA) were computed to test the distribution of cases of *Salmonella* infections for the 10-year period.

## Results

Out of 85,187 confirmed cases of *Salmonella*-associated diseases (SADs), 880 deaths were recorded between 1999 and 2008 in 14 public hospitals in Lagos State, giving a case-fatality rate of 1.03%. The highest cases of SADs were recorded in Ikeja General Hospital followed by Ebute-Metta General Hospital, and the least in Isolo General Hospital. Figure 1 shows that the highest percentage (41.1%) of the total deaths recorded in this study was

**Figure 1.** Number of *Salmonella*-associated cases and deaths recorded in 14 general hospitals in Lagos

observed in Ikeja gGeneral Hospital followed by 13.3% in Gbagada Hospital, while the lowest percentage of deaths was recorded in Surulere Hospital (0.5%). The prevalence of non-typhoidal *Salmonella*-associated illness in this study was 64.5% as compared to 35.5% recorded for typhoid fever. The mean incidence of SADs in Lagos State with a population of about 19 million people for the 10-year period was estimated to be 45 cases per 100,000 persons per year, while that of typhoid fever and gastroenteritis were 16 cases per 100,000 persons per year and 29 cases per 100,000 persons per year respectively (Table 1). The number of female patients with septicemia was significantly higher ( $P < 0.05$ ) than that of male patients, and the psychotic *Salmonella*-infected males in this study did not significantly ( $P > 0.05$ ) outnumber their female counterparts; however, the risk of septicemia cases could be as much as five times higher than that of psychosis patients (Table 2). During the period from 1999 to 2008, deaths due to *Salmonella* infections occurred in patients with typhoid fever and gastroenteritis. The number of deaths due to typhoid fever was significantly ( $P < 0.05$ ) higher than deaths due to gastroenteritis except in 2003 and 2004. The risk associated with typhoidal deaths was between 4 and 11 times higher when compared to gastroenteritis deaths between the years 2000 and 2002 (Table 3). Both diseases showed an increasing trend in both sexes between 1999 and 2001. The increase in trends of both diseases was recorded in male subjects

between years 2002 and 2006 and in female subjects between the years 2003 and 2004. The highest number of typhoid cases and deaths occurred in females in 2006 (Table 4).

*Salmonella*-associated diseases were most prevalent in adults 21 to 30 years of age (49.49%), followed by the age group 31 to 40 years (16.0%), while the lowest percentage of *Salmonella*-associated diseases was found in the age group 11 to 20 years (7.30%). More cases were observed in the year 2006 (17.8 %) than in any other year during the period under review (Figure 2). Few cases of patients with invasive *Salmonella*-associated gastroenteritis were observed, and these were mainly in children under five years of age. Also, infants and children aged 0-10 years was the third age group most affected by SADs; this group accounted for 17.7% cases and 33.5% death of typhoid fever in this study (Table 5).

## Discussion

*Salmonella* infection in humans continues to be a distressing health problem. The results of a 10-year retrospective cohort study conducted in 14 public hospitals in Lagos revealed 85,187 confirmed cases of *Salmonella*-associated diseases (SADs), of which 880 deaths were recorded, giving a case-fatality rate of 1.03%. Of the 85,187 patients, 54,919 (64.5%) had gastroenteritis and 30,210 (35.5%) had typhoid fever (Table 2). These results indicate that infections caused by *Salmonella enterica* serovars are endemic

**Table 1.** Incidence of *Salmonella*-associated diseases from 1999-2008 in Lagos State

<i>Salmonella</i> -associated diseases	Number of cases	Incidence/10 <sup>4</sup> /Yr (p = 19 x 10 <sup>5</sup> )	Number of deaths
Gastroenteritis	54,919	29	653
Typhoid fever	30,210	16	227
Septicaemia	48	0.005	0
Psychosis	10	0.001	0
<b>Total</b>	<b>85,187</b>	<b>45</b>	<b>880</b>

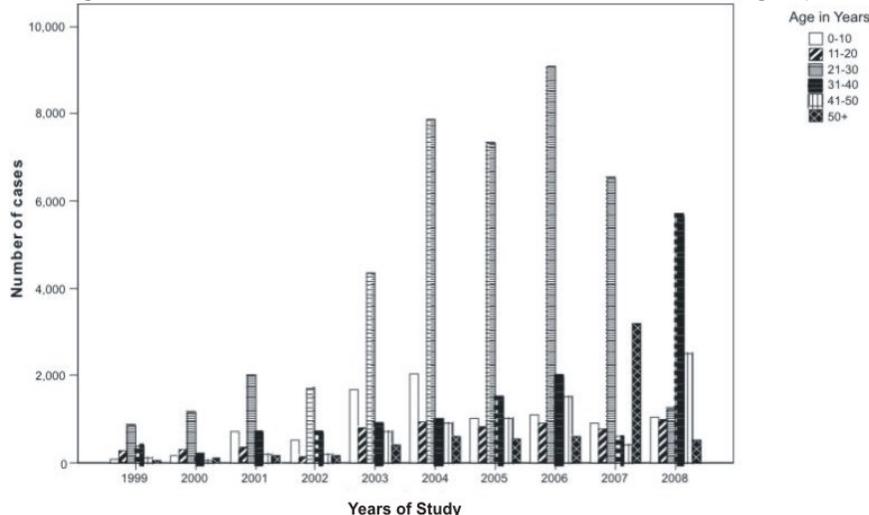
P represents the estimated population of Lagos State from population Commissions.

**Table 2.** Relative risk of *Salmonella*-associated diseases in male and female subjects in Lagos

<i>Salmonella</i> -associated diseases	Number of males (%)	Number of females (%)	Total Number (%)	Male vs Female $\chi^2$ , P [RR(95CI)]
Typhoid fever	17,610 (35.4)	12,600 (35.6)	30,210 (35.5)	0.57, 0.4 [0.99 (0.99-1.02)]
Gastroenteritis	32,168 (64.6)	22,751 (64.3)	54,919 (64.5)	0.75, 0.4 [1.01 (0.98-1.04)]
Septicaemia	20 (0.04)	28 (0.08)	48 (0.06)	5.58, 0.01 [0.51 (0.28-0.93)]
Psychosis	6 (0.01)	4 (0.01)	10 (0.01)	0.01, 0.92 [1.07 (0.27-4.48)]
Total	49,804 (100.0)	35,383 (100.0)	85,187 (100.0)	0.68, 0.4 [0.99 (0.97-1.03)]

RR = relative risk statistics; 95CI = 95% confidence intervals; P = probability;  $\chi^2$  = Chi square.

**Figure 2.** Age distribution of cases of *Salmonella*-associated diseases in Lagos (1999-2008)



in our environment and thus pose a serious threat to public health. In many developing countries, typhoid and paratyphoid are major causes of gastric illness transmitted by the faecal-oral route [9,10]. In Thailand, *Salmonella* are the main bacteria which cause gastrointestinal and systemic infections. In 2005 alone, nontyphoidal *Salmonella* contributed 89.39%, of SADs followed by typhoidal salmonellosis [11]. Recently, *Salmonella*-associated diarrhoea and fever was reported in Maseno, Kenya [12]. The severe disease has poor prognosis because of co-infection and co-endemicity with malaria [7,9]. Although no cases of typhoid perforations and hepatomegally were found in our study, a few cases of life-threatening complications such as septicemia (48; 0.06%) and typhoid psychosis (10; 0.01%) were noticed. Typhoid fever complications such as septicemia, typhoid psychosis, intestinal perforations, hepatosplenomegaly and haemorrhage have been documented to increase mortality in areas characterized by inadequate sanitation, poor hygienic practices, and drug abuse [5,7,13].

In this study, the mean incidence of SADs for the 10-year period was estimated to be 45 cases per 100,000 per year, while that of typhoid fever alone was 16 cases per 100,000 persons per year (Table 1). To our knowledge, no previous studies have examined the population-based surveillance at all the public hospitals for laboratory-confirmed *Salmonella* infections in Lagos State, Nigeria. In Mediterranean African countries, typhoid fever is considered endemic with medium incidence of 10 to 100 cases

per 100,000 persons [14,15] and in Libya the incidence rate for the year 2006 was 16 per 100,000 persons per year [16]. Egypt remains a country with intermediate incidence of one to 180 per 100,000 cases of enteric fever, below nations such as India and Indonesia which claimed more than 100 cases per 100,000 persons [17]. In Tunisia, the 2006 Bulletin of the Ministry of Health showed an incidence of typhoid fever of about one case per 100,000 per year [18]. Also, recent data in Morocco indicated an estimate of 8 cases per 100,000 of typhoid fever [19]. Therefore, the high incidence of SADs, particularly of typhoid fever recorded in the present study, may represent a surveillance artifact resulting from increased awareness of the diseases, greater access to diagnostic facilities, more sensitive diagnostic methods, and good record and reporting systems in the health-care facilities examined.

The number of deaths arising from SADs was not proportional to the number of cases in all hospitals but Ikeja General (Figure 1). During the 10-year period, deaths due to *Salmonella* infections occurred in patients with typhoid fever and gastroenteritis. The number of deaths due to typhoid fever was significantly ( $P < 0.05$ ) higher than deaths due to gastroenteritis except in 2003 and 2004. The risk associated with typhoidal deaths was between 4 and 11 times higher when compared to gastroenteritis deaths between the years 2000 and 2002. Available records revealed that most patients were from low socio-economic status, residing in areas with poor sanitation. The current surveillance data indicated

**Table 3.** Types and numbers of cases and deaths of *Salmonella*-associated diseases in Lagos for 10-year period (1999-2008)

Years	Typhoid fever (deaths)	Gastroenteritis (deaths)	RR (95%CI)	Septicemia (deaths)	Psychosis (deaths)	Total number of patients (deaths)
1999	445 (13)	1,294 (17)*	2.3 (1.0-5.0)	13 (0)	-	1,752 (30)
2000	536 (15)	1,422 (10)*	4.1 (1.7-9.8)	-	-	1,958 (25)
2001	1,342 (10)	2,767 (2)*	11.2 (2.3-74.2)	11 (0)	-	4,120 (12)
2002	906 (8)	2,483 (3)*	7.4 (1.8-35.2)	4 (0)	5 (0)	3,398 (11)
2003	3,337 (27)	5,558 (51)	0.9 (0.5-1.4)	2 (0)	-	8,897 (78)
2004	4,367 (57)	8,983 (113)	1.0 (0.7-1.5)	-	-	13,350 (170)
2005	4,313 (30)	7,901 (84)*	0.7 (0.4-1.0)	10 (0)	1 (0)	12,225 (114)
2006	4,467 (20)	10,700(180)*	0.3 (0.2-0.4)	-	3 (0)	15,170 (200)
2007	5,651 (23)	6,743 (180)*	0.2 (0.2-0.4)	8 (0)	1 (0)	12,403 (112)
2008	4,846 (24)	7,068 (104)*	0.3 (0.2-0.5)	-	-	11,914 (128)
<b>Total</b>	<b>30,210 (227)</b>	<b>54,919 (653)*</b>	<b>0.6 (0.5-0.7)</b>	<b>48 (0)</b>	<b>10 (00)</b>	<b>85,187 (880)</b>

Data were analyzed using chi-square ( $\chi^2$ ) and relative risk statistics at 95% confidence intervals (95%CI).  $P < 0.05$  was considered to be significant. \* $P < 0.05$  (typhoid fever vs. gastroenteritis). RR = Relative risk.

**Table 4.** Sex distribution of cases and deaths of *Salmonella*-associated diseases from 1999 to 2008 in Lagos

Years	Number of cases in males (%)	Number of cases in females (%)	Total Cases	Number of deaths in males (%)	Number of deaths in females (%)	Total deaths
1999	1,049 (2.1)	703 (2.0)	1,752	17 (56.7)	13 (43.3)	30
2000	799 (1.6)	1,159 (3.2)	1,958	11 (44.0)	14 (56.0)	25
2001	2,865 (5.7)	1,255 (3.6)	4,120	7 (58.3)	5 (41.7)	12
2002	2,039 (4.1)	1,359 (3.8)	3,398	8 (72.7)	3 (27.3)	11
2003	5,336 (10.7)	3,561 (10.1)	8,897	46 (59.0)	32 (41.0)	78
2004	9,236 (18.6)	4,114 (11.6)	13,350	105 (61.8)	65 (38.2)	170
2005	6,545 (13.1)	5,680 (16.1)	12,225	55 (48.3)	59 (51.7)	114
2006	6,322 (12.7)	8,848 (25.0)	15,170	94 (47.0)	106 (53.0)	200
2007	7,229 (14.5)	5,174 (14.6)	12,403	70 (62.5)	42 (37.5)	112
2008	8,384 (16.8)	3,530 (10.0)	11,914	79 (61.7)	49 (38.3)	128
<b>Total</b>	<b>49,804 (100)</b>	<b>35,383 (100)</b>	<b>85,187</b>	<b>492 (55.9)</b>	<b>388 (44.1)</b>	<b>880</b>

$\chi^2 = 16.2$ ;  $P = 0.04$ ; On the whole, a total number of 880 deaths due to salmonellosis were recorded between 1999 and 2008 in 14 hospitals in Lagos state. Single table chi-square

**Table 5.** Distribution of *Salmonella*-associated diseases in different age groups

Age in years	Number of cases with <i>Salmonella</i> -associated diseases (deaths)	Number of cases with Typhoid fever (deaths)	Number of cases with <i>Salmonella</i> -associated gastroenteritis (deaths)		Number of cases with septicemia (deaths)	Number of cases with psychosis (deaths)
			Non-invasive	Invasive		
0 - 10	9230 (139)	5337 (76)	3876 (59)	17 (4)	0 (0)	0 (0)
11 - 20	6249 (161)	1513(26)	4730 (135)	0 (0)	6 (0)	0 (0)
21 - 30	42105 (347)	14903(72)	27176 (275)	0 (0)	24 (0)	2 (0)
31 - 40	13611 (139)	4986 (30)	8608 (109)	0 (0)	13 (0)	4 (0)
41 – 50	7624 (60)	2701 (16)	4917 (44)	0 (0)	3 (0)	3 (0)
50 and above	6368 (35)	770 (8)	5595 (27)	0 (0)	2 (0)	1 (0)
<b>Total</b>	<b>85187 (880)</b>	<b>30210 (227)</b>	<b>54902(659)</b>	<b>17 (4)</b>	<b>48 (0)</b>	<b>10 (0)</b>

high incidence of SADs in areas most exposed to environmental contaminations, especially Ikeja, Ikorodu, Surulere, Ebute-Metta and Yaba. Contaminated drinking water has been documented to be one of the main sources of the disease transmission in Lagos [20]. This study was consistent with the separate findings of Khanum *et al.* [21] and Rustam *et al.*, [22] which reported high incidence of SADs among patients residing in rural and more congested areas with poor sanitation.

Interestingly, both typhoid fever and gastroenteritis showed an increasing trend in both sexes between 1999 and 2001. The increase in trends of both diseases was recorded in male subjects between the years 2002 and 2006 and in female subjects between the years 2003 and 2004. These findings were similar to those observed in a study conducted in northern Nigeria where more males were implicated but the sex-related difference in infection rates did not vary significantly ( $P < 0.05$ ) [7]. A higher incidence of SADs was reported among female patients in a study conducted in Pakistan, [21], which was consistent with the case patients recorded in 2006 in the present study (Table 4). Limited dietary choices along with poor personal hygiene and open-air defecations and urination

among the subjects studied were the likely reasons identified for the infections.

*Salmonella*-associated diseases occurred in all age groups in this study (Figure 2), with young adults (21 to 30 years) being the age group most at risk of infection, occurring in 49.49% of the patients. The few cases of patients with invasive *Salmonella*-associated gastroenteritis that were observed were found mainly in children under five years of age. Also, infants and children aged 0-10 years was the third age group most affected by SADs; this group accounted for 17.7% of the cases and 33.5% of the deaths from typhoid fever in this study (Table 5). Available information revealed that most of the infants were either breastfed for a period of one to three months or in some cases, not breastfed at all but mostly fed with baby food cereals. Studies elsewhere have demonstrated that infants infected with *Salmonella* are less likely to be breastfed and more likely to have a household member with diarrhoea than healthy infants [23-25], situations that could not be ruled out in this study. A report from northern Nigeria had implicated young adults within the 11 to 20 years and 21 to 30 years age groups to be the most vulnerable members of the community [7]. In other parts of the world, SADs particularly typhoid

fever, has been known to be a disease of the school-aged children and young adults and milder in infants [4]. The incidence of laboratory-confirmed non-typhoidal *Salmonella* infection is much greater in infants than in other age groups [4]. Infants have also been reported to suffer substantial morbidity from invasive *Salmonella* [2]6 and are at higher risk of complications from *Salmonella*-associated diarrhoeal disease [26]. In Pakistan, the highest incidence of *Salmonella* infection among children and infants aged 1 to 14 years has been reported [21]. A high percentage (13%) of typhoid fever complications in children was also found in Morocco [27] and in Egypt; children were the group most affected in outbreaks of typhoid fever and other SADs [28]. Therefore, the high rate of SADs, particularly typhoid fever, recorded in infants and children in this study calls for serious concern and the implication is the increasing childhood mortality arising from these preventable diseases if unchecked.

In conclusion, the current surveillance data indicated high incidence of SADs in areas exposed to environmental contaminations. The mean incidence of SADs in Lagos was found to be 45 cases per 100,000 persons per year, while that of typhoid fever alone was 16 cases per 100,000 persons per year. Cases of patients with invasive *Salmonella*-associated gastroenteritis, mainly in children under five years of age, were observed. The results also revealed that infections caused by *Salmonella enterica* serovars are endemic in our environment and thus pose a serious threat to public health. Therefore, the need to enhance the *Salmonella* surveillance through collaborative strategies aimed to stem the increasing tide of SADs is advocated. Improvement in the provision of clean water and sanitation are critical to reduce the overall burden of these diseases. Constant public health education campaigns are essential to avert undue epidemics. Further population-based studies are still needed. Meanwhile, information from this study will not only support and assist the policy makers and health authorities in proper planning, but also in the prevention and control of these diseases.

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