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Review Article

Salmonella Urinary Tract Infections: A Review and Update

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Abstract

Salmonella infections of the urinary tract are uncommon infections that tend to be encountered sporadically for which a high index of suspicion is required. Generally, *Salmonella* infection does occur via the ingestion of contaminated food or water via the faecal-oral route. Non-typhoidal *Salmonella* are commonly found within food and companion animals that include poultry, cattle, swine, parrots, cats, dogs as well as turtles. Eggs, milk, meat, poultry as well as contaminated vegetables commonly tend to be implicated in cases of Salmonellosis. Direct transmission of -+*Salmonella* from person to person and transmission from pets might occur. Within the setting of Salmonellosis, the source of the transmission may not appear. Generally *Salmonella* urinary tract infections do manifest with symptoms that simulate the symptoms of more common causes of urinary tract infection. Occasionally individuals who have *Salmonella* urinary tract infection could be asymptomatic. The symptoms of *Salmonella* urinary tract infection may be present contemporaneously with or develop after symptoms of enteric *Salmonella* infections with diarrhoea, abdominal discomfort, as well as other symptoms. Nevertheless, some individuals who have *Salmonella* urinary tract infections do not have any preceding or concurrent symptoms of enteric *Salmonella* infections. The clinical findings of *Salmonella* urinary tract infections are non-specific or any different from the clinical findings of more common urinary tract infection. Diagnosis of Non-typhoidal salmonellosis had traditionally been made based upon stool culture although many of the patients had tended not to seek medical attention. Not long ago, a PCR based assay has been introduced which, in addition to *Salmonella* species bacteria, also does detect *Camply-+obacter* group, *Shigella* species, *Vibrio* group, *Yersinia enterocolitica*, Shiga toxin 1 and 2, Norovirus G1 / GII, Rotavirus A as well as *Aeromonas* species. Serotyping of *Salmonella* tends to be undertaken in order to characterize outbreaks of *Salmonella* disease. Typhoid fever tends to be diagnosed by means of blood culture or stool culture. Within the developing counties of the world where laboratory facilities may not be readily available, clinicians have tended to treat suspected *Salmonella* infection empirically without the results of positive microbiology or PCR serology results based upon a high index of suspicion. *Salmonella* urinary tract infections tend to be quite often associated with chronic diseases, immunosuppression or structural abnormalities of the genitourinary tract. Utilization of 14 days course of appropriate antibiotics or longer than 14 days based upon the sensitivity pattern of the cultured *Salmonella* organism does effectively treat the infection and it is important to note the *Salmonella* organisms are tending to develop resistance to a number of antibiotics so clinicians should be aware of the antibiotic sensitivity pattern within their areas of practice. Repeat urine cultures are necessary to ascertain of the *Salmonella* urinary tract infection has successfully been treated. A thorough assessment of patients with detailed history taking, clinical examination, laboratory studies, and radiology imaging are important for the diagnosis, treatment, and follow-up of patients who have *Salmonella* urinary tract infection.

INTRODUCTION

Urinary tract infection that had been caused by non-typhoidal *Salmonella* was stated to be first reported in 1946 [1,2]. It has been iterated that urinary tract infection due to *Salmonella* is an uncommon phenomenon, that accounts for 0.01 to 0.07% of cases of UTIs that had been -+reported in various studies but there has been a notable increase with regard to the incidence of NTS infections over recent years [2,3]. Jehangir et al. [1] iterated that urinary tract infection that is caused by *Salmonella* infection is most commonly encountered in infants and patients who are older than 60 years old [4]. In a retrospective analysis of 799 isolates of NTS from urine, serotypes of groups C1 and E were more commonly associated with UTIs, in contrast to group D *Salmonella* UTI, as described in their case [5].

The modes of urinary tract infection from NTS include hematogenous spread from gastroenteritis or contamination from faecal flora via direct urethral invasion, whic-+h is more common in women [6]. It usually manifests as typical symptoms of urinary tract infection, even though cases of asymptomatic bacteriuria have been reported. UTI from NTS is usually encountered in patients with predisposing factors, including severe immune deficiency, occult urologic problems, chronic diseases (e.g., diabetes mellitus), or exposure to reptiles, such as the common green iguana [7]. Hence an episode of NTS urinary infection must be considered as a surrogate marker of underlying predisposing factor(s), namely, heretofore unrecognized immune system suppression or compromise of genitourinary anatomy. Such patients should also be evaluated for occult diabetes or

recent exposure to reptiles [6,8]. Evaluation did not suggest any evidence of immunosuppression or diabetes in our patient. Genitourinary tract abnormalities commonly reported in the literature that predispose to NTS UTI include nephrolithiasis, chronic pyelonephritis, retro-vesicular fistula, urethrorectal fistula, hydrocele, and post-TURP; our patient was conceivably predisposed to nontyphoidal *Salmonella* by his history of benign prostatic hyperplasia, as partial urinary obstruction is a major risk factor [2,9] Nonetheless, it is imperative to remember that these urinary infections can also occur in apparently healthy and immunocompetent individuals and there is data suggesting that the relationship of NTS UTI with genitourinary abnormalities and immunosuppression is likely an overestimation as a result of bias [10]. Thus, it is important to keep NTS in the differential of potential pathogens causing UTIs, including patients without any overt predisposing factors [5,6].

NTS urine infection may be difficult to treat, but early institution of antibiotics is associated with a favourable outcome [7,8] Antibiotics with high intracellular concentrations such as ciprofloxacin should be used as *Salmonella* has the tendency to grow intracellularly [8]. S Abuhasna et al. [8] stated that High frequency of complications due to *Salmonella* UTI like pyelonephritis, renal insufficiency, nephrotic syndrome, nephrolithiasis, genitourinary abscesses, recurrence, and chronic bacteriuria warrants prolonged treatment, even though recurrences may still be seen [3,6,9] In view of the fact that *Salmonella* infection of the urinary tract organs are not common, there might be difficulties in diagnosing the disease in that clinicians may not have a high index of suspicion for the infection. The ensuing article on *Salmonella* infections of the urinary tract is divided into two parts (A) Overview and (B) Miscellaneous narrations and discussions from case reports, case series, and studies related to *salmonella* infections in general and *salmonella* urinary tract infections.

AIM

To review and update the literature on *Salmonella* urinary tract infections.

METHODS

Internet Data bases were searched including: Google, Google Scholar. Yahoo, Bing, and PUBMED. The search words that were used included: *Salmonella* infections; *Salmonella* typhoid infections, *Salmonella* infections of the urinary tract, Salmonellosis of urinary tract; *Salmonella t*yphoidal infections of the urinary tract, non-typhoidal *salmonella* infections of the urinary tract, *Salmonella* typhi infections in general, non-typhoidal *salmonella* infections in general. Twenty three references were identified which were used to write the article which was divided into two parts: (A) Overview and (B) Miscellaneous narrations and discussions from Case Reports, Case Series, and studies related to *Salmonella* infections in general and *salmonella* infections of the urinary tract.

Results / Review and Update of the Literature on Salmonella Infections in General and Salmonella Urinary Tract Infections

[A] Overview:

Definition / General Statements

- It has been stated that the disease which is caused by *Salmonella* species infection is referred to as *Salmonellosis* or *Salmonella* infection [11].
- It has also been iterated even though overlap does exist with regard to *Salmonella* infection, species of *Salmonella* that cause typhoid fever as well as non-typhoidal species of *Salmonella* are quite often While overlap exists, species causing typhoid fever and nontyphoidal species often tend to be categorized separately. [11]

Essential features of *Salmonella* infection

It has been stated that *Salmonellosis* or *Salmonella* infection is regarded to be a food borne disease and that summations related to typhoid fever and infections that are caused by non-typhoidal disease are as follows: [11]

- Typhoid fever [11]

o It has been iterated that typhoid fever which at times is referred to as enteric fever relates to a life threatening illness which is caused by *Salmonella* typhi which at times is referred to *Salmonella* enterica serotype or *Salmonella* (S). para-typhi [11].

o It has been stated that *Salmonella* typhi does infect between 20 million and 30 million individuals annually and this infection tends to occur within the developing areas of the world [11].

o It has also been stated that the occurrence of typhoid fever within industrialized countries does usually tend to be associated with travellers [11].

- Nontyphoid species: [11]

o Non-typhoid species usually tend to cause self-limited gastroenteritis.

o The Centres for Disease Control and Prevention (CDC) has estimated that one million cases, 19,000 hospital admissions, and 450 deaths do occur each year within the United States of America.

o Tens of millions of cases do occur globally annually which cause an estimated 100,000 deaths.

o The disease tends to spread via ingestion of contaminated food or water and very often in a sporadic fashion but at times, via food-borne outbreaks which often tend to be associated with sub-optimal sanitary practices or food

Terminology and summations related to miscellaneous features of *Salmonella*

- It has been documented that *Salmonella* is a terminology which has been coined after the veterinarian Elmer Daniel Salmon [11].
- *Salmonella* bacteria are gram negative rods [11].
- It has been iterated that *Salmonella* bacteria species are serotype based upon the chemical content of the O antigens that are found upon the surface and the protein content of part of the flagella that is known as the H antigen [11].
- It has been stated that more than 25000 serotypes of

Salmonella had been described; nevertheless. Less than 100 serotypes of the bacterium have been known to be associated with human disease [11].

- It has been documented that serotyping of *Salmonella* is at the moment being undertaken by utilization of molecular methods [11].
- It has been iterated that *Salmonella* typhi and *Salmonella* para-typhi tend to be associated with the development of typhoid fever [11]-+.
- It has been stated that some of the more commonly encountered non-typhoidal species of *Salmonella* do include the following: [11]
  - *Salmonella*. Enteritidis
  - *Salmonella* typhimurium
  - *Salmonella* muenchen
  - *Salmonella*. adnatum
  - *Salmonella*. Give
  - As well as *Salmonella*. para-typhi could also cause non-typhoidal disease

Epidemiology:

- It has been iterated that globally more than 20 million cases of typhoid fever do occur annually and these cases mostly occur within the developing world [11].
- It has also been stated that about 1800 cases of typhoid fever do occur within the United States each year, mostly in travellers [11].
- It has been documented that from 1.0 to 1.2 million cases of non-typhoidal illness occur within the United States yearly which cause about 19,000 hospital admissions and 450 deaths [11].
- It has additionally been iterated that tens of millions of non-typhoidal illness occur worldwide, which cause more than 100,000 deaths each year [11].
- It has been iterated that the disease does occur from ingestion of bacteria, usually within food or water, eggs, milk, meat, poultry [11].
- It has also been documented that vegetables that have been contaminated with animal faeces are commonly implicated with the development of the disease.[11]
- Food borne outbreaks of *Salmonella* infections which often tend to be associated with less than sanitary conditions, are common sources of the disease [11].
  - Nevertheless, it has been documented that within the United States of America about 60% of cases do occur sporadically
- It has been iterated that faecal oral transmission of *Salmonella* could occur and that the disease develop pursuant to contact with infected animals is another source[11].
- It has been documented that *Salmonellosis* tends to be a common cause of travellers' diarrhoea[11].
- It has been iterated that all serotypes of *Salmonella* at least in theoretically could cause human *Salmonella* disease [11]
- It has also been stated that serotypes of *Salmonella* could or could not be host specific[11].
- It has been iterated that when serotypes that are specific to other species do infect human beings, severe disease might result [11].
- It has also been documented that *Salmonella* typhi is restricted to human beings [11]
- Some of the risk factors for the development of *Salmonella* infection have been documented to include: [11]
  - Lack or non-availability of access to clean water
  - Poor sanitation. especially with regard to the handling of food
  - Flooding
  - Ingestion of plants that had been fertilized with sewage
  - Living within urban environments
  - Sexual transmission of *Salmonella* infection has been reported
- The development of both typhoidal and non-typhoidal salmonellosis could occur within health care workers when they do not practice proper hand hygiene [11].
- It had been documented that travellers to the developing world often tend to be infected with S. para-typhi as well as vaccination against S. typhi tends to be commonly undertaken prior to travel [11].

Sites

Some of the sites that tend to be affected by *Salmonella* typhi infection have been documented to include: [11]

- *Salmonella* typhi could infect the entire gastrointestinal tract but typically it tends to be found within the terminal ileum, appendix and ascending colon nut non-typhoidal *Salmonella* does infects the small and large bowel [11].
- *Salmonella* typhi is said to typically spread to the liver, spleen, bone marrow and lymph nodes[11].
- Extra-intestinal spread is said to be uncommon in non-typhoidal *Salmonella* but it could occur with severe disease [11]
- On rare occasions *salmonella* infections of the urinary tract do occur which has been discussed in detail in the second part of the article.

Pathophysiology: The pathophysiology of *Salmonella* infection has been summated as follows: [11]

- *Salmonella* does possess cellular mechanisms which enable bacterial proteins to be transferred to enterocytes and M cells with subsequent growth within endosomes.
- Subsequent events do include an inflammatory response with neutrophil recruitment and mucosal damage
- The host immune response typically does control non-

typhoidal infection; nevertheless, very young individuals, the elderly, the debilitated and immunosuppressed individuals could lack the response that is necessary to control infection

- More commonly, *Salmonella*. *typhi* tends to invade M cells
- The Bacteria tend to be phagocytosed by histiocytes within the underlying lymphoid tissue
- The bacteria do proliferate and they widely disseminate via the blood vessels and lymphatic channels

5.3 Aetiology

Documented summations related to the aetiology of *Salmonella* infection do include: [11]

- *Salmonella* are gram negative bacilli.
- *Salmonella* typhi tends to be encountered only in human beings
- Non-typhoidal species of *Salmonella* tend to be encountered in human beings, domestic animals, as well as in wild animals
- Generally, *Salmonella* infection does occur via the ingestion of contaminated food or water via the faecal-oral route.
- Non-typhoidal *Salmonella* are commonly found within food and companion animals that include poultry, cattle, swine, parrots, cats, dogs as well as turtles
- Eggs, milk, meat, poultry as well as contaminated vegetables commonly tend to be implicated in cases of *Salmonellosis*
- Direct transmission of *Salmonella* from person to person and transmission from pets might occur.
- Within the setting of *Salmonellosis*, the source of the transmission may not appear.

Clinical features of *Salmonella* infection

The clinical features of *Salmonella* infection have been summarized as follows: [11]

- Symptoms of nontyphoidal salmonellosis generally start 12 - 36 hours after ingestion of bacteria but may occur after 6 - 72 hours
- Ingestion of very few organisms may cause disease
- Typically patients suffer self-limited illness characterized by diarrhoea, abdominal pain, fever, nausea and occasionally vomiting that is unpleasant but rarely life threatening
- May be life threatening in infants, elderly, immunocompromised or debilitated patients, due to dehydration or dissemination of bacteria
- Very rarely, toxic megacolon may complicate infection
- Individuals with achlorhydria or hypochlorhydria from drugs, chronic *Helicobacter pylori* infection or other causes are at higher risk of infection
- Some patients develop a reactive arthritis that may last for months and lead to chronic arthritis
- Typhoid fever causes symptoms shortly after bacteria are ingested
- Patients suffer from severe abdominal pain, bloody diarrhoea, bloating, anorexia, nausea, vomiting, headache
- A brief asymptomatic period is followed by bacteraemia with fever and flu-like illness
- Blood cultures are almost always positive at this time and antibiotic therapy may be lifesaving
- With disease progression in untreated patients, high fever and abdominal pain occurs that may mimic appendicitis; lasts for about two weeks
- If patients survive, symptoms slowly abate
- Possible extraintestinal complications include CNS disease, endocarditis, myocarditis, pneumonia, cholecystitis, osteomyelitis (patients with sickle cell disease are particularly prone to osteomyelitis)
- Disease relapses may occur

Diagnosis: Some of the summations related to the diagnosis of *Salmonella i*nfection do include: [11]

- Diagnosis of Non-typhoidal *salmonellosis* had traditionally been made based upon stool culture although many of the patients had tended not to seek medical attention
- Not long ago, a PCR based assay has been introduced which, in addition to *Salmonella* species bacteria, also does tect *Camplyobacter* group, *Shigella* species, *Vibrio* group, *Yersinia enterocolitica*, Shiga toxin 1 and 2, Norovirus G1 / GII, Rotavirus A as well as *Aeromonas* species
- Serotyping of *Salmonella* tends to be undertaken in order to characterize outbreaks of *Salmonella* disease.
- Typhoid fever tends to be diagnosed by means of blood culture or stool culture
- Within the developing counties of the world where laboratory facilities may not be readily available, clinicians have tended to treat suspected *Salmonella* infection empirically without the results of positive microbiology or PCR serology results based upon a high index of suspicion.

Factors of prognostication: The factors of prognostication of *Salmonellosis* have been summated as follows: [11]

- Non-typhoidal salmonellosis almost always tends to be a self-limited infection, with the exception of *Salmonella* infection in infants, the elderly, immunocompromised as well as in debilitated patients
- Antibiotic treatment usually tends to be effective in patients who have *salmonella* infection, even though antibiotic resistance has been stated to have become a growing problem
- If typhoid fever is not treated this may become lethal even with regard to healthy individuals but the prognosis tends to be worse with regard to infants, the elderly, immunocompromised

and debilitated patients

- Prompt commencements of antibiotic treatment greatly does improve the outcome of the patient and despite this it is important to note that antibiotic resistance is a growing problem

Typhoid perforation of the ileum and intussusception of the ileum does require resuscitation and early appropriate surgical operation plus antibiotic treatment as treatment of curative intent. Haemorrhage that emanates from a bleeding typhoid infection of the ileum may be severe enough to require blood transfusion.

Treatment

Salient points related to the treatment of *Salmonella* infection have been summated as follows: [11]

- The treatments of Non-typhoidal *Salmonella* most often:

o Only do require supportive care, and in particular hydration of the patient.

o Utilization of antibiotics are required for severe disease patients and vulnerable patients

o Utilization of Ceftriaxone and ciprofloxacin have at the moment been recommended by the CDC

o Resistance of *Salmonella* to antibiotics that are used in the treatment of *Salmonella* infection is a growing global problem

- Utilization of Antibiotic treatment for typhoid fever is obligatory and this should not be delayed for confirmatory laboratory testing

o In the past, chloramphenicol, trimethoprim-sulfamethoxazole, cephalosporins and first generation fluoroquinolones were utilized in the treatment of typhoid fever; nevertheless, antibiotic resistance had developed.

o At the moment, third generation fluoroquinolones have been recommended; however, resistance to these medicaments has been reported

o The undertaking of surgical operations could be necessitated for intestinal perforation or gallbladder disease

o An effective vaccine for *Salmonella. Typhi does* exist

- WHO recommendations for the public as well as travellers do include:

o Individuals should ensure that their food is properly cooked and hot when they are served

o Individuals should avoid drinking of raw milk and products that are made from raw milk

o Individuals should avoid ice unless the ice is made from safe water

o Individuals should utilize disinfecting tablets for water unless they are certain of the purity of the water.

o Individuals should wash their hands thoroughly with soap and water following having had contact with pets or farm animals and after they had used the toilet

o Individuals should wash their fruits and vegetables thoroughly and if possible, they should peel fruits and vegetables unless they are certain that optimal sanitary practices have taken place

- Recommendations for food handlers and producers do include:

o Food handlers and food producers should maintain a clean workspace

o Food handlers and food producers should separate raw and cooked food

o Food handlers and food producers should cook food thoroughly

o Food handlers and food producers should keep food at safe temperatures

o Food handlers and food producers should use safe water and raw materials

o Food handlers and food producers should practice good personal hygiene

o Food handlers and food producers should work if they have fever, diarrhoea, vomiting or infected skin lesions

o Food handlers and food producers should protect fields from animal contamination

Macroscopic features [11]

- It has been documented that the undertaking of colonoscopy in patients who have mild non-typhoidal salmonellosis of the bowel does show non-specific findings that include oedema as well as petechial haemorrhage and that with regard to more severe disease of the bowel the aforementioned findings tend to be associated with friability and ulceration of the mucosa of the bowel[11].

- It has also been iterated that typhoid fever does cause marked enlargement of Peyer patches and lymphoid tissue within the appendix and ascending colon which does lead to mucosal elevation along the axis of the ileum[11].

- It has also been stated that in typhoid infections of the bowel perforation of the bowel could occur [11]

- It has been documented that small grey, soft nodules that are called typhoid nodules could be seen present in the liver[11].

- There is splenomegaly and lymphadenopathy

Microscopy pathology examination features [11]: The microscopy pathology examination features of common types of *Salmonella* infections have been summated as follows: [11]

- It is a fact that organs that are infected by non-typhoidal *salmonellosis* are only biopsied on rare occasions[11].

- The microscopy examination findings tend to be a non-specific acute self -limited colitis[11].

- The crypt architecture tends to be maintained, and there tends to be evidence of increased mixed inflammatory cells within the lamina propria in a patchy distribution with foci of cryptitis and possible crypt abscesses [11].

- Microscopy pathology examination of long standing cases might demonstrate architectural distortion which tend to raise the spectre of idiopathic inflammatory bowel disease [11].

  - This is said also to be true of *S. typhimurium* infection

- Knowledge of culture results confirming the diagnosis of *Salmonella* infection is necessary to confirm a specific diagnosis of *Salmonella* infection [11].

- *Salmonella* typhi does show neutrophils, histiocytes with cytoplasmic bacteria, nuclear debris as well as haemorrhage within the lamina propria which tends to be associated with presence of a lymphoplasmacytic infiltrate [11].

- The spleen and lymph nodes in cases of *Salmonella* infection tend to show sinus histiocytosis which distorts the normal architecture [11].

- With regard to cases of *Salmonella* infection, typhoid nodules within the liver tend to show aggregates of histiocytes with necrotic debris [11].

- It has been iterated that in cases of *salmonella* infections, typhoid nodules could also be found within bone marrow and lymph nodes

Differential diagnosis: Some of the differential diagnosis of *Salmonella* infection of the bowel have been stated to include the following: [11]

- The differential diagnoses of non-typhoidal salmonellosis doe include other enteric pathogens which cause acute self-limited colitis including: (a) Shigella, and (b) Campylobacter [11].

- It has been pointed out that long standing cases of *salmonella* infection of the bowel could simulate idiopathic inflammatory bowel disease [11].

With regard to *Salmonella* urinary tract infections, the differential diagnosis would include common bacterial infections of the urinary tract and quite often it is only after the urine culture result is obtained that the clinician would be sure that the infection is truly a *Salmonella* infection in most cases.

[B] Miscellaneous narrations and discussions from some case reports, case series and studies related to Salmonella urinary tract infections / salmonella infections of organs of the urinary tract excluding Salmonella infections of the bowel

Mellon et al. [12] stated that *non-typhi Salmonella enterica* urinary tract infections (UTIs) are not often encountered and they uncommonly get reported in the literature. Mellon et al. [12] characterised the clinical manifestations and risk factors for the non-typhi enterica infection. Mellon et al. [12] undertook a retrospective study of *non-typhi Salmonella enterica* strains that had been isolated from urine cytobacteriological examinations (UCBE) which had been collected between January 1, 1996 and October 30, 2014 and which were analysed by the microbiology laboratories of the university hospitals of the western part of Île-de-France and of Paris, France. Mellon et al. [12] summarised the results as follows:

- Twenty UCBEs that were positive for *non-typhi Salmonella enterica* were analysed.

- The sex ratio was 0.53 and the average age of patients was found to be 57 years.

- The clinical manifestations of the infection included: acute pyelonephritis, acute cystitis, and prostatitis.

- Bacteraemia were found in Eight cases.

- Diarrhoea was found in half of the patients, either before-+ the urinary tract infection (UTI) or simultaneously.

- None of the patients did require to be transferred to the intensive care unit.

- Immunodeficiency and/or diabetes were noted in eight of the patients.

- Three of the patients had manifested with a uropathy.

- The prescribed antibiotics did include third generation cephalosporins and fluoroquinolones.

- The average duration of the treatment was 20 days.

- A spondylitis and a purulent pleurisy were noted and were deemed to be related to the urinary tract infection (UTI).

- The outcome of the patient was found to be always favourable following the prescription of treatment.

Mellon et al. [12] made the following conclusions:

- Non-typhi *Salmonella* enterica UTIs are rare.

- They are mainly observed in elderly patients presenting with immunodeficiency or an underlying urological disorder.

Tena et al. [3] iterated that urinary tract infection (UTI) that is caused by *non-typhoidal Salmonella* (NTS) is not common. Tena et al. [3] undertook a study to ascertain the frequency and clinical characteristics of this infection within their area. They did perform a retrospective analysis of patients who had bacteriuria caused by NTS that was diagnosed within their hospital from January 1990 to December 2005. Tena et al. [3] summarized the results as follows:

- Nineteen patients who had bacteriuria that were caused by NTS were diagnosed, that amounted to 0.07% of the UTIs that were diagnosed within their area over the same period of time.

- The mean age of the patients was 62.5 years.

- Eighteen of the patients that amounted to 94.7% of the patients did have symptoms of urinary tract infection (UTI) with 12 patients presenting with cystitis, 6 patients presenting with pyelonephritis, and 1 patient did remain asymptomatic.

- Fourteen patients that amounted to 73.6% of the patients did have chronic diseases; whilst diabetes mellitus was found in 8 of the patients that amounted to 42.1% and

7 patients that amounted to 36.8% of the patients had been undergoing immunosuppressor treatment. Eight of the patients that amounted to 42.1% of the patients did have urological abnormalities.

- *Salmonella* (S). enteritidis was the commonest serotype of *Salmonella* that was isolated in 16 of the cases.

- Eleven of the patients did require antibiotic therapy over a period of 2 or more weeks.

- Four of the patients did develop recurrent *Salmonella* UTIs that amounted to 22.2% of the cases, and in 2 of the patients, recurrence did occur pursuant to prolonged treatment of 3.5 and 5 weeks, respectively.

Tena et al. [3] made the ensuing conclusions:

- Urinary tract infection (UTI) due to NTS was predominantly found in elderly patients who had underlying diseases, particularly diabetes mellitus, urological abnormalities as well as immunosuppression.

- Prolonged antibiotic therapy should be considered in view of the high frequency of complicating conditions, even though the infection could be recurrent despite provision of prolonged treatment.

Gulcan et al. [13] reported a case of urinary tract infection (UTI) which had been caused by *Salmonella* enterica serovar Virchow in an elderly and debilitated individual who had Benign Prostatic Hyperplasia (BPH). They reported that the administration of appropriate antibiotic treatment did result in the recovery of the patient's clinical course. Gulcan et al. [13] stated the following:

- *Nontyphoid salmonella* (NTS) serotypes could cause gastroenteritis, bacteriemia, as well as focal infections.

- Nevertheless, these focal infections that include urinary tract infections (UTI), tend to be occasionally observed; in particular, the presence of many predisposing factors, including immunodeficiency and structural abnormality within the urinary tract, do increase the possibility of the development of the of infection.

Klosterman et al. [14] reported a 73-year-old Caucasian woman who had manifested with 'another episode of urine infection'. Two weeks preceding her manifestation, she had been assessed for symptoms of dysuria and nocturia. At that time, she had urinalysis with microscopy which demonstrated moderate blood with positive leucocyte esterase on a midstream collection; nevertheless, a urine culture was not undertaken. She was treated empirically with utilization of a 7-day course of macrodantin, which she had completed, but her symptoms did not improve. Her genitourinary (GU) tract history was negative for visible haematuria or renal lithiasis but positive for dysuria, nocturia and stress incontinence. Her general and systematic examinations was negative for fever, nausea, abdominal pain, emesis or diarrhoea. Her past medical history included: frequent urinary tract infections, kidney insufficiency without hypertension, gastroesophageal reflux disease, significant osteoarthritis of her knees and hips as well as depression with insomnia. Her previous surgeries had included a cystocele and repair of rectocele in the 1980s, which had been complicated by left hydronephrosis and a non-functioning kidney. She subsequently underwent left nephrectomy in 2005, which was related to an infection in the left urinary tract. She also had a previous cholecystectomy ensuing an episode of gallstone pancreatitis. Her clinical examination demonstrated a temperature of 98.1°F, blood pressure of 160/84 mm/hg, and her rate of 88 beats per minute, 16 breaths/minute and weight of 281 with body mass index of 50. The rest of her general and systematic examinations were was otherwise normal. The results of her routine haematology and biochemistry blood tests were within normal range with the exception of her baseline serum creatinine of 1.54. Her urinalysis with microscopy was found to be positive for many White Blood Cells (WBCs) as well as bacteria were visualised, but no evidence of casts or crystals was found. Her urine culture result was received 2 days later which documented that there was a growth of greater than 100,000 colony forming units / ML of *Salmonella* species that was sensitive to ampicillin, ceftriaxone, and trimethoprim/sulfamethoxazole. The *Salmonella* was additionally typed as *Salmonella Newport.* Upon a review of her previous Urinary Tract Infections (UTIs), it was found that there was no previous history of *Salmonella* within her urine culture but her only isolated Urinary Tract Infections (UTIs) were due to Klebsiella pneumonia, Citrobacter freundi, and Escherichia coli, respectively which had occurred in the years that ensued her nephrectomy. She did not have any stool cultures because she did not have any gastrointestinal tract symptoms and she did not have haematochezia. She had already been commenced on empirical treatment of trimethoprim / sulfamethoxazole at the time her urine culture results were received. She had ultrasound scan of abdomen which demonstrated a 1.2 cm hyper-echoic region upon the lower pole of her right kidney that was concerning for angiomyolipoma as well as discreet small pseudocysts of the pancreas. She had Computed Tomography (CT) scan of abdomen and pelvis which revealed a sub-centimetre renal cyst within the lower pole of her right kidney that was associated with overlying calcification of the renal fat, a pseudocyst of the pancreas with fatty infiltration as well as a mildly enlarged spleen. There was no evidence of hydronephrosis or renal or bladder stones demonstrated in the CT scan. She was treated with trimethoprim/sulfamethoxazole twice daily for a period of 14 days and she was referred to the local infectious diseases consultant. She responded well to her single oral antibiotic 14 days treatment, compared with typical urinary tract infection (UTI) treatment regimens, which in their opinion was appropriate to her *Salmonella* UTI aetiology. [6,15-18] She did not undergo any Stool studies at the time of her infectious disease visit, 6 weeks later, as the patient had already completed her trimethroprim/sulfamethoxazole regimen prior to her appointment and she was asymptomatic with no evidence of both urinary tract symptoms and Gastrointestinal Tract (GI) symptoms during her assessment. During her consultation, she reported to the specialist that she had had a week-long period of diarrhoea 3 to 4 weeks preceding her Urinary Tract Infection (UTI) symptoms, but the diarrhoea was not associated with fever, haematochezia or mucous within her stool. Her exposure risk factors had included farm animals of goats and pigs on her property but she had not had any direct contact with the animals and she had not had any exotic pets. She did recall having eaten some questionable spoiled shrimp during that time frame

period but which was not of any concern to her as it was self-limited, and she occasionally did experience similar episodes of loose stool since she had her cholecystectomy. After 14 days of treatment with trimethoprim/sulfamethoxazole, the results of her follow-up urine cultures were negative for *Salmonella*. She has also had many Urinary Tract Infections (UTIs) since then but these infections were with different bacterial species identified by urine culture which included *E. coli* and *K. pneumonia* and she was referred back to her urologist for further assessment and consideration for the provision of antibiotic prophylaxis. She had radiology imaging with post-micturition ultrasound scan which showed 0 mL of urine remaining in her bladder which demonstrated complete emptying of her urinary bladder. She was commenced on daily prophylactic antibiotics by her urologist, and she had been asymptomatic since that time.

Allerberger et al. [2] reported that thirty cases of *non-typhoidal Salmonella* bacteriuria had been identified by them though a review of cultures that had been undertaken at the Mayo Clinic (Minn.) from 1985 to 1989 and at the Federal Public Health Laboratory Innsbruck (Austria) from 1979 to 1989. Allerberger et al. [2] summarized the results as follows:

- All of the patients did have symptoms of an acute urinary tract infection (UTI).
- With regard to 24 cases non-typhoidal *Salmonella* was found to be the sole pathogen that was isolated.
- Only 1 patient had manifested with concomitant gastroenteritis and 2 did experience episodes of diarrhoea over the preceding before the development of UTI; nevertheless, 15 of the patients did have positive stool cultures with the absence of a gastrointestinal illness.
- Out of all of the positive urine cultures that were obtained at the Mayo Microbiology Laboratory, 0.015% were noted to be positive for *non-typhoidal Salmonella;* at the Federal Public Health Laboratory Innsbruck, 0.024% of the organisms that were cultured from urine were non-typhoidal *salmonellae.*
- With regard to the majority of the patients, *Salmonella* UTI had not differed clinically from UTI that were caused by other members of the Enterobacteriaceae; It was only in kidney transplant recipients that the course of genitourinary salmonellosis was more serious.
- While some urinary isolates of *non-typhoidal Salmonella* could have been faecal contaminants, all of the 30 isolates that had been recovered from urine during this study were regarded to be the cause of symptomatic UTI in the patients.

Gorelik et al. [19] undertook a study to ascertain the characteristics of symptomatic *non-typhoidal Salmonella* (NTS) urinary tract infection (UTI) without concomitant gastroenteritis (GE) as a separate clinical entity. They undertook a retrospective cohort single-centre study and they did review all cases of NTS bacteriuria between that had been encountered between 1995 and 2016. They assigned the patients to a group according to their clinical manifestation, namely, symptomatic NTS UTI without GE, GE with NTS bacteriuria or isolated asymptomatic NTS bacteriuria. They did compare the characteristics of patients within the NTS UTI group with those of the latter 2 groups. Gorelik et al. [19] summarized the results as follows:

- They found NTS bacteriuria in 77 patients, of which 61 patients did have records available for review.
- Twenty-one patients who had included 17 adults, had manifested with NTS UTI, Thirty (30) patients had manifested with features of GE with NTS bacteriuria and Ten (10) patients did have asymptomatic NTS bacteriuria.
- NTS UTI was found not to be significantly associated with older age, male sex, diabetes, immunosuppressive states or urologic abnormalities.
- There was a significant difference with regard to the proportion of patients who had an underlying urological malignancy in the NTS UTI group that consisted of 4 out of 17 patients that amounted to 23.5% in comparison with those in the other groups with 0 out of 24 patients in the P value was P = 0.023.

Gorelik et al. [15] made the following conclusions:

- They had identified a unique group of patients who had symptomatic NTS UTI without GE.
- They had demonstrated a significant association with urological malignancies in patients who had NTS UTI in comparison with those who had GE and NTS bacteriuria or asymptomatic NTS bacteriuria.

Ramos et al. [6] undertook a retrospective analysis of 28 cases of bacteriuria due to *Non-Typhoidal Salmonella* (NTS). With regard to the results, they reported that twenty-one patients that amounted to 75% of the patients did have symptoms of urinary tract infection with 16 patients having cystitis, 3 patients having pyelonephritis, and 2 patients having renal abscess, as well as 7 patients who had remained asymptomatic. Additional summations of their results included:

- With regard to 24 cases, NTS was the sole pathogen that had been isolated from the urine.
- *Salmonella* enteritidis (a *Salmonella* subgroup 1 serotype) was the serotype that was most frequently isolated with regard to16 cases, which was followed by *Salmonella enteritidis* serotype typhimurium that was found in 5 cases.
- Sixteen patients that amounted to 57% of the patients were severely immunocompromised, and 14 patients that amounted to 52% of the patients had urological abnormalities.
- Recurrence of bacteriuria did occurred in four patients.

Ramos et al. [6] suggested that with regard to cases of urinary *salmonellosis* clinicians must consider the existence of an occult urological problem or severe immunosuppression.

Yosefi and Dorreh [20] reported a 7-year-old boy who had manifested with a history of fever and chill and a 24-hour history of loin pain, dysuria, urinary frequency, haematuria, as well as secondary nocturia. He did not have any previous history of urinary tract infection (UTI) or recent gastroenteritis. He had undergone circumcision during his neonatal period. He had remained dry by day and night from 2 years and 3 years of age, respectively. He had normal micturition and bowel movement.

He was a second child in his family and he did not have any family history of immunodeficiency. He did not have any history of recurrent infection. Upon his physical examination, his temperature was noted to be 38ºC; his respiratory rate was 20 per minute; his heart rate was 100 per minute and his blood pressure was 90/55 mm Hg. There was evidence of tenderness within his costal vertebral angles. His examination was otherwise normal. His urinalysis revealed: Urine pH 8 Specific gravity 101 Blood 3+ Nitrite Negative Leukocyte Many Erythrocyte, /HPF 35 to 40. The results of his routine haematology and biochemistry blood tests revealed: Full blood count; Leukocyte, × 109/L 137; Neutrophils, % 68; Lymphocytes, % 29; Haemoglobin, g/dL 12.5; Urea, mmol/L 2.2; Creatinine, µmol/L 43. His Laboratory Fi A midstream clean-catch specimen of the urine did yield a pure growth of *Salmonella* serogroup C with a colony count of 105 colony-forming units. The organism was sensitive to ampicillin, cefotaxim, nalidixic-acid, as well as ceftriaxon. His urine culture was repeated in another clinical laboratory and the result was the similar. He was treated with 75 mg/kg of ceftriaxon for 3 days and this was continued with cefexim for 7 days. He had ultrasound scan of the renal tract which was normal. He had a voiding cystourethrography that was undertaken 3 weeks pursuant to his presentation that was normal. He had Dimercaptosuccine acid renogram (DMSA) scan which showed bilateral photopenic areas and bilateral decreased function.

Yosefi and Dorreh [20] made the ensuing summations related to *Salmonella* infections of the urinary tract:

- *Salmonella* species tend to be an uncommon cause of urinary tract infection (UTI) in children.

- Abbott and colleagues [5], in a retrospective analysis of accompanying laboratory data of more than 60 cases of salmonellosis associated with urine isolates, did suggest that this bacterium is a true and often unrecognized cause of UTI.

- *Salmonella* urinary tract infection (UTI) had been linked with a higher incidence of structural abnormalities or immunosuppressive status. A Study that was undertaken by Kapoor and colleagues did showed that urinary tract infection (UTI) due to *Salmonella* in a patient without a predisposing condition was not common and this accounted for only 0.65% of all *Salmonella* UTIs. [21].

- Their patient did have a structurally normal urinary tract and no evidence of an immunological problem. A few cases had been documented with *Salmonella* urinary tract infection (UTI) in otherwise healthy individuals who did not have a predisposing condition. [2,15]

- Whilst a significant number of *Salmonella-associated urinary tract infections* (UTIs) tend to be linked with persons who have one or more comorbid conditions, at times bacteriuria does occur in individuals who do not have known risk factors. An Australian study by Paterson and colleagues [10] on 23 cases of *Salmonella* urinary tract infections (UTIs) did not identify any immunocompromised patients in their study and only 3 who had urological abnormalities.

- Alexander and associates reported a healthy 4-year-old boy that developed UTI due to *Salmonella Stanleyville* following an episode of gastroenteritis due to the some organism, for which an ascending route for the infection was most likely [22].

- Their patient did not have any history of recent gastroenteritis. Mourani and associates [20]16 reported an 11-year-old girl who had urinary tract infection (UTI) secondary to *Salmonella typhi* that was associated with urolithiasis. With regard to their patient, they did not identify any urolithiasis. Tena and associates [3] had reported 19 patients who had bacteriuria that was caused by nontyphoid *Salmonella*, that amounted to 0.07% of the urinary tract infections (UTIs) that were diagnosed over the same period. The mean age of the patients was 62.5 years and 6 patients did have pyelonephritis. They did have chronic diseases or urological abnormalities.

- Gulcan [13] reported a case of UTI caused by *Salmonella* enterica in an elderly disabled patient with benign prostatic hyperplasia.

- In an analysis that was undertaken by Abbott and associates [5], serotypes belonging to group C and E were isolated more often from urine in comparison with from the stool. Urinary tract infection in their patient was also due to *Salmonella*

Jehangir et al. [1] reported a 62-year-old man who had a past medical history of benign prostatic hyperplasia who had manifested as emergency department with symptoms of decreased flow of his urine, inability to fully empty his urinary bladder, and visible haematuria. His general and systematic examinations were unremarkable. His urinalysis demonstrated large amount of blood and more than 700 white blood cells which had suggested a urinary tract infection. His urine culture grew *group D Salmonella* greater than 100,000 colony-forming units per ML. He was prescribed 6 weeks course of trimethoprim/sulfamethoxazole following which there was resolution of his symptoms. He did report retrospectively a 3-day history of watery diarrhoea about a week preceding the onset of his urinary symptoms which was presumed to be the hematogenous source in his case. Jehangir et al. [1] stated the following:

- Urinary tract infection from *nontyphoidal Salmonella* (NTS) is not common and it usually tends to be usually associated with immunosuppression, chronic diseases, such as diabetes or structural abnormalities of the genitourinary tract.

- Genitourinary tract abnormalities that had been previously reported within the literature that predispose to nontyphoidal *Salmonella* urinary tract infection do include: nephrolithiasis, chronic pyelonephritis, retro-vesicular fistula, urethrorectal fistula, hydrocele, and post-TURP.

Mokadem et al. [23] reported a 50-year-old man who did not have any significant past medical history, who had manifested with a 5-months history of recurrent right flank discomfort. He denied having any haematuria, passage of urinary calculi, fever, chills, vomiting, diarrhoea, constipation, or abdominal pain. He was not taking any medicament. Upon examination, he was noted to be afebrile. His abdominal examination was normal and he did have a very soft tenderness within his right flank region. He had a urine culture that was negative in that it did not grow any organism. He had radiology imaging which did include ultrasound scan and computed tomography (CT)

scan which revealed a large right renal pelvis calculi and calculi within the middle and inferior calyx. The radiology imaging also demonstrated hydronephrosis of the upper calyx as well as thin encompassing renal cortex (see Figure 1). He was offered Per-Cutaneous Nephrolithotomy (PCNL); nevertheless, he refused to undergo any per-cutaneous or laparoscopic surgery. Instead he did undergo open surgical procedure. During the operation, it was found that the upper pole of the kidney was adherent and surrounded by fibrotic tissue. Pyelolithotomy was undertaken. During the process of extracting the calculi, his urine was found to be purulent in view of this bacteriological samples were taken. A renal pelvis suturing was undertaken after a Double-J stent was inserted (Figure 1).

His pus culture grew *group D Salmonella* greater than 10^4 colony-forming units (cfu) per ML of urine. The results of his blood culture as well as HIV analysis were negative. He was prescribed third generation cephalosporin (cefotaxime 2 g3 /g intravenously) for 14 days. He made a steady recovery and on the 16th day pursuant to his admission he was discharged home. Mokadem et al. [23] stated that Pyonephrosis due to NTS had been reported twice and they had reported the first case of asymptomatic NTS pyonephrosis as well as they had presented an unusual case of an incidental per-operative discovery of pyonephrosis due to NTS in an asymptomatic immunocompetent 50-year-old man. Mokadem et al. [23] made the ensuing conclusions:

- NTS urinary tract infection is uncommon.
- When NTS urinary tract infection is diagnosed, it should lead to the undertaking of investigations looking for immunosuppressive illness and for urological abnormalities including urolithiasis.
- NTS pyonephrosis could be life threatening but asymptomatic forms could also be encountered.

CONCLUSION

- *Salmonella urinary tract infections* tend to be uncommon and they generally tend to be symptomatic.
- *Salmonella urinary tract infections* could complicate *enteric Salmonella infections*.
- In some of the patients who develop *Salmonella urinary tract infection,* the symptoms of urinary tract infection may present contemporaneously with gastrointestinal symptoms of *Salmonella infection*; nevertheless, in other patients who have *Salmonella urinary tract infection,* there may not be any associated symptoms related to enteric *Salmonella infection*.
- *Salmonella urinary tract infections* tend to be quite often associated with chronic diseases, immunosuppression or structural abnormalities of the genitourinary tract.
- Utilization of 14 days course of appropriate antibiotics or longer than 14 days based upon the sensitivity pattern of the cultured *Salmonella* organism does effectively treat the infection and it is important to note the *Salmonella* organisms are tending to develop resistance to a number of antibiotics so clinicians should be aware of the antibiotic sensitivity pattern within their areas of practice. Repeat urine cultures are necessary to ascertain of the *Salmonella* urinary tract infection has successfully been treated.
- A thorough assessment of patients with detailed history taking, clinical examination, laboratory studies, and radiology imaging are important for the diagnosis, treatment, and follow-up of patients who have *Salmonella* urinary tract infection.

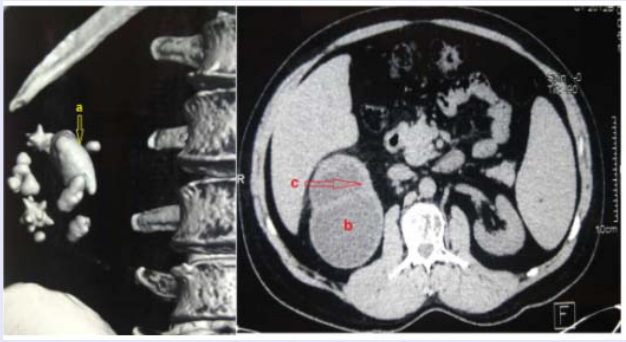

Figure 1 CT Scan demonstrating large renal calculi and upper pole hydronephrosis: (a) large right renal pelvic calculi; (b) upper calix hydronephrosis; (c) thinned surrounding renal cortex [23].

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