Incidence and Extent of Typhoid Fever in Geidam Town, Yobe State, Nigeria

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ABSTRACT

Incidence and extent of typhoid fever was conducted based on the samples collected from the patients attending general hospital of Geidam Yobe state, Nigeria and Jibo Rahama medical laboratory. Widal blood test and rapid slide titration method was used in this research work for typhoid fever injection diagnosis by putting the blood sample collected in the EDTA container, then it was place in a test tube and spun in centrifuge machine at 1000rpm (revolution per minute) for 5 minute where it separated the serum from blood. An eight (8) drops of serum was place on a clean white tiles separately, eight drops of widal antigens was dropped respectively. Mixture was mixed to give homogenous solution and the tile was rotated at least for 5 to 10 minutes, the reaction was observed visually. Out of the 24 samples collected, nine (9) were tested positive and it was more prevalent between the age classes: 1-10, 11-20, 21-30 and 30-40. It was observed that two (2) out of the nine patients are male while seven (7) were female, and this suggest that typhoid fever is more prevalent in female sex than in male sex. However, it should be noted that in this study there were more female patients than male therefore, valid conclusion cannot be made regarding the sex which suffers more. In a nutshell, improper sanitation is responsible for the wide spread of typhoid fever in most localities in developing countries like Nigeria, because the species that cause typhoid fever breed well in an unsanitary practice in preparation of food and drinks with water contaminated with fecal matter. It is known that the symptoms of typhoid fever mimics those of malaria fever, therefore proper investigation should be carried out before medication.

Index Terms: Disease, Infection, typhoid Fever, observation, Salmonella typhi, Widal test.
Introduction

Typhoid fever: is an acute infection disease caused by a mycobacterium salmonella typhoid from contaminated food or water. The germs reach the intestine through the lymph, channels. Typhoid fever is a disease caused by salmonella typhi, formerly known as bacillus typhosa in tropical or subtropical countries. (huestep, 1962) reported that the typhoid fever is a disease which flourished where the standard of hygiene is poor, and is caused by ingestion of salmonella typhi. (huestep,1962) also reported that incubation period of typhoid fever takes about 12 to 14 days and the patients remain infectious until bacteriological test are negative. The onset is gradual from 4 to 5 days and the temperature is ascending. If untreated patient become very ill during the second week with high body temperature. The stool is often pear soap in characters, and become rose coloured sports. By third week if untreated patient is delirious.

Typhoid and paratyphoid fevers, collectively referred to as enteric fever, are caused by systemic infection with Salmonella enterica sub species serovars Typhi and Paratyphi A, B, and C. (Lancet, 2017). Whereas most non-typhoidal Salmonella spp infections typically produce diarrheal, illness and less commonly cause bloodstream infection, typhoid and paratyphoid infections produce primarily bacteremia febrile illnesses, with prolonged high fever, headache, and malaise being characteristic symptoms. Without effective treatment, typhoid and paratyphoid fevers can lead to altered mental states (termed the typhoid state), ileus, gastrointestinal bleeding, intestinal perforation, septic shock, and death. Typhoid and paratyphoid infections are relatively common in countries with poor water supply and sanitation, especially south Asia, southeast Asia, and sub-Saharan Africa, where they are a major cause of death and disability, especially among children. With growing antimicrobial resistance, and intensifying conversations around typhoid vaccine policy, accurate and detailed estimates of enteric fever burden are required. The Strategic Advisory Group of Experts (SAGE) of WHO convened in October, 2017, and recommended the use of typhoid conjugate vaccines in children between 6 months and 2 years of age, with a catch-up campaign for children up to 15 years of age, where possible, and WHO prequalified the first typhoid conjugate vaccine in December, 2017. These developments give typhoid-endemic, low-income countries priority access and funding for the vaccine and could make vaccines increasingly accessible. However, data to support their introduction remain sparse. (Moore, 2017).

The occurrence of typhoid fever is a major threat globally with annual cases exceeds 20 million and approximately a quarter million deaths. The disease is mostly dominant in underdeveloped and developing countries where sanitation is poor, mainly in part of south Asia (crump and miritz, 2010). The enteric fever is caused by the etiologic agent, salmonella serovar typhi (s. typhi). With early detection and medical prevalence, the severity of the diseases can be reduced and thus decrease the fatality rate. However, the diagnosis of the diseases is commonly done with conventional methods and widal test, which specificity and sensitivity are not that high (Olopenia and king, 2000). Furthermore, the test is also limited by other factors of time, labor and cost which reduce its availability mainly in developing countries.

One of the rapid test developed for detection of s. typhi is through multiplex PCR, which is salmonella Ezplex. The system is a patented salmonella detection kit developed from laboratory of biochemical science and molecular microbiology, university Malaya (patent, P12011005414, 2011). The method of detection amplifies a 332 bp DNA marker that is specific for s. typhi. Although the DNA marker is specific for PCR detection, its sphericity to serological method remains unknown.

INCIDENCE OF THYROID FEVER

The incidence of a disease is the number of new cases per population per unit time. For typhoid fever, incidence is usually expressed as cases per 100 000 populations per year. Typhoid fever incidence is often classified as low, medium, high. (Crump, 2014), and, more recently, very high (Antillón, 2017), corresponding to incidence bands of <10, 10–100, >100–<500, and ≥500 per 100 000 per year, respectively. For burden of disease calculations, population-based incidence measured by active disease surveillance accounting for blood culture insensitivity is used. Studies combining sentinel healthcare facility surveillance with healthcare utilization surveys to account for under ascertainment are increasingly done to approximate population-based disease incidence with lower resource investment (Youssef, 2003).

Early attempts to estimate the global burden of typhoid fever were hampered by the very limited number of contemporary population-based studies of typhoid fever incidence using blood culture confirmation from typhoid-endemic areas (WHO, 1996). Data from the control arm of the burgeoning number of typhoid vaccine trials were central to the 2000 estimate of global typhoid incidence, but their use was tempered by concern for bias due to the preference for conducting vaccine trials in high-incidence settings. Since that time, a number
of studies. have been completed that bolster data on typhoid fever incidence from an increasingly diverse range of locations. Such studies include those that are truly population-based, with household surveillance for fever and blood culture in the home or by active referral to healthcare facilities (Breiman, 2012). In addition, a number of recent incidence studies rely on healthcare facility–based surveillance supplemented with healthcare utilization surveys that provide multipliers to account for under ascertainment related to healthcare access among febrile persons (Marks, 2017).

There is growing recognition of the considerable variation in typhoid fever incidence that may occur in place and over time. Whereas in 2000 typhoid fever appeared to be less common or under ascertained in Africa compared with Asia (Mweu, 2008), more recent studies confirm that typhoid fever incidence is high in some parts of Africa. Furthermore, typhoid has been demonstrated to occur at high incidence after years of little disease in some locations (Feasey, 2014) while declining markedly from high incidence levels elsewhere. Furthermore, Salmonella serovars other than Typhi play differing roles by location. Among Asian bloodstream infection studies, both typhoid fever and paratyphoid fever are common (Deen, 2012). African studies demonstrate that nontyphoidal Salmonella invasive disease is often as common or exceeds typhoid fever incidence in some locations (Reddy, 2010). Estimates from the past 5 years indicate that 11.0–17.8 million typhoid fever illnesses occur annually worldwide. Notwithstanding substantial improvements and changes in the amount of source data and methods for extrapolation, the annual number of typhoid fever illnesses have not kept pace with global population growth. However, typhoid fever still ranks high among the major causes of infectious disease illness and death (Lancet, 2017).

**MORPHOLOGY AND TYPES OF SALMONELLA**

The salmonella species are gram negative non-sporing bacillus of about 2.4x 0.54 actively motile, numerous long patrichous flagella (in some) do not passed a capsule and most strain are fimbriae. The species are classified according to their antigenic composition (Gollioili, 1930). The classification is both in osmatic and flagellate.

Salmonella typhi (salmonella typhosa).

Salmonella paratyphi A (S. American).

Salmonella paratyphi B (S. scholt millei)

Salmonella typhimurum and

Salmonella enteritis

Salmonella typhi A (typhosa) found in a contaminated food or water is causing an acute infectious disease (Huestep, 1962). In paratyphi fever the small intestine may be acutely inflamed through its length there may be ulceration of the large intestine, in most instance a septicemid and deep metastic abscesses are found. Salmonella enteritis the species that cause bacteria enteristis of food poisoning.

**WIDAL TEST REACTION**

**Table 1.1**

<table>
<thead>
<tr>
<th>ANTIGEN</th>
<th>PARA TPY</th>
<th>AH</th>
<th>1/160</th>
<th>+ve</th>
</tr>
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<tr>
<td>Salmonella</td>
<td>Para typhi</td>
<td>AO</td>
<td>1/80</td>
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<tr>
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<td>BH</td>
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<td>Salmonella</td>
<td>Para typhi</td>
<td>BO</td>
<td>1/160</td>
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<td>Salmonella</td>
<td>Para typhi</td>
<td>CH</td>
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<td>Para typhi</td>
<td>CO</td>
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<td>Salmonella</td>
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CAUSATIVE AGENT OF TYPHOID FEVER

Typhoid fever is caused by salmonella species (bacteria) known as typhoid bacillus there are about ten (10) species of salmonella of which only eight (8) species effected human health. But the commonest is salmonella typhirium which caused salmonella gastro enteritis and food poisoning. The pathogenies salmonella was linked to carrier proteins, offer several potential advantages over earlier prior – using the global burden of typhoid fever. The sustained high burden of disease, coupled with the emergence of drug-resistant strains of S. Typhi, makes prevention via vaccination a priority in the short-to-medium term. The Ty21a and Vi-polysaccharide vaccines have demonstrated efficacy at 2 years of 58% (95% CI 40–71%) and 59% (95% CI 45–69%), respectively, but have limited use in the youngest age-group of children due to inconvenience in vaccine administration and poor immunogenicity, respectively (Anwar, 2014).

School-based campaigns as well as delivery strategies of these vaccines using the available healthcare structure have been effective in terms of coverage and cost-effectiveness in Asia (Date, 2015). TCVs, in which Vi-polysaccharide is covalently linked to carrier proteins, offer several potential advantages over earlier generation typhoid vaccines. The appeal of Vi-conjugate vaccines, relates to their capacity to induce immune responses in infants, enhanced immunogenicity in terms of antibody magnitude, quality and duration, and the potential for boosting of immune responses with revaccination. Proof-in-principle of TCV efficacy is derived, primarily, from trials of a prototype Vi-rEPA vaccine, which demonstrated efficacy of up to 91% (95% CI 77–97%) at 2 years, when given as a two dose schedule in 2–5 year-old children (Lin, 2001). The VirEPA vaccine was efficacious up to at least 5 years and was compatible with Coad ministered expanded programme on immunization vaccines, but has yet to be commercialized. The most advanced TCV is the Vi-tetanus toxoid conjugate vaccine, TypharTCV, manufactured by Bharat Biotech (Hyderabad, India). This vaccine is immunogenic and safe in children from as young as 6 months of age, as well as demonstrating superior immunogenicity to a Vi-polysaccharide vaccine (Mohan, 2015).

Importantly, TypharTCV has demonstrated efficacy of between 54.6 and 87.1% in a stringent controlled human infection model, depending on the efficacy endpoint (Jin, 2017). Modelling studies have estimated a vaccine efficacy for TypharTCV of 85% based on serological data (Voysey, 2018). Cost-effective models indicate that routine infant TCV vaccination is likely to be cost-effective in medium- or high-incidence settings, depending on the intervention strategy used and at a modest vaccine cost ($2/ dose) (Antillón, 2017). Additional safety and immunogenicity data will be generated in an upcoming introduction of TCV in Navi Mumbai, India and from three-phase IV effectiveness studies conducted as part of the TyVAC consortium.

Several TCVs are currently in development, including VI-DT, VirEPA, Vi-CRM197, and Vi-tetanus toxoid conjugates, many of which have completed Phase 1 and 2/3 trials (Bhatta, 2014). In October 2017, the WHO Strategic Advisory Group of Experts on immunization recommended programmatic use of TCVs in typhoid endemic countries (WHO, 2018). The recommendations focused on the use of TCV from the age of 6 months onward, administered as a single dose, and combined with programmatic administration in combination with other childhood vaccines [72&&]. Where feasible and supported by epidemiologic data, catch-up vaccination up to 15 years of age was also recommended. The position paper highlights that the roll of TCVs should be prioritized in countries with a high burden of typhoid fever or high rates of AMR. TYPBAR-TCV was prequalified by the WHO in January 2018 and Gavi has committed an $85 million funding window to support the roll out of these vaccines in eligible countries between 2019 and 2020. Momentum to achieve control of typhoid is building, driven by the availability of effective tools and support from key stakeholders. The challenge now facing the community is to support access to typhoid vaccines where they are needed most.

CONTROL AND PREVENTION OF TYPHOID

The contribution of unsafe drinking water has been recognized as central to the spread of typhoid fever for over 150 years. Access to clean, safe drinking water – combined with investment in sanitation and hygiene interventions – will be key to reducing the global burden of typhoid fever. The sustained high burden of disease, coupled with the emergence of drug-resistant strains of S. Typhi, makes prevention via vaccination a priority in the short-to-medium term. The Ty21a and Vi-polysaccharide vaccines have demonstrated efficacy at 2 years of 58% (95% CI 40–71%) and 59% (95% CI 45–69%), respectively, but have limited use in the youngest age-group of children due to inconvenience in vaccine administration and poor immunogenicity, respectively (Anwar, 2014).

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TREATMENT OF TYPHOID FEVER

The mortality rate of enteric fever in the pre-antibiotic era was estimated to be between 10 and 30%. The availability of traditional first-line antimicrobials over the past nearly 70 years (chloramphenicol, ampicillin, and trimethoprim-sulfamethoxazole) has reduced the overall mortality rate to less than 1%. Unfortunately, their use has been limited by the emergence of so-called multidrug-resistant (MDR) strains, defined as resistance to all three of the ‘traditional’ first-line antimicrobials. Resistance in MDR strains are typically conferred via IncHI1 plasmids, harboring resistance genes such as catA, sul1, sul2, dfrA, blaTEM-1, strA, strB, tetA, tetB, tetC, and tetD on composite transposons. These MDR-associated genes have also been known to integrate within the chromosome of H58 S. Typhi in isolates from countries including India, Nepal, and Bangladesh (Wong, 2015).

MDR strains were responsible for several outbreaks of enteric fever in the 1980/1990s and led to the widespread use of fluoroquinolones as first-line therapy (Parry, 2017). Despite considerable success in treatment of MDR typhoid, the extensive use of fluoroquinolones has since led to the emergence of intermediate and fully fluoroquinolone resistant strains. Fluoroquinolone resistance occurs mainly via chromosomal mutations in the gyrA, gyrB, parC, and parE genes. Cumulative mutations correspond to the degree of fluoroquinolone, for example, a single nucleotide polymorphism (SNP) in codon S83F of gyrA will produce a low-level resistance (ciprofloxacin minimal inhibitory concentration [MIC] of 0.125–0.25mg/l) whereas additional SNPs in gyrA (D87N) and parC (S80I) confer a higher level of ciprofloxacin resistance (MIC 8–64mg/l). In 2017, the World Health Organization designated fluoroquinolone resistant Salmonella spp. as a high priority pathogen, identified as one of 12 families of bacteria thought to pose the greatest risk to human health through rising antimicrobial resistance (AMR) (Tacconelli, 2017).

Third-generation cephalosporins are commonly used in the empirical treatment of enteric fever and are a valuable empirical treatment option in the setting of MDR and of fluoroquinolone resistant isolates (Arjyal, 2016). However, a recent typhoid outbreak in Sindh, Pakistan was attributable to so-called extensively drug resistant (XDR) S. Typhi H58 defined as an MDR resistance pattern, combined with fluoroquinolone and cephalosporin resistance (Klemm, 2018). In this outbreak strain, cephalosporin resistance was mediated by the horizontal acquisition of a plasmid encoding the blaCTX-M-15 extended-spectrum β-lactamase, in addition to quinolone resistance containing genes such as qnrB2, qnrB4. The emergence of cephalosporin resistance calls for an urgent reappraisal in the use of cephalosporins for treating enteric fever in South and South-East Asia severely limits potential treatment options and emphasizes the importance of disease prevention. Azithromycin is increasingly used for the empirical treatment of enteric fever. Although currently rare, isolates with increased azithromycin MICs and treatment failure have been reported (Hassing, 2014). Azithromycin resistance is known to be mediated via the ereA, msrD, and msrA genes. The monobactam aztreonam may be a treatment option for treatment of fluoroquinolone-resistant S. Typhi, particularly in individuals allergic to penicillin. Alternative treatments include tigecycline or carbapenems, but there are relatively limited studies describing their use for the treatment of typhoid fever and widespread use may be limited by the cost of treatment (Capoor, 2019). Combination antibiotic therapy is sometimes used in the treatment of enteric fever, particularly when response to treatment is slow; susceptibilities are unknown and when the diagnosis is uncertain (Crump, 2008). Combination therapy may have synergistic effects and reduce the rate of emergence of antibiotic-resistant strains. There is currently limited evidence from randomized trials to guide this approach (Parry, 2007). Chloramphenicol, ampicillin, and trimethoprim-sulfamethoxazole were seldom used after widespread MDR strains emerged in the 1990s, but recent data suggest that sensitivity to these agents is reemerging following their declining use (Zellweger, 2017). One study spanning a 9-year period in Nepal suggesting that over 95% of isolates were sensitive to all three ‘traditional’ first-line antimicrobials (Britto, 2018). However, it is almost inevitable that MDR strains will re-emerge over time with the build-up of sufficient antimicrobial pressure via uncoordinated and widespread use of these drugs, particularly if coupled with poor surveillance systems.

Nevertheless, these drugs could be used in settings with high fluoroquinolone resistance and evolving cephalosporin resistance – possibly when used in combination or with antibiotic cycling. Analysis of a global collection of S. Typhi isolates using whole genome sequencing has demonstrated how a single S. Typhi haplotype, termed H58 (or genotype 4.3.1.), has emerged and spread globally. Strains of S. Typhi of H58 are associated with multidrug resistance and reduced fluoroquinolone susceptibility, and isolates belonging to this genotype isolates are widely prevalent is South and South-East Asia, as well as in Central/Southern Africa. Recent analysis suggests that this haplotype is displacing antibiotic-sensitive strains and may possess a fitness advantage compared with other isolates (Baker, 2013). In addition, several MDR typhoid epidemics have...
recently been described in Africa, evolving independently of the H58 haplotype, suggesting that S. Typhi is constantly adapting to new antibiotics and distinct ecological niches (Wong, 2016) enteric fever cases in regions of South Asia with high incidence of Rickettsia spp (Thompson, 2017).

Treatment of chronic carriage may require a combination of medical and surgical interventions. Fluoroquinolones are commonly used in the treatment of chronic carriage and treatment with a 28 day course of ciprofloxacin (750 mg twice daily) or norfloxacin (400 mg twice daily) can achieve clearance in over 80% of patients. Shorter courses (14 days) of fluoroquinolones may also be efficacious in the treatment of chronic carriage, with treatment success ranging from 87 to 100% in published studies. A prolonged treatment courses with azithromycin (28 days) may be of use in the management of chronic carriers infected with fluoroquinolone-resistant isolates, although this has not been formally studies in randomised controlled trials. Cholecystectomy may be required in the presence of cholelithiasis, the efficacy of which is likely to be improved by concomitant administration of antibiotics. Patients with concomitant Schistosoma infection should receive antiparasitic treatment with praziquantel to manage chronic urinary and intestinal carriage (Hsiao, 2016).

**SYMPTOMS OF TYPHOID FEVER**

The incubation period is usually 7 to 14 days but is also dependent on the infecting dose (range, 3-30 days). The clinical presentation of typhoid fever varies from a mild illness with low-grade fever, malaise, and slight dry cough to a severe clinical condition with abdominal discomfort and multiple complications. The advent and availability of antibiotic therapy has changed the presentation of typhoid fever; the classic mode of presentation with a slow and "stepladder" rise in fever and toxicity is now rare. (Bhutta, 1991)

Many factors influence the severity and overall clinical outcome of the infection. These include the duration of illness before the initiation of appropriate therapy, the choice of antimicrobial treatment, age, exposure or vaccination history, the virulence of the bacterial strain, the quantity of inoculum ingested, and several host factors affecting the immune status.

The presentation of typhoid fever may also differ according to age. Although previous data from South America and other parts of Africa suggested that typhoid may present as a mild illness in young children,10,11 this may vary in different parts of the world. There is emerging evidence from south Asia that the presentation of typhoid may be more dramatic in children younger than 5 years, with comparatively higher rates of complications and hospitalization. (Sinha, 1999) Diarrhoea, toxicity, and complications, such as disseminated intravascular complications, are also more common in infancy, with higher case fatality rates. However, some of the other features and complications of typhoid fever observed in adults, such as relative bradycardia, neurological manifestations, and gastrointestinal bleeding, are relatively rare in childhood.

Typhoid fever usually presents with high-grade fever with a wide variety of associated features, such as generalized myalgia, abdominal pain, hepatosplenomegaly, abdominal pain, and anorexia. In younger children, diarrhoea may be a more common presentation in the earlier stages of the illness and may be followed by constipation. In the absence of localizing signs, the early stage of the disease may be difficult to differentiate from other endemic diseases, such as malaria or dengue fever. In about 25% of cases, a macular or maculopapular rash (rose spots) may be visible around the 7th to the 10th day of the illness, and lesions may appear in crops of 10 to 15 on the lower chest and abdomen and may last 2 to 3 days. These lesions may be difficult to see in dark-skinned children. (Siddiqui, 2016).

**CAUSE AND PATHOGENESIS**

Typhoid fever is caused by infection with S. enterica subspecies enterica serovar typhi (S. Typhi), a Gramnegative facultative anaerobic bacillus. Paratyphoid fever results from infection with the related organism S. enterica subspecies enterica serovar paratyphi (S. Paratyphi), which is divided into three subtypes – S. Paratyphi A, B, and C. S. Typhi and Paratyphi are collectively referred to as typhoidal Salmonella serovars and infection with either can result in the clinical syndrome of enteric fever. Unlike other S. enterica serovars, S. Typhi, and Paratyphi are humanrestricted pathogens that cause a systemic illness progressing to an asymptomatic chronic carrier state in some individuals. Transmission of S. Typhi and Paratyphi occurs through consumption of contaminated food or water via short-cycle or long-cycle transmission. Short-cycle transmission is defined as the contamination of food and water in the immediate environment through
inadequate hygiene and sanitation measures, either by shedding from acute or chronic carriers. Long-cycle transmission is defined as contamination of the broader environment, such as pollution of water supplies by sewage, or inadequate treatment of piped water. The relative contribution of each transmission mode may vary depending on the epidemiological context and may differ between S. Typhi and Paratyphi (Karkey, 2013).

The clinical presentation of typhoid fever is highly variable, ranging from a mild-illness characterized by low-grade fever and malaise, through to a severe life-threatening systemic illness with multiple complications, including intestinal perforation, intestinal hemorrhage, and encephalopathy (Parry, 2002). Ingestion of bacteria and systemic invasion is followed by a short-lived period of asymptomatic primary bacteremia. The incubation period, typically lasts 7–14 days, but can range from 3 to 60 days dependent, in part, on the size of the inoculum. Symptoms are usually nonspecific and include fever, malaise, anorexia, headache, arthralgia, myalgia, nausea, abdominal discomfort, and dry cough. Sporadic, asymptomatic, shedding of the bacteria in the stool can occur prior to the development of symptomatic disease. Clinical signs may include high fever, relative bradycardia, abdominal tenderness, hepatomegaly, splenomegaly, or rose-spots. S. Paratyphi may cause a milder disease than S. Typhi (Dobinson, 2017), although field data from the largest case series todate, comprising 609 enteric fever patients in Nepal suggest that both serovars cause an indistinguishable clinical syndrome (Maskey, 2006). In the absence of effective antimicrobial therapy, approximately 1–5% of patients with acute typhoid infection are thought to become chronic carriers. Risk factors for chronic carriage include the presence of gallstones, female sex, older age, and inadequate treatment courses. Chronic carriers may be responsible for maintaining low-level transmission of disease and thus could complicate disease eradication efforts through sanitation and vaccination programs (Baker, 2011). Accurate identification and treatment of chronic carriers will likely form an important component of future disease control efforts. The pathogenesis of enteric fever and host response to infection are reviewed by Dougan and Baker (Dougan, 2014). A key virulence factor expressed by most strains of S. Typhi is a polysaccharide capsule, termed the Vi (virulence) antigen. The Vi-capsule is encoded by the viaB locus, which comprises several genes required for biosynthesis and export of the capsule. In the absence of the Vi-capsule, S. Typhi is inherently more sensitive to killing in serum than other serovars, such as S. Typhimurium (Hart, 2016). The Vi-capsule possesses immunomodulatory properties that are thought to contribute to disease pathogenesis, including limiting complement deposition, reducing immune activation, assisting with phagocytosis evasion, and inhibiting serum bactericidal activity (Raffatellu, 2005). The Vi capsule forms the principal component of parenteral typhoid vaccines, including new conjugate vaccines. Vi-antigen is expressed by other bacteria including Citrobacter freundii, S. Paratyphi C, and S. Dublin.

Advances in genomics studies offer insights into the pathogenic mechanisms of S. Typhi and Paratyphi. The genome of S. Typhi is notable for the accumulation of multiple pseudogenes, thought to reflect the host-restriction properties of typhoidal Salmonella as a similar process has been observed in other host-restricted pathogens (Parkhill, 2001). In addition, S. Typhi possess approximately 300–400 specific genes not found in other S. serovars. Many of these gene products are encoded on Salmonella pathogenicity islands relatively unique to S. Typhi (e.g., SPI-5, SPI-15, SPI-17, and SPI-18) [6]. For example, S. Typhi and Paratyphi A possess a recently described exotoxin termed the typhoid-toxin, which is postulated to have a central role in pathogenesis of enteric fever (reviewed in ref. (Galán, 2016). The characterization of virulence factors that may have an important role in disease pathogenesis could aid the development of novel vaccines for typhoidal Salmonella.

Recent data from the Typhoid Fever Surveillance in Africa Program highlighted marked differences in incidence rates between sites in Africa with adjusted rates ranging from 0 in Sudan to 383/100 000 person years in Burkina Faso. This study also demonstrated marked intra-country variation, with higher rates in rural Ghana compared with urban settings (Marks, 2017). Data from ongoing surveillance studies suggest that an estimated 27% of typhoid fever cases requiring medical attention occur in children aged 0–4 years, of which a substantial proportion (30%) occur at ages below 2 years (SAGE, 2017). These data are supported by a recent meta-analysis, underlining the large burden of disease in preschool children (Britto, 2017). Age-specific incidence may vary by country, risk factors, and force of infection. Ongoing surveillance studies (including the Surveillance of Enteric Fever in Asia Project, Severe Typhoid in Africa Program, and the Strategic Typhoid Alliance across Africa programs aim to better characterize the burden of severe typhoid disease, refine our understanding of age distribution, and to better characterize the role of chronic carriers in transmission dynamics. It is hoped that data generated from these studies will help to inform future prevention strategies (Meiring, 2017).
TRANSMISSION OF TYPHOID FEVER

The mode of *Salmonella* Typhi transmission is considered to be largely indirect and predominantly vehicle-borne through contaminated water or food (Luby, 1998). Water and food usually serve as passive vehicles for *Salmonella* Typhi. While *Salmonella* Typhi may survive for extended periods on vehicles, multiplication of *Salmonella* Typhi in water and food is uncommon (Mitscherlich, 1984). Some group *Salmonella* Typhi transmission into 2 broad patterns. In short-cycle transmission, food and water are contaminated by fecal shedding in the immediate environment, and transmission is mediated through inadequate hygiene and sanitation measures. In long-cycle transmission there is contamination of the broader environment, such as pollution of untreated water supplies by human feces and use of raw human feces or untreated sewage as a crop fertilizer (González-Guzmán, 1989). Epidemiologic investigations underscore the important role of chronic carriers in short-cycle foodborne typhoid outbreaks in countries with low typhoid incidence (Olsen, 2003), and the potentially large scale of long-cycle waterborne transmission in many high-incidence settings (Mermin, 1999). The means by which the source is contaminated and type of vehicles involved vary considerably from location to location, underscoring the importance of local epidemiologic investigations for informing non-vaccine control measures.

DIAGNOSIS OF TYPHOID FEVER

The test used to diagnose typhoid fever infection in laboratory is known as widal test it was discovered by an American scientist. Called widal T.D in 1903. The test is up two (2) method namely as rapid slide titration and tub agglutination. Blood cultures: approximately 10 cc. of blood is added aseptically to 100 cc. of Tryphosa phosphate broth and a second 10 cc. of blood to 100 cc. of bite broth. If no growth occurs in either medium, a second culture is made of 30 cc. of blood added to bacilli occurs, in either medium, a second culture is made of 30 cc. of blood added to 300 cc. of bite broth. If growth of gram negative bacillus occurs, the organisms are tested for motility and identified biochemically (Martin, 2016).

There remains a pressing need to improve upon current enteric fever diagnostics and to develop a new generation of tests that are accessible, cost-effective, sensitive, and specific (Andrews, 2015). Bone marrow culture is considered the 'gold-standard' diagnostic test for enteric fever, but frequently impractical to perform in many endemic settings. Blood culture is the mainstay of typhoid and paratyphoid diagnosis. A recent systematic review estimated the average diagnostic sensitivity of blood culture to be 61.1% [95% confidence interval (CI) 51.9–70.3%] (Mogasale, 2016). Rapid diagnostic tests (RDTs) for typhoid and paratyphoid fever could theoretically be combined with clinical algorithms to differentiate febrile patients to guide management, particularly in areas lacking well-equipped laboratory facilities. Several RDTs for enter fever diagnosis have been developed, the most commonly of which are the Typhidot/ Typhidot-M test, the TUBEX test and Test-It Typhoid. The current generation of typhoid RDTs has only modest sensitivity and specificity determined in meta-analyses and there is insufficient evidence to support their exclusive use for the diagnosis and management of enteric fever (Wijedoru, 2017). Other diagnostics in development include antibody-in-lymphocyte-supernatant (ALS), which has demonstrated good sensitivity and specificity in endemic settings (Darton, 2017). Several polymerase chain reaction (PCR)-based methods have also been developed and demonstrate promising results in some small-scale studies, but there are currently no widely used and validated assays in general use, and remain poorly sensitive. The sensitivity of PCR-based assays can be improved by incorporating a pre-enrichment step (Zhou, 2010). Limited laboratory infrastructure, cost, and the length of time required to obtain results currently serve as deterrents to scalability and expansive deployment for both molecular diagnostics and ALS. Future directions for diagnostic biomarker discovery include the application of high-throughput technologies on clinical specimens, including mass spectrometry (Kuhns, 2012), next-generation sequencing, and antigen arrays (Darton, 2017). Using mass spectrometry on serum samples from enteric fever patients, Na’sstro’m and colleagues have identified a set of metabolites...
Material and Method

EQUIPMENT/MATERIAL REQUIRED

i. EDTA container  
ii. Syringes  
iii. Cotton wool  
iv. Tourniquet  
v. White tiles  
vi. Serum sample  
vii. Applica stall  
viii. Widal antigens  
ix. Centrifuge machine  
x. Test tube  
xi. Dropper

COLLECTION OF SAMPLE

The blood sample for the test (diagnoses) were collected from the left hand of the patient tourniquet, using antiseptic, cotton wools, sterile syringe and needles, EDTA and container. All the thirty (30) sample were obtained from the General Hospital Geidam, Jibo Rahama Lab. And Millennium Development Goal (MDG’S) Hospital.

TEST/METHOD OF TYPHOID FEVER DETECTION

The rapid slide titration method was used in this research for the typhoid fever injection diagnosis, stain febrile antigen is the reagents necessary for this test which contains four (4) blue and four (4) red febrile antigen and are specific to the somatic “O” antigen while the red stain antigens are specific to the flagella “H” antigen as indicated below:

STAINED FEBRILE ANTIGENS

Table 2.1

<table>
<thead>
<tr>
<th>S.</th>
<th>Typhi</th>
<th>“H”</th>
<th>5ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.</td>
<td>Paratyphi</td>
<td>“A”</td>
<td>5ml</td>
</tr>
<tr>
<td>S.</td>
<td>Paratyphi</td>
<td>“B”</td>
<td>5ml</td>
</tr>
<tr>
<td>S.</td>
<td>Typhi</td>
<td>“C”</td>
<td>5ml</td>
</tr>
<tr>
<td>S.</td>
<td>Paratyphi</td>
<td>“O”</td>
<td>5ml</td>
</tr>
<tr>
<td>S.</td>
<td>Paratyphi</td>
<td>“A”</td>
<td>5ml</td>
</tr>
<tr>
<td>S.</td>
<td>Paratyphi</td>
<td>“B”</td>
<td>5ml</td>
</tr>
<tr>
<td>S.</td>
<td>Paratyphi</td>
<td>“C”</td>
<td>5ml</td>
</tr>
</tbody>
</table>

The blood sample collected in the EDTA container was put in test tube and was spinned in centrifuge machine at 1000rpm (revolution per minute) for 5 minute where it separated the serum from blood. An eight (8) drops of serum was place on a clean white tiles separately, eight drops of widal antigens was dropped respectively. Mixture was mixed to give homogenous solution and the tile was rotated at least for 5 to 10 minutes, the reaction was observed visually. The result was interpreted and recorded as in the figures below:

Agglutination seen in circle diameter shown in each circle is indication of their respective titter. If the circle remained cleared without agglutination after rotation is in significant (negative result) or typhoid free, while others with agglutination were significantly positive respectively as shown below:
Result

TABLE 3.1: AGE CLASSIFICATION OF TYPHOID FEVER POSITIVE PATIENT.

<table>
<thead>
<tr>
<th>Age class</th>
<th>+ve male</th>
<th>+ve female</th>
<th>Total positive</th>
<th>Total negative</th>
<th>Total number of patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-10</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>11-20</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>21-30</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>31-40</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>41-5-</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>2</td>
<td>7</td>
<td>9</td>
<td>15</td>
<td>24</td>
</tr>
</tbody>
</table>

TABLE 3.2: DISTRIBUTION OF TYPHOID POSITIVE OR NEGATIVE PATIENT BY SEX

<table>
<thead>
<tr>
<th>Sex</th>
<th>No of +ve patient</th>
<th>No of –ve patient</th>
<th>% of +ve patient</th>
<th>% -ve patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>2</td>
<td>6</td>
<td>35.2%</td>
<td>30.7%</td>
</tr>
<tr>
<td>Female</td>
<td>7</td>
<td>9</td>
<td>64.8%</td>
<td>69.3%</td>
</tr>
<tr>
<td>Total</td>
<td>9</td>
<td>15</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Discussion

Typhoid fever remains a major public health problem, affecting millions of people every year and disproportionately impacting low- and middle-income countries. The global enteric fever landscape has transformed steadily over the past two decades, illustrated by the emergence and dissemination of multidrug-resistant (MDR) and fluoroquinolone resistant strains of Salmonella Typhi, an increasing burden of S. Paratyphi A infection in Africa and the development of a new generation of typhoid conjugate vaccines (TCVs). The recent approval and impending deployment of TCVs is a cause for optimism in efforts to achieve control of enteric fever globally. Nevertheless, several challenges remain. This study aims to investigate the incidence and extent of typhoid fever among patients attending general hospital of Geidam and Jibro Rahama medical laboratory.

As shown in table 3.1 above, 9 patients are tested positive out of the total of 24, it was more prevalent in the age classes of 1-10, 11-20, 21-30, and 31-40; this means that most patient of typhoid fever belong to the age grade of 1-40 years and occurrence or incident level decreases with increase in age. It is also observed as shown in table 3.2 that out of 9 patients 2 were male or 35.2% while 7 were female or 64.8% this suggested that typhoid fever is more prevalence in female than in males however, it should be noted that in this study there were more male than female patient therefore valid conclusion cannot be made regarding the sex which suffer more. Geidam town has modern entities like pipe borne water system however majority of the people depend on hand-dug shallow well for water. Most frequently, well are contaminated with fecal matter containing salmonella typhi, the causative agent of typhoid fever, therefore, it is not surprising that the incidence of mainly Geidam town. It is not unlikely that the incidence level obtained in this study (9 out of 24) is typical of rural areas in Nigeria characterized by unhygienic way of disposing of human exacta or animal fecal matter which often are transmitted to available sources of water on wards to consumables mainly perishable food items.

Conclusion

In conclusion improper sanitation is responsible for wide spread of typhoid fever in most localities in developing countries like Nigeria, because the species of salmonella that cause typhoid fever breed well in unsanitary practice in preparation of food and drinks with water contaminated with fecal matter. It is known that the symptoms of typhoid fever mimics those of malaria fever, therefore proper investigation should be carried out before medication.
Recommendation

i. There is need to educate food handlers, house wives and personnel in food processing establishment of the need to maintain good hygienic practices during food preparation.

ii. Sanitary slaughtering and processing of meat (chicken, beef etc.) should enforced by sanitary inspectors.

iii. All infected and exposed individuals should be identified and excluded from handling food or drink.

iv. Sellers of food including meat and chicken should supply the consumer with a safe and wholesome product.

v. Hand should be thoroughly washed with detergent, disinfectant or soap before consumption of food; fruits should be washed before consumption to avoid infection.

References


