SALMONELLA GASTROENTERITIS: EPIDEMIOLOGY, CLINICAL MANIFESTATIONS AND TREATMENT OUTCOME

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Thematic Paper
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SALMONELLA GASTROENTERITIS: EPIDEMIOLOGY, CLINICAL MANIFESTATIONS AND TREATMENT OUTCOME

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ABSTRACT

Background: *Salmonella* species that contribute to gastroenteritis are a significant food-borne pathogen affecting the general population and have made an alarming contribution to the emergence of drug resistant strains.

Objectives: The aim of this study is to identify the prevalence of *Salmonella* gastroenteritis and antibiotic-resistant *Salmonella* in admitted patients of Samutsakhon Hospital.

Methods: A descriptive cross-sectional retrospective study was conducted which included patients of all ages admitted to Samutsakhon Hospital with acute gastroenteritis and sent for stool culture from year 2013 to 2015. Clinical manifestations, treatment outcomes and antimicrobial susceptibility patterns were obtained from patients with *Salmonella* gastroenteritis and analyzed.

Results: The prevalence of *Salmonella* gastroenteritis was 529/7,575 episodes of acute diarrhea (6.9%). Among 529 episodes, 351 cases of *Salmonella* gastroenteritis were investigated for epidemiology, clinical manifestations, treatment and treatment outcome. More than half of these 351 patients (56.1%) were children aged less than 5 years. *Salmonella* serogroup B was the most predominant serogroup found, infecting 48.4% of children and 31.9% of adult patients. The prevalence of antibiotic resistant *Salmonella* in patients suffering gastroenteritis was 71.5%. Most of the *Salmonella* strains from child-aged patients were resistant to ampicillin (62.6%) and ciprofloxacin (42.2%). In adults, resistance to ciprofloxacin was 46.3% and ampicillin was 45.6%. Of the 351 cases, only 123 (35.0%) were treated with appropriate antibiotic. The mortality rate resulting from *Salmonella* gastroenteritis was 1.7%. Of the 6 mortalities, only 2 of these patients were treated with the appropriate antibiotic. Eleven patients had multiple admissions of *Salmonella* gastroenteritis within 3 years (24 episodes). Nearly half of these (45.5%) were treated inappropriately at the first time of infection.

Conclusion: Children aged less than 5 years were the most common age group found suffering from *Salmonella* gastroenteritis. Antibiotic resistance of *Salmonella* gastroenteritis was very high despite of its low prevalence. Use of inappropriate antibiotics may be contributing to death and repeated infection.

KEY WORDS: *SALMONELLA* GASTROENTERITIS / PREVALENCE / ANTIBIOTIC-RESISTANCE / SEROGROUPS

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LIST OF ABBREVIATIONS

Abbreviations	**Term**
TS	Typhoidal *Salmonella*
NTS	Non-typhoidal *Salmonella*
SGE	*Salmonella* gastroenteritis
S. enterica ser. Enteritidis	*Salmonella enterica* serovar Enteritidis
spp.	Species
MMWR	Morbidity & Mortality WeeklyReport
CDC	Center for Disease Control and Prevention
WHO	World Health Organization
UNICEF	United Nations Children's Emergency Fund
GI tract	Gastrointestinal Tract
HIV	Human Immunodeficiency Virus
MDR	Multidrug Resistance
DT 104	Definitive type 104
PCR	Polymerase Chain Reaction
ORT	Oral Rehydration Therapy
CI	Confidence Interval
IQR	Interquartile Range
WBC	White Blood Cells
RBC	Red Blood Cells

LIST OF ABBREVIATIONS (cont.)

Abbreviations	Term
BUN	Blood Urea Nitrogen
Na^+	Sodium
K^+	Potassium
Cl^-	Chloride
HCO_3^-	Bicarbonate
TMP/SMX	Trimethoprim/sulfamethoxazole
%R	Percentage Resistance
µm	Micro-meter
dL	Deciliter
mg	Milligram
mEq	Milliequivalent

CHAPTER I
INTRODUCTION

Salmonella is the worldwide prevalent illness among the foodborne diseases, which can cause enteric fever and gastroenteritis. It is revealed that *Salmonella* infection can evoke ten millions human cases per year and mortality of hundred thousand each year in the publication of World Health Organization.(1) The incidence in the developed countries such as in the United States was also high despite of good sanitation. World Health Organization (WHO) issued a report in 2009 for the global burden of childhood diarrhea stated that diarrhea stands in the second most leading cause of mortality in children under five years of age affecting the whole world. It means that diarrhea is killing nearly one in five children, approximately 1.5 million annually.(2)

The study published in year 2011 showed that *Salmonella* and Shiga toxin-producing *Escherichia coli* obligate about 1.2 million cases of gastrointestinal illness, 22,000 hospitalization and 400 deaths per annum.(3) An epidemiological chronicle of salmonellosis in Poland, 2012 specified that a very high hospitalization percentage of about 69.4% in the total of 8,444 cases of salmonellosis where *Salmonella* gastroenteritis took the maximum fragment, more than 90% of the illness. The incidence rate was 21.9 per 100,000 populations. *Salmonella enterica* serovar Enteritidis (*S. enterica* ser. Enteritidis) is the most etiological agent in Poland triggering the disease over 77% of the total cases.(4)

There were many outbreaks of *Salmonella* infection occurred and many kinds of food could be the common sources of infection. An outbreak in several states of United States in 2013 because of the cucumbers imported from Mexico contaminated with *Salmonella* Saintpaul, instigating illness to total of 84 people with 28% hospitalization whereas there is no mortality reported.(5) The Mortality and Morbidity Weekly Report conveyed an outbreak of *Salmonella* Newport infections linked to cucumbers in the United States in 2014 in which 275 patients from 29 states

and District of Columbia are affected. The affected patients are approximately 42 years, 66% were female. Thirty four percent were hospitalized and there is one case of mortality reported by Centers for Disease Control and Prevention(6) CDC reported multistate outbreaks occurred in this year with many foods as common sources including pork, cucumbers, raw, frozen, stuffed chicken entrees and frozen raw tuna.(7) Contacting with live poultry also caused four outbreaks involving with 252 cases in 43 states.(8)

In the etiology of acute gastroenteritis, *Salmonella* stands in the foremost reason of bacterial diarrhea in which it is the prominent cause of mortality and morbidity among children less than 5 years old and the normal population with the estimated incidence rate of 1,140/100,000 persons-year globally.(9)

In a study making research for enteric bacterial pathogens in children in Niger initiated that *Salmonella* was the second most frequent enteropathogen giving prevalence of 9.2% after *Escherichia coli*. This study was performed on 4,020 children of under five years of age with diarrhea during 2010 to 2012.(10)

In Thailand, few studies showed the prevalence or incidence of *Salmonella* gastroenteritis, especially in adult patients. In a study of the soldiers of United States who were training in Thailand during year 2000-2001, 182 cases of acute diarrhea for less than 96 hours were enrolled. NTS was the second most common pathogen found in two years, 13.8% in year 2000 (Nakhon Sri Thammarat, Southern Thailand) and 34.2% in year 2001 (Phitsanulok, Northern Thailand).(11)

Another study was done in Thai children (aged 3 months to 5 years) at Kanchanaburi province (Western Thailand, near Thai-Myanmar border).(12) This study compared enteric pathogens found in children with acute diarrhea and children without symptom. *Salmonella* were the third most common pathogen found both in cases (6%) and controls (9%).

Last study was retrospective study in Bangkok, Thailand, during 2009 to 2010.(13) This study aimed to describe antibiotic prescription in adult patients with acute diarrhea at King Chulalongkorn Memorial Hospital, which was the tertiary and university hospital. 390 adult patients older than 15 years of age who presented with acute diarrhea were enrolled but only 36 patients had sent stool culture. *Salmonella* was found in two cases (5.6%).

From the Annual Epidemiology Surveillance Report of the Bureau of Epidemiology, Thailand in 2013, acute diarrhea had the highest morbidity rate, 1,756 cases per 100,000 populations.(14) Food poisoning was also in the fifth rank with morbidity rate of 204 cases per 100,000 populations.(15) *Salmonella* organism was reported as one of the most common causes of both acute diarrhea and food poisoning.(15, 16) There were 93 outbreaks of food poisoning in 33 provinces in the year 2013. Bacteria were identified in 73.1% which is the most common cause of these outbreaks. *Vibrio parahaemolyticus* was the most common bacteria (44.3%) and *Salmonella* spp. was the second most common (35.6%). Both NTS and TS were found in the human specimens. NTS comprised of 118 serovars which *Salmonella* Enteritidis was the most common serovars (19.0%). TS comprised of 2 serovars, *Salmonella* Typhi and *Salmonella* Paratyphi A.(15)

Samut Sakhon is the province in the central part of Thailand with coastal area in the southern part. Therefore fishery is one of the most important occupations in the province. Myanmar workers for the fishery increased every year. From the Annual Epidemiology Surveillance Report 2013 of the Bureau of Epidemiology, Thailand, Samut Sakhon was in the seventh rank of the highest rate of acute diarrhea in Thailand (3,073 cases/100,000 populations) (Figure 1.1).The report suggested that the area which had many immigrant workers was one of the risk factor for the high incidence rate of acute diarrhea.(16)

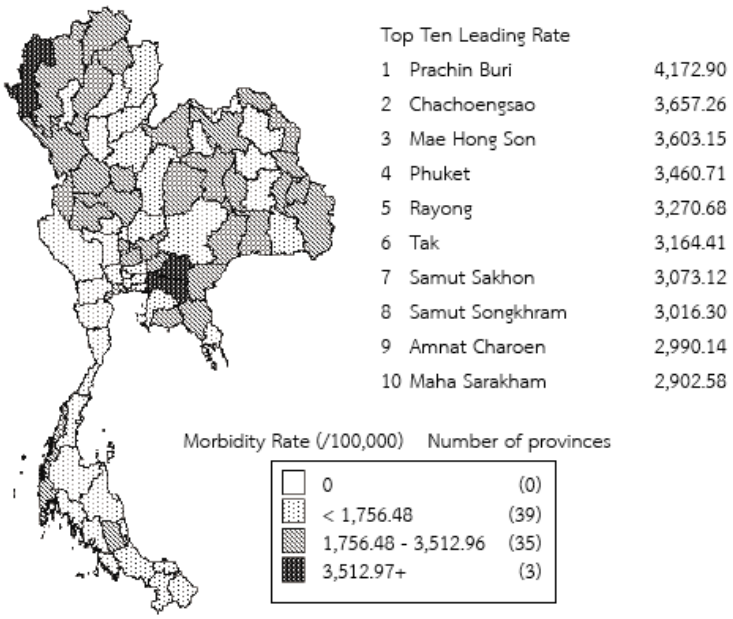


Figure 1.1 Reported cases of acute diarrhea per 100,000 population by province, Thailand, 2013(16)

Antibiotic resistance non-typhoidal *Salmonella*, a serious threat regarded by Center of Disease Control and Prevention (CDC) stated that this concern will be getting urgent without preventive measures and continuous monitoring system. In 2013 in United States, drug resistant *Salmonella* caused 100,000 illnesses per year.(17)Drug resistance of non-typhoidal *Salmonella* isolates which was resistant to at least one antibiotic started to give burden to community by giving 20-30% resistance in 19th century and when it turned to 20th century, its percentage of resistance rose up to 70% in some continents of the world.(18)

Therefore we will conduct the retrospective study to identify the prevalence of *Salmonella* gastroenteritis in Samutsakhon hospital. Clinical manifestations, treatment outcome and antibiotic susceptibility of patients with *Salmonella* gastroenteritis will also be described and will be benefit for useful information of the real situation in Samut Sakhon Province.

CHAPTER II
LITERATURE REVIEW

2.1 Microbiology of *Salmonella* species

Salmonella are gram-negative, non-spore-forming, significantly motile enterobacteria which has cell diameters of roughly 0.7 and 1.5 µm, lengths from 2 to 5 µm, and peritrichous flagella (flagella that are all around the cell body). They obtain their energy from oxidation and reduction reactions using organic sources, so they are named as chemoorganotrophs and are facultative anaerobic, capable of surviving with or without oxygen. *Salmonella* is a ubiquitous pathogen for human and animals affecting all over the world.(19) The genus *Salmonella*, which includes in the family Enterobacteriaceae, was denominated after Daniel E. Salmon, an American veterinarian who first isolated *Salmonella* Choleraesuis from pigs with hog cholera in 1884.(20)

The genus *Salmonella* encloses two species, *Salmonella enterica* and *Salmonella bongori*. *S. enterica*, is further confidential into six subspecies: enterica (subsp. I), salamae (subsp. II), arizonae (subsp.IIIa), diarizonae (subsp. IIIb), houtenae (subsp. IV) and indica (subsp. VI). *Salmonella* strains correspond to over 50 serogroups based on the O antigen, and to over 2,500 serotypes. Most of these serotypes belong to one single *Salmonella* subspecies, *enterica*.(21)

O antigen, H antigen and Vi antigen are antigens that have found out in *Salmonella* species. O antigen is positioned on the cell wall of the bacterium and it can also be two or more in numbers. For H antigen, it is an antigen which has a flagella for the motility of the bacterium and it can be ruined by heat and also have two forms called phase 1 and phase 2. The last antigen is known to be the Vi antigen, is named because of its virulence for the bacterium, located upon the O antigen.(19)

Salmonella species are differentiated into two types; typhoidal *Salmonella* (TS) which includes *Salmonella enterica* serovars Typhi, Paratyphi A, Paratyphi B, and Paratyphi C whereas next serovars are named as non-typhoidal *Salmonella* (NTS). Typhoid fever and paratyphoid fever is caused by TS strains, which are human-host

restricted organisms, together mentioned to as typhoid fever. NTS strains may infect the widespread range of vertebrate animals or restricting to the nonhuman animal species.(22)

For TS, low and mid-income countries are at high risk where these strains are endemic because of lack of sanitation and poor adherence to safe food and water. Global Burden of Disease project 2010 stated that typhoid fever causes ultimately 21.7 million infections and 216,000 mortalities and paratyphoid fever about 5.4 million illnesses during 2000.(23) For the view of high-income countries, the disease is acquired which has the association with travelling to endemic areas.(24)

2.2 Epidemiology of Salmonella species

Non-typhoidal *Salmonella* gives the burden to the whole world by 93.8 million illnesses and 155,000 deaths in 2006. The region which mostly need to take account is Southeast Asia region causing 29 million cases per year with morbidity of 49,200 cases/year and approximate incidence rate of 1440 cases/100,000 person-years. In industrialized countries like United States and Europe, the incidence rate is 250 cases and 690 cases/100,000 person-years respectively.(9) Global Burden of Disease project issued that 4.8 million disease illnesses and 81,000 deaths were instigated by NTS in the year of 2010 calculated by the Institute for Health Metrics and Evaluation.(25) *Salmonella* gastroenteritis played a crucial role in causing most of the illnesses and mortality in all around the globe in the whole population including children less than five years of age and elderly ones.(9) In a study aiming to find the prevalence of selected enteropathogens completed in Barbados established that non-typhoidal *Salmonella* were the most corporate isolates followed by rotavirus. They set up that prevalence of *Salmonella* was 21.1% among 571 children of under fifteen years of age admitted with acute diarrhea or gastroenteritis and more than 77% of cases were children less than five years of age.(26)

In United States, estimate nineteen thousand cases and hospitalizations of 4,000 illnesses was caused by foodborne illnesses which were reported in morbidity and mortality weekly report (MMWR) 2014. The occurrence of death is 71 cases. Among them, *Salmonella* incidence was 15.45 per 100,000 population. Amid the top

six serotypes of *Salmonella* isolation, the incidence per 100,000 population of *Salmonella* Enteritidis stayed in the first rank (2.9) whilst *Salmonella* Typhimurium and *Salmonella* Newport stood in second (1.67) and third (1.5), correspondingly.(27)

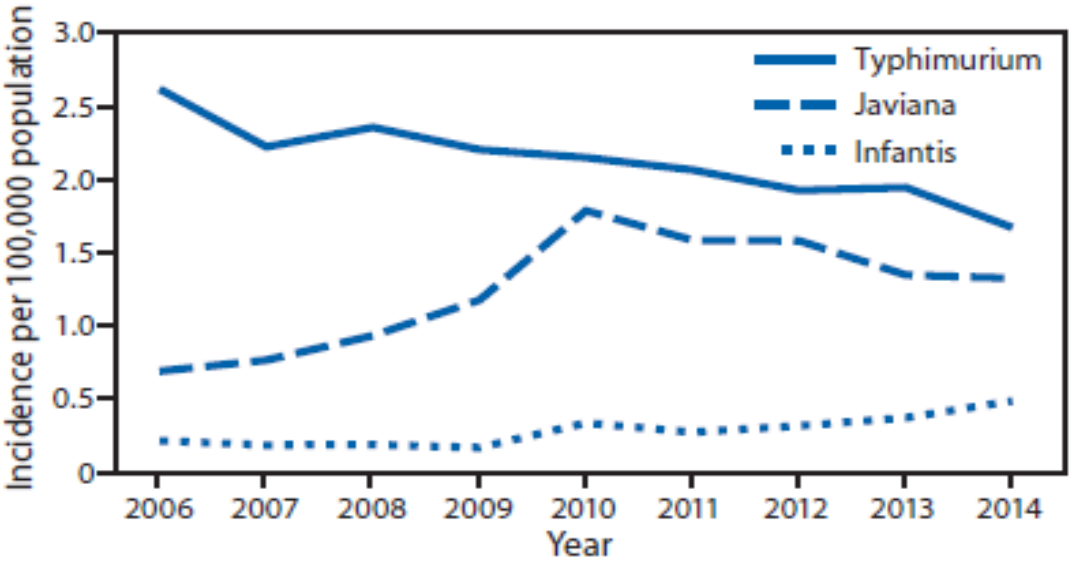


Figure 2.1 Incidence per 100,000 population of culture-confirmed infection with *Salmonella* serovars Typhimurium, Javiana and Infantis, by year- Foodborne diseases Active Surveillance Network United States, 2006-2014.(27)

Salmonella serovar Typhimurium incidence was considerably poorer in 2014 compared to 2006-2008 (27% decrease, CI 15-35%), however significantly higher for Infantis (162% increase, 100-244%), and Javiana (131%, CI 83-191%) by Foodborne Diseases Active Surveillance Network United States 2006-2014. (Figure 2.1)(27)

NTS accounts for 3.4 million invasive infections and 681,000 deaths; 57% of these illnesses and deaths arose in Africa by the year 2010.

Although appropriate antimicrobial therapy was administered, mortality from invasive NTS infection was still elevated in all subgroups. Adults with HIV infections who had case fatality ratios from African case series were 50% early in the HIV epidemic.(28)

An outbreak in Germany occurred because of uncommon variant of monophasic *Salmonella* Typhimurium in 2013specified that salmonellosis is the

second most frequently acquainted bacterial disease (23.2/ 100.000 persons in 2013). *Salmonella* Typhimurium, the most recently determined serovar, is accounted for 41%of human *Salmonella* isolates in 2013.*Salmonella*Enterica serovar 4- is deliberated to be a monophasic variant of serovar Typhimurium 4. The monophasic variant which can be most commonly isolated from pigs has been progressively labelled throughout the world and both sporadic and outbreak-associated cases of human salmonellosis ensue with high prevalence of hospitalization.(29)

A study about the serogroup and serovar distribution of *Salmonella* infection in Thailand was conducted at Siriraj hospital from 2011-2012. 583 isolates of *Salmonella* were found from various specimens, most from feces (67%). Serogroup B was the most common serogroup found in fecal specimen. No *Salmonella* Typhi was found and the author suggested that it was due to the improvement of hygiene and sanitation in Thailand.(30)

A research article about community acquired diarrhea among children and adults in urban settings in Senegal by BMC infectious disease stated that *Salmonella* infection are more prone in the rainy seasons comparing to the dry seasons.(31)27 million cases worldwide are exaggerated by enteric fever each year, which leads to mortality between 216,000 to 600,000 cases. The mainstream of cases were reported in South Asia, India and Pakistan whilst Indonesia has the intermediate incidence and China and Vietnam with the lowest incidence.

Public Health of England reported in 2012 that 354 cases of enteric fever were confirmed by laboratory in England, Wales and Northern Ireland of which 303 cases are UK residents whose ethnicity are Indian, Pakistan or Bangladesh who had travelled abroad to South Asia. 50% of cases are due to *Salmonella* Typhi whereas the rest is because of *Salmonella* Paratyphi.(32)

A study in the Lebanon by the year 2014 indicated that typhoid fever is still enduring to be a serious global health problem in the developing world which is also a key reason of morbidity and mortality. High endemic areas include South-central Asia, Southeast Asia and Southern Africa.(33)

A study of typhoid fever completed in five Asian countries; China, India, Indonesia, Pakistan and Vietnam, specified that among the age group of 5-15years, the incidence rate per 100,000 is 24.2 and 29.3 for Vietnam and China correspondingly,

and 180.3 to Indonesia, 412.9, 493.5 for Pakistan and India, respectively. This study reported in conclusion that burden of typhoid fever is geographically heterogeneous in endemic areas of Asia; the incidence is high in India and Pakistan, intermediate in Indonesia, lowest in China and Vietnam. They anticipated that countries in South Asia, possibly South-East Asia partake a high burden of typhoid fever.(34) The incidence of typhoid fever is high in Asian countries and African countries. (Figure 2.2)(35)

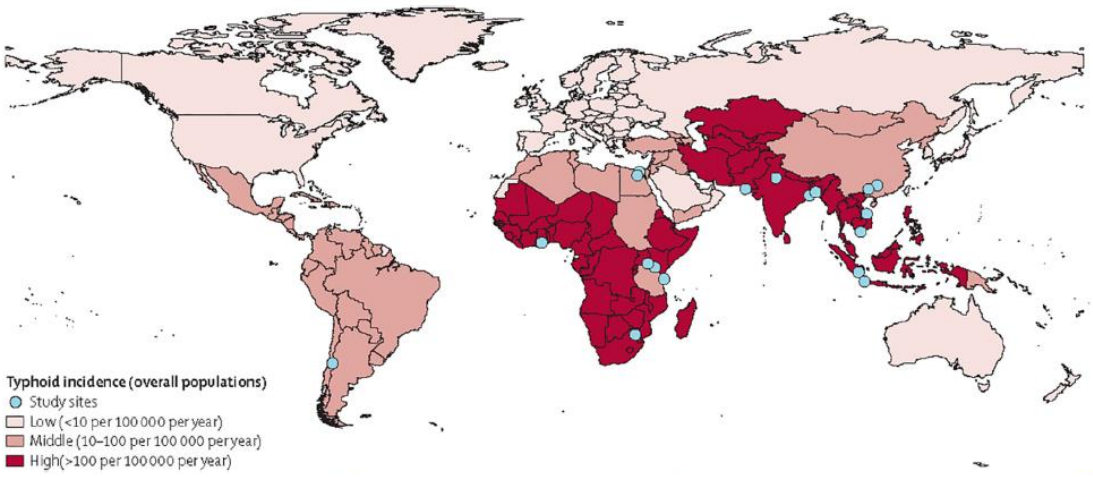


Figure 2.2 Incidence of typhoid fever in low and middle-income countries(35)

2.3 Pathogenesis

Salmonella infection arises primarily through ingestion of contaminated water and food products. When it touches the small intestine (distal ileum and proximal colon) leading to the inflammation of the intestinal cells which contributes the consequence of gastroenteritis. Initial host responses comprise neutrophil infiltration, tracked by the arrival of lymphocyte and macrophages.(19)

On behalf of *Salmonella* Typhimurium, the bacterium adhesions attach to the receptors on the membrane of the intestinal cells points to development of membrane “ruffles” by distorting the natural architecture of the intestinal cells. There is a process called pinocytosis, a form of endocytosis, where the ruffling membrane let the *Salmonella* Typhimurium to be engulfed (Figure 2.3).

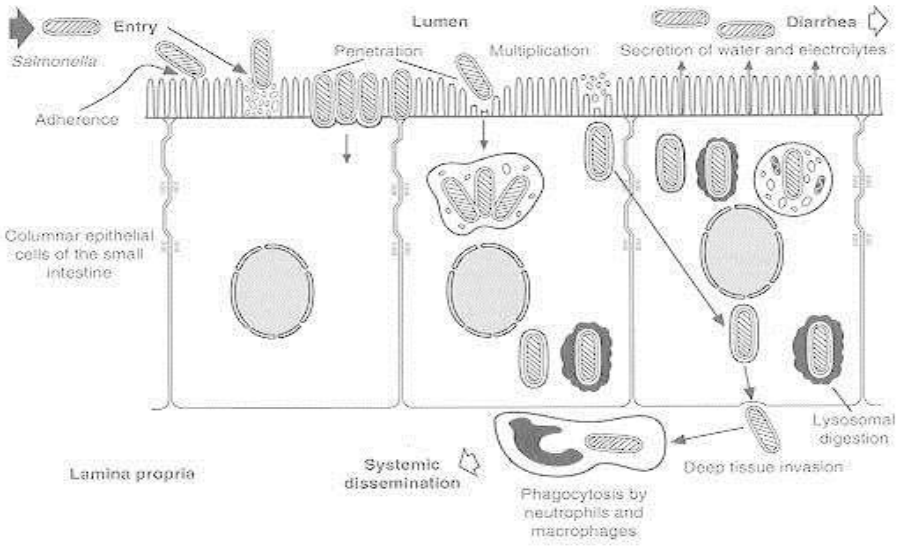


Figure 2.3 Pathogenesis of *Salmonella*: invasion of intestinal mucosa.(19)

Certain species of *Salmonella* infections can pass in the lymphatic system and stimulate extensive infections in many major organs if they are virulent enough to be able to penetrate the intestinal walls. Some complications such as septicemia, GI tract ulceration, gut wall perforation, hemorrhage and ischemia may occur if the *Salmonella* is widespread throughout the body.

The infectious dose required for clinical illness is varied in previous studies. One study administered *Salmonella* organisms from laboratory to healthy human volunteers. Median infectious dose was 10^6 bacteria.(36) Studies from many outbreaks suggested lower infectious doses such as 200 bacteria could produce non-typhoidal gastroenteritis. This variation can be explained by different strain of *Salmonella* organisms. In patients had condition making higher gastric pH such as using proton-pump inhibitor, had higher susceptibility to *Salmonella* infection so infection may occur after ingesting a smaller quantity of bacteria.(37)

Host factors for susceptibility of *Salmonella* infection depend on the age extremity, patients who have chronic granulomatous disease, iron overload, diabetes mellitus and rheumatological conditions. Patients who were immunocompromised or have been using immunosuppressive medications or antibiotics may reduce the competitive effect of the normal intestinal flora. The last but not the least is

hypoacidity which can frequently affects in infants, patients who suffer from pernicious anemia and with the use of antacid medications.(38, 39)

Salmonella produces two toxins; endotoxin and enterotoxin, of which the latter is associated with the incidence of gastroenteritis.

2.4 Clinical Manifestations

Gastroenteritis

The effect of NTS infection is to impose a burden on the people's health by giving the disease of gastroenteritis in mainly underdeveloped and industrialized countries. *Salmonella* spp. contributes gastroenteritis worldwide leading to approximately 155,000 deaths annually. *Salmonella* survey supported foodborne disease surveillance network by World Health Organization data supported that from 2001 to 2005, *Salmonella* Enteritidis was the utmost common serotype worldwide (65% of the isolates), shadowed by *Salmonella* Typhimurium (12%) and *Salmonella* Newport (4%).

NTS is transmitted by consumption of food products originated from animal sources, non-animal food products, and usages of contaminated water or by contact with the animals. For industrialized countries, NTS is transmitted mainly from farm animals, which are the major reservoir such as chickens, ducks, sheep, goats, pig, reptiles, birds, pets, rodents, dogs and cats.(40)

The symptoms starts with nausea, vomiting and subsequent diarrhea for 3-4 days; other symptoms may include fever fluctuating from 100.4 to 102.2 F, chills, abdominal pain, myalgia, arthralgia and headache, 6-12 hours after ingestion of contaminated food. These symptoms are usually self-limited and not associated with intestinal perforation. Sporadically, severe right quadrant pain may be mimicked with appendicitis.(41)A retrospective study conducted in a pediatric hospital in Bangkok, Thailand with 134 children showed that common clinical manifestations of *Salmonella* gastroenteritis were watery diarrhea for 99.3%, fever for 93% and nausea/vomiting for around 50%.(42)

Features of underlying diseases such as anemia, advanced HIV disease and malnutrition habitually exhibit in patients with invasive NTS. Respiratory symptoms are frequently present such as chest crepitation or tachypnea, and diarrhea is often not a noticeable feature in young children. However, symptoms and signs of lower respiratory tract infection are conjoint in invasive NTS infection, these may be recurrently prompted by other pathogens. Other extra-intestinal manifestations are meningitis, encephalopathy, endocarditis, pneumonia, empyema, abscess, urinary tract infection, osteomyelitis, cellulitis or arthritis. Non-typhoidal *Salmonella* meningitis may take place among children and it reasons for high fatality ratio with poor outcomes.(40)

Enteric fever

The incubation period arrays from 7 to 14 days, with a range of 3 to 60 days in which clinical manifestations and complications of enteric fever are similar with *Salmonella* Typhi and Paratyphi.

Sign and symptoms of typhoid fever describe that headache (which is a frequent symptom), diarrhea or constipation, and abdominal pain are specific complaints whereas non-specific complaints are loss of weight, chills and cough, myalgia. Low-grade fever tracked by high sustained fever may precede up to 4 weeks. Other findings include coated tongue (typhoidal tongue), relative bradycardia in less than 50% of cases, blanching erythematous maculopapular rash 2-4mm (rose spot) which can be found in 30% of cases. Hepatomegaly, splenomegaly and altering mental status can also be an outcome of this disease. Children under 1 year and immunosuppressed patients are of high risk groups in which the disease could be more severe in this population.

The most common gastrointestinal complication is bleeding secondary to erosion of Peyer's patches. Other complications for example hepatitis, cholecystitis, pancreatitis, peritonitis and intestinal perforation more frequently occur in the ileum can also manifest. Enteric fever can affect the vital organs of the body as its complications; i. Meningitis, hemorrhages, seizures, encephalopathy, Guillain-Barre´s syndrome, and peripheral neuropathy for central nervous system, ii. Myocarditis, endocarditis, pneumonia, and pleural effusion for cardio-pulmonary complications; iii.

Renal complications: acute renal failure, glomerulonephritis, pyelonephritis; iv. Hematologic: disseminated intravascular coagulation, bone marrow suppression, thrombosis v. Other: infection in bone, joints, liver, spleen, and musculoskeletal system.

Bacteremia and vascular infection

Bacteremia is the most common complication of gastroenteritis which affects not only immunocompetent patients (1-4%), but also infants, elderly and immunologically weak people (AIDS, transplant recipients, patients with malignancy or autoimmune diseases). HIV-infected persons are up to a 100-fold riskier for salmonellosis compared to the general population. Anti-retrovirals and trimethoprim-sulfamethoxazole are protective, not only against *Pneumocystis jiroveci* pneumonia, but also against *Salmonella*. So, a reduction in the incidence of salmonellosis has been observed among HIV patients who received anti-retrovirals and trimethoprim-sulfamethoxazole.(38)A retrospective study at Children's hospital, Boston stated that immunocompromised children are more prone to develop focal infection (7 in 25) whilst immunocompetent are not (5 in 132) ($p < 0.01$).(43) Endovascular complications known as mycotic aneurysm and venous thrombophlebitis may come about in patients with bacteremia with seeding of atherosclerotic plaques or aneurysms primarily in the aorta.(38)

Localized Infection

Possible localized complications of enteric fever are thrombophlebitis, cerebral thrombrosis, encephalopathy, pneumonia, cholecystitis, osteomyelitis, meningitis,endocarditis. Reiter syndrome which is significant of arthritis, conjunctivitis, urethritis is also comprise in the effect of *Salmonella* infection. Non-typhoidal *Salmonella* can virtually conceive at any anatomical site hematogenously and may evolve into local infection, even if the bacteremia is successfully treated. Focal infections should be drained or debrided at any time possible. For the treatment of a surgically eradicated soft-tissue focus in a normal host, antimicrobial therapy of at least 2 weeks is recommended.(43)

Chronic carrier

Chronic carrier means if a person's stool is positive for culture for more than 12 months after an acute infection and it is concerned with the public health status. *Salmonella* Typhi ordinarily spreads when chronic carrier's feces are contaminated with food products or water sources. The chronic, asymptomatic carrier state is thought to be a key feature to continue the maintenance of the bacterium within human populations. Penetrating for chronic carriers and eliminating the carrier status is essential for transmission elimination and disease prevention since *Salmonella* Typhi only has humans as a reservoir. Enteric fever spreading in the community usually occur among street food vendors. One to 4% of patients with enteric fever may become chronic carriers, as well as people who have no history of the disease.

Carrier state was likely to be more common in women, infants and elderly, and in cholelithiasis patients. It is submitted that the liver is the organ where *Salmonella* Typhi can persist and it is intermittently excreted into the gallbladder. There are several reports proposing the association of carcinoma of the gallbladder with chronic typhoid carriage.

Laboratory confirmed NTS infection occurs in 0.1 to 1% cases because non-typhoidal *Salmonella* is less frequent than typhoidal *Salmonella*. Animals, instead, remain repeatedly colonized by NTS than humans. Risks factors associated with NTS carriage include young age, female, and presence of gallstones or kidney stones.NTS chronic carriers are not responsible for most human infections worldwide.(40)

2.5 Laboratory Diagnosis

Diagnostic tests and laboratory investigations are necessary to detect the convalescent *Salmonella* infection and to know about the chronic fecal carrier which exists in typhoid fever and to estimate the burden of typhoidal *Salmonella* for the concern of the general population. Strength of diagnosis is the microbiological culture which can be stool or blood, whereas antigen and antibody detection and nucleic acid amplification test take particular restrictions. To achieve the decisive diagnosis of enteric fever, *Salmonella enterica* isolation could be conducted from normally sterile sites typically blood and bone marrow is critical. The result of blood culture can be

positive for 80% or more if the enteric fever is remained untreated. The results of blood culture can be decrease to 40% if the antimicrobial therapy is habitually yield in people who lived in endemic areas. If this condition occur, bone marrow culture is preferable with sensitivity of more than 80%.(24, 44)

For *Salmonella* gastroenteritis, conventional stool culture is the gold standard method for laboratory diagnosis and freshly passed stool is the best for isolation of organism. Stool or rectal swab specimens are collected and saved in Cary-Blair transport medium to maintain the bacteria. Then the samples are cultured promptly into MacConkey (MC) agar, thiosulfate citrate bile salt sucrose medium (TCBS) and Xylose Desoxycholate Citrate Agar (XDCA) and all inoculated media were incubated at 37°C for 18-24 h. For serotyping, *Salmonella* species were conditionally serotyped consuming slide agglutination techniques with specific antisera and following the methods of Edwards and Ewing (1986).(45)

For typhoidal *Salmonella*, the blood volume taken for the blood culture also plays an important role because of the content of the number of viable bacteria. The first or second week of the disease is the best period for detecting the circulating organisms in the bloodstream. If the patient is suffering from severe disease and also have complications, culture of bone marrow may become frequently positive. Isolation of *Salmonella enterica* can be done from feces in up to 30% of patients with typhoidal *Salmonella* and in <1% of urine samples. In doing fecal culture, the sensitivity increases to 30% by testing multiple cultures whereas there is only 10% sensitivity in single culture method. Various authorities indorse handling of *Salmonella* Typhi and Paratyphi A under biosafety level 3 conditions because they have remained a communal cause of laboratory-acquired infection.

Serologic assays

In patients who were doubted for typhoid fever, serological assays such as agglutinating antibodies against LPS (O) and flagellar (H) antigens of *Salmonella* Typhi can be diagnosed by measuring Widal test. Acute-phase serum and convalescent-phase serum can be taken approximately 10 days apart and increase of antibody titer (4-fold rise) suggested a positive result. Nevertheless, patients who are infected have their antibody titers increase earlier than the onset of clinical symptoms,

so it makes a difficult way for the necessary 4-fold rise of antibody titers between first and subsequent.(24, 46) A study from Vietnam established that Widal test can make diagnosis in estimately 74% of positive blood culture patients with a cut point titer of ≥200 for O agglutination or ≥100 for H agglutination in patients suffering from typhoidal *Salmonella* and also in patients with fever or healthy.(24, 47)

Molecular assays

Conventional PCR and real-time PCR which are so called as nucleic acid amplification tests can be used for the detection of typhoidal *Salmonella* (*Salmonella* serovars Typhi, Paratyphi A) predominantly in blood. This methods can be used for amplifying small numbers of organisms, bacteria which cannot be cultured and also the deceased organisms.

PCR method have sensitivity which can surpass 90% in some of the studies without improvement in cases of positive blood-culture, even though there are other reported studies which have inferior sensitivities more dependable with the number of bacteria in the blood.(24, 48)

2.6 Treatment

The mainstream for treatment of acute gastroenteritis is oral rehydration therapy (ORT) and to maintain the fluid and electrolyte balance. The usage of ORT is ecologically safe and can decrease the rate of hospitalizations in both developed and developing countries. WHO and UNICEF recommend the new formula of low osmolality oral rehydration salts (ORS) which contains sodium 75mmol/L, chloride 65mmol/L, anhydrous glucose 75mm0l/L, potassium 20mmol/L and trisodium citrate 10mmol/L.

Antibiotics therapy is mostly not indicated in non-invasive *Salmonella* gastroenteritis. On the other hand, empirical antimicrobial treatment is required for invasive or inflammatory diarrhea.(49)Antimicrobial therapy is recommended only in febrile or invasive diarrhea where it was thought to be moderate or severe illness. However, suitable antibiotics administration will reduce the duration of illness, decrease the morbidity rate and may be life-saving. In Western countries, antibiotics

are not prescribed where the treatment is only restricted to rehydration and to maintain the electrolytes. During the recent years, fluoroquinolones or broad spectrum cephalosporins are the drug of choice for the treatment of NTS, but nowadays, increasing numbers of multidrug resistance strains are occurred throughout the world due to the excessive unnecessarily use of antibiotics.(50) Risk groups who may need the antibiotics treatment are extreme of ages (infants, elderly) and immunocompromised individuals. To initiate the empiric antibiotic treatment, local epidemiology and local resistance pattern of each country should be observed and surveillance of etiological pathogens of acute diarrhea should be continued in each and every country. Recommended antibiotics for children is ceftriaxone 100 mg/kg/day in two equally divided doses for 7-10 days or azithromycin 20 mg/kg/day once a day for 7 days. Recommended antibiotics for adults is levofloxacin 500 mg (or other fluoroquinolone) once a day for 7-10 days or azithromycin once a day for 7 days. Duration of levofloxacin or azithromycin should be prolonged to 14 days if the patient is immunocompromised. Azithromycin 500mg for 5 days shows the proven efficacy in *Salmonella* infectious diarrhea in adults.(50)

2.7 Antimicrobial resistance

Antibiotic resistance is now threatening all over the world by causing approximately 2 million illnesses and 23,000 deaths by both bacteria and fungus in United States in the year 2013 according to the report of CDC. Resistant strains of *Salmonella* to antimicrobial agents also have grown into a worldwide health problem. Antibiotic resistance of *Salmonella* is regarded as a serious threat as it will get worsen and become urgent without further prevention and monitoring activities.(17)*Salmonella* Enteritidis and Typhimurium are the most prevalent serovars among others and increasing display of antimicrobial resistance of these strains are overwhelming the whole world.(51) Nowadays, people are using antimicrobial agents for veterinary to promote growth and for therapeutic use. Drug resistance bacteria from animals are getting to humans by eating of improperly cooked meat, drinking of contaminated water and eating of fresh vegetables which are contaminated by the

feces of animals. This is the way how antibiotic resistance is spreading in the community.(17)

Overall antimicrobial resistance of *Salmonella* infection showed an obvious ascend from 20-30% in the early years of 1990 to as increase as 70% in some continents of the world at the turn of 20th century.(18) In the year 1990 in United States, the prevalence of drug resistance *Salmonella* was 31% and in 1993 in Greece, it reached up to 66%. By the turn of the century, the prevalence was 71% in Spain in 2001 and 69% in Taiwan in 2003.(18) In United States, *Salmonella* was giving an estimate of 1 million infections and 100,000 illnesses by drug-resistant *Salmonella* per year in 2013.(17)A foremost origin of illness in humans and animals in Europe, especially the United Kingdom is triggered by a distinct strain of *Salmonella enterica* serotype Typhimurium, known as definitive type 104 (DT104), which has become resistant to five major antibiotics ampicillin, chloramphenicol, streptomycin, sulfonamides, and tetracycline. Within the past fifteen years, the number of cases of *Salmonella* Typhimurium by Public Health Laboratory Information System reported to CDC still remained constant. In contrast, the proportion of isolates with the five-drug pattern of resistance has increased from less than 1 percent in 1979–1980 to 34 percent in 1996.Since 1995, 91 percent of isolates that were phage typed were identified and the great majority of these isolates are probably DT104. It is estimated that the 40,000 *Salmonella* isolates reported yearly, 3400 are *Salmonella* Typhimurium with the five-drug pattern of resistance. Investigations in the United States have found associations between *Salmonella* Typhimurium DT104 infections in humans and the consumption of unpasteurized dairy products and direct contact with livestock.(52)

By encouraging the judicious use of antimicrobial agents in food animals and termination the use of growth-promoting agents in food animals of agents used in human medicine, such as penicillin and tetracycline, World Health Organization group reaffirmed recommendations to minimize the further emergence of resistance to antimicrobial agents to which five-drug–resistant *Salmonella* Typhimurium DT104 is resistant.(52)

Table 2.1 Global status of antimicrobial resistance in non-typhoidal *Salmonella* isolates(18)

Country	Year of study	Number of isolates	% resistance (to at least one antibiotic)
United States	1990	758	31%
Greece	1993	58	66%
Turkey	1996	259	20%
United Kingdom	1996	5849	90%
Spain	2001	1051	73%
Taiwan	2003	675	69%

Antibiotic resistance of non-typhoidal *Salmonella* is affecting in various ways to each country of the world. Table 2.1 show the percentage resistance of non-typhoidal Salmonella isolates to antibiotic in countries of the world.(18)In 2006 in England, resistance to ampicillin and tetracycline was around 40%, TMP/SMX was 18%and in Germany in 2014, resistance to ampicillin was 78%, tetracycline was 77.6% and TMP/SMX was 15%. The resistances to these drugs were much higher in developing countries like Ethiopia, which showed resistance of ampicillin (100%), tetracycline (100%) and TMP/SMX (85%). Resistance to ciprofloxacin was approximately 0.6 to 5.5% in all countries.(53-55)

Study from Chiang Mai, Thailand, during 2005-2007, was conducted by using 183 strains (21 serotypes) of *Salmonella enterica*.(56) All of human isolates (52 strains) obtained from patients stools. All of these represented resistance to ampicillin, chloramphenicol and spectinomycin. Resistance to other antibiotics were varied; ciprofloxacin (31%), gentamicin (21%), nalidixic acid (27%), tetracycline (90%), streptomycin (85%), sulfamethoxazole (44%) and trimethoprim (63%).

In a retrospective study conducted in Shanghai, China made 1833 children presented to the clinic with acute diarrhea and 316 patients had stool culture positive for non-typhoidal *Salmonella*. Overall prevalence of antibiotic resistant *Salmonella* was 60.5% and resistances to first line antibiotic were high (ampicillin- 58.6%, TMP/SMX- 32.4%). In China, *Salmonella* contamination in raw food of animal origin is common and environmental contamination and exposure might be associated with NTS infection.(57)

Chloramphenicol was used as a main treatment for enteric fever in earlier 1970s. After that period, chloramphenicol-resistant *Salmonella enterica* serovar Typhi outbreaks were reported from many countries of the world, such as in India, Vietnam, South Korea, and Bangladesh.

Because of the chloramphenicol resistance, two first-line drugs, ampicillin and trimethoprim-sulfamethoxazole were used for taking place of chloramphenicol. And then, multidrug resistant *Salmonella enterica* serovar Typhi had been spreading, so fluoroquinolones such as ciprofloxacin was used as an alternative drug for typhoidal *Salmonella*. Distribution of antibiotic resistance of *Salmonella* Typhi globally was shown in Figure 2.4.(58)

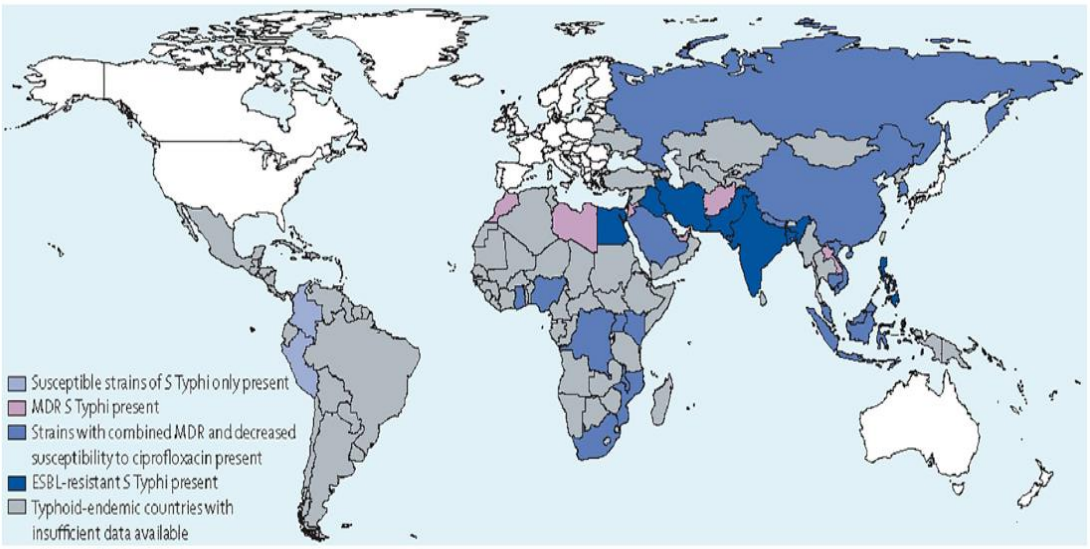


Figure 2.4 Distribution of antimicrobial drug resistance in *Salmonella enterica* serovar Typhi globally.(58)

Azithromycin which is an azalide antimicrobial agent showed proven efficacy in uncomplicated typhoid fever which have been facing with a high resistant to both MDR and fluoroquinolone in many clinical researches. Another choice of drug is extended-spectrum cephalosporins (e.g., ceftriaxone) which has tendency to be used for the treatment of typhoid fever. Azithromycin can penetrate into most tissues with excellent rate and its intracellular concentrations inside macrophages and neutrophils are 10 to 100 times higher than serum concentrations, with sluggish release from this

intracellular site. The use of azithromycin has been established by Clinical and Laboratory Standard Institutes guidelines in 2015.(24)

CHAPTER III
OBJECTIVES

3.1 Primary objective

3.1.1 To identify the prevalence of *Salmonella* gastroenteritis admitted in Samutsakhon hospital

3.1.2 To identify the prevalence of antibiotic-resistant *Salmonella* gastroenteritis admitted in Samutsakhon hospital

3.2 Secondary objective

3.2.1 To describe the epidemiology of *Salmonella* gastroenteritis admitted in Samutsakhon hospital

3.2.2 To describe clinical manifestations of *Salmonella* gastroenteritis admitted in Samutsakhon hospital

3.2.3 To compare clinical manifestations and treatment outcome between patients with antibiotic-resistant *Salmonella* gastroenteritis and patients with antibiotic-sensitive *Salmonella* gastroenteritis admitted in Samutsakhon hospital

CHAPTER IV
MATERIALS AND METHODS

4.1 Study site

The study was carried out at Samutsakhon Hospital, Thailand.

4.2 Study period

The study was conducted during November 2015 to January 2016.

4.3 Type of study

This study is a descriptive cross-sectional retrospective study.

4.4 Study subjects

Inclusion criteria

1. All ages
2. Patients admitted in the hospital
3. Patients had diagnosis of diarrhea or gastroenteritis
4. Patients had diagnosis of diarrhea or gastroenteritis, with stool culture positive for *Salmonella* species

Exclusion criteria

1. Patients whose diarrhea started after admission
2. Patients who could not retrieve the inpatient records of the diarrheal episode

4.5 Sample size estimation

There are 2 primary objectives in this study. First is to identify the prevalence of *Salmonella* gastroenteritis admitted in Samutsakhon Hospital. Prevalence of *Salmonella* gastroenteritis was 6% from previous study in Bangkok, Thailand.(13) Then the sample size calculation by using this prevalence is as the following.

$n = (Z_{1-\alpha/2})^2 p*(1-p) / d^2$

n = estimated sample size

$\alpha = 0.05$

Z = reliability coefficient for 95% CI$\rightarrow Z_{0.975} = 1.96$

p = prevalence of *Salmonella* gastroenteritis = 0.06

d = precision error = 0.02

$n = (1.96)^2 *0.06* 0.94 / (0.02)^2$

$= 541.6$

So the numbers of patients with diarrhea or gastroenteritis, admitted in Samutsakhon Hospital required for this study, are 542 persons.

Another primary objective is to identify the prevalence of antibiotic-resistant *Salmonella* gastroenteritis in Samutsakhon Hospital. Prevalence of ciprofloxacin-resistant *Salmonella* infectionwas 31% from previous study in Thailand.(56) Then the sample size calculation by using this prevalence is as the following.

$n = (Z_{1-\alpha/2})^2 p*(1-p) / d^2$

n = estimated sample size

$\alpha = 0.05$

Z = reliability coefficient for 95% CI$\rightarrow Z_{0.975} = 1.96$

p = prevalence of ciprofloxacin-resistant *Salmonella* infection = 0.31

d = precision error = 0.05

$n = (1.96)^2 *0.31* 0.69 / (0.05)^2$

$= 328.6$

So the numbers of patients with *Salmonella* gastroenteritis with diarrhea or gastroenteritis, admitted in Samutsakhon Hospital required for this study, are 329 persons.

The process to recruit patients for this study will be as the followings. First step is searching for the number of patients admitted in Samutsakhon Hospital with diarrhea or gastroenteritis and had results of stool culture in 2014. If this number is more than 542 patients, we will use data of the patients in 2014 only. If this number is less than 542 patients, then search again in year 2013. This step will do until total number of all years more than 542 patients. We recruit all patients in the same years because we would like to identify the seasonal variation of the disease. The second step is searching for the number of patients with diarrhea or gastroenteritis admitted in Samutsakhon Hospital in the same time period of the first step and identify who had stool culture positive for *Salmonella* spp. Then we can calculate the prevalence of *Salmonella* gastroenteritis from these two numbers. Third step is to calculate the prevalence of antibiotic-resistant *Salmonella* gastroenteritis. This step needs total number of patients with diarrhea or gastroenteritis admitted in Samutsakhon Hospital and had stool culture positive for *Salmonella* spp. at least 329 patients. Find out the results of antibiotic susceptibility test in this group of patients to find the number of antibiotic-resistant *Salmonella* gastroenteritis. The last step is to fill the data of patients with *Salmonella* gastroenteritis admitted in Samutsakhon Hospital in the case record forms.

Antibiotic susceptibility were determined by disk diffusion method BBL™Sensi-Disc™ Antimicrobial Susceptibility Test at Samutsakhon Hospital. . In this study, antimicrobial susceptibility testing for five antibiotics were recorded (cefotaxime, ciprofloxacin, trimethoprim/sulfamethoxazole, ampicillin, nalidixic acid).

Disk diffusion method

Disk diffusion method was first described by Barry and Thornsberry, 1985 and it was again modified by Kirby-Bauer's method (Bauer et al., 1966) using Mueller Hinton agar as the test medium.

Extensive diversity of antimicrobial agents comprising discs were applied to the surface of Mueller Hinton agar plates which have been inoculated with pure culture of clinical isolates. After incubation, the plates were looked for and measured the diameters (mm) of the zone of inhibition surrounding the disc for each antimicrobial agent and paralleled with the conventional zone size ranges to define

which antimicrobial agent was most proper to use for antimicrobial treatment. Zone diameter used for interpretive standards for antimicrobial susceptibility test is described in Table 4.1.

Table 4.1 Zone diameter interpretive standards for antimicrobial susceptibility test

	Zone diameter interpretive standards (mm)		
Antimicrobial agent	Resistant	Intermediate	Susceptible
Cefotaxime	≤ 14	15-22	≥ 23
Ciprofloxacin	≤ 15	16-20	≥ 21
Trimethoprim/sulfamethoxazole	≤ 10	11-15	≥ 16
Ampicillin	≤ 13	14-16	≥ 17
Nalidixic acid	≤ 13	14-18	≥ 19

4.6 Study procedures

Approval was achieved from the Ethics Committee at the Faculty of Tropical Medicine, Mahidol University.

The medical records will be delivered by the department of registration of Samutsakhon Hospital.

As an alternative of full names and/or the hospital registration number, the logbook system with a specific code was used for reasons of confidentiality.

Records of the medical history, physical examination, laboratory, treatment and outcome are filled in the Case Record Form (CRF).

The data obtained was recorded in a Microsoft Excel file followed by the verification and validation of the data. Statistical software SPSS, Version 20.0.0 was used for statistical analysis.

4.7 Statistical analysis

- Descriptive statistics will be used for percentage, measurement of central tendency in combination with tables and graphs where the clinical manifestations of patients with *Salmonella* gastroenteritis are described.
- The statistical significance was set with a significant level of 0.02 to calculate the total number of acute diarrhea cases and 0.05 was set for the prevalence of total cases of *Salmonella* gastroenteritis.
- Categorical data will be described as frequency and percentage.
- Continuous data will be described as mean, standard deviation, minimum, maximum or interquartile range (IQR) depending on data distribution.
- In case of a skewed distribution, use of median, range and interquartile range was applied.
- Parametric tests will be applied for normal distribution whereas non-parametric tests will be used to analyze the difference between continuous data sets.

4.8 Study methods

The data will be collectedfrom hospital medical records of Samutsakhon Hospital under the authority of hospital administration. The data were used for determination of prevalence of *Salmonella* gastroenteritis in admitted patients of the Samutsakhon Hospital. During the period of 2013-2015 at Samutsakhon Hospital, we chose the patient records of all ages who were admitted to hospital with diarrhea or gastroenteritis according to ICD-10. We included the patients of all ages and gender admitted to the hospital with diarrhea or gastroenteritis and excluded the patients who did not come to the hospital with diarrhea or who had diarrhea after admission to the hospital

The data collection will include

- Demographic data: age, sex, ethnicity, weight, height, occupation
- Patients' history including underlying disease, co-morbidities, smoking, alcohol drinking and drug abuse

- Clinical manifestations including symptoms before admission, physical examination on admission, and laboratory findings
- Stool culture results including serogroups of *Salmonella*, other bacterial infection (if detected), and antibiotic susceptibility
- Treatment, outcome and complications

4.9 Ethics

Ethical approval

The study proposal will be scientifically and ethically evaluated by the Ethical Committee of the Faculty of Tropical Medicine, Mahidol University. As our study is retrospective, only the patients' record will be reviewed. Also, informed consent will not be obtained because patients are not directly involved in our study.

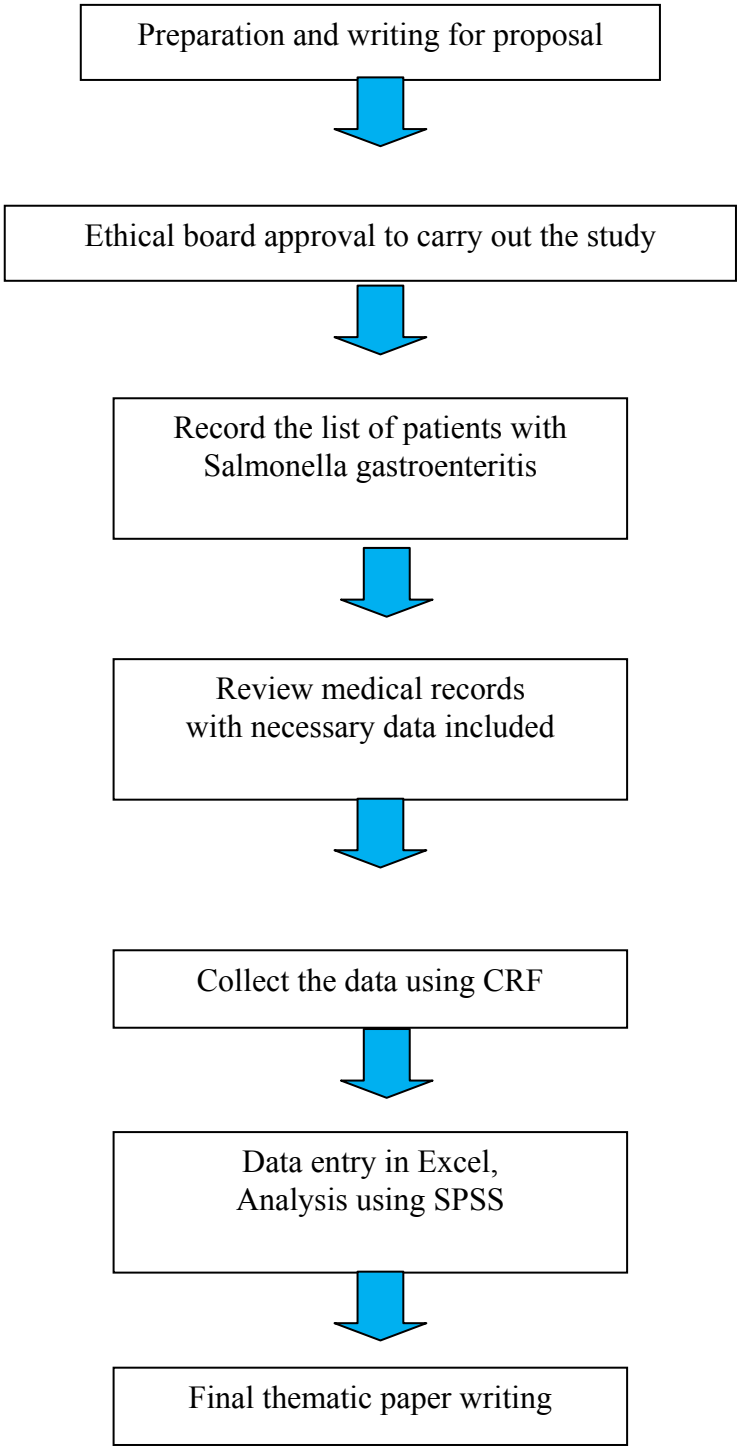
Confidentiality

For patients' confidentiality and privacy, their names are not identified on CRF or database but will be exclusively coded with numerical numbers to identify each and every patient. Only the investigators can access to the records and data.

4.10 Funding

The research fund will be provided by Faculty of Tropical Medicine, Mahidol University, academic year 2015.

4.11 Study flow chart



CHAPTER V
RESULTS

Total 7,575 episodes of acute diarrhea were recorded and sent stool culture at Samutsakhon Hospital within the year 2013-2015. Among these stool specimens, 529 specimens were positive for *Salmonella* species giving prevalence of 6.9% for *Salmonella* gastroenteritis in Samutsakhon Hospital. The process of recruitment of study population is shown in Figure 5.1. A total of 351 cases of *Salmonella* gastroenteritis, which satisfied our inclusion criteria, were included in this study. In 351 cases, 11 cases had multiple infections during 2013 to 2015.

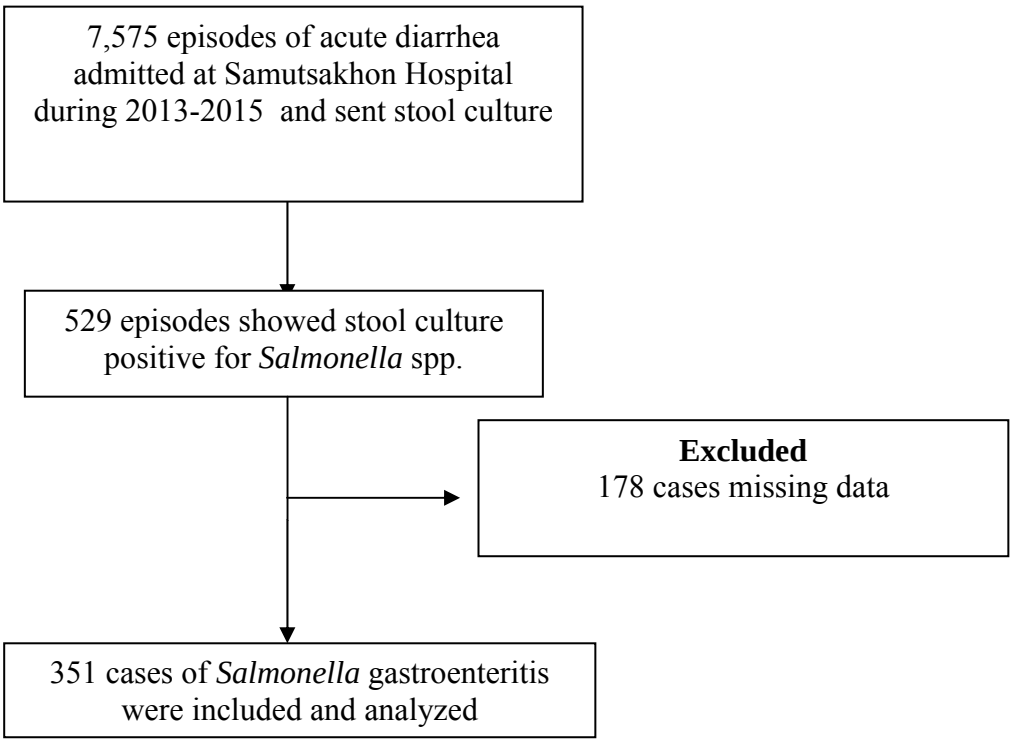


Figure 5.1 Flow diagram showing study population

Demographic characteristics and clinical manifestations of *Salmonella* gastroenteritis

Table 5.1 represents the demographic characteristics of *Salmonella* gastroenteritis in 351 patients. Median age for all patients was 2.0 year (IQR=0.7-40.0year). Male proportion was greater than female (56.7% vs. 43.3%). Median body weight for all patients was found to be 10.6kg (IQR=8.0-45.8kg). 78.3% of patients were within normal weight. 20.5% of all patients were factory workers and 16.0% were elderly patients. 74.4% of the patients had no comorbid diseases. Most common comorbid diseases in all patients were hypertension (10.3%) and diabetes mellitus (7.7%).

There were 213 cases of children (60.7%) and 138 cases of adults (39.3%) included in this study. Most of the children (92.5%) were under five years old. Median age for children was 0.8 year (IQR=0.5-1.0 year) whereas for adults was 49 years (IQR=33.0-72.2 years). There were males comprising of 64.3% in children group and 44.9% in adult group.

Body mass index was calculated for the adult patients and half of the patients were in normal weight (51.2%). Median body weight of adults was found to be 53.5 kg (IQR=46.7-64.0kg). Majority of children (89.2%) were within normal weight according to weight for age by World Health Organization. Median body weight of children was 8.8 kg (IQR=7.3-11.0 kg). Twenty-two percent of adult patients were underweight which was higher than children patients (4.4%). Among the adult patients, most of them were factory workers (52.2%) and elderly (40.6%). Most of both children and adults patients with *Salmonella* gastroenteritis were Thai (85.0% and 83.3% respectively).

55.1% of patients presented with underlying comorbid diseases in adult groups but only 6.6% had comorbid conditions in children group. Common comorbidities in adult patients were hypertension (26.1%) and diabetes mellitus (19.6%). For children, common comorbidities were congenital heart diseases (1.4%), thalassemia (0.9%) and epilepsy (0.9%). Other comorbidities such as Down syndrome, lactase deficiency were presented in children and autoimmune diseases and pelvic inflammatory diseases were presented in adults.

Table 5.1 Demographic characteristics of admitted patients with *Salmonella* gastroenteritis at Samutsakhon Hospital during 2013-2015

Characteristics	N	All patients N (%)	N	Children N (%)	N	Adults N (%)
Median age (IQR) (years)	351	2.0 (0.7-40.0)	213	0.8 (0.5-1.0)	138	49.0 (33.0-72.2)
Gender: Male	351	199 (56.7)	213	137 (64.3)	138	62 (44.9)
Median body weight (IQR)	300	10.6 (8.0-45.8)	206	8.8 (7.3-11.0)	94	53.5 (46.7-64.0)
Body weight: Underweight	286	27 (9.4)	204	9 (4.4)	82	18 (22.0)
Normal weight		224 (78.3)		182 (89.2)		42 (51.2)
Over weight		33 (11.5)		13 (6.4)		20 (24.4)
Obese		2 (0.7)		0 (0)		2 (2.4)
Occupation: Factory worker	351	72 (20.5)	213	0 (0)	138	72 (52.2)
Elderly		56 (16.0)		0 (0)		56 (40.6)
Student		19 (5.4)		14 (6.6)		5 (3.6)
Farmer		1 (0.3)		0 (0)		1 (0.7)
Fisherman		1 (0.3)		0 (0)		1 (0.7)
Business		1 (0.3)		0 (0)		1 (0.7)
Unemployed		2 (0.6)		0 (0)		2 (1.4)
Others		199 (56.6)		199 (93.4)		0 (0)
Race: Thai	351	296 (84.3)	213	181 (85.0)	138	115 (83.3)
Myanmar		50 (14.2)		29 (13.6)		21 (15.2)
Cambodia		4 (1.1)		2 (0.9)		2 (1.4)
Laos		1 (0.3)		1 (0.5)		0 (0)
Smoking	100	22 (22.0)	213	0 (0)	100	22 (22.0)
Alcohol drinking	98	16 (16.3)	213	0 (0)	98	16 (16.3)

Table 5.1 Demographic characteristics of admitted patients with *Salmonella* gastroenteritis at Samutsakhon Hospital during 2013-2015 (cont.)

Characteristics	N	All patients N (%)	N	Children N (%)	N	Adults N (%)
Comorbidities: Hypertension	315	36 (10.3)	213	0 (0)	138	36 (26.1)
Diabetes mellitus		27 (7.7)		0 (0)		27 (19.6)
CKD		10 (2.8)		0 (0)		10 (7.2)
HIV, CA, steroids		15 (4.3)		0 (0)		15 (10.9)
Pulmonary disease		7 (2.0)		0 (0)		7 (5.1)
CVD & CHD		9 (2.6)		3 (1.4)		6 (4.3)
CLD		2 (0.6)		0 (0)		2 (1.4)
Others		25 (7.1)		7 (3.3)		18 (13.0)
Thalassemia		2 (0.6)		2 (0.9)		0 (0)
Epilepsy		2 (0.6)		2 (0.9)		0 (0)
Comorbidity: None	351	261 (74.4)	213	199 (93.4)	138	62 (44.9)
1 comorbid		54 (15.4)		13 (6.1)		41 (29.7)
2 comorbidities		27 (7.7)		1 (0.4)		26 (18.8)
≥3 comorbidities		9 (2.6)		0 (0)		9 (6.5)

IQR = Interquartile range, CKD = Chronic kidney diseases, HIV = Human Immunodeficiency Virus, CA = Cancer, CVD = Cardiovascular diseases, CHD = Congenital heart diseases, CLD = Chronic liver diseases

Clinical manifestations and treatment outcome are shown in Table 5.2. Median duration of diarrhea for all patients was 1 day (IQR=1.0-2.0day) and median frequency of bowel movements was 4 times (IQR=3-8 times). 98.0% of all patients presented to the hospital with less than and equal to 10 times of diarrhea with watery stool (93.3%). Other presenting symptoms for all patients included fever (72.0%), abdominal pain (67.6%), nausea/vomiting (68.6%). Abdominal distension was found only in 4.4% of all patients and abdominal tenderness was presented in 16.2% of the patients. Half of the patients (51.5%) presented with mild dehydration and 26.4% of all patients came with moderate dehydration.

The median duration of diarrhea for both children and adults before admitted to hospital were 1 day (IQR=1-2 days). Median frequency of bowel movements in children was 4 times (IQR=3.0-6.0) which was significantly lower than in adults [5 times (IQR=3.0-10.0) (P value=0.001)]. Firstly for children, mainstream of

patients presented with watery stool (90.5%) and bowel movements of less than or equal to 10 times (99.5%). Patients also had other symptoms such as fever (81.8%), nausea/vomiting (69.7%) and abdominal pain (57.1%). These findings could also be compared with adults. Almost all of the adults came with frequency of diarrhea less than or equal to 10 times (95.7%) with watery stool (97.7%). They had fever in 56.9%, nausea/vomiting in 66.9% and abdominal pain in 71.2%. Abdominal distension was rarely noted in both groups of children and adults (6.3%, 1.6%).

In children, mild dehydration was manifested generally (57.9%) whereas adults presented with moderate dehydration (38.8%) or mild dehydration (36.7%).

In comparison of the children and adult groups, adults had bowel movements more than 10 times which was significantly higher than children (4.3% vs. 0.5%, P=0.016). In contrast, children presented mucous or bloody diarrhea in the significantly higher proportion than adults (9.5% vs. 2.3%, P=0.009). Fever was presented in children more significantly than in adults (81.8% vs. 56.9%, P<0.001). And also abdominal distension seen in children was significantly higher than adult group (6.3% vs. 1.6%, P=0.048). But, adults had abdominal tenderness, which was significantly higher than children 34.4% vs. 4.3%, P<0.001).

Table 5.2 Clinical manifestations of admitted patients with *Salmonella* gastroenteritis at Samutsakhon Hospital during 2013-2015

Clinical manifestations	All	Children	Adults	P value
	Numbers (%)	Numbers (%)	Numbers (%)	
Median duration of diarrhea (IQR) (days)	(n=351) 1.0 (1.0-2.0)	(n=213) 1.0 (1.0-2.0)	(n=138) 1.0 (1.0-2.0)	0.758
Median frequency of bowel movements (IQR) (times)	(n=351) 4.0 (3.0-8.0)	(n= 213) 4.0 (3.0-6.0)	(n=138) 5.0 (3.0-10.0)	0.001
Frequency of bowel movements ≤10 times >10 times	(n=351) 344 (98.0) 7 (2.0)	(n=213) 212 (99.5) 1 (0.5)	(n=138) 132 (95.7) 6 (4.3)	0.016
Stool characteristics Watery Mucous or bloody	(n=343) 320 (93.3) 23 (6.7)	(n=211) 191 (90.5) 20 (9.5)	(n=132) 129 (97.7) 3 (2.3)	0.009

Table 5.2 Clinical manifestations of admitted patients with *Salmonella* gastroenteritis at Samutsakhon Hospital during 2013-2015 (cont.)

Clinical manifestations	All	Children	Adults	P value
	Numbers (%)	Numbers (%)	Numbers (%)	
History of present illness				
Fever	(n=346) 249 (72.0)	(n=209) 171 (81.8)	(n=137) 78 (56.9)	< 0.001
Abdominal pain	(n=139) 94 (67.6)	(n=35) 20 (57.1)	(n=104) 74 (71.2)	0.125
Nausea/vomiting	(n=283) 194 (68.6)	(n=165) 115 (69.7)	(n=118) 79 (66.9)	0.624
Abdominal distension	(n=316) 14 (4.4)	(n=191) 12 (6.3)	(n=125) 2 (1.6)	0.048
Abdominal tenderness	(n=309) 50 (16.2)	(n=187) 8 (4.3)	(n=122) 42 (34.4)	< 0.001
Dehydration No Mild Moderate Severe	(n=163) 25 (15.3) 84 (51.5) 43 (26.4) 11 (6.7)	(n=114) 16 (14.0) 66 (57.9) 24 (21.1) 8 (7.0)	(n=49) 9 (18.4) 18 (36.7) 19 (38.8) 3 (6.1)	0.057

Laboratory findings of *Salmonella* gastroenteritis

Hematological test results are presented in Table 5.3. Median values of hematocrit, hemoglobin and platelets were within normal limits. The median value of white blood cell count was relatively high in children (12.2 □ 10^9/L; IQR=9.1-17.2) and in adults (10.3 □ 10^9/L; IQR=7.3-14.0). Median neutrophil percentage was only high in adults 84.7% (IQR=76.8-89.1%). The findings of hematological test results among children and adults were statistically different ($p<0.001$) except in percentages of eosinophil.

The blood chemistry results are also shown in Table 5.3. Blood urea nitrogen (BUN) and creatinine of both children and adult patients were within normal range. Results of serum electrolytes except potassium and bicarbonate are in normal limit in both children and adult groups. Blood chemistry results in these two groups showed difference statistically ($p<0.001$).

Fecal simple smears were prepared seeking white and red blood cells. The results of stool examination are shown in Table 5.4. Only white blood cells were found in 28.6% of children and 21.0% of adults. Only red blood cells were found in children statistically higher than in adults (22.5% vs. 8.7%, P=0.001).

Table 5.3 Hematological & blood chemistry test results in admitted patients with *Salmonella* gastroenteritis at Samutsakhon Hospital during 2013- 2015

	Children	Median (IQR)	Adults	Median (IQR)	P value
	n		n		
Hematocrit (%)	212	34.6 (31.9-36.9)	135	37.0 (32.7-42.9)	< 0.001
Hemoglobin (g/dL)	212	11.3 (10.4-12.0)	135	12.5 (10.7-14.4)	< 0.001
Platelets ($x10^9$/L)	212	353.0 (289.2-437.3)	135	251.0 (186.0-315.0)	< 0.001
WBC ($x10^9$/L)	212	12.2 (9.1-17.2)	135	10.3 (7.3-14.0)	< 0.001
Neutrophil (%)	212	49.6 (37.9-64.7)	135	84.7 (76.8-89.1)	< 0.001
Eosinophil (%)	212	0.1 (0.0-0.8)	135	0.1 (0.0-0.5)	0.194
BUN (mg/dL)	27	9.0 (7.0-14.0)	127	18.0 (11.0-30.0)	< 0.001
Creatinine (mg/dL)	27	0.4 (0.3-0.5)	128	1.1 (0.8-1.6)	< 0.001
Na^+ (mEq/L)	179	137.0 (135-139)	135	135.0 (132-137)	< 0.001
K^+ (mEq/L)	179	4.1 (3.6-4.4)	135	3.4 (3.0-3.7)	< 0.001
Cl^- (mEq/L)	179	107.0 (105-110)	135	103.0 (100-105)	< 0.001
HCO^-_3 (mEq/L)	179	15.2 (12.8-17.1)	135	18.9 (16.1-21.8)	< 0.001

** IQR= interquartile range, WBC= white blood cells, BUN= blood urea nitrogen, Na^+= sodium, K^+= potassium, Cl^-= chloride, HCO_3^-= bicarbonate,

Table 5.4 Stool examination of admitted patients with *Salmonella* gastroenteritis at Samutsakhon Hospital during 2013-2015

Laboratory test	Children (n=213)	Adults (n=138)	P value
	Numbers (%)	Numbers (%)	
Only WBC found	61 (28.6)	29 (21.0)	0.110
Only RBC found	48 (22.5)	12 (8.7)	0.001
Any WBC or RBC found	69 (32.4)	30 (21.7)	0.030

** WBC= white blood cells, RBC= red blood cells

Treatments and treatment outcomes of *Salmonella* gastroenteritis

Treatment and treatment outcomes of all patients, children and adult groups are shown in Table 5.5. In all patients, *Salmonella* strains were resistant for 71.5%. First antibiotic commonly used in all patients was ceftriaxone (30.2%) and second antibiotic was cefotaxime (23.9%). 95.7% of all patients received intravenous fluid during hospital admission and median duration of intravenous fluid used was 3 days (IQR=2-3days). 51.0% of all patients received antiemetic drugs. Shock was presented in 2.8% of all patients, renal failure in 2.0% and heart failure in 0.6%. Hyponatremia was seen in 34.4% of patients, hypokalemia in 30.9%, metabolic acidosis in 82.8% and high creatinine in 22.6% of all patients.

From the test of antibiotic susceptibility, we found that children had significantly higher percentage of antibiotic resistant *Salmonella* strains than in adults (75.6% vs. 65.2%, P=0.036).Antibiotic usage patterns between children and adult groups were statistically different (P<0.001). Most used intravenous antibiotic in children was cefotaxime (39.4%) and in adult was ceftriaxone (51.4%). Almost all of the patients received intravenous fluid for 97.2% in children and 93.5% in adults. Median duration of intravenous fluid used was 3 days (IQR=2-3days) in both groups. The antiemetic drugs were used in adults significantly higher than in children (60.1% vs. 45.1%, P=0.006). There was no use of anti-motility drugs in children, only 1.4% of adult used. Treatment outcome between children and adults were different (P=0.008). 99.1% in children group and 94.2% in adult group got improved. Median duration of hospital stay in adults was 4 days (IQR-3.0-6.0) which was less than in children (5 days) (IQR-3.0-6.0) (P=0.012). Complications found in adult group were significantly higher than in children (93.5% vs. 84.0%, P=0.008). Shock was seen in adults more than children (7.2% vs. 0%, P<0.001). Renal failure found in adult groups was higher than in children (5.1% vs. 0%, P=0.001). Bacteremia was found more in adult than children (28% vs. 4%, P<0.001). Hyponatremia (Na <135 mEq/L) in adults was significantly higher than in children (48.1% vs. 24%, P<0.001). Hypokalemia (K < 3.5 mEq/L) in adults was also more than in children (53.3% vs. 14%, P<0.001). High creatinine (Cr >1.5g/dL) was seen in adults higher than in children (26.6% vs. 3.7%, P=0.010). But metabolic acidosis (HCO_3< 21.0 mEq/L) in children was significantly higher than in adults (93.9% vs. 68.1%, P<0.001).

Table 5.5 Treatment and treatment outcomes of admitted patients with *Salmonella* gastroenteritis at Samutsakhon Hospital during 2013-2015

	All (n=351)	Children (n=213)	Adults (n=138)	P value
Antibiotic: Sensitivity	100 (28.5)	52 (24.4)	48 (34.8)	0.036
Resistant	251 (71.5)	161 (75.6)	90 (65.2)	
Antibiotic: Not used	100 (28.5)	60 (28.2)	40 (29.0)	< 0.001
Ceftriaxone	106 (30.2)	35 (16.4)	71 (51.4)	
Cefotaxime	84 (23.9)	84 (39.4)	0 (0)	
Ampicillin	16 (4.6)	16 (7.5)	0 (0)	
Ciprofloxacin	7 (2.0)	1 (0.5)	6 (4.3)	
Ceftriaxone + Metronidazole	10 (2.8)	0 (0)	10 (7.2)	
Cefotaxime + Ampicillin	7 (2.0)	7 (3.3)	0 (0)	
Ceftriaxone + Ciprofloxacin	4 (1.1)	2 (0.9)	2 (1.4)	
Others	17 (4.8)	8 (3.8)	9 (6.5)	
Intravenous fluid	336 (95.7)	207 (97.2)	129 (93.5)	0.094
Duration of IVF used, days median(IQR)	3 (2-3)	3 (2-3)	3 (2-3)	0.435
Anti-motility drugs	2 (0.6)	0 (0)	2 (1.4)	0.154
Anti-emetic drugs	179 (51.0)	96 (45.1)	83 (60.1)	0.006
Duration of diarrhea after treatment, days median(IQR)	4 (3-5)	4 (3-6)	4 (3-5)	0.017
All complications	308 (87.7)	179 (84.0)	129 (93.5)	0.008
Shock	10 (2.8)	0 (0)	10 (7.2)	< 0.001
Renal failure	7 (2.0)	0 (0)	7 (5.1)	0.001
Heart failure	2 (0.6)	1 (0.5)	1 (0.7)	1.000
Bacteremia (n=149)	18 (12.1)	4 (4.0)	14 (28.0)	< 0.001
Hyponatremia (n=314)	108 (34.4)	43 (24.0)	65 (48.1)	< 0.001
Hypokalemia (n=314)	97 (30.9)	25 (14.0)	72 (53.3)	< 0.001
Metabolic acidosis (n=314)	260 (82.8)	168 (93.9)	92 (68.1)	< 0.001
Creatinine >1.5 mg/dL (n=314)	35 (22.6)	1 (3.7)	34 (26.6)	0.010
Outcome				0.008
Improved	341 (97.2)	211 (99.1)	130 (94.2)	
Referred	0 (0)	0 (0)	0 (0)	
Dead	6 (1.7)	0 (0)	6 (4.3)	
Leave against advice	4 (1.1)	2 (0.9)	2 (1.4)	
Duration of hospital stay, days median(IQR)	4.0 (3.0-6.0)	5.0 (3.0-6.0)	4.0 (3.0-6.0)	0.012

All in Number (%), IVF = Intravenous fluid, IQR = Interquartile Range

Serogroups of *Salmonella*

Salmonella serogroups are revealed in Table 5.6. In all patients, the most frequently found serogroups were serogroups B, C, D and E. Among these serogroups, serogroup B was the commonest of all (41.9%), accounting for 48.4% of children and 31.9% of adults. And another important serogroup in adults was serogroup E (30.4%). Two serogroups (A and H) were not found in both groups of patients. The findings of

serogroups of *Salmonella* in children and adult groups are statistically significant (P=0.007).

Table 5.6 *Salmonella* serogroups found in admitted patients with *Salmonella* gastroenteritis at Samutsakhon Hospital during 2013- 2015

Salmonella serogroups	All (n=351)	Children (n=213)	Adults (n=138)	P value
	Numbers (%)	Numbers (%)	Numbers. (%)	0.007
A	0 (0)	0 (0)	0 (0)	
B	147 (41.9)	103 (48.4)	44 (31.9)	
C	72 (20.5)	43 (20.2)	29 (21.0)	
D	42 (12.0)	26 (12.2)	16 (11.6)	
E	71 (20.2)	29 (13.6)	42 (30.4)	
F	1 (0.3)	1 (0.5)	0 (0)	
G	4 (1.1)	3 (1.4)	1 (0.7)	
H	0 (0)	0 (0)	0 (0)	
I	7 (2.0)	3 (1.4)	4 (2.9)	
Spp	7 (2.0)	5 (2.3)	2 (1.4)	

Epidemiology and clinical manifestations of *Salmonella* gastroenteritis according to Salmonella serogroups

In the findings of *Salmonella* serogroups, we established that serogroup B, C, D and E were the most common serogroups found in all patients of children and adults. Other serogroups, A, F, G, H, I and *Salmonella* spp, were not commonly found in both groups of patients. So, we categorized *Salmonella* serogroups into B, C, D, E and others.

In children, among the serogroups of *Salmonella*, serogroup B was the most resistant giving serogroup, 89.3% out of 103 patients were resistant (P<0.001). *Salmonella* serogroup B was the one, which infected the youngest age of patients [0.7 year (IQR= 0.5-1.0 year, P=0.026)]. Male is predominantly affected by all serogroups. Key symptoms caused by all serogroups were watery diarrhea and in addition with frequency of diarrhea within 1 to 10 times. Other presenting symptoms such as fever, abdominal pain and nausea/vomiting were also manifested. Median duration of diarrhea and median frequency of bowel movements are statistically similar among the

serogroups. These results are presented in Table 5.7. The median duration of diarrhea after treatment in children was statistically different among *Salmonella* serogroups (P=0.024). Serogroup D had the longest duration of diarrhea after treatment [5 days (3.8-7.3 days)]. Complications between these serogroups have similar findings statistically.

Table 5.7 Epidemiology, clinical manifestations and outcomes of *Salmonella* gastroenteritis according to *Salmonella* serogroups in children at Samutsakhon Hospital during 2013- 2015

	Group B (n= 103)	Group C (n= 43)	Group D (n= 26)	Group E (n= 29)	Others (n= 12)	P value
Resistant	92 (89.3)	33 (76.7)	19 (73.1)	11 (37.9)	6 (50.0)	< 0.001
Median age (years)	0.7 (0.5-1.0)	1 (0.6-2)	1 (0.7-3)	0.9 (0.3-2)	0.9 (0.4-1.8)	0.026
Age <5 years	98 (95.1)	39 (90.7)	22 (84.6)	24 (82.8)	12 (100.0)	0.117
Male gender	67 (65.0)	24 (55.8)	18 (69.2)	19 (65.5)	9 (75.0)	0.687
Race: Thai	88 (85.4)	38 (88.4)	21 (80.8)	24 (82.8)	10 (83.3)	0.789
Myanmar	14 (13.6)	3 (7.0)	5 (19.2)	5 (17.2)	2 (16.7)	
Cambodia	1 (1.0)	1 (2.3)	0 (0)	0 (0)	0 (0)	
Laos	0 (0)	1 (2.3)	0 (0)	0 (0)	0 (0)	
Body weight (n=171)						0.950
Underweight	11 (14.3)	5 (13.5)	2 (8.0)	2 (8.3)	1 (12.5)	
Normal weight	58 (75.3)	28 (75.7)	21 (84.0)	20 (83.3)	6 (75.0)	
Overweight	8 (10.4)	3 (8.1)	2 (8.0)	2 (8.3)	1 (12.5)	
Obese	0 (0)	1 (2.7)	0 (0)	0 (0)	0 (0)	
Comorbidity: None	97 (94.2)	39 (90.7)	24 (92.3)	27 (93.1)	12 (100.0)	0.759
1 comorbidity	6 (5.8)	3 (7.0)	2 (7.7)	2 (6.9)	0 (0)	
2 comorbidities	0 (0)	1 (2.3)	0 (0)	0 (0)	0 (0)	
Duration of diarrhea, days median(IQR)	1.0 (1-2)	1.0 (1-2)	1.0 (1-2)	1.0 (1-2)	1.0 (1-1)	0.762
Frequency of bowel movements, times median(IQR)	5.0 (3-7)	3.0 (3-5)	3.0 (3-5.3)	4.0 (2.5-6.5)	3.0 (3-5.5)	0.140
Fever (n=209)	81 (79.4)	35 (83.3)	23 (92.0)	22 (75.9)	10 (90.9)	0.477
Abdominal pain (n=35)	7 (50.0)	4 (50.0)	3 (100.0)	4 (57.1)	2 (66.7)	0.588
Nausea/vomiting (n=165)	56 (71.8)	23 (63.9)	16 (69.6)	14 (73.7)	6 (66.7)	0.922
Dehydration (n=114): No	6 (11.1)	5 (20.8)	2 (18.2)	2 (13.3)	1 (10.0)	0.903
Mild	31 (57.4)	14 (58.3)	6 (54.5)	10 (66.7)	5 (50.0)	
Moderate	13 (24.1)	4 (16.7)	3 (27.3)	1 (6.7)	3 (30.0)	
Severe	4 (7.4)	1 (4.2)	0 (0)	2 (13.3)	1 (10.0)	

Table 5.7 Epidemiology, clinical manifestations and outcomes of *Salmonella* gastroenteritis according to *Salmonella* serogroups in children at Samutsakhon Hospital during 2013- 2015 (cont.)

	Group B (n= 103)	Group C (n= 43)	Group D (n= 26)	Group E (n= 29)	Others (n= 12)	P value
Outcome						
Duration of IVF used, days median(IQR)	3 (2-3)	3 (3-3)	3 (2-3)	3 (3-3)	2 (2-3)	0.079
Duration of diarrhea after treatment, days median(IQR)	4 (3-6)	4 (3-5)	5 (3.8-7.3)	4 (3-5)	3.5 (3-5.5)	0.024
Complication (n=213)	84 (81.6)	36 (83.7)	20 (76.9)	27 (93.1)	12 (100.0)	0.238
Bacteremia (n=99)	3 (6.1)	0 (0)	1 (6.7)	0 (0)	0 (0)	0.683
Hyponatremia (n=179)	19 (22.4)	7 (20.0)	9 (42.9)	8 (30.8)	0 (0)	0.062
Hypokalemia (n=179)	10 (11.8)	4 (11.4)	4 (19.0)	5 (19.2)	2 (16.7)	0.799
Metabolic acidosis (n=179)	80 (94.1)	32 (91.4)	19 (90.5)	25 (96.2)	12 (100.0)	0.771
Duration of hospital stay, days median(IQR)	5.0 (3-7)	4.0 (3-5)	5.0 (4-8)	4.0 (3-6.5)	4.0 (3-6)	0.196

All in Number (%), IVF = Intravenous fluid, IQR = Interquartile Range

Table 5.8 represents the epidemiology and clinical manifestations of *Salmonella* gastroenteritis according to *Salmonella* serogroups in adult patients. *Salmonella* serogroup B was the most prevalent one than other serogroups in adults. Resistances found between these serogroups were statistically different ($p<0.001$).Serogroup B caused the highest resistant rate (88.6%) among all serogroups. After group B, group D was the second most resistant group (81.3%). The major clinical symptoms presenting in all serogroups were watery diarrhea with less than or equal to ten times frequency in addition with fever, abdominal pain and nausea/vomiting. Affected percentages of male patients were more predominant than female patients in serogroup B (56.8% vs. 43.2%) and in serogroup D (68.8% vs. 31.3%). Although in other serogroups, female patients were more infected than male patients (P=0.029). Presence of complication and presence of hypokalemia in adult patients infected with different serogroups of *Salmonella*, were statistically different (P=0.003 and 0.002, respectively). Adult patients infected with *Salmonella* serogroup E had the lowest complication rate and hypokalemia rate than patients infected with other serogroups.

Table 5.8 Epidemiology, clinical manifestations and outcomes of *Salmonella* gastroenteritis according to *Salmonella* serogroups in adults at Samutsakhon Hospital during 2013- 2015

	Group B (n= 44)	Group C (n= 29)	Group D (n= 16)	Group E (n= 42)	Others (n= 7)	P value
Resistant	39 (88.6)	21 (72.4)	13 (81.3)	12 (28.6)	5 (71.4)	< 0.001
Age in years, median(IQR)	46.5 (35.0-68.8)	65.0 (42.0-74.5)	45.5 (26.8-78.0)	43.5 (25.0-67.3)	72.0 (54.0-76.0)	0.079
Age ≥60 years	14 (31.8)	17 (58.6)	6 (37.5)	15 (35.7)	4 (57.1)	0.117
Male gender	25 (56.8)	10 (34.5)	11 (68.8)	13 (31.0)	3 (42.9)	0.029
Race: Thai	40 (90.9)	25 (86.2)	12 (75.0)	31 (73.8)	7 (100.0)	0.304
Myanmar	4 (9.1)	4 (13.8)	3 (18.8)	10 (23.8)	0 (0)	
Cambodia	0 (0)	0 (0)	1 (6.3)	1 (2.4)	0 (0)	
Body weight (n=117)						0.305
Underweight	2 (5.4)	1 (4.0)	3 (20.0)	2 (5.7)	0 (0)	
Normal weight	31 (83.8)	17 (68.0)	11 (73.3)	29 (82.9)	5 (100.0)	
Overweight	3 (8.1)	7 (28.0)	1 (6.7)	4 (11.4)	0 (0)	
Obese	1 (2.7)	0 (0)	0 (0)	0 (0)	0 (0)	
Comorbidity: None	20 (45.5)	11 (37.9)	7 (43.8)	24 (57.1)	0 (0)	0.175
1 comorbidity	9 (20.5)	9 (31.0)	5 (31.2)	13 (31.0)	5 (71.4)	
2 comorbidities	12 (27.3)	7 (24.1)	3 (18.8)	3 (7.1)	1 (14.3)	
≥3 comorbidities	3 (6.8)	2 (6.9)	1 (6.3)	2 (4.8)	1 (14.3)	
Duration of diarrhea in days, median(IQR)	1.0 (1-2)	1.0 (1-2)	1.0 (1-2)	1.0 (1-1)	1.0 (1-2)	0.445
Frequency of bowel movements in times, median(IQR)	6.0 (3-10)	4.0 (3-7.5)	7.0 (3-10)	5.0 (3-10)	4.0 (3-7)	0.486
Fever (n=137)	29 (67.4)	12 (41.4)	9 (56.2)	25 (59.5)	3 (42.9)	0.241
Abdominal pain (n=104)	23 (69.7)	11 (61.1)	10 (71.4)	26 (76.5)	4 (80.0)	0.831
Nausea/vomiting (n=118)	23 (67.6)	14 (60.9)	10 (66.7)	29 (70.7)	3 (60.0)	0.943
Dehydration (n=49): No	4 (25.0)	1 (14.3)	1 (12.5)	3 (18.8)	0 (0)	0.076
Mild	0 (0)	6 (85.7)	4 (50.0)	7 (43.8)	1 (50.0)	
Moderate	10 (62.5)	0 (0)	3 (37.5)	5 (31.3)	1 (50.0)	
Severe	2 (12.5)	0 (0)	0 (0)	1 (6.3)	0 (0)	

Table 5.8 Epidemiology, clinical manifestations and outcomes of *Salmonella* gastroenteritis according to *Salmonella* serogroups in adults at Samutsakhon Hospital during 2013- 2015 (cont.)

	Group B (n= 44)	Group C (n= 29)	Group D (n= 16)	Group E (n= 42)	Others (n= 7)	P value
Outcome						
Duration of IVF used, days median(IQR)	3 (2-3)	3 (2-3)	3 (3-3)	3 (2.8-3)	3 (2-3)	0.168
Duration of diarrhea after treatment, days median(IQR)	4 (3-7)	3 (3-5.5)	4 (3-5)	3 (2-4)	4 (3-4)	0.097
Complication (n=138)	43 (97.7)	29 (100.0)	16 (100.0)	34 (81.0)	7 (100.0)	0.238
Bacteremia (n=50)	5 (27.8)	3 (20.0)	3 (50.0)	3 (33.3)	0 (0)	0.588
Hyponatremia (n=135)	18 (41.9)	14 (48.3)	10 (62.5)	18 (45.0)	5 (71.4)	0.451
Hypokalemia (n=135)	29 (67.4)	21 (72.4)	7 (43.8)	13 (32.5)	2 (28.6)	0.002
Metabolic acidosis (n=135)	27 (62.8)	22 (75.9)	12 (75.0)	27 (67.5)	4 (57.1)	0.716
Creatinine >1.5mg/dL (n=128)	11 (29.7)	8 (28.6)	4 (25.0)	9 (22.5)	2 (28.6)	0.961
Renal failure	4 (9.1)	0 (0)	2 (12.5)	1 (2.4)	0 (0)	0.210
Shock	4 (9.1)	1 (3.4)	2 (12.5)	3 (7.1)	0 (0)	0.727
Mortality	2 (4.5)	3 (10.3)	0 (0)	1 (2.4)	0 (0)	0.453
Duration of hospital stay, days median(IQR)	4.0 (3-13.)	4.0 (3-12.0)	4.0 (3-5)	4.0 (3-5)	4.0 (3-4)	0.140

All in Number (%), IVF = Intravenous fluid, IQR = Interquartile Range

Antimicrobial susceptibility test for *Salmonella*

The results of antimicrobial susceptibility testing for *Salmonella* are shown in Table 5.9 and 5.10. Antimicrobial susceptibility test results are described in three categories, sensitive, intermediate and resistant. In order to find antibiotic resistant *Salmonella* gastroenteritis, we combined the intermediate and resistant group. Prevalence of antibiotic-resistant *Salmonella* in this study was found to be 71.5% among 351 cases of *Salmonella* gastroenteritis. Resistance of ampicillin was found to be highest in children groups (62.6%) whereas ciprofloxacin was the highest resistance in adults (46.3%).

Table 5.9 Antibiotic susceptibility test done in children at Samutsakhon Hospital during 2013-2015

	Number of strains tested for antibiotics susceptibility test	Sensitive		Intermediate		Resistant	
		N	%	N	%	N	%
Cefotaxime	107	73	68.2	7	6.5	27	25.2
Ciprofloxacin	204	118	57.8	80	39.2	6	2.9
TMP/SMX	188	138	73.4	0	0	50	26.6
Ampicillin	211	79	37.4	0	0	132	62.6
Nalidixic acid	75	48	64.0	19	25.3	8	10.7

* N = numbers, TMP/SMX = Trimethoprim/sulfamethoxazole

Table 5.10 Antibiotic susceptibility test done in adults at Samutsakhon Hospital during 2013-2015

	Number of strains tested for antibiotics susceptibility test	Sensitive		Intermediate		Resistant	
		N	%	N	%	N	%
Cefotaxime	88	53	60.2	8	9.1	27	30.7
Ciprofloxacin	136	73	53.7	52	38.2	11	8.1
TMP/SMX	135	116	85.9	2	1.5	17	12.6
Ampicillin	136	74	54.4	0	0	62	45.6
Nalidixic acid	78	49	62.8	13	16.7	16	20.5

* N = numbers, TMP/SMX = Trimethoprim/sulfamethoxazole

Antibiotics resistance pattern among *Salmonella* serogroups

The results of antibiotic resistance among the serogroups of *Salmonella* are shown in Table 5.11 and 5.12 for children and adults respectively. Between the five antibiotics tested in children, all antibiotics came across various degrees of resistance whilst ampicillin was the one giving most resistance pattern in children and ciprofloxacin was the highest resistant drug in adults. Trimethoprim/sulfamethoxazole

was also the one, which is found to be the most effective against *Salmonella* in both groups. In children, ciprofloxacin got 42.2% and ampicillin had 62.6% resistance. Also in adults, ciprofloxacin had 46.3% resistance and ampicillin got 45.6% resistance.

In children patients, ampicillin resistance was found most commonly in *Salmonella* serogroup B (80.6%). Resistance with cefotaxime and ciprofloxacin was found most commonly in serogroup C (50.0% and 52.4% respectively). Resistance with trimethoprim/sulfamethoxazole and nalidixic acid was found most commonly in serogroup D (50.0% and 100.0% respectively).

Table 5.11 Antibiotics resistance pattern among *Salmonella* serogroups in children at Samutsakhon Hospital during 2013-2015

Salmonella serogroups	Cefotaxime		Ciprofloxacin		TMP/SMX		Ampicillin		Nalidixic acid	
	N	%R	N	%R	N	%R	N	%R	N	%R
B (n=103)	50	38.0	98	42.9	94	22.3	103	80.6	40	30.0
C (n=43)	24	50.0	42	52.4	41	34.1	42	57.1	21	52.4
D (n=26)	14	0	26	23.1	22	50.0	25	68.0	3	100.0
E (n=29)	13	23.1	28	39.3	23	13.0	29	13.8	7	0
Others (n=12)	6	0	10	50.0	8	12.5	12	33.3	4	25.0
All	**107**	**31.8**	**204**	**42.2**	**188**	**26.6**	**211**	**62.6**	**75**	**36.0**

*N = number of strains tested for each antibiotics, %R = percentage resistance

In adults, resistant to cefotaxime, trimethoprim/sulfamethoxazole and ampicillin was found most frequently in *Salmonella* serogroup B (67.9%, 28.6%, 74.4%) correspondingly. Resistance to ciprofloxacin was found mostly in serogroup C (60.7%). Resistance with nalidixic acid was found most commonly in serogroup D (54.5%).

Table 5.12 Antibiotics resistance pattern among *Salmonella* serogroups in adults at Samutsakhon Hospital during 2013-2015

Salmonella serogroups	Cefotaxime		Ciprofloxacin		TMP/SMX		Ampicillin		Nalidixic acid	
	N	%R	N	%R	N	%R	N	%R	N	%R
B (n=44)	28	67.9	43	51.2	42	28.6	43	74.4	23	47.8
C (n=29)	19	36.8	28	60.7	29	13.8	29	51.7	18	44.4
D (n=16)	13	15.4	16	56.2	15	13.3	16	43.8	11	54.5
E (n=42)	25	24.0	42	26.2	42	2.4	41	14.6	23	17.4
Others (n=7)	3	33.3	7	57.1	7	0	7	28.6	3	0
All	**88**	**39.8**	**136**	**46.3**	**135**	**14.1**	**136**	**45.6**	**78**	**37.2**

*N= number of strains tested for each antibiotic, %R= percentage resistance

Comparison of the clinical manifestations and treatment outcome between antibiotic sensitive and antibiotic resistant groups

In children of 213 patients, there were 52 patients (24.4%) with antibiotic sensitive (sensitive to all antibiotic tested) and 161 patients (75.6%) with antibiotic resistant. For 138 adults, antibiotic sensitive was 48 patients (34.8%) and antibiotic resistant was 90 patients (65.2%).The clinical manifestations and treatment outcome of 351 admitted patients with *Salmonella* gastroenteritis with respect to antibiotic resistant and antibiotic sensitive are presented in Table 5.13 and 5.14.

In children, antibiotic resistant group had patients <5 years old in the higher proportion than antibiotic sensitive group (93.8% vs. 84.6%, P=0.048).Gender and race were not significantly different in antibiotic resistant and sensitive groups and the clinical symptoms such as frequency of bowel movement and the characteristics of stool in these two groups were also the same. Fever was presented in antibiotic resistant groups significantly higher than in antibiotic sensitive group (84.8% vs. 72.5%, P=0.048). Other symptoms prior to admission in children were similar in both groups. Median duration of intravenous fluid used in both groups was 3 days (IQR=2-3 days). The use of antibiotic, anti-emetic drugs, intravenous fluid for treatment and

outcome of the disease were not significantly different between both groups. These results for children are shown in Table 5.13.

Table 5.13 Comparison of the clinical manifestations and treatment outcome between antibiotic resistant and antibiotic sensitive groups among children at Samutsakhon Hospital during 2013-2015

	Resistant strains (n=161)	Sensitive strains (n=52)	P value
Median age (years)	0.8 (0.5-1.0)	0.9 (0.4-2.0)	0.787
Age: <5 years	151 (93.8)	44 (84.6)	0.048
5-14.9 years	10 (6.2)	8 (15.4)	
Male gender	104 (64.6)	33 (63.5)	0.882
Race: Thai	136 (84.5)	45 (86.5)	0.736
Non-Thai	25 (15.5)	7 (13.4)	
Body weight (n=171)			0.757
Underweight	17 (13.2)	4 (9.5)	
Normal weight	98 (76.0)	35 (83.3)	
Overweight	13 (10.1)	3 (7.1)	
Obese	1 (0.8)	0 (0)	
Duration of diarrhea in days, median(IQR)	1.0 (1-2)	1.0 (1-2)	0.215
Frequency of bowel movements in times, median(IQR)	4.0 (3.0-6.0)	4.0 (3.0-8.0)	0.251
Stool characteristic (n= 211): Watery	142 (88.8)	49 (96.1)	0.170
Mucous or bloody	18 (11.2)	2 (3.9)	
Fever (n= 209)	134 (84.8)	37 (72.5)	0.048
Abdominal pain (n= 35)	14 (56.0)	6 (60.0)	1.000
Nausea/vomiting (n= 165)	87 (69.6)	28 (70.0)	0.962

Table 5.13 Comparison of the clinical manifestations and treatment outcome between antibiotic resistant and antibiotic sensitive groups among children at Samutsakhon Hospital during 2013-2015 (cont.)

	Resistant strains (n=161)	Sensitive strains (n=52)	P value
Dehydration (n=114): None	12 (14.0)	4 (14.3)	0.362
Mild	52 (60.5)	14 (50.0)	
Moderate	18 (20.9)	6 (21.4)	
Severe	4 (4.7)	4 (14.3)	
Antibiotics used	114 (70.8)	39 (75.0)	0.559
IV fluid used	156 (96.9)	51 (98.1)	1.000
Duration of IVF used, days median(IQR)	3 (2-3)	3 (2.3-3)	0.776
Duration of diarrhea after treatment, days median(IQR)	4 (3-6)	4 (3-5)	0.189
Anti-emetic drugs used	71 (44.1)	25 (48.1)	0.616
Complications	133 (82.6)	46 (88.5)	0.316
Bacteremia (n=99)	4 (5.6)	0 (0)	0.572
Hyponatremia (n= 179)	32 (23.9)	11 (24.4)	0.939
Hypokalemia (n= 179)	17 (12.7)	8 (17.8)	0.394
Metabolic acidosis (n= 179)	124 (92.5)	44 (97.8)	0.295
Duration of hospital stay, days median(IQR)	5.0 (3-7)	4.0 (3-5.75)	0.308
Outcome: improved	160 (99.4)	51 (98.1)	0.430

The findings for adult patients are shown in Table 5.14. In comparison of antibiotic resistant and sensitive groups, demographic characteristic were not statistically different. Clinical manifestations of diarrhea, frequency of bowel movements, stool characteristic, fever, abdominal pain, nausea/vomiting were also not significantly different in these groups. Both groups also had similar findings for treatment, complications and outcome. The antiemetic drugs were used in antibiotic

sensitive group significantly more than in antibiotic resistant group (72.9% vs. 53.3%, P=0.025).

Table 5.15 shows the comparison of the clinical manifestations and treatment outcome between antibiotic resistant and antibiotic sensitive groups in all patients. For age group distribution, the results between these two groups were statistically significant (P=0.035). In antibiotic resistant group, 60.2% of the patients were <5 years old and 21.9% were within 15-59.9 years. In antibiotic sensitive group, 44.0% of patients were <5 years old and 27.0% were 15-59.9 years old. Presenting stool characteristic between two groups was statistically different (P=0.035). Mucous or bloody diarrhea was seen in antibiotic resistant group in significantly higher proportion than in antibiotic sensitive group (8.5% vs. 2.1%, P=0.035). Antiemetic drugs were used in antibiotic sensitive group more significantly than in antibiotic sensitive group (60.0% vs. 47.4%, P=0.033).

Table 5.14 Comparison of the clinical manifestations and treatment outcome between antibiotic resistant and antibiotic sensitive groups among adult patients at Samutsakhon Hospital during 2013-2015

	Resistant strains (n=90)	Sensitive strains (n=48)	P value
Median age (years)	48.0 (33.0-70.25)	51.0(32.3-74.5)	0.712
Age: >60 years	55 (61.1)	27 (56.2)	0.307
Male gender	44 (48.9)	18 (37.5)	0.200
Race: Thai	76 (84.4)	39 (81.3)	0.149
Non-Thai	14 (15.6)	9 (18.7)	
Body weight (n=117)			0.820
Underweight	6 (7.5)	2 (5.4)	
Normal weight	62 (77.5)	31 (83.8)	
Overweight	11 (13.8)	4 (10.8)	
Obese	1 (1.3)	0 (0)	
Duration of diarrhea in days, median(IQR)	1.0 (1.0-2.0)	1.0 (1.0-1.8)	0.484

Table 5.14 Comparison of the clinical manifestations and treatment outcome between antibiotic resistant and antibiotic sensitive groups among adult patients at Samutsakhon Hospital during 2013-2015 (cont.)

	Resistant strains (n=90)	Sensitive strains (n=48)	P value
Frequency of bowel movements in times, median(IQR)	5.0 (3.0-10.0)	5.0 (3.0-10.0)	0.604
Stool characteristic (n= 132): Watery	85 (96.6)	44 (100.0)	0.550
Mucous or bloody	3 (3.4)	0 (0)	
Fever (n= 137)	48 (53.9)	30 (62.5)	0.334
Abdominal pain (n= 104)	46 (70.8)	28 (71.8)	0.911
Nausea/vomiting (n= 118)	50 (67.6)	29 (65.9)	0.853
Dehydration (n=49): None	4 (13.8)	5 (25.0)	0.794
Mild	11 (37.9)	7 (35.0)	
Moderate	12 (41.4)	7 (35.0)	
Severe	2 (6.9)	1 (5.0)	
Antibiotics used	67 (74.4)	31 (64.6)	0.224
IV fluid used	82 (91.1)	47 (97.9)	0.162
Duration of intravenous fluid used in days, median(IQR)	3.0 (2.0-3.0)	3.0 (3.0-3.0)	0.020
Duration of diarrhea after treatment, days median(IQR)	4.0 (3.0-5.0)	4.0 (3.0-4.8)	0.945
Anti-emetic drugs used	48 (53.3)	35 (72.9)	0.025
All complications	86 (95.6)	43 (89.6)	0.276
Bacteremia (n=50)	10 (28.6)	4 (26.7)	1.000
Shock	6 (6.7)	4 (8.3)	0.739
Duration of hospital stay, days median(IQR)	4.0 (3.0-8.0)	4.0 (3.0-5.0)	0.390
Outcome: improved	83 (92.2)	47 (97.9)	0.360

Table 5.15 Comparison of the clinical manifestations and treatment outcome between antibiotic resistant and antibiotic sensitive groups in all patients at Samutsakhon Hospital during 2013-2015

	Resistant strains (n=251)	Sensitive strains (n=100)	P value
Median age (years)	1.0 (0.7-35.0)	9.5 (0.8-49.0)	0.046
Age: <5 years	151 (60.2)	44 (44.0)	0.035
5-14.9 years	10 (4.0)	8 (8.0)	
15-59.9 years	55 (21.9)	27 (27.0)	
>60 years	35 (13.9)	21 (21.0)	
Stool characteristic (n= 343): Watery	227 (91.5)	93 (97.9)	0.035
Mucous or bloody	21 (8.5)	2 (2.1)	
Anti-emetic drugs used	119 (47.4)	60 (60.0)	0.033

Complications and treatment outcome among the patients who received antibiotic or not

Among 351 patients, 60 patients did not get treatment with antibiotic. In patients who received antibiotic treatment, 123 patients got appropriate antibiotic and 63 got inappropriate antibiotic treatment. The rest 105 patients who also received antibiotic but the antibiotic susceptibility tests were not matched with the antibiotics they received. For complications such as shock, renal failure, heart failure, hyponatremia, metabolic acidosis, high creatinine and outcome, there is no significant difference between these groups. Only hypokalemia and bacteremia showed statistical significance between these groups (p=0.019, 0.032) correspondingly. Patients who received inappropriate antibiotic treatment group had significantly highest percentage of hypokalemia than other groups (41.1%, P=0.019). Highest percentage of bacteremia was found significantly in patients who had appropriate antibiotic treatment than other groups (22.4%, P=0.032). These results are shown in Table 5.16.

Table 5.16 Complications and treatment outcome among the patients who received antibiotic or notat Samutsakhon Hospital during 2013-2015

	Antibiotic not used (n=60) N (%)	Appropriate antibiotic used (n=123) N (%)	Inappropriate antibiotic used (n=63) N (%)	No susceptibility test (n=105) N (%)	P value
Complications (n=351)	50 (83.3)	114 (92.7)	54 (85.7)	90 (85.7)	0.210
Shock (n=351)	1 (1.7)	4 (3.3)	2 (3.2)	3 (2.9)	0.940
Renal failure (n=351)	0 (0)	4 (3.3)	2 (3.2)	1 (1.0)	0.355
Heart failure (n=351)	0 (0)	1 (0.8)	0 (0)	1 (1.0)	0.776
Hyponatremia (n=314)	12 (24.0)	36 (31.3)	19 (33.9)	41 (44.1)	0.080
Hypokalemia (n=314)	9 (18.0)	42 (36.5)	23 (41.1)	23 (24.7)	0.019
Creatinine >1.5 mg/dL (n=155)	4 (26.7)	13 (20.6)	9 (23.7)	9 (23.1)	0.958
Bacteremia (n=149)	1 (10.0)	11 (22.4)	4 (11.8)	2 (3.6)	0.032
Co-infection (n=351)	11 (18.3)	22 (17.9)	11 (17.5)	20 (19.0)	0.994
Outcome (n= 347): Dead	0 (0)	2 (1.6)	1 (1.6)	3 (2.9)	0.611

Demographic characteristic, treatment and complications of dead patients

The results of demographic characteristic, treatment and complications of dead patients are shown in Table 5.17. There were 6 patients died after admission. They were all in adult groups with 4 male and 2 female patients. Among 6 patients, 4 patients had underlying comorbidities. Chronic kidney disease and hypertension were the most common underlying disease found in 50% of patients. *Salmonella* serogroups affecting these patients were serogroups C (3 patients), B (2 patients) and E (1 patient). All patients had received antibiotic treatment and only 2 patients got appropriate antibiotic treatment.

Table 5.17 Demographic characteristic, treatment and complications of dead patientsat Samutsakhon Hospital during 2013-2015

	Case 1	**Case 2**	**Case 3**	**Case 4**	**Case 5**	**Case 6**
Age	49	40	60	67	74	70
Gender	Male	Male	Female	Female	Male	Male
Underlying disease	ESRD	Hypertension	No	Hypertension, ESRD, stroke	No	DM, Hypertension,CKD
Duration of hospital stay	8	1	44	2	1	92
Salmonella serogroup	E	C	C	C	B	B
Antibiotic used	Ceftriaxone IV	Ceftriaxone IV	Metronidazole IV, Meropenem IV, Norfloxacin oral	Ceftriaxone IV, Metronidazole IV	Ceftriaxone IV	Ciprofloxacin IV
Appropriate antibiotic or not	Appropriate	N/A	N/A	N/A	Inappropriate	Appropriate
Co-infection	No	No	UTI	No	No	UTI
Bacteremia	Mixed growth	N/A	No	No	N/A	Gram negative bacilli
Complications	Shock Renal failure Respiratory failure Hyperkalemia Metabolic acidosis	Severe anemia Metabolic acidosis	Severe anemia Metabolic acidosis Hyponatremia Hypokalemia Volume overload	Cardiac arrest Metabolic acidosis Hypokalemia	Shock High creatinine Hypokalemia	Sepsis Renal failure Anemia Hyponatremia Hypokalemia Metabolic acidosis

*ESRD= End stage renal disease, DM= Diabetes mellitus, CKD= Chronic kidney disease, UTI= Urinary tract infection, N/A= Not available

Comparison of demographic characteristic, treatment and complications between dead patients and improved patients

In comparison of patients who died after admission and patients who clinically improved after treatment, there was statistical significance in age group (p=0.003).In dead patients group, highest proportion was seen in ≥60 years of age (66.7%). In improved patients group, the highest proportion (56.6%) was found in < 5 years of age and ≥ 60 years age group got improved only in 14.7%. Numbers of comorbidities between these two groups were statistically difference (P<0.001). In dead patients group, 33.3% of patients had 1 comorbid condition and another 33.3% had ≥ 3 comorbidities. In improved patients group, the highest proportion (75.4%) had no comorbid condition and only 2.1% had ≥ 3 comorbid conditions. For no comorbid conditions, improved patients had significant higher proportion than dead patients (75.4% vs. 33.3%). *Salmonella* serogroups and the use of antibiotics among the two groups were similar (P> 0.5, *data not shown*). Shock was seen in dead patients significantly higher than improved patients (33.3% vs. 2.1%, P=0.009). Also renal failure was presented more significant in dead patients than improved patients (33.3% vs. 1.2%. P=0.004). High creatinine could be seen in dead patients in the significantly higher proportion than in improved patients (80.0% vs. 20.3%, P=0.009). These findings are shown in Table 5.18.

Table 5.18 Comparison of demographic characteristic, treatment and complications between dead patients and improved patients at Samutsakhon Hospital during 2013-2015

	Dead (n=6)	Improved (n=341)	P value
Age (n=347)			0.003
<5 years	0 (0)	193 (56.6)	
5-14.9 years	0 (0)	18 (5.3)	
15-59.9 years	2 (33.3)	80 (23.5)	
≥60 years	4 (66.7)	50 (14.7)	
Gender (n=347)			0.703
Male	4 (66.7)	194 (56.9)	
Female	2 (33.3)	147 (43.1)	

Table 5.18 Comparison of demographic characteristic, treatment and complications between dead patients and improved patients at Samutsakhon Hospital during 2013-2015 (cont.)

	Dead (n=6)	Improved (n=341)	P value
Comorbidities (n=347)			<0.001
No	2 (33.3)	257 (75.4)	
1 comorbid	2 (33.3)	51 (15.0)	
2 comorbidities	0 (0)	26 (7.6)	
≥3 comorbidities	2 (33.3)	7 (2.1)	
Bacteremia (n=147)			0.066
Yes	2 (50.0)	15 (10.5)	
No	2 (50.0)	128 (89.5)	
Any complications (n=347)			1.000
Yes	6 (100.0)	298 (87.4)	
No	0 (0)	43 (12.6)	
Shock (n=347)			0.009
Yes	2 (33.3)	7 (2.1)	
No	4 (66.7)	334 (97.9)	
Renal failure (n= 347)			0.004
Yes	2 (33.3)	4 (1.2)	
No	4 (66.7)	337 (98.8)	
Heart failure (n=347)			0.034
Yes	1 (16.7)	1 (0.3)	
No	5 (83.3)	340 (99.7)	
Hyponatremia (n=310)			0.423
Yes	3 (50.0)	105 (34.5)	
No	3 (50.0)	199 (65.5)	
Hypokalemia (n=310)			0.378
Yes	3 (50.0)	93 (30.6)	
No	3 (50.0)	211 (69.4)	
Metabolic acidosis (n=310)			1.000
Yes	5 (83.3)	252 (82.9)	
No	1 (16.7)	52 (17.1)	
Creatinine >1.5 mg/dL (n=153)			0.009
Yes	4 (80.0)	30 (20.3)	
No	1 (20.0)	118 (79.7)	

Demographic characteristic, treatment and treatment outcome of patients with multiple admissions

Among 351 cases, there were 11 cases, which had *Salmonella* gastroenteritis and admitted more than 1 time in the study period (multiple admissions). Among them, 9 patients had 2 times admissions and 2 patients had 3 times admissions. The results of demographic characteristic, treatment and treatment outcome of multiple admitted patients are shown in Table 5.19.In 9 patients out of 11 patients (81.8%) who had multiple admissions, they were infected with same *Salmonella* serogroup in each time of hospital admissions. Only 1 patient (Case no. 1) received appropriate antibiotic treatment in the first time of admission. Five patients received inappropriate antibiotic treatment and five patients received antibiotic, which didn't had the antibiotic susceptibility test.

Table 5.19 Demographic characteristic of patients with multiple admissions with *Salmonella* gastroenteritis at Samutsakhon Hospital during 2013-2015

Case no.	Age (year)	Gender	Underlying disease	Time of infection	*Salmonella* serogroup	Duration after previous infection (month)
1	29	Male	HIV	First	D	
				Second	D	3
2	25	Male	DM	First	E	
				Second	E	7
3	69	Female	No	First	C	
				Second	C	1
4	1.3	Male	No	First	E	
				Second	B	14
5	0.6	Male	No	First	B	
				Second	B	12
6	1	Male	No	First	B	
				Second	B	0.2
7	0.6	Female	No	First	C	
				Second	C	6
8	0.4	Male	No	First	B	
				Second	B	4

Table 5.19 Demographic characteristic of patients with multiple admissions with *Salmonella* gastroenteritis at Samutsakhon Hospital during 2013-2015 (cont.)

Case no.	Age (year)	Gender	Underlying disease	Time of infection	*Salmonella* serogroup	Duration after previous infection (month)
9	0.3	Male	G6PD deficiency	First	E	
				Second	E	3
10	0.4	Female	Lactase deficiency	First	D	
				Second	D	1.4
				Third	D	0.3
11	23	Female	HIV	First	C	
				Second	B	2
				Third	B	0.1

Table 5.20 Treatment and treatment outcome of patients with multiple admissions with *Salmonella* gastroenteritis at Samutsakhon Hospital during 2013-2015

No.	Episode	Antibiotic	Appropriate ATB Used	Co-infection	Bacteremia	Outcome
1	First	Ceftriaxone	Appropriate	No	Gram negative bacilli	Improved
	Second	Ceftriaxone+ Ampicillin	Appropriate	UTI	Gram negative bacilli	Improved
2	First	Not used	Inappropriate	No	N/A	Improved
	Second	Ceftriaxone	N/A	No	N/A	Improved
3	First	Norfloxacin oral	N/A	No	N/A	Improved
	Second	Not used	Inappropriate	No	N/A	Improved
4	First	Cefotaxime	N/A	No	No	Improved
	Second	Ampicillin	Inappropriate	Bronchiolitis	N/A	Improved
5	First	Cefotaxime	N/A	No	N/A	Improved
	Second	Not used	Inappropriate	No	N/A	Improved
6	First	Not used	Inappropriate	URI	N/A	Improved
	Second	Not used	Inappropriate	No	N/A	Improved
7	First	Not used	Inappropriate	Bronchitis	N/A	Improved
	Second	Not used	Inappropriate	Pneumonia	N/A	Improved
8	First	Ceftriaxone	Inappropriate	No	No	Improved
	Second	Not used	Inappropriate	No	N/A	Improved

Table 5.20 Treatment and treatment outcome of patients with multiple admissions with *Salmonella* gastroenteritis at Samutsakhon Hospital during 2013-2015 (cont.)

No.	Episode	Antibiotic	Appropriate ATB Used	Co-infection	Bacteremia	Outcome
9	First	Norfloxacin oral	N/A	No	N/A	Improved
	Second	Not used	Inappropriate	Bronchitis	N/A	Improved
10	First	Ceftriaxone	N/A	UTI	No	Improved
	Second	Not used	Inappropriate	Pneumonia	N/A	Improved
	Third	Cefotaxime	Inappropriate	No	No	Improved
11	First	Ceftriaxone	Inappropriate	No	N/A	Improved
	Second	Ceftriaxone + Metronidazole	N/A	No	Gram negative bacilli	Improved
	Third	Ciprofloxacin + Co-amoxiclav	Appropriate	No	Not done	Improved

N/A= Not available, URI= upper respiratory tract infection, UTI= urinary tract infection

Comparison of the demographic characteristic, treatment and treatment outcome between single admitted patients and multiple admitted patients

The results of the comparison of demographic characteristic, treatment and treatment outcome between single admitted and multiple admitted patients are shown in Table 5.21. By comparing single admitted patients and multiple admitted patients, there are no significant differences in demographic characteristics and *Salmonella* serogroups. The antibiotic usage, complications and treatment outcome also did not have any statistical difference between single admission group and multiple admissions group.

Table 5.21 Comparison of demographic characteristic, treatment and treatment outcome between single admitted patients and multiple admitted patients at Samutsakhon Hospital during 2013-2015

	Single admission (n=340)	Multiple admissions (n=11)	P value
Age (n=351)			0.771
<5 years	188 (55.3)	7 (63.6)	
5-14.9 years	18 (5.3)	0 (0)	
15-59.9 years	79 (23.2)	3 (27.3)	
≥60 years	55 (16.2)	1 (9.1)	
Gender (n=351)			0.763
Male	192 (56.5)	7 (63.3)	
Female	148 (43.5)	4 (36.4)	
Salmonella serogroups (n=351)			0.719
Serogroup B	144 (42.4)	3 (27.3)	
Serogroup C	69 (20.3)	3 (27.3)	
Serogroup D	40 (11.8)	2 (18.2)	
Serogroup E	68 (20.0)	3(27.3)	
Others	19 (5.6)	0 (0)	
Antibiotic (n=351)			0.409
Used	283 (83.2)	8 (72.7)	
Not used	57 (16.8)	3 (27.3)	
Antibiotic used (n=246)			0.213
Appropriated antibiotic used	122 (50.8)	1 (16.7)	
Inappropriated/No antibiotic used	118 (49.2)	5 (83.3)	
Comorbidities (n=351)			0.204
No	254 (74.7)	7 (63.6)	
1 comorbid	50 (14.7)	4 (36.4)	
2 comorbidities	27 (7.9)	0 (0)	
≥3 comorbidities	9 (2.6)	0 (0)	
Bacteremia (n=149)	17 (11.7)	1 (25.0)	0.406
Co-infection (n=351)	62 (18.2)	2 (18.2)	1.000
Complication (n=351)	299 (87.9)	10 (90.9)	1.000
Outcome (n=347)			1.000
Improved	330 (98.2)	11 (100.0)	

CHAPTER VI
DISCUSSION

This study was piloted at Samutsakhon Hospital including 351 cases of *Salmonella* gastroenteritis of all ages during the fiscal year 2013 to 2015.

Ministry of Public Health Thailand published an Annual Epidemiology Surveillance Report stated that there were 15,800 reported cases of acute diarrhea in Samut Sakhon Province in the year 2013.(59) In present study the prevalence of *Salmonella* gastroenteritis among the admitted patients of acute diarrhea which was sent stool culture at Samutsakhon Hospital was 6.9% from the year 2013 to 2015. This finding could be compared with a case-control study conducted at Western Thailand to find the etiology of diarrheal diseases, the prevalence of *Salmonella* was found to be 6% during 2001-2002. 236 children aged from 3 month to 5 years who came with acute diarrhea were collected to get stool specimens.(12) Another study about enteropathogen in diarrhea patients was a one-year prospective study in Stockholm, Sweden. *Salmonella* was one of the most frequent enteropathogens found in that study with the prevalence of 7% in 851 adult patients presented with diarrhea or gastroenteritis. (60) We could compare these two studies with ours because they were also made only in inpatient units and laboratory diagnosis was done by stool culture.

There were other issued studies, which had greater prevalence than our study. A retrospective study of 571 children in Barbados in 2014, found out that acute gastroenteritis was in the third place among the causes of hospital admission in children less than 15 years. In this study, they investigated for prevalence of *Salmonella* species, which was 21.1%, more advanced than the finding of our study. Since in Barbados, acute diarrheal was responsible for 9-13.5% of all pediatric hospital admission. (26)Another study was conducted at National University Hospital, Singapore researching the prevalence of bacterial diarrheal in 1992 in 4,508 patients of all ages presented to hospital with diarrhea found out that *Salmonella* was the supreme communal finding being isolated in 10.8%.(61)

There were other published studies, which showed lower prevalence rate than our study. Firstly, this study was conducted in Lagos, Nigeria over 6 months period (December-May) with 215 fecal samples from children less than 5 years. Amongst 215 patients who came with diarrhea, *Salmonella* was cultured in 3.3% of the stool samples. This research may yield less prevalence than our findings may be because this study was made in the dry season of the year. In Lagos, the dry season started from November and ends in May of the year.(45)*Salmonella* gastroenteritis has the seasonal variation with highest incidence during the rainy seasons. (51) Another 6 months study revealed that *Salmonella* account for 4% in total of 350 rectal swabs in patients approached with diarrhea in non-AIDS condition conducted at Nonthaburi, Thailand. In this study, they compared the prevalence of AIDS patients with diarrhea and non-AIDS patients with diarrhea and found the prevalence of *Salmonella* for 5.7% and 4% respectively. They might have the limitations of detection from a single stool specimen or getting not enough stool specimens from some patients.(62)Gold standard for laboratory diagnosis of *Salmonella* gastroenteritis is conventional stool culture with freshly passed stool for best isolation and consecutive stool culture for 3 days is recommended for detection of organisms.(51)

In the report of Annual Epidemiology Surveillance Report of Thailand, it could be seen that children aged less than five years were the majority of the population who had been affected by acute diarrhea with the incidence rate of 7,774/100,000 populations in 2013.(16) These were agreeable with our findings that 56.1% of the patients who presented with diarrhea in our study were under five years of age. Previously, a study on activity of serogroups of non-typhoidal *Salmonella,* majority of patients (70%) was determined to be 0-4 years of age, which was concordant with our findings.(63) Kumar A et al. also stated that over 77% of *Salmonella* isolates found in their study was within 0-5 years of age. Their study was done retrospectively with 571 children who were under 15 years of age within 3-year study period.(26) Young children under five years of age have more risk to get *Salmonella* infection because the immune systems of the children are still in developing stage compared to adults and they also have increased likelihood of hand-to face contact and contact with the environment. Good hand washing practice also play an important role in *Salmonella* gastroenteritis.(64)

Salmonella gastroenteritis may manifest with clinical symptoms like loose and watery stool with moderate volume without blood, only in rare cases may present as large volume associated with tenesmus. Other symptoms including fever, abdominal cramps, nausea/vomiting were described commonly.(51) In this present study in both children and adult groups, *Salmonella* gastroenteritis presented with watery diarrhea and frequency of bowel movements with less than or equal to ten times for more than ninety percent of patients. Further symptoms encompassed were fever (>37.5 °C) for 81.8% in children and 56.9% in adults, abdominal pain for 57.1% in children and 71.2% in adults, and nausea/vomiting giving 69,7% in children group and 66.9% in adult group. From these clinical findings in children, *Salmonella* gastroenteritis should be in the differential diagnosis in children aged less than 5 years presented with fever and diarrhea. Our study had the similar findings with other published studies. Firstly, there was a study made in 394 Thai children with *Salmonella* gastroenteritis at Nonthaburi, Thailand found that 83.3% of the patients came with watery stool and in additional symptoms with fever for 74.7% and abdominal pain for 59%.(65) Another study, which was held in Bangkok, Thailand in 2009, was a retrospective study of 134 children who had positive stool culture for *Salmonella* species. Clinical manifestations of *Salmonella* gastroenteritis in that study were watery diarrhea for 99.3%, fever for 93.3% and nausea/vomiting for 48.5% in which these findings were concordant with our study.(42)

In this study, we established that *Salmonella* serogroup B was the most mutual serogroup, 48.4% in children and 31.9% in adults. Serogroup C was the second most common one in children, which took about 20.2% whilst serogroup E was the one which took part in adults for 30.4%. This outcome could be compatible with a study, which discovered the prevalence of *Salmonella* serogroups and serovars during 2011 to 2012 at Siriraj Hospital. Prevalence of serogroup B was 32.6% predominantly and serogroup C was 22.8%.(30) Another study, which had similar findings with our study, was done in Bamrasnaradura Hospital, Nonthaburi, Thailand with 394 children who came with *Salmonella* diarrhea. 56.1% of the isolates were affected by *Salmonella* serogroup B. 87% of patients were under two years of age.(65)An additional study found out serogroup B was the most frequent serogroup giving 58% of the isolates tracked by serogroup C which was 13%. This study was done in 1,419

children with acute diarrhea in Ho Chi Minh City, Vietnam from 2009-2010.(66)*Salmonella* Typhimurium (43.5%), which belongs to serogroup B, and *Salmonella* Enteritidis (17.1%), which belongs to serogroup D, are the most prevalent *Salmonella* serovars globally. Therefore, *Salmonella* serogroup B was the most common serogroup among the other serogroups. And also *Salmonella* Typhimurium is causing antimicrobial resistance globally than *Salmonella* Enteritidis.(51)

Antibiotic resistance had fully-fledged into a vast problem intimidating the whole world. Newly recognized resistant strains, which were so-called as nightmare bacteria by the world health leaders, could blowout easily between continents and also cross the international borders threatening each and every people all over the world. Center for disease control and prevention (CDC) reported that antibiotic resistance was causing illnesses in at least 2,049,442 people and mortality in 23,000 people of United States in the year 2013.(17)

Since antibiotic resistance had increasing trend in all health problems, antimicrobial susceptibility testing played a role for treating bacterial diarrhea cases not only to choose appropriate antibiotic for treatment but also to monitor the ascending route of antimicrobial resistance. In daily practice of treating acute gastroenteritis cases at Samutsakhon Hospital, ceftriaxone was the most commonly used antibiotics in adult patients (50.7%) whilst in children, cefotaxime was the one mostly used (42.3%). For antibiotic susceptibility testing at Samutsakhon Hospital, there were 123 patients who received antibiotic treatment but did not do the susceptibility test that matched to their antibiotic uses. Therefore the antibiotic susceptibility test should include all antibiotics commonly used to treat *Salmonella* infection, especially ceftriaxone. Nalidixic acid and ciprofloxacin should also be included in first priority as quinolone resistance was increasing trend for *Salmonella* gastroenteritis. After testing of antibiotic susceptibility, if the patient infect with *Salmonella* resistant to first line antibiotic, they should be treated with azithromycin or levofloxacin (or other fluoroquinolone). Monitoring of antibiotic susceptibility test should be done once each antibiotic is started to use.

In present study, overall prevalence of antibiotic resistant *Salmonella* (resistance to at least one antibiotic) was 71.5% among 351 cases of *Salmonella* gastroenteritis. In a study demonstrating antimicrobial resistance of *Salmonella* in a

global extent shown that in the years of 1990s, prevalence of antibiotic resistant *Salmonella* was around 20-30%. As the time travelled to 20th century, the prevalence reached up to 70% in some parts of world.(18)Liang Z, et al. demonstrated that prevalence of antibiotic resistant *Salmonella* in Guangdong, China, was 72% in the year 2015. It was made in 40,572 patients of all ages came with diarrhea and found that 1,826 cases was culture positive for *Salmonella*.(67)Another study was conducted in Shanghai, China with 1,833 children with 316 culture-positive *Salmonella* found the prevalence of drug resistance *Salmonella* was 60.5% in 2014. In these two studies made in China, the leading cause of drug resistance *Salmonella* was due to overuse or misuse of antibiotics in veterinary.(57)A study that found the prevalence of overall antimicrobial resistance in *Salmonella* was 40.2% in which it took part in Saudi Arabia testing 17,436 fecal samples of all patients admitted with acute diarrhea or gastroenteritis.(68)

Table 6.1 Drug resistance of non-typhoidal *Salmonella* all over the world

Country	**Year**	**Ampicillin**	**Tetracycline**	**Chloramphenicol**	**TMP/SMX**	**Nalidixic acid**	**Ciprofloxacin**
Ethiopia(55)	2014	100%	100%	71.4%	85.7%	10.7%	0%
China(57)	2014	58.6%	N/A	N/A	32.4%	69.6%	5.5%
USA(69)	2014	13.4%	N/A	8.3%	2.8%	6.4%	0.6%
Germany(54)	2014	78.3%	77.6%	14.6%	15.7%	4.7%	0%
Bangladesh(70)	2011	10.1%	N/A	0%	3.1%	N/A	2.1%
England(53)	2006	42%	51%	N/A	18%	13%	N/A

Drug resistance of non-typhoidal *Salmonella* to each antibiotic all over the world is shown in Table 6.1. In this study, we found that resistance was high for ampicillin (62.6%) and ciprofloxacin (42.2%) in children and ampicillin (45.6%) and ciprofloxacin (46.3%) for adults. Resistance to nalidixic acid, which was used to test

for quinolone resistance, caused 36.0% resistance in children and 37.2% resistance in adults.

In a study made in Shanghai, China with 1,833 cases of children with acute diarrhea found out that resistance for previously used empirical antibiotics were high (ampicillin 58.6%, trimethoprim/sulfamethoxazole 32.4%) whilst currently used antibiotic ciprofloxacin resistance was 5.5%.(57) A cross-sectional study conducted in Ethiopia 384 patients of all ages presented to outpatient department with acute diarrhea published that resistance for ampicillin and tetracycline was 100%, chloramphenicol was 71.4%, trimethoprim/sulfamethoxazole was 85.7%. Antibiotics, which were not easily available over the counter in Ethiopia, had low rate of resistance (nalidixic acid10.7%, ciprofloxacin 0%).(55) In developing countries like England and Wales, antimicrobial drugs that were giving resistance were nalidixic acid coupled with decreased susceptibility to ciprofloxacin tested in 43,563 human isolates of *Salmonella*. This combination of resistance for *S.* Enteritidis was increased from 43% to 76% and for *S.* Typhimurium was ascending from 9% to 13% from the year 2000 to 2004.(53)

A published research made in Bangkok, Thailand in 2001 which established ampicillin as the most resistant giving drug (50%), trimethoprim/sulfamethoxazole gave 7% and nalidixic acid resistance was 14% in that study.(62)Another study conducted in Thailand and Vietnam to compare the antibiotic resistance of diarrhea pathogens also listed 37% resistance trimethoprim/ sulfamethoxazole, 28% resistance ampicillin, 21% resistance nalidixic acid and ciprofloxacin resistance was <1% found in Thai patients. This study was done over 3 years study period including both children and adults.(71)Non-typhoidal *Salmonella* strains were also presenting their resistance to ampicillin (31.3%), trimethoprim/sulfamethoxazole (20.9%) in a study made in Saudi Arabia in a retrospective study of all patients admitted with acute diarrhea or gastroenteritis.(68)

Therefore, the outcomes of the contemporary study were consistent with other issued studies aiming that *Salmonella* strains were increasing resistance to a wide variety of antibiotics treatment. Local epidemiology of a country or a city also played in a crucial role for antibiotics resistance strains and clinicians should be aware of the results of antimicrobial susceptibility test. Fluctuating patterns of antibiotics

resistance should always be cautiously monitored for the benefits of the patients.(68)In our study, there were 105 patients who were not tested for antibiotic susceptibility test that matched with their antibiotics used. Among 6 dead patients, only 2 patients received appropriate antibiotic treatment, therefore, it may be another crucial issue to get appropriate antibiotic to reduce the morbidity and mortality of *Salmonella* infection. Multiple infections with *Salmonella* may be decreased if the patient is tested for antibiotic susceptibility prior giving treatment and treated with right antibiotic. In Samutsakhon Hospital, only serogroup of *Salmonella* can be tested, serovars of *Salmonella* cannot be identified and 9 patients out of 11 patients who had multiple admission have same *Salmonella* serogroups in each time of hospital admission (serovars may be presumably same but serovars are not tested).

Nowadays, antibiotic resistance strains are emergent and scattering from human to human or non-human sources such as food. Center for disease control and prevention (CDC) specified that there would be four fundamental phases to avoid the spread of resistance strains. Firstly, preclude getting infection and then track the resistance bacteria. By cultivating the use of current antibiotics and by endorsing the progress of new antibiotics and new diagnostic tests for resistant bacteria, we hope to preserve new resistance from developing and to avert the resistance that already exists from spreading.(17)

Since it was a descriptive retrospective study, it had limitations in obtaining various information. There were lots of missing data or not recorded data about the demographic characteristic, history of illness, clinical signs and symptoms. Bearing in mind the retrospective nature of the study, we couldn’t get the information about the volume of diarrhea. In addition, due to the limitations of laboratory technique, we couldn’t identify the serotypes of *Salmonella* isolates. Hence, a prospective study with a longer duration of study and standardized diagnostic techniques for serotyping, faster and accurate stool culture method and antimicrobial susceptibility testing would be needed to solve the problems that we were facing with *Salmonella* gastroenteritis.

CHAPTER VII
CONCLUSION

In Samut Sakhon Province, the prevalence of *Salmonella* gastroenteritis among all cases of acute diarrhea admitted to the hospital and sent stool culture was 6.9%. Children less than five years old were the most common age group found in *Salmonella* gastroenteritis. Most commonly identified serogroup in patients admitted to hospital was *Salmonella* serogroup B. In study of 351 cases of *Salmonella* gastroenteritis, the mortality rate of *Salmonella* gastroenteritis was 1.7%. Inappropriate antibiotic used might be attributed to death and repeated infection.

Prevalence of antibiotic resistant *Salmonella* gastroenteritis was 71.5%. Prevalence of antibiotic resistant of *Salmonella* gastroenteritis was relatively high regardless of its low prevalence. Thus, antibiotic usage should be taken into caution to prevent from getting antibiotic resistant strains in the community and to provide better health care and treatment for the patients. Results of antibiotic susceptibility test showed that ampicillin was the most resistant drug against *Salmonella* species in children followed by ciprofloxacin. In adults, ciprofloxacin was the most resistant one and the second drug was ampicillin. Antibiotic resistance for these drugs may be higher because these are the first line antimicrobial drugs used in Thailand. It is important to get appropriate antibiotic treatment to decline morbidity and mortality of *Salmonella* infection and thus, antibiotic susceptibility test should be done and monitored the changing trends of antibiotic resistance.

We would like to conclude that *Salmonella* species were still causing the global burden affecting all ages of population and hence, drug resistant *Salmonella* were also threatening public health in a serious situation. A prospective study with a broader panel of diagnostic techniques representing the general population, not only admitted patients, will be needed in the future. Physicians should bear in mind about drug resistance strains before starting antibiotics for treatment of *Salmonella* gastroenteritis.

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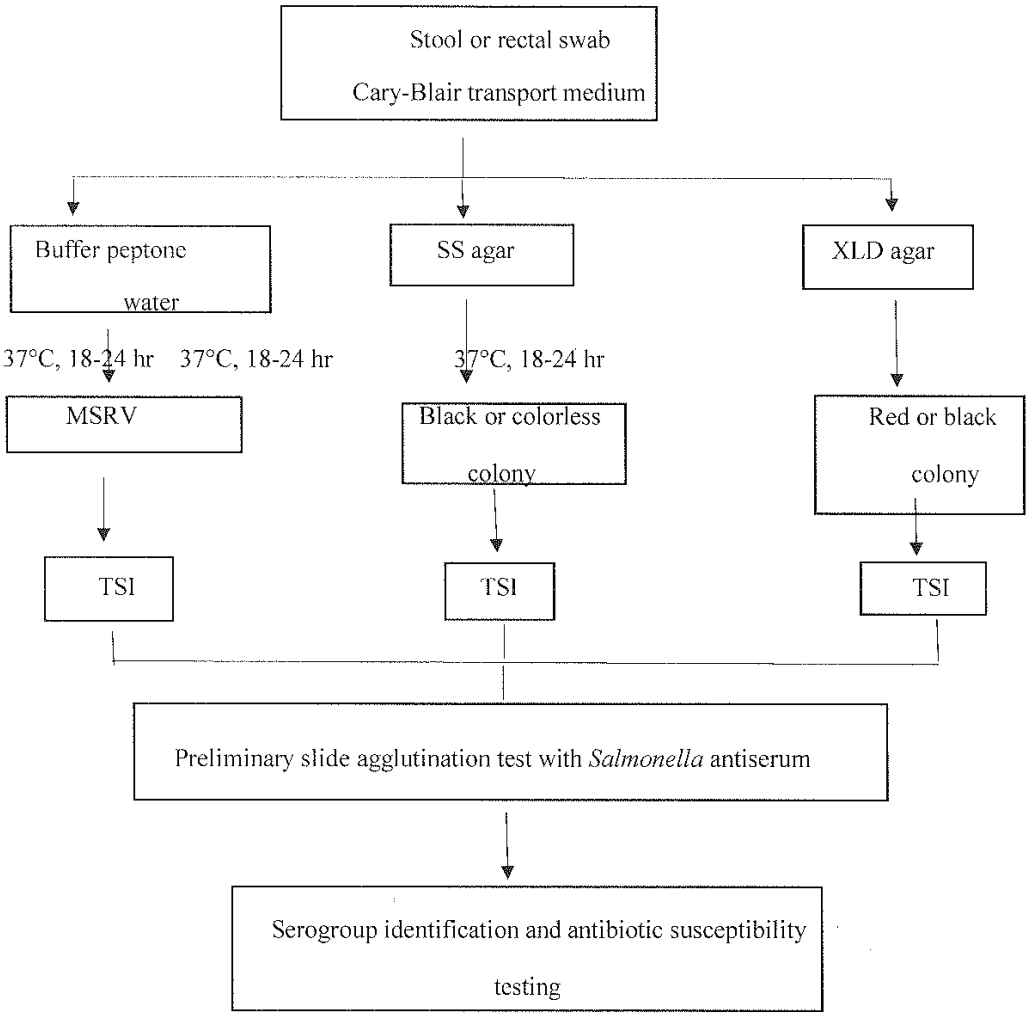
APPENDICES

APPENDIX A

FLOW DIAGRAM FOR PROCESS OF STOOL CULTURE



SS agar – Salmonella-Shigella agar

XLD agar – Xylose Lysine Decarboxylate agar

MSRV – Modified Semi Solid Rappaport Vassiliadis medium base

TSI – Triple Sugar Ion

APPENDIX B

Laboratory values used in Samutsakhon Hospital

Hct (%)	37.0-50.0
Hb (g/dL)	12.0-16.5
Platelets ($\times 10^9$/L)	140.0-440.0
WBC ($\times 10^9$/L)	4.0-11.0
Neutrophil (%)	37.0-80.0
Eosinophil (%)	0.0-7.0

BUN (mg/dL)	7-18
Creatinine (mg/dL)	0.6-1.3
Na^+(mEq/L)	135-145
K^+ (mEq/L)	3.6-5.2
Cl^- (mEq/L)	100-108
HCO_3^-(mEq/L)	21.0-32.0

APPENDIX C

Case Record Form Study ID. No_____

Salmonella gastroenteritis: epidemiology, clinical manifestations and treatment outcome

Patient information

1. Age _____ years
2. Gender ☐ (1) Female ☐ (2) Male
3. Weight _____kg, height _____cm.
4. Occupation ☐ (1) Farmer ☐ (2) Fisherman ☐ (3) Factory worker
   ☐ (4) Officer ☐ (5) Business ☐ (6) Student ☐ (7) Unemployed
   ☐ (8) Unspecified employee ☐ (7) Others (specify) _____
5. Race ☐ (1) Thai ☐ (2) Myanmar
   ☐ (3) Lao ☐ (4) Others (specify) _____
6. Smoking ☐ (0) No ☐ (1) Yes ☐ (9) Unknown
7. Alcohol ☐ (0) No ☐ (1) Yes ☐ (9) Unknown
8. Comorbidities ☐ (0) No ☐ (1) Yes
   (1) DM ☐ (0) No ☐ (1) Yes ☐ (9) Unknown
   (2) Hypertension ☐ (0) No ☐ (1) Yes ☐ (9) Unknown
   (3) Steroid therapy ☐ (0) No ☐ (1) Yes ☐ (9) Unknown
   (4) HIV ☐ (0) No ☐ (1) Yes ☐ (9) Unknown
   (5) Chronic liver disease ☐ (0) No ☐ (1) Yes ☐ (9) Unknown
   (6) Chronic kidney disease ☐ (0) No ☐ (1) Yes ☐ (9) Unknown
   (7) Others (specify) _____
9. Date of admission (DD/MM/YYYY) ☐☐/☐☐/25☐☐
10. Date of discharge (DD/MM/YYYY) ☐☐/☐☐/25☐☐
11. Date of first visit in this illness (DD/MM/YYYY) ☐☐/☐☐/25☐☐

Before admission

12. Diarrhea ☐ (0) No ☐ (1) Yes, duration _____ days, frequency _____ times/day
13. Stool characteristic ☐ (1) Watery ☐ (2) Mucous or bloody ☐ (9) Unknown
14. Fever ☐ (0) No ☐ (1) Yes, duration _____ days ☐ (9) Unknown
15. Abdominal pain ☐ (0) No ☐ (1) Yes, duration _____ days ☐ (9) Unknown
16. Nausea/vomiting ☐ (0) No ☐ (1) Yes, duration _____ days ☐ (9) Unknown

Case Record Form Study ID. No_____

Salmonella gastroenteritis: epidemiology, clinical manifestations and treatment outcome

Physical exam on admission

17. Temperature _____°c, BP _____/_____ mmHg, PR _____/min
18. Dehydration ☐ (0) No ☐ (1) Mild ☐ (2) Moderate ☐ (3) Severe ☐ (9) Unknown
19. Abdominal distension ☐ (0) No ☐ (1) Yes ☐ (9) Unknown
20. Abdominal tenderness ☐ (0) No ☐ (1) Yes ☐ (9) Unknown

Investigations		**First time**	**Second time**	**Third time**
	Date	/ /25	/ /25	/ /25
Hematocrit	(%)			
Hemoglobin	(g/dL)			
WBC	($x10^9$/L)			
Neutrophil	(%)			
Eosinophil	(%)			
Platelet	($x10^9$/L)			
	Date	/ /25	/ /25	/ /25
BUN	(mg/dL)			
Cr	(mg/dL)			
Na	(mEq/L)			
K	(mEq/L)			
Cl	(mEq/L)			
HCO_3	(mEq/L)			
Stool exam	**Date**	/ /25	/ /25	/ /25
WBC	(/LPF)			
RBC	(/LPF)			
Mucous				
Character				

21. Stool culture (DD/MM/YYYY) ☐☐/☐☐/☐☐☐☐
22. Result of stool culture: Salmonella serogroup ☐ (1) A ☐ (2) B ☐ (3) C ☐ (4) D ☐ (5) E ☐ (6) F ☐ (7) G ☐ (8) H ☐ (9) I ☐ (10) Spp.

Antibiotic susceptibility

23. Cefotaxime ☐ (0) Sensitive ☐ (1) Intermediate ☐ (2) Resistant
24. Ciprofloxacin ☐ (0) Sensitive ☐ (1) Intermediate ☐ (2) Resistant
25. TMP/SMX ☐ (0) Sensitive ☐ (1) Intermediate ☐ (2) Resistant
26. Tetracycline ☐ (0) Sensitive ☐ (1) Intermediate ☐ (2) Resistant
27. Nalidixic acid ☐ (0) Sensitive ☐ (1) Intermediate ☐ (2) Resistant

Case Record Form Study ID. No_____

Salmonella gastroenteritis: epidemiology, clinical manifestations and treatment outcome

28. Bacteremia ☐ (0) No ☐ (1) Yes, specify _____ ☐ (9) Hemoculture not done

Treatment	Not used	Started Date	Stopped Date	Dose (mg/day)
Intravenous				
Ceftriaxone		/ /25	/ /25	
Ciprofloxacin		/ /25	/ /25	
Metronidazole		/ /25	/ /25	
		/ /25	/ /25	
		/ /25	/ /25	
Oral antibiotics				
Ciprofloxacin		/ /25	/ /25	
Ofloxacin		/ /25	/ /25	
Norfloxacin		/ /25	/ /25	
Azithromycin		/ /25	/ /25	
Co-trimoxazole		/ /25	/ /25	
		/ /25	/ /25	
		/ /25	/ /25	
IV fluid		/ /25	/ /25	Total _____ cc
Antimotility drugs		/ /25	/ /25	
Anti-emetic drugs		/ /25	/ /25	

29. Diarrhea stopped date (DD/MM/YYYY) ☐☐/☐☐/25☐☐

30. Fever stopped date (DD/MM/YYYY) ☐☐/☐☐/25☐☐

31. Complication ☐ (0) No ☐ (1) Yes

(1) Shock ☐ (0) No ☐ (1) Yes ☐ (9) Unknown

(2) Renal failure ☐ (0) No ☐ (1) Yes ☐ (9) Unknown

(3) Heart failure ☐ (0) No ☐ (1) Yes ☐ (9) Unknown

(4) Others: _____

32. Co-infection ☐ (0) No ☐ (1) Yes, _____

33. Outcome ☐ (0) Improved ☐ (1) Referred ☐ (2) Dead ☐ (3) Leave against advice

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