THE SOCIAL AND CLINICAL CORRELATES OF TYPHOID FEVER INFECTION IN ZARIA, NORTHERN NIGERIA

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ABSTRACT

The study was carried out to assess the socio-demographic and clinical variables in typhoid infection in Zaria, Northern Nigeria. Such parameters as age, sex, occupation and places of residence as well as the prescription pattern for typhoid treatment were evaluated. This retrospective, non experimental study involved the collection of case records (files) of patients admitted in Ahmadu Bello University Teaching Hospital, Zaria for typhoid fever for a five-year period. Retrieval of the data was done manually. A total of 118 cases were analyzed, some of the records required for analysis were missing, and were excluded. Most of the typhoid infections studied (66.5%) occurred during the rainy season in Zaria (May – November) with 40.7% of cases at the beginning of the rainy season (May/June). More females (55.3%), of all age and occupational groups were affected with higher incidences in young adults and students. Most of the patients (66.5%) were urban dwellers and the incidence between patients using well water and tap water was similar. Ciprofloxacin and ceftriaxone were the most frequently prescribed antibiotics; chloramphenicol use is still relatively common despite the 12.4% mortality and 28% relapse rate recorded. The findings of this study highlight the public health and social services challenges of typhoid infection in the Zaria metropolis. Communities, health authorities and governments should therefore focus more attention on preventive measures in view of the high costs of these newer antibiotics which now form the core of treatment of typhoid fever. Most patients will find this treatment modality unaffordable, taking into cognizance the socio-economic environment of Zaria.

Keywords: Antibiotics, enteric fever, preventive measures for typhoid fever, typhoid fever.

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INTRODUCTION AND BACKGROUND INFORMATION

Typhoid fever diagnosis and management have been a topical issue in recent times. This is because definitive diagnosis and clinical management of typhoid have been controversial (Onuigbo, M.A. 1989:25; Odugbemi and Animashaun 1994: 98). Despite the profuse information on the subject, typhoid fever has remained a major cause of morbidity and mortality in Nigeria (Onyiah 2001:74).

The nature and transmission of the causative organism, Salmonella typhi, interacted to make typhoid fever difficult to manage. The faeco-oral mode of transmission implies that its control in poor sanitary environments, characterised by unsafe sources of drinking water, is problematic (Hornick et al 2001:340). In addition, communities in poor countries indiscriminately use antibiotics too treat virtually all poorly treated or chloroquine-resistant malaria which are often perceived as typhoid fever. Most cases of typhoid fever initially mimic malaria. Symptoms as intermittent fever, anorexia, headache, malaise, and sore throat are treated initially as malaria, and then if fever persists, antibiotics are introduced inappropriately, usually by non-qualified personnel (Irabor, 2003: 93). Sometimes typhoid infection manifests as psychosis (Baiyewu & Oluboye 1991:265; Stanley and Andrew 2002:33)

In the medical world, the management of typhoid fever had consisted essentially of chloramphenicol since the early 1960s. Resistance to this drug and its association with epidemics of the 1970s are well documented (Meskin et al 1992: 446). However, in many parts of Nigeria, the use of chloramphenicol as the first drug of choice in typhoid fever is still high (Philip 2003:1). In mild cases, outpatient treatment of typhoid fever consists of chloramphenicol with good therapeutic responses. The efficacy of ampicillin and amoxicillin is said to be somewhat inferior but useful for their decreased harmful effects compared to other antibiotics. Sometimes chloramphenicol may be combined with tetracycline to reduce the carrier state. When chloramphenicol is contraindicated, drugs such as ciproxin and augmentin have been found useful (Onyiah 2001: 74). Cotrimoxazole (trimethroprim and sulphamethoxazole) is also found to be effective with similar period of defervescence i.e. stage of an illness during which fever subsides (about five days).

In severe cases, treatment takes a multi-dimensional approach including intravenous infusions of dextrose in water and antibiotics, depending on the severity. Most patients require oral antibiotics and intravenous gentamicin. More severely affected ones require stronger antibiotics such as intravenous Zinacef (Philip 2003:75). The quinolines such as ciprofloxacin and cephalosporins such as ceftriaxone are used in most cases of chloramphenicol-resistant typhoid fever. However, carriers have been treated with oral quinolines with excellent therapeutic results. Moreover, Hopkins et al (2008:341) reported that quinolines, apart from being highly effective against multi-resistant strains of Salmonella typhi, have low relapses and convalescence carrier rates; they are now the drugs of choice for the treatment of adult typhoid fever. Quinolines

are however contraindicated in children and pregnant mothers because they damage cartilage tissues (Philip 2000:5). In another study, Manitoba (2005) reported a 5-day course of ceftriaxone intravenously was found as effective as a conventional 14-day chloramphenicol treatment.

Notwithstanding, other studies have advanced other treatment modalities. For example, metronidazole and chloramphenicol are used in surgical perforations due to typhoid (Ameh et al 2000:57; Irabor 2003:93; Jenner 2003:23). Short term high doses of corticosteroid treatment such as dexamethasone 3mg per kilogramme body weight six hourly for eight doses combined with specific antibiotics and supportive care reduce mortality rates in critically ill patients (Miller, G.M. 2005). However, most complicated cases of typhoid perforation require surgical management. The usual case-fatality rate of 10% can be reduced to less than 1% with prompt antibiotic therapy, while relapses occur in 15-20% of cases treated with appropriate antibiotics (Taiwo 2003:6). New typhoid vaccines such as the V1 polysaccharide vaccine which, unlike others, can be used in children from age 2 years and over may be the hope of many typhoid-prone communities (Guerrant and Kosek 2001:1322).

PURPOSE OF THE STUDY

This retrospective study aimed at evaluating the socio-demographic variables of typhoid patients and the treatment of typhoid infection in Zaria against the background of current global recommendations. This was determined from records of prescriptions for the treatment of cases diagnosed as typhoid fever. The study also examined the therapeutic efficacy of the drugs prescribed as measured by the recovery rate of patients, the relapse rates as well as the mortality rates with a view to recommending a prescription policy for the hospital. Such a policy, when combined with effective public health education, will contribute to the management of typhoid fever.

MATERIALS AND METHODS

Data were collected from the Medical Records Department of the Teaching Hospital after due permission was granted. The study was a retrospective non-experimental study of 188 patients with typhoid fever admitted between June 2000 and June 2005 in Ahmadu Bello University Teaching Hospital, Tudun-wada, Zaria. Relevant records of all the patients admitted into the medical wards with a diagnosis of typhoid fever over the 5-year period were manually sorted out from the patients' files using a self-constructed guide designed to collect information related to the research objectives. Typhoid fever diagnosis was mainly by a combination of blood, stool and urine tests, including Widal tests. Descriptive statistics were used to analyse the data to provide answers to the research questions. The drugs or the combination of drugs prescribed for the individual patients were noted and the patients' length of the hospital stays were also

correlated with the drugs or combinations of drugs used by the patients. Therapeutic responses were evaluated by examining the number of patients discharged home with complete recovery, the number who relapsed (assessed on days of re admission or retreatment after initial discharge from hospital) and the number of deaths. There were no records of adverse effects of the drugs used. Sources of drinking water of affected patients were equally noted. Some patients whose records of treatment could not be found were excluded from this study.

RESULTS

A total of 188 patients were admitted with a diagnosis of typhoid fever within the study period (June 2000 to June 2005). The disease appeared to have a higher cumulative incidence between the months of May and June for the five years under study. October to March had relatively low incidences. However, on the whole, the incidence ranged from 20 cases in 2000 to 53 cases in 2005 with a mean incidence of 31.5 per year (Table 1).

The study also showed a seasonal variation of typhoid fever occurrence in Zaria with the peak frequency of 20.2% (n=38) and 20.7% (n=39) in May and June respectively for the five-year period. The pattern for May/June was consistent for the 5 years. The data showed that there were 125 cases (66.5%) during the rainy season and only 63 cases (33.5%) for the dry season. The means for the rainy season (May–October) and dry season (November–April) were 20.8 and 10.7, representing a ratio of 2:1 for the wet (rainy) and dry seasons respectively. This means there were twice as many cases of typhoid infection during the rainy season as in the dry season. Typhoid fever occurred throughout the months of the years under review except in September–December 2004 when there were no recorded cases of typhoid infection on admission (this period coincided with industrial action by health workers). It was also noted that the months of September–February had a low incidence (with the lowest incidence in December) throughout the five years under review

Table 1: Monthly and Seasonal Incidence of Typhoid fever in Zaria

Month of the Year	2000	2001	2002	2003	2004	2005	Total	Percentage (%)
January	-	2	1	1	4	0	8	4.3
February	-	2	0	4	2	0	8	4.3
March	-	4	1	6	5	11	18	9.6
April	-	3	1	2	5	4	15	7.9
May	-	5	5	5	5	18	38	20.2
June	4	7	2	3	3	20	39	20.7

July	2	1	3	4	3	-	13	6.9
August	2	5	10	5	1	-	23	12.2
September	0	0	3	2	0	-	5	2.7
October	11	4	1	0	0	-	7	3.7
November	0	5	3	2	0	-	10	5.3
December	1	0	11	1	0	-	4	2.1
Total	20	38	41	35	28	35	188	100

Sources: Hospital Records

An analysis of the socio-demographic variables of the patients indicated that there were more females (55.3%; n=104) than males (44.7%; n=84) representing a male: female ratio of 1:1.2. Similarly, the age distribution shows that 66.0% (n=124) of the patients were between the ages of 11–30 years. Patients aged 21 – 30 years had the highest frequency (39.6%; n=65). The elderly (61 years and older) constituted only 1.6% (n=3) of the total sample.

Table 2: Age and Sex Distribution of Typhoid Patients in Zaria

Age (in years)	**Female**	**Male**	**Total**
11 – 20	27 (14.4%)	32 (17.0%)	59 (31.4%)
21 – 30	40 (21.3%)	25 (13.3%)	65 (39.6%)
31 – 40	16 (8.5%)	19 (10.1%)	35 (18.6%)
41 – 50	6 (3.2%)	3 (1.6%)	9 (4.8%)
51 – 60	13 (6.9%)	4 (2.1%)	17 (9.0%)
61+	2 (1.1%)	1 (0.5%)	3 (1.6%)
Total	104 (53.4%)	84 (44.6%)	188 (100%)

The occupational affiliations of the patients showed that students accounted for 39.4% of the cases, housewives 29.3%, civil servants 11.2% business people 10.6% farmers 7.4% and those simply labelled children, 2.1% (Table 3). Most of these patients (66.5%, n=125) lived in urban settlements mainly in Zaria metropolis while 33.5% (n=63) were rural dwellers.

Table 3: Occupation of Patients with Typhoid Fever in Zaria

Occupation	Frequency	Percentage (%)
Children (Pupil)	4	2.1
Students	74	39.4
Housewives	55	29.3
Farmers	7	3.7
Civil servants	21	11.2
Business people	20	10.6
Artisans / others	7	3.7
Total	188	100

Results indicated that the major sources of drinking water were tap (pipe-borne) water (44%), and well water (42.3%). Only 9.0% (n=17 of the patients used water from the borehole while 4.4% used water from streams.

Table 4: Sources of Drinking water of patients admitted for typhoid fever in Zaria

Sources	Number	Percentage (%)
Tap (pipe-borne) water	80	42.6
Well water	77	41.0
Borehole	17	9.0
Stream	8	4.3
Nil record	6	3.1
Total	188	100

Sources: Hospital Records

Table 5 shows the commonly prescribed antibiotics for the treatment of typhoid fever in Zaria. These drugs were usually prescribed with other (adjunctive) therapies such as intravenous infusions, haematinics, multivitamins, and antimalarials. In most cases, the antibiotics were prescribed in combination with other drugs. Ciprofloxacin was the most commonly prescribed antibiotic (37.7%), followed by ceftriaxone (about 24%) and chloramphenicol in about 21% of the cases. Amoxil and other penicillin derivatives were prescribed in only about 10% of cases, usually in combination with other drugs.

Table 5: Antibiotics prescribed in the Treatment of typhoid fever in Zaria

Antibiotics	Prescription frequency	Percentage (%)
Chloramphenicol	35	20.9
Ciprofloxacin	63	37.7
Ceftriaxone	40	24.0
Gentamicin	12	7.2
Amoxicillin/amoxiclav	17	10.2
Total	167	100

Sources: Hospital Records

These antibiotics were used with adjunctive therapies. For example, haematinics and multivitamins were used in most cases (92.2%) while antimalarial drugs, mainly artesunate in 43% of cases and sulphadoxine/pyrimethamine in 4%. In 24.5%, metronidazole was used as adjunctive therapy. Most patients admitted for typhoid fever also had fluid and electrolyte replacements.

Table 6 and Figure 1 show the overall treatment outcomes for the various antibiotics used during the period under review. Ceftriaxone and ciprofloxacin appear to have produced the best overall recovery rates (therapeutic responses). As many as 88.7% (n=30) of the patients on ceftriaxone had 73.5% recovery rate within 6 – 10 days of admission, while 88.2% of those on ciprofloxacin had 62.7% recovery rate within the same period of admission. Chloramphenicol appeared to have a higher relapse rate (28%) compared to ceftriaxone (8.8%) and ciprofloxacin (about 3%). Patients treated with chloramphenicol also had the highest mortality rate (12.4%).

Table 6: Antibiotics therapy and Treatment Outcomes in Typhoid infections in Zaria

S/ no.	Antibiotics and days On admission	Treatment outcomes			Total
		Discharge	Relapse	Death	
1.	Chloramphenicol:	1 (3.1%)			
	1 – 5	10 (31.2%)	1 (3.1%)	2 (6.2%)	4 (12.5%)
	6 – 10	8 (25%)			
	> 10	19 (59.4%)	4 (12.5%)	2 (6.2%)	16 (50%)
	Total		4 (12.5%)	0	12 (37.5%)
			9 (28.1%)	4 (12.4%)	32 (100%)

2.	Ciprofloxacin: 1 – 5 6 – 10 > 10 Total	 10 (16.9%) 37 (62.7%) 5 (8.5%) 52 (88.2%)	 1 (1.7%) 0 1 (1.7%) 2 (3.4%)	 3 (5.1%) 0 2 (3.4%) 5 (8.5%)	 14 (23.7%) 37 (62.7%) 8 (13.6%) 59 (100%)
3.	Ceftriaxone: 1 – 5 6 – 10 > 10 Total	 5 (14.7%) 21 (61.8%) 2 (5.9%) 28 (82.4%)	 0 3 (8.8%) 0 3 (8.8%)	 1 (2.9%) 1 (2.9%) 1 (2.9%) 3 (8.8%)	 6 (17.7%) 25 (73.5%) 3 (8.8%) 34 (100%)
4.	Gentamicin: 1 – 5 6 – 10 > 10 Total	 0 (0.0%) 7 (70.0%) 2 (20.0%) 9 (90.0%)	 0 0 0 0	 0 1 (10%) 0 1 (10%)	 0 8 (80%) 2 (20%) 10 (100%)
5.	Amoxicillin/ Amoxiclav: 1 – 5 6 – 10 > 10 Total	 1 (6.3%) 2 (12.5%) 9 (56.2%) 12 (75%)	 1 (1.6%) 0 2 (12.5%) 3 (18.8%)	 1 (6.3%) 0 0 1 (6.3%)	 3 (18.8%) 2 (12.5%) 11 (68.7%) 16 (100%)

DISCUSSION OF FINDINGS

The incidence of typhoid fever in Zaria, as seen retrospectively for five years in the teaching hospital records, showed monthly and seasonal variations. The peak incidence of typhoid infection in Zaria coincided with the beginning of the rainy season which is May/June each year. The result showed that 41% of all typhoid cases occurred at this time. This finding is most likely associated with increased microbial (bacterial) contamination of flowing surface water at this period of the year. Similarly, the finding that typhoid fever occurs twice as often in the rainy season as in the dry season can be linked to the transmission of Salmonella typhi through water contamination during the rainy season. Poor sewage disposal contributes to these findings. In most parts of Zaria, sewage disposal is indiscriminate. Sewage is usually washed into water sources mainly the surrounding streams and rivers. It is also likely that the perennial water supply problem evident in most parts of Zaria explains the consistent incidence of typhoid fever. In other studies, similar assertions have been made. For example, Ikeme and Anan (1999) reported prevalence of typhoid in western Nigeria with high positive correlation with the rainy season. They implicated the contamination of drinking water as the most potent transmission factor. In Lagos, Nigeria, three peak incidences of typhoid infection in April, July and November had been reported (Ogunbiyi & Onabowale, 1996) coinciding with rain fall. Similarly, Ozumba et al (1997) reported a definite seasonal incidence with two peaks coinciding with two rainy seasons in Ghana. However, Ogunbiyi and Onabowale (1996) noted in contrast to these other findings that in Kenya,

higher incidence of typhoid fever is in hot dry season (months of January–March). But they also implicated poor water supplies and poor personal hygiene in cases of typhoid infection.

The incidence of the infection in the male and female patients (45.7% and 55.3% respectively) in this study indicates that the infection occurs significantly in both sexes. However, females are slightly more affected than males. The male: female ratio of 1:1.2 found in this study thus appears to be different from most of previous findings where males were found to be more affected. For instance, Olubuyide (1992) found a 1.7:1 male: female incidence of typhoid infection on the ward. In another study, Irabor (2003) also reported a male: female ratio of 1.5:1. A possible explanation for higher incidence in females in Zaria may be that women more likely to present themselves for treatment than men in this area.

Although all ages were affected in this study, the incidence was higher in the highly mobile age group of 11–30 years (66.0%; n=124). This trend becomes even more apparent in view of the high incidence found among students (39.4%). The incidence of typhoid fever however cuts across all occupational groups, with students mostly affected. These students coincidently are mainly in the more affected age group (11 – 30 years). This group of patients are commonly found outside their homes and thus may become prone to eating food and drinking water from contaminated sources. As reported elsewhere, the peak age group for typhoid infection is 21 – 30 years, with most of the patients being between 21 and 40 years (Onabowale and Ogunbiyi 1996: 46). Typhoid fever thus appears to be a disease of the young adult. This can be linked to the age structure of the general population in Nigeria which has more young people. However, babies and the aged were also infected. Olubuyide (1992) reported typhoid in a two-month old baby boy and a 68-year woman in Ibadan, Nigeria.

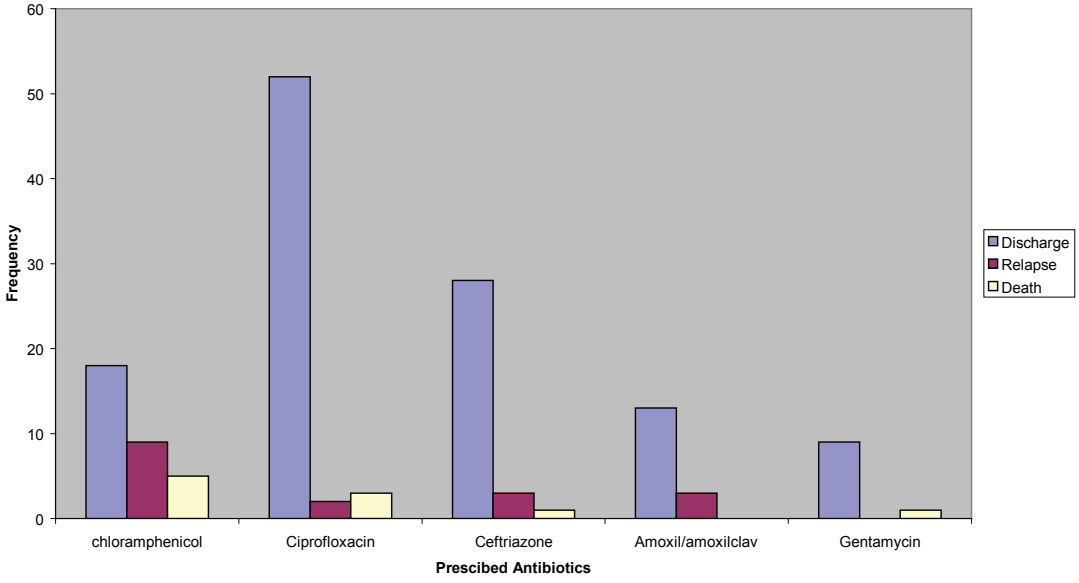
The incidence of typhoid fever noted seems to further point to the problem of general water supply in most parts of Zaria metropolis. Findings show that patients used tap water and well water for drinking had similar incidences (42.6% and 41%). An explanation for this is the possible inadequate treatment of tap (pipe-borne) water, especially during the rainy season, a period often associated with high microbial contamination of surface flowing water usually without a proportionate increase in chlorination (treatment) of tap water.

Ciprofloxacin and ceftriaxone were the most frequently prescribed antibiotics with a lesser preference for chloramphenicol. This conforms to documented current recommendations in the management of typhoid fever (Manitoba, 2001; Philip 2000; Hopkins et al 2008) but also with the attendant high cost of these drugs. However, it is found that chloramphenicol was prescribed in 12.4% of cases, indicating that the drug is still being considered as a drug of choice for typhoid treatment. This position had been corroborated by Meskin et al (1992) that the use of chloramphenicol for treating typhoid infection is still widespread due to accessibility and affordability, regardless of

its relatively high relapse rates. In this study, relapse rate was 28% for chloramphenicol compared with the previously documented rate of 15–20% (Meskin et al 1992:447). In addition, new emerging strains of Salmonella resistant to ciprofloxacin and ceftriaxone now pose new challenges to typhoid antimicrobial treatment (Threlfall et al 2005: 170; Davis et al 2007: 1584).

Similarly, adjunctive therapy recommended for typhoid treatment such as haematinics, multivitamins, antimalarials and infusions are being prescribed. For example, in more than 92% of the cases treated within the period under study (2000 – 2005), antimalarials were used concurrently. This is the practice because Zaria, the study area, is an endemic malaria area where it is recommended that all fevers should receive malarial treatment in addition to the normally prescribed treatment regimens. In almost all cases, haematinics/ multivitamins were also prescribed.

Fig. 1: Treatment Outcomes for typhoid patients on Prescribed antibiotics



CONCLUSIONS AND RECOMMENDATIONS

The results of this study highlight the public health and social services challenges of typhoid fever infection in Zaria metropolis as well as the increasing cost of treatment as indicated by the types of antibiotics being used in its management. In view of these findings, public health efforts and community resources should be channelled towards ensuring the availability of appropriate social infrastructures (sewage disposal, water treatment plants and environmental sanitation) and health facilities such as typhoid vaccines and affordable standard drugs. Most patients will find the current antibiotic treatment modality for typhoid infection unaffordable, taking the socio-economic

environment of Zaria into consideration. There is a need for the economic infrastructural enhancement of Zaria to address the low economic level and poverty in the area. In addition, prescribers need to take patients' economic status into consideration, especially if there are more affordable alternatives. More research on enhancing the potency of affordable and available drugs such as chloramphenicol in combination with other affordable options such as penicillin-related substances may offer solutions to outbreaks of typhoid fever in Zaria.

Programmes similar to those designed for HIV/AIDS (National Action on AIDS) and malaria (Roll Back Malaria Initiative) should also be formulated and implemented urgently, to address the staring problem of typhoid infection in the community. Furthermore, health education should be directed towards particularly vulnerable groups such as the young adults and women, especially food handlers. Primary carers and those who administer antibiotics should equally be educated to comply with regimes of antibiotic medication to prevent development of resistance to the new antibiotics. Equally important is the need for proper and adequate health record format for keeping all relevant clinical and social data of patients, including records of therapeutic as well as adverse effects of drugs, by those involved in the clinical care of patients and health record officers. Such information should be made more retrievable from computerised database systems.

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