TYPHOID FEVER IN ZARIA.

DISSERTATION SUBMITTED TO THE
NATIONAL P0ST GRADUATE MEDICAL COLLEGE
OF *NIGERIA IN PART FULFILLMENT FOR*
DIPLOMA OF FELLOWSHIP IN SURGERY

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C E R T I F I C A T I O N

I certify that the study of TYPHOID FEVER IN ZARIA, which is the subject of this dissertation, was carried out in the Department of Surgery, Ahmadu Bello University Teaching Hospital, Zaria, under my supervision.

The bacteriological aspects of the study were supervised by Dr. C.S.S. Bello of the Department of Medical Microbiology of this hospital.

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DEDICATION

To Jumeyi, Iko and Ibe - the three who make homecoming a joy.

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SUMMARY

This is a two part study on the epidemiology and surgical complications of typhoid fever, and, the prognostic factors in typhoid perforation.

The first part of the study is a retrospective review of 185 cases of typhoid fever seen over a 5 year period, from January, 1981 to December, 1985. In the prospective part of the study which covered a period of 1 year, 64 cases of typhoid were studied.

In the combined study the peak age group incidence was in the second quinquenium and males were more affected than females. Most of the patients came from areas of inadequate water supply and poor environmental sanitation. A definite seasonal frequency was observed with most patients presenting during the rainy season.

Intestinal perforation which occurred in 24.5% was the commonest complication, ranking third among the causes of acute abdominal emergencies during the period.

Post operative wound infection occurred in 54.55% of patients with typhoid perforation.

The mortality rate for all patients was 21.19%, while for typhoid perforation, it was 55.77%. There was no significant difference in mortality rate between the retrospective and prospective studies.

Important prognostic factors identified in patients with typhoid perforation were blood urea level and duration of perforation before admission. Further research on this important disease is recommended.

CHAPTER I

INTRODUCTION

Typhoid is a widespread and potentially lethal infection, which follows ingestion of Salmonella typhi, with initial lesions in the bowel, bacteriaemia and subsequent affection of many tissues (1). It is endemic in the economically under-developed parts of the world, particularly in countries of Africa, Asia, Central and South America, posing a pressing clinical problem.

The surgical complications of typhoid are as varied and numerous as the medical, ileal perforation and intestinal haemorrhage being the most common and dreaded of them all.

The clinical pattern of the disease in the Southern parts of Nigeria has been reviewed from Ibadan (2, 3, 4), Ilesha (5, 6), Lagos (7) and Ife (8). Although typhoid is said to be common in Zaria (9, 10), there is a dearth of information about the clinical pattern of this disease there.

The ABU, Hospital, Zaria located in the heart of Northern Nigeria serves a large local population of about 5 million people and acts as a referral centre for most parts of Northern Nigeria.

The study was designed to:-

1. Determine the pattern of surgical complications of typhoid fever in Zaria.

2. Identify the determinants of morbidity and mortality in typhoid perforation.

SCOPE AND LIMITATIONS

This study was conducted in two parts:-

Part 1 was a retrospective study of all cases of proven typhoid fever treated at the Ahmadu Bello University Hospital, Zaria during the 5 year period - January, 1981 to December, 1985. Part II was a prospective study of typhoid fever in the Zaria Hospital from May, 1986 to April, 1987.

It was not possible on many occasions to do bone marrow aspiration for culture before antibiotic therapy was commenced. This was because the investigation could only be done during official working hours. This might have influenced the relative recovery of the organism from the bone marrow as compared to blood culture.

The absence of post mortem examinations of the patients who died seriously hampered the understanding of the causes of death. The patients' relations and the local community, for religious reasons stoutly refuse any attempt at post mortem examinations.

CHAPTER II

LITERATURE REVIEW

Though typhoid has been recognized for many centuries, it was only in 1659 that Thomas Willis gave a classic description of the disease and it was not until 1880 that Carl Joseph Eberth discovered the typhoid bacillus. Gaffky in 1884 produced the first successful culture of Salmonella typhi. Along with Virchow he stressed that the infection was water borne, and not air borne (11).

Although the causative organism of typhoid fever was discovered over a century ago, gaps still remain in the understanding of the disease.

While some authorities define typhoid fever as being due to infection caused by Salmonella typhi or Salmonella para-typhi A, B or C (12) others like Stewart and Beswick (13) advocate that the terms 'typhoid fever' and 'paratyphoid fever', often used synonymously with 'enteric fever' should imply a bacteriological diagnosis of infection with Salmonella typhi or Salmonella para-typhi A, B and C respectively. The organisms of enteric fever belong to the genus Salmonella, comprising over 1800 different serotypes (14). The Salmonellae are gram-negative, motile, non-sporing, non-capsulate bacilli morphologically indistinguishable from Escherichia coli. They are non-indole producing and non-urea hydrolysing. They do not ferment lactose but with the exception of Salmonella typhi ferment maltose, glucose and mannitol producing both acid and gas (13). The Salmonellae belong to two basic groups:

1. The enteric fever group including S. typhi and paratyphoid bacilli, are found in the intestinal tract of man for whom they have a high degree of pathogenicity.

2. The food poisoning group including S. enteritidis, S. typhimurium which are essentially parasites of animals from whom man is occasionally infected.

The nomenclature of the Salmonellae has undergone several changes. To avoid proliferation of names, the antigenic formula of the organism has been adopted as the new method of designation. Using the O antigen composition the species can be classified into some 40 serological groups, each group characterized by the possession of an O antigen not present in other groups. The organisms most commonly encountered fall into the first five of these - A, B, C, D and E. S. typhi the most important pathogen to man belongs to group D and it possesses O antigens 9, 12, d flagella or H antigens and some strains also possess Vi antigens (13).

The typhoid bacillus is shown in figure I.

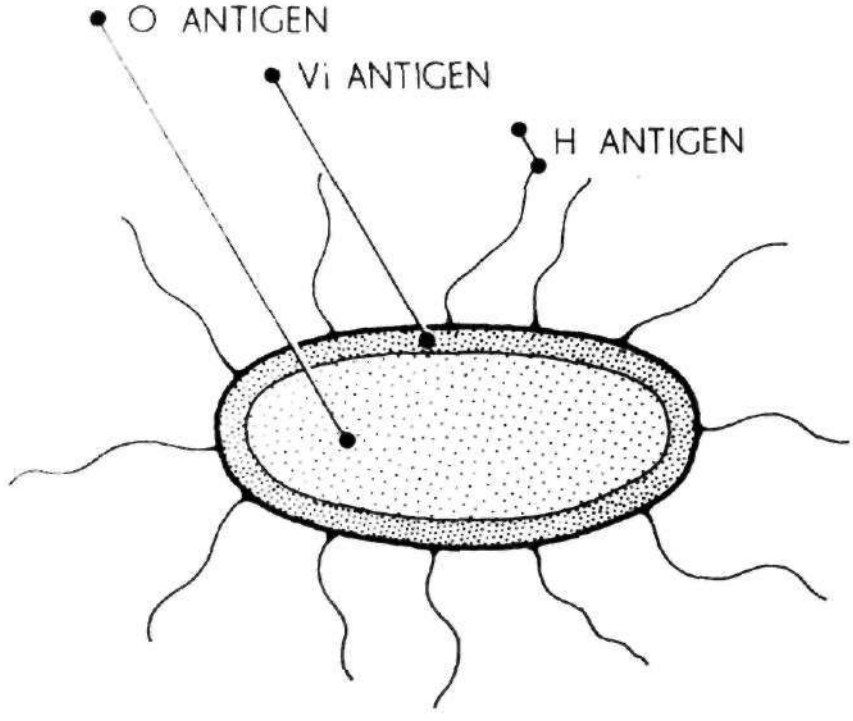


Fig I TYPHOID BACILLUS (11)

S. para-typhi A and B infections are similar to but less severe than S. typhi infection.

Typhoid fever is a disease with worldwide prevalence (3). It has however undergone a marked decline in incidence in the industrialized nations. There the disease is mainly imported by travellers from endemic areas. Typhoid fever is common in Africa (2, 3, 8, 9, 11, 15, 16) where it poses a grave socio-medical problem.

Most of the reports from the West African sub-region have emanated from teaching hospitals (3, 7, 8, 15, 17) and large mission hospitals (5, 6). Since all levels of health care delivery from the dispensary through the health centre and general hospital to the teaching hospital are confronted with typhoid disease, the figures quoted by these authors represent perhaps the tip of the iceberg. Apart from gross under reporting of cases seen, many clinical cases are not included for lack of facilities for confirming diagnosis. Often times only seriously ill patients are treated in the teaching hospitals. What this means is that the problem of typhoid fever is much larger than reported.

Most authors report a seasonal variation in the incidence of typhoid and typhoid perforations. Ikeme and Anan (3) reported a higher incidence during the rainy season and although no studies of the transmission method of the disease or case tracing were carried out, they concluded that contamination of drinking water is the most potent factor in the dissemination of disease in Western Nigeria. Archampong (17) also reported a definite seasonal incidence with 2 peaks coinciding with the 2 rainy seasons in Accra, Ghana. But Huckstep's findings (11) contrasted sharply with those stated above. He noted a higher incidence in the hot dry months of January - March in Kenya and blamed it on contaminated water supply and the poor personal hygiene of the African people.

In Lagos (7); 3 peaks were reported - April, July, November, but it does appear as if the disease was present all year round. To highlight the importance of environmental sanitation on disease transmission, it was shown that 70% of patients came from areas of Lagos characterized by over-crowding and poor sanitation.

In tropical countries, carriers among the public food handlers, dealing with high risk food and beverages such as cold dishes, fresh fruits and cold drinks, especially those that involve much handling during preparation, play an important role in maintaining endemic infection (14).

While no age seems to be immune (18), typhoid fever is most common in the older child and young adult. The peak age incidence is in the 2nd and 3rd decades of life (4, 7). But an earlier report from Zaria (10) showed that in a series of 64 patients 64% were under 15 years with a mean age of 9 years. Idoko et al (9) suggested that this age distribution might be more of a reflection of our young population in addition to a greater level of immunity acquired by the adult.

Pathogenesis

Infection in enteric fever is by ingestion, followed by penetration through the intestinal mucosa. The severity of the disease and the speed at which it develops, depend on the size of the dose of organisms swallowed. In volunteers, 10^9 organisms were needed to induce infection in most, whereas only a quarter of the volunteers became infected with 10^5 organisms. Variation in pathogenicity and host factors such as gastric hypo-acidity may influence the size of infecting dose (14). Other factors that may increase host susceptibility include sickle cell anaemia and the presence of schistosomiasis (16).

After evading the acid barrier in the stomach, the organisms multiply in the 2nd part of the duodenum before penetrating the bowel mucosa. Although the exact site of penetration is

uncertain, the organisms invade the lymphatics to reach the mesenteric lymph nodes where they undergo a brief period of multiplication before reaching the blood stream (transient primary bacteraemia) via the thoracic duct.

From the blood stream, there is a generalised dissemination of organisms to the liver, spleen and other reticulo-endothelial tissues. After a period of silent multiplication at these sites, the organisms re-enter the blood stream in huge numbers (secondary bacteraemia) heralding the onset of the clinical illness. During this phase very few organs in the body escape involvement.

The gall bladder is affected in every case and through the bile where rapid multiplication occurs, a heavy re-infection of the intestinal tract occurs.

Although the jejunum, appendix and colon could be affected in typhoid fever, the Peyer's patches in the ileum are most heavily involved and bear the brunt of tissue destruction (1). The changes occurring here have been divided into four stages occurring at weekly intervals but this convenient time table is often greatly accelerated in Africa (19).

1. Hyperplasia - swelling of Peyer's patches and lymphoid follicles from congestion, oedema, accumulation of lymphocytes, red blood cells, and mono-nuclear cells (typhoid cells) which phagocytose bacilli.

2. Necrosis - involves the mucosa and submucosa and the mechanism probably being local toxaemia with thrombosis of small vessels.

3. Ulceration - this is by far the most dangerous stage and it may lead to haemorrhage and/or perforation. The ulcers are deepest and most frequent in the last 45 cm of the ileum

where they are situated on the anti-mesenteric border of the gut and are generally oval or longitudinal in shape. There is marked peritoneal reaction on the serosal surface of the ulcerated bowel and during the progress of the disease, the bowel may become paper thin and bacterial penetration can occur before macroscopic perforation takes place.

4. Healing - occurs by granulation and little scarring results.

One of the areas of controversy with respect to the pathogenesis of typhoid fever is the question of what causes the prolonged fever and toxicmic state, which set typhoid fever apart from other Gram-negative septicaemias.

Traditionally the pyrexia and toxicity of typhoid were thought to result from continuous liberation of endotoxin by typhoid bacilli. However, work in induced typhoid by Hornick et al (20) has shown that volunteers rendered endotoxin tolerant by repetitive intravenous administration developed typhoid fever in no way different from the control group. Also it was not possible to produce a state of prolonged fever by continuous infusion of endotoxin. Therefore it does not appear that endotoxaemia is the major mechanism for the sustained pyrexia and toxicity of typhoid fever. The work of Butler et al (21) lends considerable support to this view. They employed a sensitive indicator of endotoxaemia, the Limulus lysate test, in 21 cases of untreated typhoid but found no evidence of circulating endotoxin. Hornick and Greisman (22) suggested that the sustained pyrexia of typhoid is due to the local effects of endotoxin which stimulates the synthesis and release of endogenous pyrogen by the inflammatory cells at those sites where S typhi is actively multiplying.

The study by Butler et al (21) also found that out of 28 patients with typhoid fever, 17 had thrombocytopenia (platelet $< 150 \times 10^9/L$), 9 had

hypofibrinogenaemia (fibrinogen < 1.5mg/L) and 20 had elevated fibrinogen - related antigens (titre > 1.8). These tests returned to normal during convalescence and intestinal bleeding did not correlate with abnormalities of coagulation tests. They, therefore, concluded that although disseminated intra-vascular coagulation occurred commonly in typhoid fever, it appeared to be a subclinical event. But the thrombocytopenic index used by Butler et al is much higher than the 70 x 10^9/L level published for non-caucasians.

Diagnosis

Since typhoid mimics many other diseases, clinical suspicion alone is not enough to make a diagnosis of the condition.

Every effort must be made to recover the organism from the blood, bone marrow, stool or urine and/or to demonstrate a rising antibody titre to the O antigen of S typhi. Klotz et al (23) stated that a diagnosis of typhoid fever may be made on the basis of any of the following criteria:-

1. Isolation of S. typhi from the blood.

2. Isolation of S. typhi from the stool in conjunction with a compatible clinical illness.

3. A four fold titre rise in antibody or titre of greater than or equal to 1:160 to the O antigen of S. typhi with a compatible clinical illness.

But Bala and Auty (10) working in Zaria suggested that either recovery of the organism from blood or a Widal agglutination titre for Salmonella 'O' antibody exceeding 1:64 or a two fold rise in Widal agglutination during the disease was accepted as diagnostic. This is based on the unpublished work of Greenwood and Whittle which showed low antibody titres in the Zaria area despite the endemicity of typhoid infection.

The diagnostic value of a single Widal test in areas endemic for typhoid fever was the subject of intense research by Levine et al (24). From their studies the following conclusions were made regarding interpretation of a single Widal test in non vaccinated individuals:

1. Elevated S. typhi O and H antibody titre (greater than or equal to 1:40 and 1:80 respectively) are indeed helpful in making a presumptive diagnosis of typhoid fever.

2. Elevated levels also offer diagnostic value for children less than 10 years in endemic areas.

3. Because of the high prevalence of antibody amongst healthy older individuals in areas of high endemicity, particularly teenagers and young adults, a single Widal test provides minimal, if any, diagnostic assistance. Rather in those above 10 years of age a negative Widal test serves to rule against typhoid fever.

Of all these tests a culture of the bone marrow aspirate is the most sensitive (25). In a prospective comparative study of 62 patients with typhoid fever, most of whom had received antibiotics before presentation, S. typhi was isolated from the bone marrow in 56 patients (90%). In contrast, S. typhi was recovered from blood in only 25 patients (40%), from stool in 23 (37%) and urine in 4 (7%) (26). The prospective study of Gilman et al offers conclusive evidence of the superiority of bone marrow cultures in the diagnosis of typhoid fever. Although a painful procedure and requiring some technical expertise, it is especially suitable in areas where self prescription is common and antibiotics are easily procurable.

Clinical Features and Complications

In stating the variety and diverse ways in which typhoid and its complications present, Huckstep (11) aptly quoted from Shakespeare's Seven Ages of Man - "One man in his time plays many parts". He further states that a case of typhoid fever

> may present as a disease clinically indistinguishable from malaria, progress to a bacillary dysentery, mimic a case of acute bronchitis, simulate a full-fledged lobar pneumonia, cause an acute abdomen with perforation, and finally in convalescence, with its evil spent, linger on as an orchitis, a myocarditis or a peripheral neuritis. In agreement, Parry (16) noted that there is no one group of signs which is characteristic of typhoid, but the very absence of signs in a patient who has had a fever for a few days and who looks ill, lies listless, speaks little, and likes to be left alone, suggests typhoid.

Surgical complications of typhoid fever include pharyngitis, tonsillitis, parotitis, intestinal haemorrhage, intestinal perforation (ileal, caecal), acute cholecystitis, paralytic ileus, intestinal obstruction, typhoid appendicitis, intussusception, rupture of a mesenteric gland, purulent abscess of the liver, orchitis pyelitis, cystitis, retention of urine empyema of chest, typhoid arthritis, typhoid osteomyelitis and typhoid spine (11).
Others include lung abscess, deep venous thrombosis (3) abortion, premature labour (27), peritonitis without perforation (5) and such general complications as typhoid abscess, boils, bed sores myositis otitis media, Zenker's degeneration, severe mental confusion, deafness, severe dehydration. Rowland (28) has classified the complications of typhoid fever according to different etiological groups:-

1. Due to typhoid organisms - relapse, meningitis, endocarditis and abscess of bone.
2. Due to toxaemia - myocarditis, hyperpyrexia, liver and bone marrow damage.
3. Due to local lesions in the gut - dysentery, haemorrhage, perforation and paralytic ileus.
4. Due to severe illness - parotitis, bed sores and pneumonia.

5. Due to treatment - marrow damage and hypersensitivity. Although a convenient pathophysiological basis for looking at the diverse complications of typhoid fever, it does not explain all the significant complications, for example arthritis.

The incidence of complications in typhoid fever varies very widely and the factors responsible for this are not well understood. Thus Rowland (28) reporting from Iran in 1961 found a complication rate of 16.3% in patients who received at least 48 hours treatment with chloramphenicol and compared this to the 56.3% earlier reported by Stuart and Pullen in 1946 (pre chloramphenicol era) and felt the introduction of chloramphenicol was responsible for the significant change.

But Gupta et al (18) in 1985 reported a complication rate of 48.0% at a time when antibiotic usage was fairly well standardized.

With the advent of chloramphenicol and other antibiotics effective against S. typhi the mortality in typhoid fever has shown a sharp decline. But not so the dreaded complications of perforation and haemorrhage (29). The pattern of complications reported by different workers varies. While in the Indian sub continent, peripheral circulatory failure is more common than intestinal perforation (when the 2 commonest lethal complications are compared) (18), intestinal perforation stands out as the more important common and challenging surgical complication of typhoid in the West African sub-region. Here it accounts for the greatest proportion of mortalities in this disease. Little wonder, the attention of most authors has been focused on typhoid perforations.

Olurin et al (4) in Ibadan cited from the literature an incidence of typhoid perforation ranging from 0.5% to 15.3% and compared to his own experience of 33.6%. Also the incidence in Accra was 17.9% and typhoid perforation was the commonest cause of peritonitis after acute appendicitis (30).

Management

Opinion is still divided about the role of surgery in the management of typhoid perforation. Huckstep (31), the Chief protagonist of conservative approach to management based his arguments on:-

1. The poor tolerance of typhoid patients to general anaesthesia either due to the poor state of the myocardium and respiratory system or to the added effects of the anaesthetic agents on an already deranged liver function.
2. The friability of the bowel which can be likened to blotting paper and which would make surgical repair impossible.
3. The sterility of the peritoneal spill in chloramphenicol treated patients and;
4. The tendency for the perforation to heal.

He further cited the work of Bailey (1958) and Webb-Johnson (1917) whose mortality rates for patients who had operative treatment were 80% and 100% respectively and compared these to his own mortality rate of 30% following conservative treatment to buttress his point. Rains and Ritchie (32) noting that laparotomy under local anaesthesia and closure of perforation yielded poor results advocated conservative therapy. Conservative treatment involves chloramphenicol therapy, intravenous fluid and electrolyte replacement and nasogastric decompression. However, the experience of other surgeons recommend operative management. Dickson and Cole (2), treated 31 patients by operation 15 of whom died while all the 7 patients treated conservatively died. Given the fact that a large proportion (98%) of patients perforated before presentation in Archampong's series (17), the peritoneal spill is unlikely to be sterile. Chloramphenicol alone is insufficient to treat E. coli, Streptococcus faecalis and to seal the perforation. Given also the sound surgical principles of cleaning out the peritoneal cavity and removing a source of continuous contamination, and the fact that in a large number of cases it may be impossible to rule out other causes of peritonitis like acute appendicitis,

operative management is now advocated. To further buttress the arguments in favour of operative treatment Li (33) published figures from his study of 20 patients with perforation. All 20 had laparotomy and simple closure but only 2 died and in those two there was no evidence of re-perforation. In his series, operative findings did not show any signs of localization of disease and peritonitis was often generalised.

The following surgical procedures can be employed in the management of typhoid perforations:-

1. Suture, lavage.
2. Bypass end-to-side ileo-transverse colostomy.
3. Bypass side-to-side
4. Wedge resection
5. Resection with anastomosis
6. Exteriorization resection
7. Lateral tube ileostomy
8. Ileostomy
9. Suture and total parenteral nutrition (34)

The choice of operative procedure is mainly dictated by the state of the terminal ileum (4). The factors in favour of simple closure in 2 layers are that it is a simple and quick procedure which avoids the danger of prolonged anaesthesia in an already compromised patient, and that decompressing the bowel through the perforation and continuing the chloramphenicol therapy reduces the risk of re-perforation. Resection and anastomosis are indicated when there are multiple perforations in a short segment of bowel in the presence of severe disease of the bowel. Although the bypass procedures were introduced to rest the diseased bowel and avoid extensive resections especially in children, they may prove inadequate in patients with disease extending to the jejunum and transverse colon. In Ile-Ife, Badejo et al (8) compared the result of 3 modalities of management of typhoid perforation in 210 patients. These were:-

1. Conservative treatment (30 cases)

2. Laparotomy, closure of perforation without post-operative irrigation (15 cases).
3. Extensive laparotomy, closure of perforation (110 cases) resection of ileum (55 cases) and post-operative irrigation with dextran solution containing chloramphenicol and trasylol.

They cited mortality rates of 66.6%, 33% and 3.03% respectively. With these results they advocated post-operative peritoneal irrigation for all patients with typhoid perforation. However it is not certain that all of these patients had typhoid fever as only 77 had bacteriological or serological confirmation of the infection. Furthermore the comparison was carried out for patients treated under different settings likely to influence outcome of treatment.

All surgical procedures used have had a high rate of post operative complications, with wound infection as the commonest complication.

Prognosis

In a prospective study of 231 patients with typhoid perforation carried out in Ghana over a 5 year period by Archampong (15) a critical attention was paid to factors which might be important in prognosis. Of the parameters studied which included haemoglobin level, sickling status, peripheral circulatory failure, perforation before admission, perforation after admission, number of perforations, number of days ill, number of days perforated before admission, fluid volume transfused before surgery, urinary output before surgery, blood urea, plasma potassium, and plasma sodium, the following were found to strongly influence prognosis:-

1. The duration of illness before admission
2. The number of days perforation had occurred before admission and;
3. The correction of fluid and electrolyte imbalance.

These results command respect as the numbers are relatively large and appropriate statistical analysis was done.

There is no agreement in the literature about the influence of age (35) and sex (5, 17) on prognosis.

CHAPTER III

METHODOLOGY

PART 1 (RETROSPECTIVE STUDY)

The diagnostic index of the Central Medical Records Library was checked for all cases of typhoid fever seen in the hospital between January, 1981 and December, 1985. The operation registers and the case summary files of the Department of Surgery for the same period were checked for all surgically treated complications of typhoid fever. The relevant case notes including information about the total number of hospital admissions were retrieved from the Medical Records Department. The histology reports on typhoid perforations were obtained from the Histopathology Laboratory. The figures for rainfall were obtained from the Institute of Agricultural Research, Samaru.

The diagnostic criteria used were similar to those suggested by Klotz (23) except that a two-fold rise in antibody titre and/or a value higher than 1:64 during the disease (10) was accepted as diagnostic.

From the available case notes, information on patients who met the diagnostic criteria were abstracted unto the proforma sheets (see appendix 1).

PART II (PROSPECTIVE STUDY)

This covered a period of 1 year from May, 1986 to April, 1987.

All the patients admitted to Ahmadu Bello University Teaching Hospital, Zaria with a clinical suspicion of typhoid fever were included in the study. The relevant information about the patient was entered into a proforma sheet (see appendix 1).

Before antibiotic treatment was commenced in most cases, and depending on the age of the patient, 10-20ml sample of venous blood was obtained for the following laboratory tests:

1. Two and half millilitres of this sample was put in a bottle containing ethylene diamine tetra acetic acid (EDTA) for the determination of the full blood count. The haemoglobin level was determined using the cyanomethaemoglobin method described by Dacie and Lewis (36). The total white blood cell count was done with the Coulter counter model Zfn. Platelet count was determined by a method using ammonium oxalate as the diluent.

2. Ten millilitres (5ml in children) of clotted blood was put into a bottle for serum urea, electrolytes, liver enzymes and bilirubin levels..

3. Using strict aseptic technique, 1-2ml of blood was put into 2 sterile blood culture bottles (McCartney bottle with screw cap which has a perforation) containing 10-15ml of thioglycolate broth. In the microbiology laboratory specimen was incubated at $37^{o}C$ aerobically for 48 hours then sub-cultured to blood agar, chocolate agar, McConkey agar. These were incubated for 24 hours at $37^{o}C$, the chocolate agar being incubated in CO_2 and air. The subculture plates were then examined and the growths identified. A further subculture was performed on the seventh day and a negative report issued if no growth was found on the subcultures. Serological tests using slide agglutination to Salmonella O antisera enabled identification of any isolate in the somatic groups but final identification to the serotype was not possible due to lack of Salmonella H antigens. Sensitivity tests were carried out on positive cultures by the standard disc method described by Auer et al using Oxoid Multodiscs (37).

4. Two to four millilitres of blood was put in the Universal bottle to obtain serum for Widal agglutination test. The antigen used was the Wellcome Salmonella typhi "O" antigen suspension and the agglutinations were performed in the wells of a micro-titre plate.

Bone marrow was obtained from either the posterior iliac spine, or upper end of the tibia using strict aseptic techniques. The site chosen was cleaned with acetavlon or spirit and about 5ml of local anaesthetic agent (lignocaine 1%) injected down to the periosteum. Through the same puncture site, the Salah marrow aspiration needle was introduced up to the periosteum and by drilling the needle was negotiated past the cortex into the marrow cavity. Two to five millilitres of marrow was aspirated using a 20ml syringe and aseptically introduced into a blood culture bottle. Further treatment of the specimen is similar to that described for blood above.

Stool and urine cultures were obtained in most patients.

The clinical progress of the patient was followed treated. Radiological investigations were ordered where these were deemed necessary. Surgical complications were diagnosed and treated.

In patients presenting with perforation, particular attention was paid to time of perforation, and the duration of perforation before admission. At surgery the number of perforations, distance of perforation from ileocaecal valve, state of the gut and mesenteric nodes were noted. Specimen of the peritoneal spill was obtained for culture and sensitivity tests, biopsies of the edge of perforation and mesenteric node were sent to the laboratory in formalin, for histopathological studies.

All the information obtained from these studies including the type of treatment given, the outcome of treatment were then entered into the proforma. Only patients with at least one

confirmatory laboratory evidence of typhoid fever were accepted for the study.

The author personally examined 52 (81.25%) of the patients, performed 30 (90%) of all the bone marrow aspirations and operated on 5 of the 8 patients who had laparotomy for typhoid perforation, and followed up the patients on the ward till discharge.

METHODS OF STATISTICAL ANALYSIS

The data used for analysis in this study was a hospital based one.

The urban: rural ratios for typhoid and the seasonal frequency of typhoid fever were analyzed with the Chi square test. Also tested by the Chi square analysis is the ratio of the perforated to the non perforated cases of typhoid fever for the sexes.

The prognostic factors were evaluated by a simple numerical system and the comparisons carried out by means of the Student's t test.

PART ONE

CHAPTER IVA

RESULTS: RETROSPECTIVE STUDY

Between January 1981 and December 1985 567 clinical cases were seen. Of these only 454 case folders could be traced (80% retrieval rate) but only 185 met the diagnostic criteria of typhoid fever. The criteria used were:-

1. Isolation of S. typhi from the blood.
2. Isolation of S. typhi from the stool or urine in conjuction with a compatible clinical illness.
3. A two - fold rise in antibody titre and/or a value higher than 1:64 to the O antigen of S. typhi with a compatible clinical illness.

The total hospital admissions for the period was 70,146, which means 0.26% (185/70,146) of total hospital admissions were for patients coded as having typhoid fever.

When the aetiology of all acute abdominal emergencies was considered, typhoid was the third commonest cause (Table I).

TABLE 1

CAUSES OF ACUTE ABDOMINAL EMERGENCIES IN ABU HOSPITAL, ZARIA (JANUARY, 1981 - DECEMBER, 1985)

CAUSES	NUMBER	%
Appendicitis	528	40.81
Strangulated external hernia	484	37.46
Typhoid acute abdomen	65	5.03
Intestinal obstruction from adhesions	46	3.56
Volvulus	28	2.17
Intussusception	26	2.01
Intra abdominal abscesses	23	1.78
Perforated peptic ulcer	22	1.70
Primary peritonitis	12	0.93
Cholecystitis	10	0.77
Others	48	3.72
TOTAL	1292	100.00

Age and Sex Distribution (Table 2)

The peak age incidence was in the second quinquennium in both males and females. Overall 64.32% of the patients were between 5 and 19 years. The disease was more common in males with a male: female ratio of 1.72:1.

TABLE 2

AGE AND SEX DISTRIBUTION OF TYPHOID FEVER IN ZARIA (RETROSPECTIVE STUDY)

AGE GROUP	MALE	FEMALE	TOTAL	%
0-4	9	7	16	8.65
5-9	38	22	60	32.43
10-14	20	16	36	19.46
15-19	17	6	23	12.43
20-24	12	9	21	11.35
25-29	8	4	12	6.49
30-34	5	1	6	3.24
35-39	2	1	3	1.62
40 +	6	2	8	4.32
TOTAL	117	68	185	99.99

Place of Domicile (Table 3)

Fifty eight percent of the patients came from Zaria. Compared with the figures of a consecutive count of general admissions to various wards of the hospital over a six - month period, there was a significantly higher proportion of rural dwellers presenting with typhoid than with other conditions. The urban/rural ratio for typhoid was 1.38:1 while the ratio for total hospital admissions was 1.92:1. This was found to be statistically significant. Twenty one patients had no information on place of domicile.

TABLE 3

PLACE OF DOMICILE

DOMICILE	TYPHOID FEVER PATIENTS : NUMBER	%	OVERALL HOSPITAL ADMISSIONS : NUMBER	%
URBAN	95	57.93	1328	65.71
RURAL	69	42.07	693	34.29
TOTAL	164	100.00	2021	100.00

$X^2 = 4.06$

$P < 0.05$

Occupation of patients (Table 4)

Children accounted for 44.51% of the cases while students (post primary and post secondary) constituted 26.22%. Only 1.22% of patients were top professionals.

TABLE 4

OCCUPATION OF PATIENTS WITH TYPHOID FEVER IN ZARIA

OCCUPATION	NUMBER	%
CHILDREN	73	44.51
STUDENTS	43	26.22
HOUSE WIVES	19	11.59
FARMING	7	4.27
TRADING	3	1.83
TEACHING	2	1.22
MISCELLANEOUS*	17	10.37
TOTAL	164	100.01

*All other occupations not mentioned.

Seasonal Frequency of Typhoid Fever in Zaria (Table 5)

The peak frequency of typhoid fever was in October with 25 cases. The monthly difference in frequency was significant by the Chi square analysis. In Zaria there are two main seasons - wet (May - October) and dry (November - April). There were 117 and 68 cases during the wet and dry seasons respectively with a ratio of 1.72:1. This seasonal variation in frequency correlated well with the average monthly rainfall in Zaria (Fig 2).

TABLE 5

MONTHLY INCIDENCE OF TYPHOID FEVER IN ZARIA

(RETROSPECTIVE STUDY)

MONTH OF THE YEAR	NUMBER	%
JANUARY	9	4.86
FEBRUARY	7	3.78
MARCH	11	5.95
APRIL	14	7.57
MAY	14	7.57
JUNE	16	8.65
JULY	19	10.27
AUGUST	21	11.35
SEPTEMBER	22	11.89
OCTOBER	25	13.51
NOVEMBER	12	6.49
DECEMBER	15	8.11
TOTAL	185	100.00

$X^2_{25} = 21.20 \quad P < 0.05$

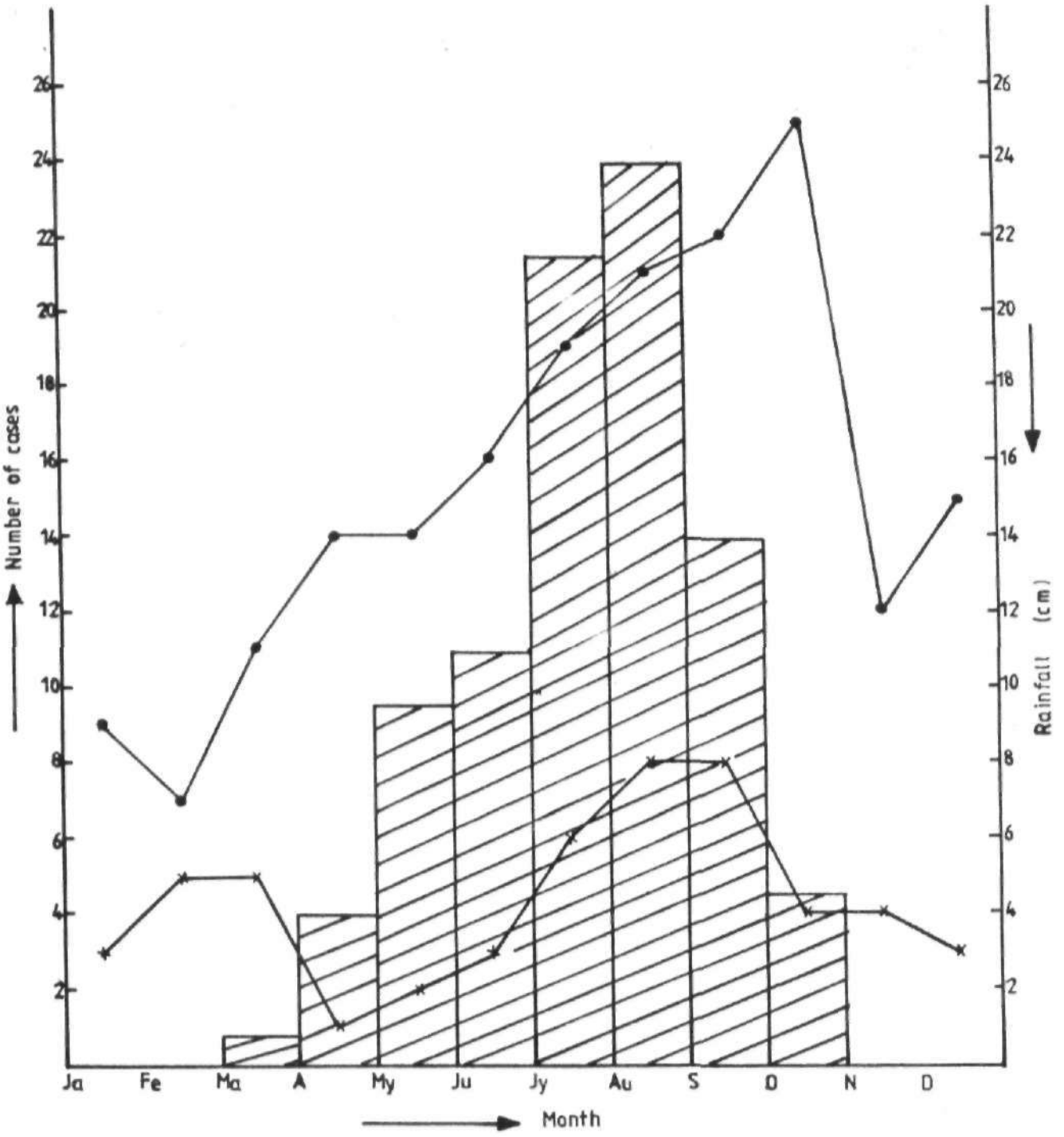


Fig. 2. Seasonal frequency of typhoid fever cases and perforations in A B U Hospital, Zaria (1981-1985).

Average monthly rainfall

Perforated typhoid cases

All cases

Clinical Features of Typhoid Fever In Zaria (Tables 6 and 7)

The case folders of 13 patients with typhoid perforation could not be found and so were not analyzed for clinical features.

The commonest symptom of typhoid fever in Zaria was fever followed by abdominal pain, vomiting, headache and diarrhoea. Half of the patients had tachycardia and 45.93% were dehydrated on admission. Abdominal tenderness which occurred in 47.67% of cases was not limited to cases with perforation or peritonitis. In this series 26.16% of patients had a normal temperature on admission.

TABLE 6

PRESENTING SYMPTOMS OF TYPHOID FEVER IN ZARIA
n = 172

SYMPTOM	NUMBER	%
FEVER	140	81.40
ABDOMINAL PAIN	103	59.88
VOMITING	88	51.16
HEADACHE	70	40.76
DIARRHOEA	69	40.12
ANOREXIA	42	24.42
COUGH	33	19.19
CONSTIPATION	31	18.02
CHILLS	21	12.21
WEAKNESS	17	9.88
BLOOD IN STOOL	16	9.30
JOINT PAIN	10	5.81
ABNORMAL BEHAVIOUR	8	4.65
CONVULSION	8	4.65
PRECEDING DIARRHOEA	8	4.65
PRECEDING CONSTIPATION	7	4.07
CHEST PAIN	7	4.07
JAUNDICE	5	2.91
ABDOMINAL DISTENSION	5	2.91
BACK ACHE	5	2.91

TABLE 7

DISTRIBUTION OF CLINICAL SIGNS IN 172 CASES OF TYPHOID (n = 172)

PHYSICAL SIGN	NUMBER	%
Tachycardia (pulse >100/min)	86	50.00
Abdominal tenderness	82	47.67
Dehydration	79	45.93
Temperature - Normal	45	26.16
up to 38.3^{o}C	58	33.72
> 38.3^{o}C	69	40.12
Hepatomegaly	66	38.37
Splenomegaly	61	35.47
Pallor	56	32.56
Abdominal distension	27	15.70
Guarding	26	15.12
Toxicity	25	14.53
Rebound Tenderness	16	9.30
Confusion	15	8.72
Diminished bowel sound	14	8.14
Absent bowel sound	11	6.40
Drowsiness	13	7.56
Jaundice	10	5.81
Meningism	6	3.49
Bronchitic signs	6	3.49

Period before Presentation

Fifty two and half percent of patients presented within the first week of illness while only 3.16% presented after the fourth week of illness. The mean period before presentation was 8.96 days.

Concurrent Diagnoses (Table 8)

The commonest associated diagnoses in patients with typhoid fever were urinary tract infection mainly E. coli infection), intestinal helminthic infestation and sickle cell anaemia. Pregnancy was an associated condition in two patients.

TABLE 8

CONCURRENT CONDITION IN 172 CASES OF TYPHOID FEVER IN ZARIA

CONCURRENT CONDITION	NUMBER	%
Urinary Tract Infection	16	9.30
Intestinal helminthiasis	15	8.72
Sickle cell anaemia	10	5.82
Schistosomiasis	6	3.49
Malaria	5	2.91
Oral Thrush	4	2.33
Deafness	3	1.74
Other Septicaemia	3	1.74
Angular Stomatitis	3	1.74
Pregnancy	2	1.16
Amoebiasis	2	1.16
Tuberculosis	2	1.16
Measles	2	1.16
Miscellaneous	20	11.63

Diagnosis (Table 9)

Urine culture was positive in 2 patients, negative in 50 and unavailable in 120 patients. Stool culture was positive in 30 patients, negative in 18 and unavailable in 124 patients. Blood

culture was positive in 42 negative in 53 and unavailable in 77 patients.

Widal agglutination reaction was diagnostically positive in 90 of 114 patients while histological examination of the edge of perforation in the bowel and/or mesenteric lymph node showed evidence typical of typhoid inflammation in 16 of 18 patients. In some patients, some of these tests were either not done or the results could not be traced.

Salmonella organisms were isolated in 75 patients. 63 (84%) of these were Salmonella typhi while the rest belonged to Salmonella of serogroups A, B, C and E.

TABLE 9

LABORATORY RESULTS IN DIAGNOSIS OF TYPHOID FEVER IN ZARIA
(n = 172)

INVESTIGATION	NOT AVAILABLE	NUMBER AVAILABLE	NUMBER POSITIVE	POSITIVE (%)	NUMBER POSITIVE FROM THIS TEST ONLY
URINE	120	52	2	3.85	-
STOOL CULTURE	124	48	30	62.50	15
BLOOD CULTURE	77	95	42	44.21	16
WIDAL TEST	58	114	90	78.95	61
PERITONEAL FLUID	47	5	1	20.00	1
HISTOLOGY	34	18	16	88.89	14

Sensitivity of the Organism to Antibiotics

Table 10 shows the general sensitivity of the organisms to 10 commonly tested antibiotics at the Zaria hospital. S. typhi remains very sensitive to chloramphenicol but very poorly sensitive to sulphonamides.

TABLE 10

GENERAL SENSITIVITY OF THE ORGANISMS TO THE ANTIBIOTICS TESTED BY THE DISC DIFFUSION METHOD

ANTIBIOTIC	NUMBER TESTED	NUMBER SENSITIVE	%
Chloramphenicol	41	39	95.12
Ampicillin	32	27	84.38
Tetracycline	44	37	84.09
Kanamycin	10	7	70.00
Co trimoxazole	33	23	69.70
Gentamycin	22	15	68.18
Penicillin	13	8	61.54
Colistin Sulphate	40	16	40.00
Streptomycin	28	10	35.71
Sulfonamide	23	2	8.70

Haematological Findings

Anaemia: Full blood counts were carried out on 138 patients, and 60 (43.48%) were found to have Hb of less than 10g/dl on admission. Only 4 (2.90%) had Hb levels below 4g/dl.

Thrombocytopenia: Of 30 patients whose platelet counts were determined, 13 (43%) had counts below 100 x 10^9/l. Five (16.67%) had counts below 50 x 10^9/l.

Leucopenia: The normal range of leucocyte count used for analysis in this study is 3.2 - 10.85 x 10^9/L with a mean of 6.44 $\pm$ 1.7 (38) and 95% confidence limits of 6.31 - 6.57x10^9/L. The leucocyte counts were studied in 137 patients and found to be less than 3 x 10^9/L in 27 (19.71%). The range was 1.7-21.4 with a mean of 5.57 $\pm$ 2.77 and 95% confidence limits of 5.11-6.03 x 10^9/L. This mean is significally lower than the normal value ($t = 3.43$, $P < 0.001$).

Biochemical Findings (n = 112)

Thirty five (31.25%) patients had urea $>$ 7mmol/L. While 59(52.21%) had hyponatraemia (Na^+ $<$ 136 mmol/L). Fifty two (46.43%) patients had hypokalaemia (K^+ $<$ 3.8 mmol/L), 58 (51.79%) had hypochloraemia (Cl^- $<$ 95 mmol/L) while 22 (19.82%) had bicarbonate levels below 20 mmol/L.

Of the liver enzymes, SGOT was elevated in 47(67.15%) SGPT in 30 (42.25%) while alkaline phosphatase was elevated in 15 (20.55%). The serum total bilirubin was elevated in 6 (9.09%).

Complications of typhoid fever in Zaria (Tables 11 and 12)

Eighty six (46.49%) of all the patients in the retrospective series developed complications. Seventy four of the patients had surgical with or without medical complications while 12 had only medical complications. As shown in table 11, intestinal perforation was by far the commonest surgical complication of typhoid fever in Zaria, followed by intestinal haemorrhage and peritonitis (without macroscopic perforation). The two patients who were pregnant both lost their fetuses; one at 13 weeks and the other at 30 weeks of gestation.

One 30 year old male patient had acalculous angrenous cholecystitis with isolation of *S. typhi* from the gall bladder contents.

The commonest medical complication of typhoid fever was pneumonia which occurred in 13 patients. The others were as shown in table 12. Comparing tables 11 and 12, surgical complications exceeded medical complications by a ratio of 4.48:1.

TABLE 11

SURGICAL COMPLICATIONS IN 185 PATIENTS WITH TYPHOID IN ZARIA

COMPLICATION	NUMBER	%
ILEAL PERFORATION	52	28.11
INTESTINAL HAEMORRHAGE	6	3.24
PERITONITIS	5	2.70
SHOCK	5	2.70
INTESTINAL OBSTRUCTION		
- ADHESIONS	3	1.62
- ILEUS	1	0.54
MESENTERIC LYMPHADENITIS	2	1.08
APPENDICITIS	2	1.08
PERIAPPENDICITIS	1	0.54
EMPYEMA THORACIS	2	1.08
SUBCUTANEOUS ABSCESSES	2	1.08
EPISTAXIS	2	1.08
TONSILLITIS	2	1.08
PHARYNGITIS	2	1.08
ABORTION/PREMATURE LABOUR	2	1.08
GANGRENOUS CHOLECYSTITIS	1	0.54
URINARY RETENTION	1	0.54
ARTHRITIS	1	0.54
D.I.C.	1	0.54
ACUTE RENAL FAILURE	1	0.54

TABLE 12

MEDICAL COMPLICATIONS IN 185 PATIENTS WITH TYPHOID FEVER IN ZARIA

COMPLICATION	NUMBER	%
PNEUMONIA	13	7.03
PSYCHOSIS	4	2.16
HEART FAILURE	2	1.08
MENINGITIS	1	0.54
MALNUTRITION	1	0.54

Treatment

The resuscitative measures carried out for most patients admitted with typhoid fever were fluid and electrolyte replacement and nasogastric decompression. Chloramphenicol was the sole antibiotic used in 143 (83.14%) of the patients and in combination with other antibiotics in 12 (6.98%) other patients. Table 13 shows the antibiotics used in the treatment of typhoid fever and its complications in Zaria.

Sixty five operative procedures were carried out for the surgical complications of typhoid as shown in Table 14. Fifty two (80%) of these operations were done for typhoid perforation.

TABLE 13

ANTIBIOTICS USED IN THE TREATMENT OF TYPHOID FEVER AND ITS COMPLICATIONS IN ZARIA (n = 172)

ANTIBIOTIC USED	NUMBER OF CASES	%
Chloramphenicol	155	90.12
Gentamycin	8	4.65
Metronidazole	6	3.49
Ampicillin	4	2.33
Co-trimoxazole	4	2.33
Ampiclox	3	1.74
Penicillin	3	1.74
Amoxycillin	1	0.50

TABLE 14

INDICATIONS FOR OPERATION IN TYPHOID FEVER IN ZARIA

OPERATIVE PROCEDURE CARRIED OUT FOR	NUMBER	%
Ileal perforation	52	80.00
Typhoid peritonitis	5	7.69
Appendicitis/Periappendicitis	3	4.62
Empyema thoracis	2	3.08
Intestinal obstruction	2	3.08
Cholecystitis	1	1.54
TOTAL	65	100%

Post Operative Complications (Table 15)

The post operative complications seen in 53 patients are shown in table 15. The commonest post operative complication was wound infection which occurred in 30.19%.

TABLE 15

POST OPERATIVE COMPLICATIONS IN PATIENTS WITH SURGICAL TYPHOID FEVER IN ZARIA (n = 53)

COMPLICATION	NUMBER OF CASES	%
Wound Infection	16	30.19
Wound dehiscence	6	11.32
Anastomotic leak	6	11.32
Pneumonia	4	7.55
Intestinal obstruction (adhesions)	2	3.77
Jaundice	2	3.77
Confusional state	2	3.77
Prolonged ileus	1	1.89
D.I.C.	1	1.89
Pressure sores	1	1.89
Fluid overload	1	1.89
Additional perforation	1	1.89

Outcome of Treatment

One hundred and thirty one (70.81%) patients recovered completely, 2 (1.08%) suffered a relapse, 1 (0.54%) absconded from hospital, while 39 (21.08%) died. The overall mortality rate for the 173 cases of known outcome came to 22.54%. Typhoid perforation was responsible for 61.54% of the deaths.

No post mortem examinations were carried out. Therefore definite causes of death could not be identified. However a number of factors which contributed to death were identified as toxaemia with or without myocarditis in 23, shock in 13, electrolyte disturbances and acid base imbalance in 11, penumonia in 2, acute renal failure in 2 and disseminated intravascular coagulation in 1.

CHAPTER IVB

TYPHOID PERFORATIONS

(a) The proportion of patients presenting with typhoid perforation expressed as a percentage of total admissions for typhoid during the study period showed a steady decline in incidence up till 1984 (Fig. 3).

(b) Thirty one (59.62%) of the perforations occurred in the age bracket 5 to 19 years. Perforations were more common in males than females with a 3:1 ratio. The sex ratio of perforated to non-perforated cases was significant (Table 16).

(c) The duration of stay in hospital ranged from 1 day to 65 days with a mean of 16.18 days. The mean for the non perforated cases was 11.03 days.

TABLE 16

SEX	NON PERFORATED	PERFORATED	TOTAL
MALE	78	39	117
FEMALE	55	13	68
TOTAL	133	52	185

$$\chi^2 = 4.30$$

$$P < 0.05$$

(d) Abdominal pain (82.50%), fever (65%) and vomiting (57.50%) were the commonest symptoms while abdominal tenderness (90%), dehydration (57.50%) and abdominal distension (55%) were the commonest signs.

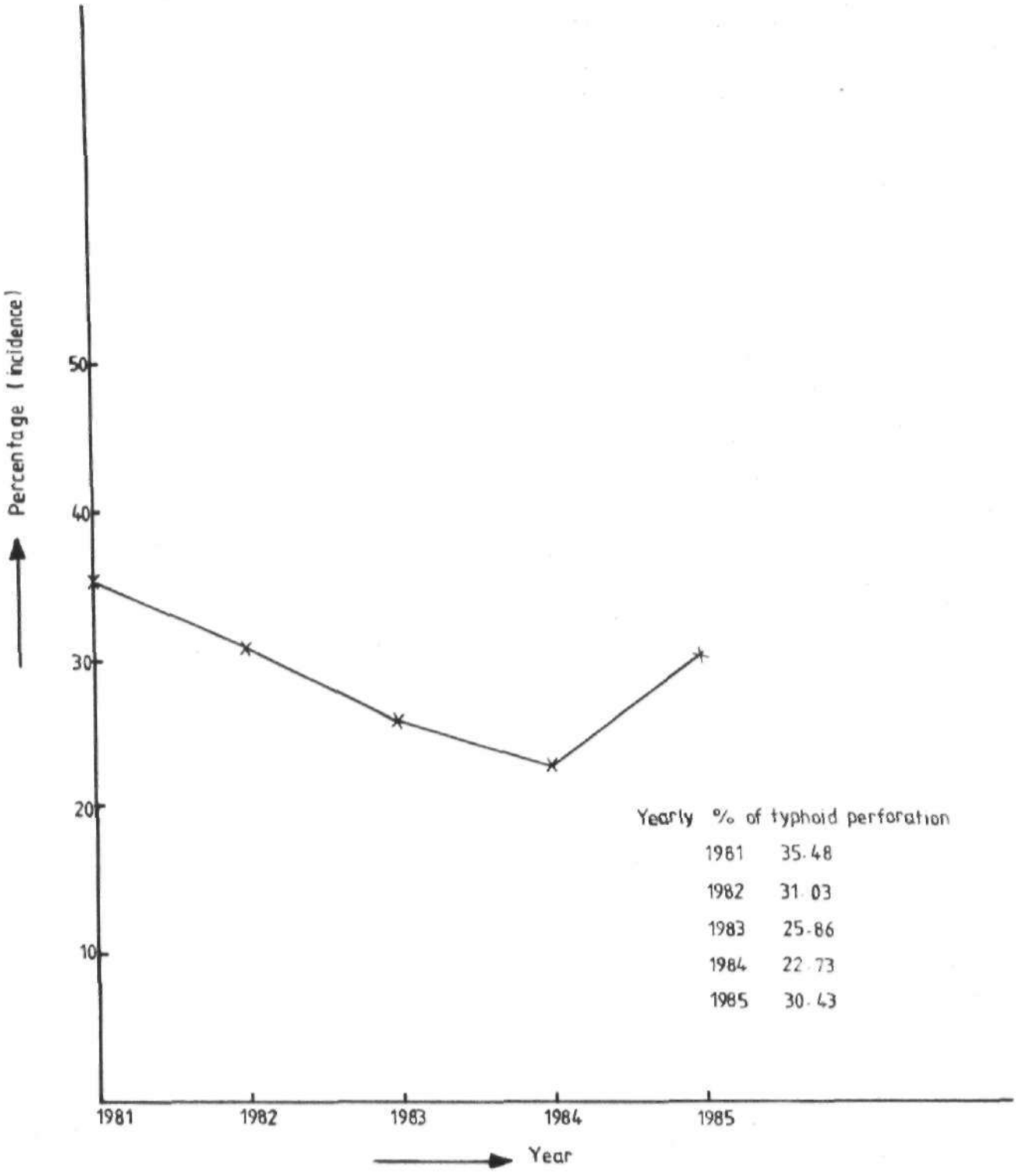


Fig. 3. Graph showing typhoid perforation as a percentage of the total cases of typhoid fever seen in A B U Hospital, Zaria (1981-1985)

(e) Diagnosis of perforation was made largely on clinical grounds. Abdominal and/or chest radiographs in 18 cases demonstrated free air under the diaphragm in 8. However in all 52 patients, bowel perforation was confirmed at laparotomy.

(f) Table 17 shows the week of perforation for 36 patients. There was no direct relationship between duration of illness before perforation and mortality rate.

(g) Table 18 shows the duration of perforation before admission for 21 patients. The mean duration of perforation before presentation was 2.62 days. All 4 who stayed at home for 4 or more days died.

(h) Table 19 shows the location of perforation in 52 patients. 69.23% of the perforations were within 30 cm of the ileocaecal valve.

(i) Seventy five percent of the perforations were single (Table 20).

TABLE 17

WEEK OF PERFORATION IN 36 CASES OF TYPHOID FEVER IN ZARIA

TIME OF PERFORATION	NUMBER	%
Week 1	19	52.78
Week 2	8	22.22
Week 3	8	22.22
Week 4	1	2.78
TOTAL	36	100.00

TABLE 18

NUMBER OF DAYS PERFORATED BEFORE ADMISSION IN 21 CASES OF TYPHOID PERFORATION IN ZARIA

DURATION BEFORE ADMISSION (DAYS)	NUMBER	%
1 Day	2	9.52
2 Days	10	47.62
3 Days	5	23.81
4 Days	2	9.52
5 Days	2	9.52
TOTAL	21	100.00

TABLE 19

LOCATION OF PERFORATION IN 52 CASES OF TYPHOID FEVER IN ZARIA

DISTANCE FROM ILEOCECAL VALVE (CM)	NUMBER	%
0 - 9	4	7.69
10 - 19	13	25.00
20 - 29	19	36.54
30 - 39	4	7.69
40 - 49	3	5.77
> 50	2	3.85
Unspecified	7	13.46
TOTAL	52	100.00

TABLE 20

NUMBER OF PERFORATIONS

NUMBER OF PERFORATIONS	NUMBER	%
1	39	75.00
2	5	9.62
3	4	7.69
4	1	1.92
5	1	1.92
Unspecified	2	3.85
TOTAL	52	100.00

(j) Operative Procedures and Mortality (Table 21)

Simple closure of the perforations in one or two layers was performed in 45 (86.54%) patients while resection and end to end anastomosis was done in 7 (13.46%) patients.

TABLE 21

OPERATIVE PROCEDURES AND MORTALITY IN 52 CASES OF TYPHOID PERFORATION IN ZARIA

OPERATIVE PROCEDURE	NUMBER OF PATIENTS	OUTCOME UNKNOWN	ALIVE	DEAD	MORTALITY %
SIMPLE CLOSURE -					
One Perforation	37	7	14	16	53.33
Two Perforations	5	1	1	3	75.00
Multiple Perforations	3	2	1	-	-
RESECTION, Multiple perforations	7	1	1	5	83.33
TOTAL	52	11	17	24	58.54

(k) Most of the post operative complications from this group are already reflected in Table 15. These patients contributed the most to these complications.

(l) The mortality rates for the perforated and non-perforated cases were 58.54% ($^{24}/_{41}$) and 11.36% ($^{15}/_{132}$) respectively. Thus mortality rate is increased five folds in patients with typhoid perforation.

PART TWO

CHAPTER VA

RESULTS: PROSPECTIVE STUDY

During the study period which lasted 12 months (May, 1986 - April, 1987), the diagnosis of typhoid fever was confirmed in 64 cases. These constituted 0.63% of total hospital admissions for the same period. Typhoid perforation was the third commonest cause of acute abdominal emergencies, accounting for 6.56% of 259 abdominal emergencies treated during the period (Table 22).

TABLE 22

CAUSES OF ACUTE ABDOMINAL EMERGENCIES IN ABU HOSPITAL, ZARIA (MAY, 1986 - APRIL, 1987)

CAUSES	NUMBER	%
Appendicitis	129	49.81
Strangulated external hernia	63	24.32
Typhoid acute abdomen	17	6.56
Intestinal obstruction from adhesions	12	4.63
Intussusception	9	3.47
Intra-abdominal abscess	6	2.32
Volvulus	4	1.54
Intestinal obstruction from tumours	4	1.54
Perforated peptic ulcer	3	1.16
Primary peritonitis	2	0.77
Miscellaneous	10	3.86
TOTAL	259	99.98

Age and Sex Distribution (Table 23)

The peak incidence was in the age group 5 - 9 years. 54.69% of patients fall into the age range 5 - 19 years. 2 (3.13%) of the patients were neonates and on the whole 37 (57.81%) were children. There was no preponderance of disease in any sex as the male: female ratio was 1.13:1.

TABLE 23

AGE AND SEX DISTRIBUTION OF TYPHOID FEVER PATIENTS IN ZARIA (PROSPECTIVE STUDY)

AGE GROUP	MALE	FEMALE	TOTAL	%
0 - 4	6	3	9	14.06
5 - 9	11	6	17	26.56
10 - 14	5	6	11	17.19
15 - 19	1	6	7	10.94
20 - 24	1	4	5	7.81
25 - 29	6	1	7	10.94
30 - 34	2	1	3	4.69
35 - 39	-	-	-	
40 +	2	3	5	7.81
TOTAL	34	30	64	100.00

Place of Domicile

Fifty six percent of the patients came from Zaria or other urban areas while 43.75% came from the surrounding rural areas. Compared with the figures of a consecutive count of general admissions to the various wards of ABU hospital, there was a higher proportion of rural dwellers presenting with typhoid than with other conditions.

The urban/rural ratio for typhoid was 1.29:1 ($^{36}/_{24}$) while the ratio for total hospital admissions was 1.92:1 (1328/693).

This was however statistically insignificant by the Chi square analysis ($P < 0.50$).

Occupation of Patients (Table 24)

For children and dependants, the occupation of the father and/or husband was used for analysis. Farming was the commonest occupation, accounting for 39.06% of the patients.

TABLE 24

OCCUPATION OF PATIENTS WITH TYPHOID FEVER IN ZARIA (Prospective Study)

OCCUPATION	NUMBER	%
FARMING	25	39.06
TRADING	14	21.88
CATTLE REARING	4	6.25
SCHOOLING/STUDENT	4	6.25
TEACHING	3	4.69
SOLDIER	2	3.13
BUSINESS (TOP LEVEL)	2	3.13
MISCELLANEOUS*	10	15.63
TOTAL	64	100.00

*All other occupations not mentioned.

Seasonal Frequency (Table 25 Fig. 4)

The peak incidence of typhoid fever was in August with 11 cases. The monthly difference in frequency was significant by the Chi square analysis. There were 48 and 16 cases during the wet and dry seasons respectively with a ratio of 3:1. This seasonal variation in frequency correlated with the monthly rainfall.

TABLE 25

MONTHLY FREQUENCY OF TYPHOID FEVER IN ZARIA (PROSPECTIVE STUDY)

MONTH	NUMBER	%
JANUARY	3	4.69
FEBRUARY	4	6.25
MARCH	2	3.13
APRIL	2	3.13
MAY	10	15.63
JUNE	9	14.06
JULY	5	7.81
AUGUST	11	17.19
SEPTEMBER	7	10.94
OCTOBER	6	9.38
NOVEMBER	2	3.13
DECEMBER	3	4.69
TOTAL	64	100.03

$X^2 = 21.88$

$P < 0.05$

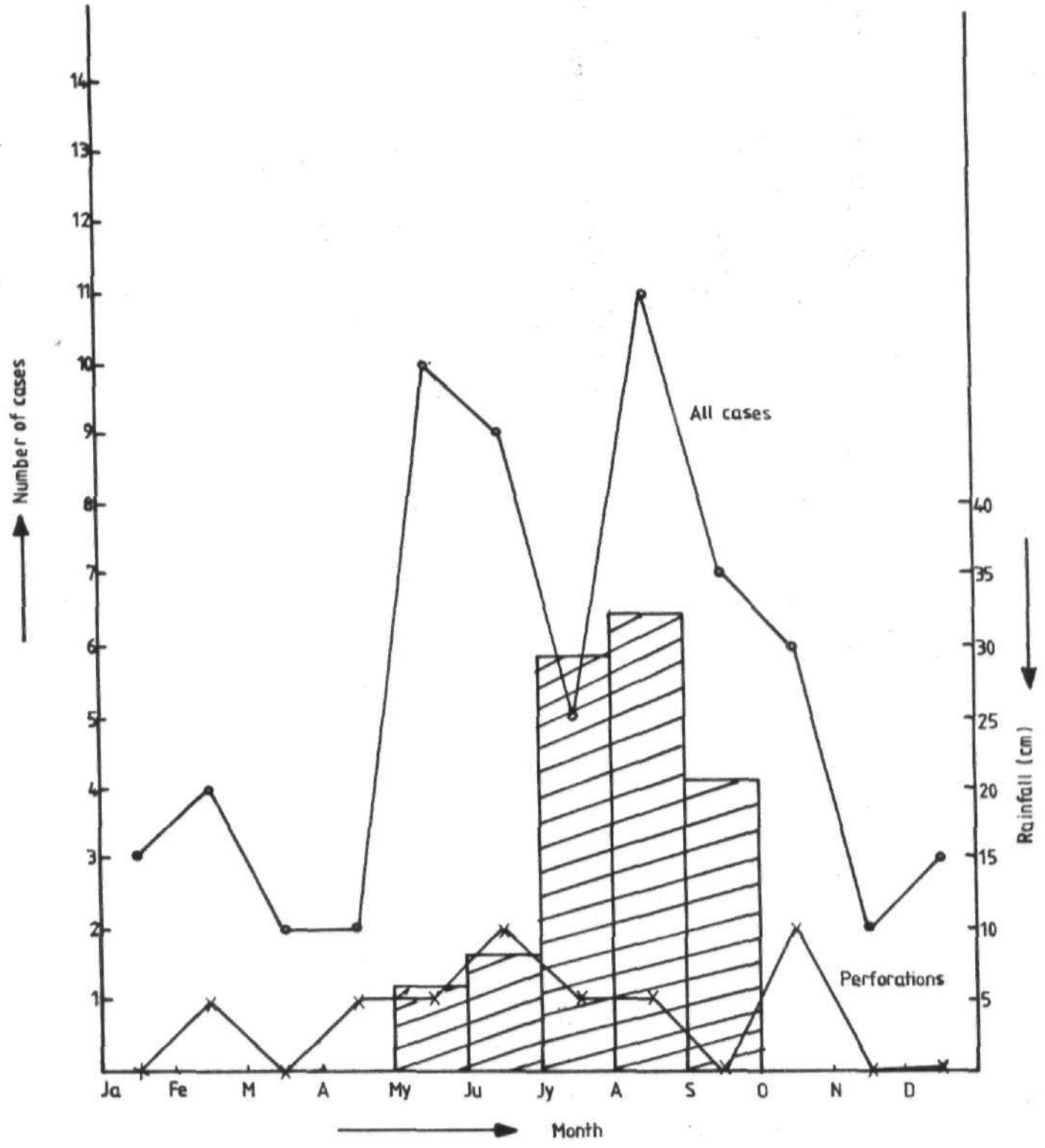


Fig. 4. Seasonal incidence of typhoid fever cases and perforations in A B U Hospital, Zaria (1986/87)

Rainfall

All cases

Typhoid perforations

Clinical Features of Typhoid Fever in Zaria (Tables 26 and 27)

The commonest symptoms of typhoid fever in Zaria were fever, vomiting, headache, diarrhoea and abdominal pain. The other symptoms encountered in the 64 patients are tabulated in Table 26.

Tachycardia is the commonest physical sign followed by dehydration abdominal tenderness, pallor and hepatomegaly in that order. A quarter of the patients had normal temperature on admission (Table 27). None of the patients developed any rose spots.

Fifty nine percent of the patients presented during the first week of illness and the mean number of days spent at home/elsewhere before seeking help in this hospital was 9.25.

TABLE 26

PRESENTING SYMPTOMS OF TYPHOID FEVER IN ZARIA
(Prospective Study) n = 64

SYMPTOMS	NUMBER	%
Fever	58	90.63
Vomiting	33	51.56
Headache	29	49.31
Diarrhoea	28	43.75
Abdominal Pain	28	43.75
Cough	21	32.81
Anorexia	17	26.56
Constipation	17	15.63
Abdominal distension	9	14.06
Chills	7	10.94
Jaundice	6	9.38
Convulsion	6	9.38
Dizziness	6	9.38
Dysuria	5	7.81
Blood in stool	5	7.81
Abnormal behaviour	5	7.81
Irritability	4	6.25
Preceding Constipation	4	6.25

TABLE 27

DISTRIBUTION OF PHYSICAL SIGNS IN 64 CASES OF TYPHOID FEVER IN ABU HOSPITAL, ZARIA (Prospective Study)

PHYSICAL SIGN	NUMBER	%
Tachycardia (pulse >100/min)	38	59.38
Dehydration	29	45.31
Abdominal tenderness	27	42.19
Pallor	26	40.63
Hepatomegaly	26	40.63
Temperature - normal	16	25.00
up to 38.3^{oC}	28	37.50
$>38.3^{oC}$	28	37.50
Splenomegaly	22	34.38
Toxicity	15	23.44
Abdominal distension	14	21.88
Jaundice	11	17.19
Rebound tenderness	11	17.19
Guarding	8	12.50
Absent bowel sound	7	10.94
Bronchitic signs	7	10.94
Free peritoneal fluid	6	9.38
Drowsiness	5	7.81
Diminished bowel sounds	4	6.25
Rigidity	4	6.25

Concurrent Conditions (Table 28)

The concurrent conditions in 64 patients with typhoid fever are shown in table 28, with helminthic infestations occurring in 13 patients. Five of the patients had sickle cell anaemia while 2 of the patients were pregnant.

The miscellaneous conditions included systemic lupus erythematosus (SLE), rheumatic fever, chronic leg ulcer and hypospadias among others.

TABLE 28

CONCURRENT CONDITIONS IN 64 CASES OF TYPHOID FEVER IN ZARIA

CONDITION	NUMBER	%
Intestinal helminthiasis	13	20.31
Urinary tract infection	6	9.38
External herniae	6	9.38
Sickle cell anaemia	5	7.81
Schistosomiasis	4	6.25
Other Septicaemia	4	6.25
Pregnancy	2	3.13
Cardiac valvular lesion	2	3.13
Miscellaneous conditions	15	23.44

Diagnosis

Each of the 64 patients had at least one laboratory confirmation of typhoid fever. S. typhi was isolated from urine, stool, blood and bone marrow in 6.25%, 20.03%, 43.86% and 58.82% respectively of patients tested (Table 29).

Thirty one of these patients had cultures of both blood and bone marrow aspirate. The yield of S. typhi was 11 and 19 for blood and bone marrow respectively and the difference was statistically significant at $P < 0.05$. In 11 patients the bone marrow cultures yielded S. typhi while blood cultures were negative. Conversely in 3 patients, the blood cultures yielded S. typhi while the bone marrow cultures were negative (Table 30). Six of the nine who had

negative cultures from both sites had prior antibiotic therapy before hospital admission. Six of the eleven with positive bone marrow culture but negative blood culture also had prior antibiotic therapy.

The relationship between the duration of illness and relative positivity of the various diagnostic tests is shown in Fig. 5. During the third and fourth weeks of illness, the recovery of Salmonella organism was 75% from bone marrow but a mere 33% from blood.

None of the bone marrow puncture sites became infected.

Twelve out of twenty seven and seven out nine patients had positive confirmation of typhoid fever by Widal agglutination and histological studies respectively. Some of the features of typhoid inflammation are shown in Figs. 6, and 7.

Of a total 57 Salmonellae recovered from 52 patients, 48 (84.21%) were S. typhi, 4 (1.75%) were S. poly-group E, 2 (3.51%) belonged to poly-group C and 1 (1.75%) each to poly-groups A, B and S.

TABLE 29

LABORATORY RESULTS IN DIAGNOSIS OF TYPHOID FEVER IN ZARIA (n = 64)

INVESTIGATION	NOT AVAILABLE	NUMBER AVAILABLE	NUMBER POSITIVE	% POSITIVE
URINE CULTURE	32	32	2	6.25
STOOL CULTURE	33	31	9	20.03
BLOOD CULTURE	7	57	25	43.86
BONE MARROW CULTURE	30	34	20	58.82
WIDAL TEST	37	27	12	44.44
HISTOLOGY	4	9	7	77.77

TABLE 30

SENSITIVITY OF BLOOD AND BONE MARROW (BM)

CULTURES IN TYPHOID FEVER

RESULT OF TEST	NUMBER	%
BLOOD POS. BM NEG.	3	9.67
BLOOD NEG. BM POS.	11	35.48
BLOOD POS. BM POS.	8	25.81
BLOOD NEG. BM NEG.	9	29.03
TOTAL	31	99.99

BLOOD POSITIVE	$^{11}/_{31}$	35%
BM POSITIVE	$^{19}/_{31}$	61.3%

$X^2 = 4.133$

$P < 0.05$

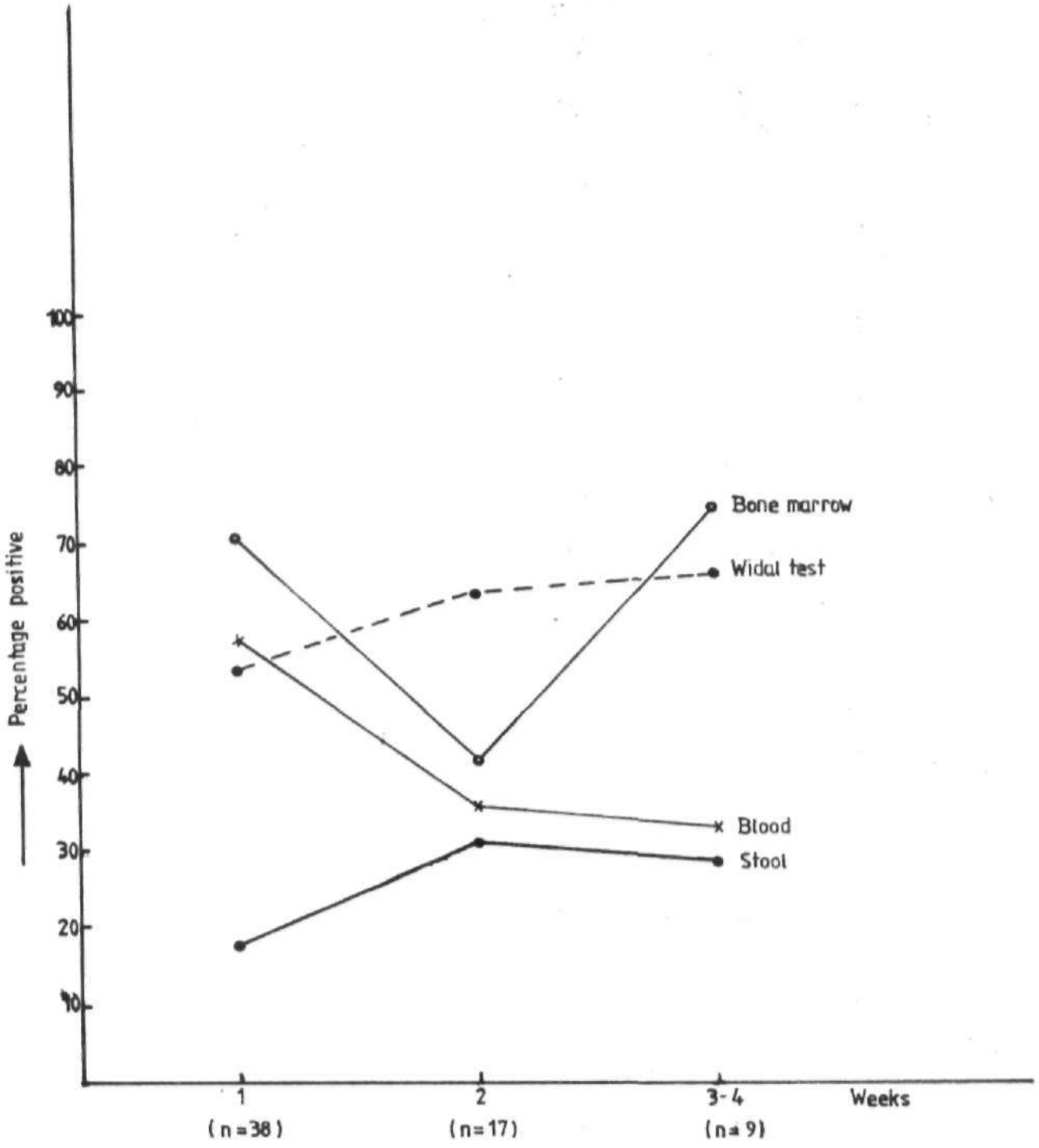


Fig. 5. Relation between duration of illness and relative percent positivity of diagnostic test for typhoid fever

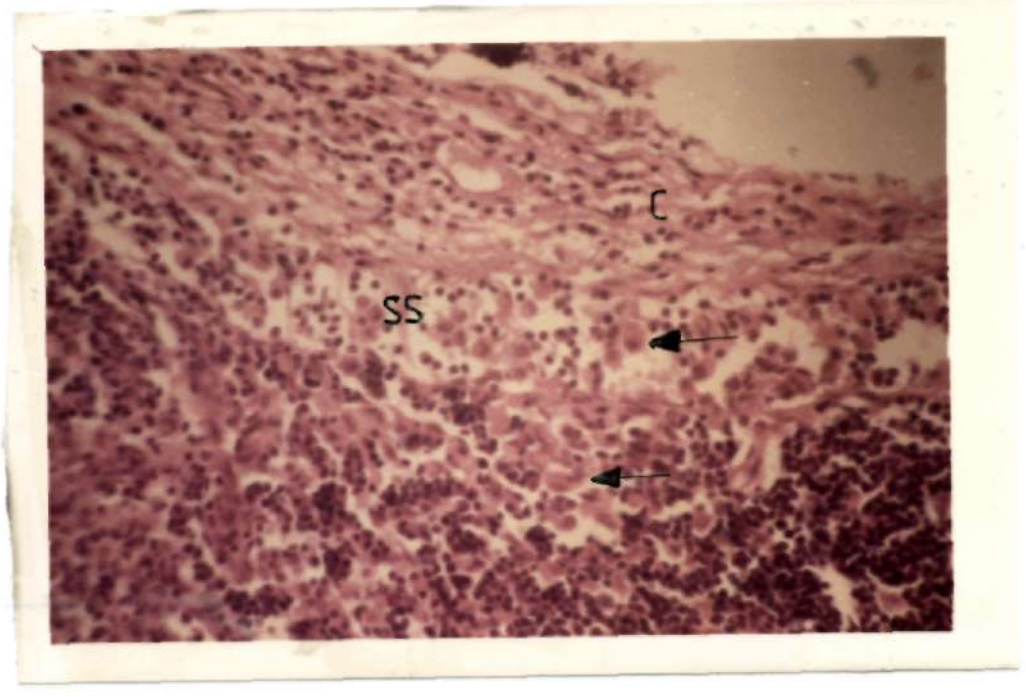


FIG. 6 Mesenteric lymph node showing infiltration of the subcapsular sinus(SS) with characteristic mononuclear cells: macrophages, plasma cells and lymphocytes (arrow). The capsule (C) is loose, oedematous and infiltrated by mononuclear cells. H and E X 400

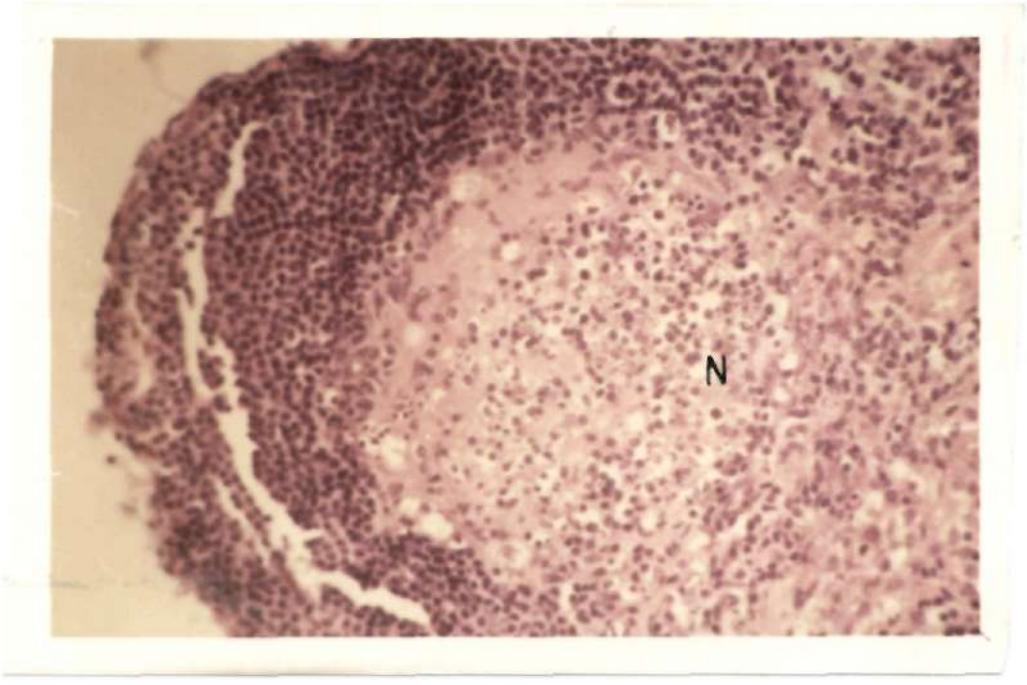


FIG. 7 Focal necrosis (N) in a mesenteric lymph node in a case of typhoid fever. H and E x 400

Sensitivity of the Organisms to Antibiotics (Table 31)

Table 31 shows the general sensitivity of the organisms to 10 antibiotics. The Salmonellae showed high sensitivity to ampicillin, colistin sulphate and chloramphenicol but low sensitivity to the sulphonamides.

TABLE 31

GENERAL SENSITIVITY OF THE ORGANISMS TO THE ANTIBIOTICS TESTED BY THE DISC DIFFUSION METHOD

ANTIBIOTIC	NUMBER TESTED	NUMBER SENSITIVE	%
Ampicillin	40	37	92.5
Colistin sulphate	42	37	88.10
Chloramphenicol	22	19	86.36
Tetracycline	42	36	85.71
Cotrimozazole	35	15	42.86
Streptomycin	34	14	41.18
Sulphonamide	29	10	34.48
Nalidixic acid	10	6	60.00
Furadantin	6	4	66.67
Gentamycin	3	3	100.00

Haematological Findings

Anaemia

Forty seven percent of the patients had Hb of less than 10 g/dl on admission. Four of the patients who presented with significant intestinal haemorrhage had Hb levels below 6 g/dl.

Thrombocytopenia

In most patients, platelet counts were reported as adequate. Only in 15 patients were they actually counted and in 7 of these the counts were below 100 x 10^9/L.

Leucopenia

White blood cell counts were estimated in 52 patients, with 10 (19.23%) having counts below 3 x 10^9/L (leucopenia). The values ranged from 1.2 - 21.4 with a mean of 5.71 $\pm$ 2.36 and a 95% confidence interval of 5.07 - 6.35 x 10^9/L. The mean was significally lower than that reported from Ibadan (38) for normal Nigerians.

Biochemical Findings

Twenty three (45.10%) patients had urea level $>$ 7 mmol/litre. While no patient had hypernatraemia (Na^+ $>$ 148 mmo/l), 28 (54.90%) had hyponatraemia.

Hypokalaemia was a common finding occurring in 68.62% of patients on admission. The potassium level was normal in only 2 of the 9 patients with typhoid perforation. Hypochloraemia and low bicarbonate levels were noted in 29 (56.86%) and 30 (58.82%) patients respectively.

Of the liver enzymes, SGOT was elevated in 24 (71.11%) while SGPT was elevated in 14 (41.18%) patients. Alkaline phosphatase was elevated in only 2 (11.76%) patients. The serum total bilirubin was elevated in 9 (26.47%) patients.

Complications of Typhoid Fever in Zaria (Table 32 and 33)

Forty (62.5%) of the patients developed complications in the course of their disease 12 (18.75%) patients had solely surgical complications, 18 (28.12%) had solely medical complications, while 10 (15.63%) had both surgical and medical complications. As shown in table 32, intestinal perforation, the commonest surgical complication occurred in 14.06% of cases.

The abscesses were located in the subcutaneous plane in 3 patients submandibular region in 1 and intra abdominal (ruptured mesenteric adenitis) in another.

In one patient, culture of the pus obtained from an inflamed gall bladder yielded Salmonella typhi. The only patient who presented with epistaxis had a platelet count of 83 x $10^9/_1$.

Of the 2 patients who were pregnant, one had a still birth at 8 months of gestation while the other delivered a normal baby 1 month after discharge from hospital. None of the patients including the sicklers developed osteomyelitis during hospitalization and up to the first visit in follow up clinic.

The medical complications encountered are shown in table 33. Pneumonia and psychosis were the commonest complications. Myocarditis resulting in heart failure was seen in one patient. Acute renal failure occurred in two patients in whom there was bacteriological confirmation of typhoid fever. One of these two had thrombocytopenia.

TABLE 32

SURGICAL COMPLICATIONS IN 64 PATIENTS WITH TYPHOID FEVER IN ZARIA

COMPLICATIONS	NUMBER	%
Ileal perforation	9	14.06
Abscesses	5	7.81
Peritonitis	5	7.81
Intestinal haemorrhage	4	6.25
Tonsillitis	3	4.69
Intestinal obstruction:adhesions and ileus	2	3.13
Empyema of gall bladder	1	1.56
Still birth	1	1.56
Pressure sore	1	1.56
Otitis media	1	1.56
Epistaxis	1	1.56

TABLE 33

MEDICAL COMPLICATIONS OF TYPHOID FEVER IN 64 PATIENTS SEEN AT ABU HOSPITAL ZARIA

COMPLICATION	NUMBER	%
Pneumonia	9	14.06
Psychosis	6	9.38
Salmonella Schistosoma Complex	4	6.25
Nephropathy	2	3.13
Carditis	1	1.56
Drug reaction (Chloramphenicol)	1	1.56
Miscellaneous	6	9.38

TREATMENT

Upon admission, usual resuscitative measures were carried out for the patient. After obtaining blood for culture antibiotic therapy was commenced usually with chloramphenicol in a dose of 25mg/kg for children and 40 - 50 mg/kg in adults given in 4 divided doses. For patients who had laparotomy, a combination of antibiotics was used in order to deal with the mixed flora especially for anaerobes and Pseudomonas. Table 34 shows the antibiotics used in the treatment of 64 patients with typhoid fever and its complications in Zaria. Hydrocortisone therapy was utilized in only 4 patients; 3 who remained in septic shock and 1 who was very toxic.

TABLE 34

ANTIBIOTICS USED IN THE TREATMENT OF TYPHOID FEVER AND ITS COMPLICATIONS IN ZARIA (n = 64)

ANTIBIOTIC USED	NUMBER OF CASES	%
Chloramphenicol	53	82.81
Ampicillin	8	12.50
Metronidazole	5	7.81
Gentamycin	5	7.81
Ampiclox	4	6.25
Co-trimoxazole	2	3.13
Neomycin	1	1.56
Penicillin	1	1.56

Eighteen procedures were carried out for the surgical complications of typhoid fever as shown in table 35. At laparotomy, the perforation was suture-closed and the peritoneal cavity thoroughly irrigated with saline or sterile water. The fascia was closed using mono-filament nylon sutures and the skin was left open. No drains were left in the peritoneal cavity. In one patient with peritonitis without evident perforation, debridement of ruptured necrotic mesenteric nodes was done.

TABLE 35

INDICATIONS FOR OPERATION IN TYPHOID FEVER IN ZARIA (Prospective Study)

OPERATIVE PROCEDURE CARRIED OUT FOR	NUMBER	%
Ileal Perforation	8	44.44
Typhoid peritonitis	5	27.78
Intestinal obstruction	2	11.11
Empyema of gall bladder	1	5.56
Subcutaneous abscess	2	11.11
TOTAL	18	100.00

Post Operative Complications (Table 36)

The post operative complications seen in the 16 patients who had laparotomy are shown in (Table 36). Peri-operative mortality occured in 4 (25%) patients.

TABLE 36

POST OPERATIVE COMPLICATIONS IN PATIENTS WITH SURGICAL TYPHOID FEVER IN ZARIA (n = 16)

COMPLICATION	NUMBER	%
Wound infection	4	25.00
Suture line leak	2	12.50
Pressure sores	2	12.50
Wound dehiscence	1	6.25
Additional perforation	1	6.25
Intra-abdominal abscess	1	6.25
Pneumonia	1	6.25

Outcome of Treatment (Table 37)

Of the eleven deaths typhoid perforation was responsible for 5, typhoid peritonitis was responsible for 3, while acute renal failure pneumonia, multiple end organ failure, accounted for 1 death each.

TABLE 37

OUTCOME OF TREATMENT OF 64 PATIENTS
WITH TYPHOID FEVER IN ZARIA

OUTCOME	NUMBER OF CASES	%
Recovered	49	76.56
Relapsed	1	1.56
Died	11	17.19
Absconded	3	4.69
TOTAL	64	100.00

CHAPTER VB

TYPHOID PERFORATIONS

(a) Perforation occurred in 7 males and 2 females for a prevalence rate of 20.59% and 6.67% respectively.

(b) The clinical features observed in these patients were not different from those stated in Chapter IVB.

(c) Diagnosis of perforation was made largely on clinical grounds. Abdominal and/or erect chest radiograph in 5 cases demonstrated free air under the diaphragm in 4. The only patient who was managed conservatively showed radiological evidence of air under the diaphragm and S. typhi was cultured from his blood. However bowel perforation was confirmed in all 8 who had operation.

(d) Five (55.56%) of the perforations occurred within the first week of illness, 2 (22.22%) in the second week and 2 (22.22%) in the third week.

(e) The average duration of perforation before presentation was 2.88 days. Two of the patients presented after 5 days of perforation.

(f) In 6(75%) patients, the perforations were located within 30 cm of the ileo caecal valve.

(g) Six patients had single perforations, one had 2 perforations and another one had 3 perforations.

(h) Operative Procedures

One patient was unable to supply surgical materials and was not operated upon. The procedures for the remaining eight are as shown in table 38

TABLE 38

OPERATIVE PROCEDURES AND MORTALITY IN 8 CASES OF TYPHOID PERFORATION IN ZARIA

OPERATIVE PROCEDURE	NUMBER OF PATIENTS	ALIVE	DEAD	% MORTALITY
SIMPLE CLOSURE				
Single perforation	6	3	3	50.00
Double perforation	1		1	100.00
RESECTION triple perforation	1	1	-	-
TOTAL	8	4	4	50.00%

(i) Mortality

Five (55.58%) of the patients with perforation died. The only patient who did not have operative treatment died after 3 days. He could not afford antibiotics, intravenous fluids and surgical supplies.

All patients who presented beyond 4 days of perforation died. The two people with perforations located beyond 30 cm of the ileo caecal valve died, while 3 of the 6 patients with perforations located within 30 cm of the ileocaecal valve died.

(j) Most of the post operative complications from this group have been referred to in table 36. Again, these patients contributed the most to these complications.

(k) The mortality rates for the perforated and non-perforated cases were 55.56% and 10.91% respectively. Thus the mortality rate is increased five times in patients with perforated typhoid.

CHAPTER VI

PROGNOSTIC FACTORS IN TYPHOID PERFORATION

The data available were insufficient to properly assess the effect of the admission - operation interval on mortality. In the retrospective study, this factor was difficult to determine. However in the prospective study there was no difference in mortality between the 4 patients who were operated upon within 24 hours and the 4 who were operated upon after 24 hours. The mortality rate was 50% for each group.

As shown in Table 39, various factors were tested by means of the Student's t test for probable influence on mortality in typhoid perforation. A probability (p value) of less than 0.05 is accepted as significant. Thus age, sex, number of days ill before admission, presence of diarrhoea, haemoglobin level and white blood cell count on admission were found to be of no value as predictors of mortality. Also found to be insignificant were the plasma levels of sodium and potassium, the number of perforations, distance of the perforation, from the ileocaecal value, the operative procedure carried out and the presence of post operative wound infection or anastomotic leak.

However the blood urea level and the duration of perforation before admission were found to have significant effects on the occurrence of mortality. 3 of 11 patients who had normal blood urea (2 - 6.5 mmol/1) died while 16 of 25 with elevated urea level ($>$ 7 mmol/1) died (Table 40). The mean duration of perforation before admission was 1.5 days for those who survived but 2.4 days for those who died. Comparison of these means by the Student's t test show a significant difference in their influence on outcome of treatment (Table 41).

TABLE 39

PROGNOSTIC FACTORS IN TYPHOID PERFORATION IN ZARIA (COMBINED RETROSPECTIVE AND PROSPECTIVE STUDIES)

PARAMETER	t Value	d.f	P Value
Age	0.78	49	>0.10
Sex	0.07	48	>0.10
Number of days ill	1.50	41	>0.10
Diarrhoea	0.66	28	>0.10
Haemoglobin level	1.70	32	>0.05
Plasma sodium level	0.79	34	>0.10
Plasma potassium level	0.56	34	>0.10
Number of perforations	0.59	46	>0.10
Distance of perforation from ICV	1.36	41	>0.10
Operative procedure carried out	0.89	48	>0.10
Wound infection	0.90	34	>0.10
Anastomotic leak	1.31	38	>0.10
Blood urea	2.83	35	<0.01
Period perforated before admission	2.43	26	<0.05

TABLE 40

BLOOD UREA AND MORTALITY IN TYPHOID PERFORATION

BLOOD UREA LEVEL	NUMBER	DEAD	% MORTALITY
< 7 mmol/L	11	3	27.27
> 7 mmol/L	25	16	64.00
TOTAL	36	19	52.78

$t = 2.83$

$P < 0.01$

TABLE 41

PERIOD PERFORATED BEFORE ADMISSION
AND MORTALITY IN 27 CASE OF TYPHOID PERFORATION

OUTCOME	MEAN (DAYS)
SURVIVED	1.5 ± 0.67
DIED	2.47 ± 1.36

$t = 2.43$

$P < 0.05$

CHAPTER VII
DISCUSSION

This is the most comprehensive study of typhoid fever in Zaria. The results of this study show that typhoid fever is common in Zaria and that the surgical complications pose a serious clinical problem. The yearly frequency of typhoid fever and in fact the yearly percentage of total hospital admissions for typhoid do not show any definite pattern. The peak frequency of 58 cases seen in 1983 coincided with the period of a prospective study carried out on the medical wards of ABU Hospital, Zaria (9). When the annual frequency of 64 cases seen in 1975/76 by Bala and Auty (10), is compared to the frequency for 1983 and the present prospective study (64 cases) it becomes clear that the annual frequency of typhoid fever in ABU Hospital, Zaria has not changed much. The low figures for the year 1981, 1982, 1984 and 1985 could be due to insufficent attention to the possibility of diagnosis and inadequate efforts to get confirmation of a clinical suspicion of the disease. This might not be entirely the physicians fault as the decline in the number of confirmed cases in 1984 and 1985 occurred at a time of severe scarcity of laboratory reagents for diagnosis and treatment in the hospital. However the author was obliged to reject many cases who had clinical but not laboratory confirmation of the infection.

Typhoid perforation is the most common complication of typhoid fever in Zaria. It ranked third among the causes of acute abdominal emergencies during the five year period covered by the retrospective study. This contrasts to the report attributed to Davey by Dickson and Cole (2) that there was only one case of perforation of the terminal ileum (? due to typhoid fever) per year in a hospital located in the Northern part of Nigeria in 1959. Bala and Auty (10) reported only 3 cases of typhoid perforation in ABU Hospital, Zaria in 1975/76. It is either that the incidence of typhoid perforation has increased dramatically or that there was under reporting of cases in the earlier reports. The latter appears to be the case.

The peak age group incidence in both the retrospective and prospective studies was in the second quinquennium (5-9 years) followed closely by the third quinquennium. This contrasts with the findings by other authors elsewhere (2, 3, 4, 18) but conforms with the pattern earlier reported from this institution (10). Typhoid appears to be a disease of the older child and young adult. Although no age is exempt, only few patients above 30 years developed typhoid fever in the present study. The explanation for this age distribution may lie in the age structure of the general population and/or in the fact that very young children, most of whom are breast fed are probably not as greatly exposed to the infecting organism as in late childhood when they become more adventurous. Opportunities for contamination during bottle feeding are many. Acquisition of immunity which increases with age presumably from sub-clinical infections may explain the declining incidence of typhoid fever with increasing age (10).

In the prospective study, two 4 - day old babies who were investigated for fever yielded S. typhi from their blood. In one, the mother had a febrile illness with a temperature of 38.2^{o}C coupled with premature rupture of membranes at 8 months gestation. Because her cervix was long, firm and closed, she had caesarean section. Although there was no record of blood culture in this mother there was a suspicion of transplacental passage of Salmonella typhi. In the second, baby was delivered per vaginam at term. Although baby had a fever, the mother was not clinically ill. This raised the probability of infection through the oral route due to contamination of the lower birth canal with faecal material containing S. typhi. The report by Freedman et al (39) lends credence to these suppositions.

In the retrospective study, the disease was more common in males with a male : female ratio of 1.72:1, somewhat similar to Bala and Auty's findings (10) in 1975/76. But this male : female ratio had decreased to 1.13:1 in the prospective study, more in agreement with the reports from Lagos (7) and Ibadan (3).

A larger male:female ratio was expected given the religious practices that allow males more ready access to hospital than females but that was not the case. It is either that children who form the bulk of the patients do not suffer such inhibition or that the level of awareness in the community has improved to an extent that there is a real increase in the number of female hospital attendance or both. The combined studies showed that typhoid perforation occurred predominantly in males. This is in agreement with other authors (4, 5, 15, 17, 40). There is no ready explanation for this male preponderance.

The Ahmadu Bello University Hospital though a teaching hospital functions essentially as a general hospital. It is often the first port of call for most patients from the surrounding villages. The relatively higher proportion of rural dwellers presenting with typhoid than with other conditions to this hospital may be a reflection of the illiteracy, low level of personal hygiene and inadequate water supply that characterise the rural environment. Most of the patients from the urban areas actually came from the slums of Zaria. The level of sanitation of those parts are marginally better than the rural areas. Thus typhoid remains a disease of the poor environment whether urban or rural in which water supply is inadequate.

In the retrospective study the occupational distribution of the patients does not lend itself to further deductions as the occupation 'children' does not indicate the socio-economic status of the patients. However, in the prospective study most of the patients belonged to the group of farmers and traders. The various occupational groups could be divided into 3 broad socio-economic levels namely high, middle and low socio economic classes. The professionals and top civil servants belong to the high group; students, traders and those in the middle level manpower belong to the middle group while the subsistence farmers and poor housewives belong to the low group. Though a crude classification it is helpful in this study.

Only 10.95% of the patients in the prospective study belong to the high socio-economic group while 67.19% of the patients belong to the low socio-economic group. People of a higher socio economic level are likely to enjoy better sanitation and thus be protected from Salmonella infection.

Cases of typhoid fever were encountered throughout the year but with a definite clustering of cases during the rainy season (May to October). In the prospective study there were two peaks; one which coincided with the onset of rains in May and the other with the height of rains in August. These findings agree with those of Ikeme and Anan (3), and Gupta et al (18) but contrasted with findings by other authors (9, 10, 11). As explained by Ikeme and Anan (3) contamination of drinking water is the most potent factor in the dissemination of the disease. Most people from the rural areas around Zaria and the slums of Zaria obtain their drinking water from largely unprotected wells. Therefore during the rainy season when flooding of surface water takes place contamination of water from the wells is very likely. The increase in fly breeding close to homes during the dry season along with the concentration of the organisms in the partially dry wells and rivers may serve to maintain infection all year round. Similar to reports by other authors (4, 2, 17) of a definite seasonal incidence of typhoid perforation, more cases were seen during the rainy season than in the dry season by a ratio of 2:1 in the combined study.

The clinical features of typhoid in Zaria are not different from those reported from other centres (5, 7, 9, 18, 23, 35) although the relative proportions of the various features vary. The absence of rose spots is attributed to the difficulty of recognition of these in the black skin (14). Relative bradycardia was practically not noticed in any of the patients in this study even though over 50% of the patients in the combined study presented within the first week of illness. The reason for the absence of this valuable clinical sign is inexplicable and

serves to buttress the fact that no set of features are pathognomonic for typhoid fever. Thus clinical suspicion coupled with awareness of the variety of symptoms and signs of the disease is the best way to improve diagnosis. In the retrospective study, it was difficult to separate the of patients who perforated prior to admission from those who perforated while on admission. In the prospective series all the 9 patients with perforation had definite features suggestive of peritonitis and/or perforation on admission. The syndrome of enteric fever perforation is more readily recognized by hospital personnel now than in the past but as encountered in the present study several of the cases were operated upon for acute appendicitis or intestinal obstruction only to find at laparotomy that the problem was typhoid perforation or typhoid peritonitis. Careful interpretation of clinical features is required as signs are in abeyance due to extreme toxaemia in these patients (17).

The disparity in numbers between the clinical and proven cases of typhoid fever in the retrospective study highlights the difficulty in confirming diagnosis of the infection in Ahmadu Bello University Hospital Zaria. The introduction of bone marrow aspiration has improved the situation. Gerbasi (1939) who claims credit for the first systematic study of typhoid infection in children by examination of the bone marrow, stated that, sternal marrow culture remained positive throughout the course of illness (41). Huckstep (1960) noted that the bone marrow, unlike the blood, is not sterilized within 2 hours by chloramphenicol therapy (31). Piaggio-Blanco (42) stated that it was more reasonable as a diagnostic measure to search for the causal agent where it is multiplying in the pre-clinical stage than to attempt to track it down in a situation where it appears only transitorily as in blood or by the route of elimination, the excreta. The 61.3% and 35.5% positivity rates for bone marrow and blood cultures respectively in this study compare with the 64.3% and 52.5% of Hirsowitz from Johannesburg (41) and the 69% and 43% of Robertson from Cairo (25). However these values are

lower than the 90% and 40% reported by Gilman from Mexico city (26). The low value for blood culture is probably due to prior antibiotic therapy which invalidates this useful diagnostic test.

During the study, it was often not possible to do the two tests simultaneously and often the bone marrow was delayed for upwards of 48 hours. The blood cultures were repeated in a number of these patients while the bone marrow culture was done once. If these two factors were eliminated, a further amplification of the difference in diagnostic sensitivity of blood and bone marrow cultures in typhoid fever would be expected. The diagnosis of typhoid fever would have been missed in 8 patients had bone marrow culture not been included in the diagnostic tests. These findings agree with those of Robertson (25) that bone marrow culture is easily the most sensitive diagnostic tool. It is a simple, inexpensive procedure, easily learnt and taught, does not require any extensive preparation and is more likely to be positive after prior antibiotic therapy than other cultures. It also is more sensitive during the later stages of the disease. Blood culture on the other hand suffers from invalidation after chloramphenicol therapy and a declining sensitivity with the duration of clinical illness.

The haematological findings are in consonance with those of Scragg et al (35). A possible diagnostic role of the haemogram in typhoid fever is of great interest to many authors. Yap et al (43) found a 32% thrombocytopenia rate in his group of patients and concluded that thrombocytopenia is a common feature in typhoid fever and that the association of fever with leucopenia and thrombocytopenia should alert one to the diagnosis of typhoid in an endemic region. Olurin et al (4) noted the diagnostic value to the surgeon of a total white cell count of between 2 - 8 x 10^9/L in a patient with generalised peritonitis. They felt the most probable diagnosis in such a case would be typhoid fever until disproved.

While Ogunbiyi and Onabowale (7) found leucopenia to be supportive of a diagnosis of typhoid fever; they did not think that high leucocyte count would exclude the diagnosis of the disease. Using the Ibadan values for normal leucocyte counts (38) only 19.64% of the patients in the combined study had absolute leucopenia. The mean leucocyte count for patients with typhoid fever is $5.61 \pm 2.44 \times 10^9/L$ with a 95% confidence interval of $5.26 - 5.96 \times 10^9/L$. While there was no statistically significant difference between the means for the perforated and non-perforated groups, the difference between the mean for all cases of typhoid fever and the mean for normal was however significant ($P < 0.001$). Thus patients with typhoid fever exhibit a certain degree of decreased leucocyte count.

Helminthic infestations are common in the tropics and their frequent occurence in patients with typhoid is not surprising. However the association between sickle cell anaemia and schistosomiasis and typhoid fever is very well established. Due to low levels of serum complements (C_3 and C_4) and a defective alternate complement pathway function in patients with sickle cell anaemia, there is a reduction of complement mediated serum opsonizing activity for Salmonella. This in addition to other abnormalities of reticulo-endothelial system function predispose to salmonellosis in sicklers (44). Idoko et al (45) cited other authors in summarising the probable mechanisms of the symbiotic relationship between Salmonellae and Schistosomes. These are: a decreased anti-Salmonella activity in the serum of patients with Salmonella - Schistosoma complex, enhanced mutiplication of Salmonella in the gut and tegumen of schistosomes and the occurence of tegumental receptors for Salmonella.

In the present combined study 96 (38.55%) patients developed surgical complications, of which typhoid perforation was the most common. The pattern of complications reported by different workers vary (4, 7, 18, 28, 30, 35) and this appears to be related to the geographical area.

The overall frequency of typhoid perforation in this study was 24.50%. This is higher than the 18.9% reported for Accra (15) but lower than the 33.6% for Ibadan (4) and the 78.57% for Ile-Ife (8).

The high proportion of typhoid perforation in this series results from the fact that the private clinics managed the mild cases but referred the more severe and complicated cases with peritonitis to the hospital. This is probably not sufficient explanation. Although the injudicious use of corticosteroids was thought to contribute to the frequency of perforation in India (18) there is no evidence that this is common practice in Zaria. Thus the factors contributing to the high hospital incidence of perforation are not fully understood.

In Zaria intestinal haemorrhage (4%) is far less common than the 13.6% in Ilesha (5) and the 9.3% in Lagos (7). However there are no standardized criteria for making the diagnosis of this 4complication. In the Zaria series only patients with melaena or frank blood in stool were regarded as having this complication.

There were 4 pregnant women in the combined study. Only one, who was treated, carried her pregnancy to term. The others lost their fetuses. Ikeme and Anan (3) reported a similar experience. One of the patients with typhoid peritonitis in whom a perforation had probably been missed, was explored on the basis of pelvic inflammatory disease with spreading peritonitis. This report should help to increase the awareness of hospital personnel working on an obstetrics - gynecology service about the possibility of typhoid being a differential diagnosis in women with pelvic inflammatory disease or complications of pregnancy. Duff et al have summarized the special risks of typhoid to the fetus and pregnant woman (27).

In 2 comparative clinical trials from Santiago, Chile, Snyder et al (46) found that oral chloramphenicol was more effective than parenteral chloramphenicol in the management of typhoid fever. So they recommend the use of oral chloramphenicol where drug sensitive Salmonella is involved. During the initial period of acute fever, however, it was necessary to give parenteral chloramphenicol. Our practice in Zaria is in full accord. 99% and 86% of the Salmonellae isolated in the retrospective and prospective studies respectively showed sensitivity to chloramphenicol. Thus there is no evidence for resistance to chloramphenicol yet in Zaria. Chloramphenicol being readily available and cheaper than ampicillin and co-trimoxazole remained the preferred drug for treating typhoid in Zaria. Indeed in the prospective series there was a 4 year old child whose treatment was begun with ampicillin but remained febrile for 5 days until he had been put on chloramphenicol for 2 days.

Ileal perforation was the major reason for surgical intervention in typhoid fever in Zaria. Except for the experience in Lagos (7) where peritonitis (without perforation) was a more common indication for surgery than perforation the pattern here is similar to the experience in most other places (4, 5). It is likely that the relatively higher incidence of operations for typhoid peritonitis noted in the prospective study is a reflection of the higher index of suspicion, more aggressive operative approach to management and a more thorough search for diagnosis demonstrated during the period.

The major post-operative problem following surgery for typhoid fever is wound infection. This has been defined as clear collection of pus in the wound which empties itself spontaneously or after incision (47). The wound infection rate for the combined study was 29% and there was practically no difference in rate between the two study groups. According to Gilmore (48), operations performed in the presence of pus carry an infection rate of 40 - 50%.

The lower rate obtained in these patients when compared to the 79.31% wound infection rate reported by Olurin et al (4) may be related to the following.

1. The possibility that only severe wound infection was entered into the case notes of the retrospective group of patients.
2. The established practice in ABU Hospital of giving anti-anaerobic anti-microbial agents usually flagyl in addition to anti-aerobic antibiotics to all patients presenting with peritonitis coupled with the practice of delayed primary closure in cases of severe purulent peritoneal contamination.
3. The fact that in this analysis wound dehiscence, which practically occurred in association with wound sepsis, was separately categorized.

The overall mortality rate for both the retrospective and prospective studies was 21.19%. This is similar to the 20.2% rate in Lagos (7), the 24.0% rate in Ibadan (3) 24.5% rate in Uganda (49) but much higher than the 14.3% in Ilesha (5), the 7% rate in Durban (35) and 8.8% in Haryana, India (18). A number of reasons may be responsible for the high mortality rate:

1. The high incidence of perforation in the study group (perforation accounted for 59.18% of deaths).

2. The possibility that milder cases were treated elsewhere while the more seriously ill cases were brought to ABU Hospital.
3. Due to the economic depression and the resultant decrease in hospital subventions, patients were required to provide drugs, intravenous fluids, surgical materials; in many instances either patients were unable to provide these items at all (or in adequate quantities) or they delayed in providing them thereby compromising surgical management.

As explained by Scragg et al (35) the striking variation in mortality rates in typhoid fever treated with chloramphenicol may well be due to variation in the severity of the disease in different parts of the world. Could the disease seen in Zaria be the severe type? Are there host factors responsible for the mortality of the disease? To answer these questions a well planned and controlled immunological study is necessary.

The probable causes of death in Zaria are not too different from those seen elsewhere (11). Toxaemia with or without myocarditis and septic shock remain the major causes. But this is largely conjectural as no electrocardiographs were done for these patients and no post mortem examinations were conducted. The absence of post mortem examinations in this study was a major drawback as proper elucidation of the cause(s) of death was impossible. The reason for the lack of post mortem examinations has been stated earlier (see page 2).

TYPHOID PERFORATION

The classical text book description of typhoid perforation was aptly summarized by Dunkerley (40) in 1976 that perforation occurs in less than 5% of total typhoid cases but contributes 30% to mortality, is usually more common in patients with diarrhoea, meteorism and intestinal haemorrhage. It is more common in the third week of disease, generally located within 30 cm of the ileocaecal valve and 2 or more perforations occur in 10% of cases. Mortality rate in that era (pre-chloramphenicol) was in the region of 75-95%.

Issues relating to the incidence, clinical features, sex ratio, seasonality and perforations prior to hospital admission have been discussed above. The age and sex distribution is consonant with Archampong's findings (17).

In the combined study, 53.33% perforated within the first week of illness according to the histories obtained from patients. Although most textbooks stress that typhoid perforations usually occur during the third week (19, 40), many other reports confirm a greater number occur in the first week (2, 4, 17, 33, 40). It would appear the disease seen in ABU Hospital, Zaria has an accelerated course.

Whether this is due to a highly virulent local strain of S. typhi or due to lowered immunological response by the host is yet to be worked out. Biopsies from early perforations with positive blood culture do not show the typical typhoid lesions but rather aggregations of lymphocytes and plasma cells reminiscent of an allergic response (17).

The patients still present late to hospital. Most of them stay at home for 2 or more days before seeking help at the hospital. This may be due to the rampant practice of self medication be it from patent medicine stores or from herbalists, and the attitude of seeking help only when all else fail.

Seventy percent of the perforations were located within 30 cm of the ileo caecal junction. This is in conformity with the findings of most authors (33, 40, 50). Solitary perforations were the commonest occurring in 75% of the cases. This figure is comparable to the 60.3% from Ibadan (4) and the 71.9% from Accra (17) but lower than the 83.33% from Addis Ababa (51) and the 95% from Baltimore (50).

Eighty seven percent of the surgical procedures for typhoid perforation were simple closure. In the combined study resection and end to end anastomosis (which was done in 13.33%) was used only for multiple perforations and/or severely diseased bowel. This method of approach conforms to that advocated by many authors (2, 4, 17, 30, 33, 40, 51). What is required is the most simple and least

traumatic procedure that stops further peritoneal contamination and cleans out the peritoneal cavity. Simple closure in 2 layers using a suitable non-absorbable suture coupled with thorough irrigation of the peritoneal cavity does that well in most cases. This avoids prolonged anaesthesia in an already compromised patient.

The case of the patient in the prospective study with clinical and radiologic evidence of typhoid perforation but who could not provide materials for adequate management illustrates one of the major problems of management in Zaria. Typhoid perforation alone is bad news. To be incapacitated by the lack of facilities for adequate care is unfortunate.

The pattern of post-operative complications show that most of the problems following surgery for typhoid fever can be attributed to typhoid perforation surgery. That is to say, surgery for other complications of typhoid fever do not invite much morbidity and mortality. The overall wound infection rate for typhoid perforation surgery is 54.55%. This is still lower than the figure cited from Ibadan (4). It is worthy of note that disseminated intravascular coagulation (DIC) occurred as a clinical event in only one patient in this study. This is in agreement with Butler et al (21) who stated that although DIC occurred commonly in typhoid fever, it appeared to be a sub-clinical event. Post-operative complications were in most cases best dealt with by re-operation. This line of management is also advocated by other authors (2, 4). This is because at the stage the patient is developing post-operative complications, the typhoid fever is usually under control.

In this study, of the 28 deaths due to typhoid perforation, 15 occurred within 48 hours of admission or surgery. Most of these deaths were due to toxaemia and gram negative shock. The major causes of death and/or morbidity in the later post-operative period were, pneumonia, wound sepsis, pelvic abscess, faecal fistula, anastomotic leak, post-operative bowel obstruction, prolonged ileus, and acute renal failure.

Two patients presented with acute oliguria. In one the initial diagnosis was indeed acute glomerulonephritis. However further investigations confirmed the diagnosis of typhoid fever. In the other diagnosis of typhoid perforation was made at admission and S typhi was recovered from blood. Despite appropriate therapy in both instances the patients died from renal failure. Although no post mortem examinations were performed on these 2 patients, the clinical course was reminiscent of that of the 6 patients dying of renal falure in the series by Lwanga and Wing (52). Histopathological findings in their patients who developed acute renal failure included acute tubular necrosis, tubular casts of haemoglobin and proliferative glomerulonephritis possibly due to an immunologic process. Thus while earlier writers attributed renal failure in typhoid fever to bacteraemic shock, they attributed this to the occurrence of massive intravascular hemolysis and would expect it to be more common in areas where G.6.PD deficiency is more common. To properly understand the renal complications of typhoid fever in our environment where autopsies are stoutly refused, a prospective study of renal biopsies in typhoid fever patients would be necessary.

The influence of various factors on the prognosis of typhoid perforation have been assessed. The age was not a significant influence and this agreed with Mulligan (5) and Scragg et al (35) but contrasted with Ikeme and Anan (3). Women are not more susceptible than men. This contrasts with the findings of Archampong (17) but is consonant with Mulligan's (5). In this study, the number of days ill before presentation to hospital was not a significant prognostic factor. This contrasts sharply with Archampong (15) and Efem (53). The fact that most of the perforations occurred in the first week and that most of the patients presented 2 -3 days after the event may explain why the duration of illness before presentation was not a sensitive prognostic factor in this study. The number of perforations or the operative procedure eventually carried out did not influence the outcome of treatment.

This must mean that all things being equal, once a patient is on the operating table, no case should be considered unsalvageable. Adequate pre-operative resuscitation with correction of electrolyte abnormalities before surgery blunts the effects of hypokalaemia and hyponatraemia and may explain their worth as prognostic factors. Two factors, however stand out clearly as good indicators of prognosis in this study; the blood urea level and the duration of perforation before admission. This is in total agreement with Archampong (15). To improve the prognosis in typhoid perforation, patients must present early to hospital and be adequately and energetically resuscitated before surgery is performed. Late presentation to hospital may not entirely be the patients fault as some private clinics or general hospitals keep these patients for days usually without adequate resuscitation and refer them only when the patients pursue a down hill course.

CHAPTER VIII

CONCLUSIONS AND RECOMMENDATIONS

PART A: CONCLUSIONS

From both the retrospective and prospective studies, the following conclusions can be drawn:-

1. Typhoid fever is a common disease in Zaria.

2. It is more common in males than females.

3. It is most common in the second quinquenium (5 - 9 years).

4. Most of the affected patients come from areas characterized by inadequate water supply and poor sanitation.

5. There is a definite seasonal variation in incidence with most of the cases seen during the rainy season.

6. The clinical features of this disease are not different from those noted elsewhere.

7. The commonest concurrent condition with typhoid fever was urinary tract infection.

8. Culture of bone marrow aspirate is the most sensitive diagnostic test. Sensitivity is high even later in the disease. It is simple, inexpensive and practicable in many hospitals.

9. Surgical complications were more common and more problematic than medical complications of typhoid fever.

10. Intestinal perforation is the commonest complication of typhoid fever in Zaria. It ranked third among the causes of surgical abdominal emergencies during the period covered by the study. The hospital incidence of perforation is 24.50%.

11. The mortality rate of typhoid fever in Zaria is high (21.19%) and the complication of perforation accounts for 59% of deaths.

12. The commonest post operative complication in Zaria is wound sepsis.

13. The Salmonellae showed high sensitivity to chloramphenicol, ampicillin and tetracycline. Chloramphenicol is the commonest antibiotic used in the treatment of typhoid fever in Zaria.

14. Blood urea level and duration of perforation before admission are the most significant prognostic factors in typhoid perforation.

15. A common problem in management which has an important bearing on prognosis is the unavailability of resuscitative materials and reliance on the patient to provide same.

PART B: RECOMMENDATIONS

1. The government should provide good water supply to our city slums and rural areas.

2. The present national environmental sanitation exercise is a welcome development, but it should be intensified along with public education on personal and communal hygiene.

3. There is a need for research into the host immunological response to typhoid infection with a view to identifying factors that may help in reducing the mortality.

4. Further work needs to be done to elucidate the kidney response to typhoid infection. This should include a prospective study of renal biopsies in patients with typhoid fever.

5. Bone marrow aspiration for culture is recommended for incorporation into the diagnostic armamentarium of teaching and state specialist hospitals.

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APPENDIX 1

SURGICAL COMPLICATIONS OF TYPHOID FEVER IN ZARIA

BY: DR. J.A. AKOH

A. PERSONAL DATA:

Serial No: ..... Hospital No: .....

Name: .....Age: ..... Sex:.....

Address:.....

Occupation:..... Religion:.....

Marital Status: ..... Ward:.....

Date of Admission: ..... Discharge:.....

Month of Year.

B. CLINICAL FEATURES: (Code Number)

1. Symptoms: .....
2. Signs: .....
3. Period before presentation: .....
4. Concurrent conditions: .....

C. LABORATORY DATA:

1. C.B.C. & Differential: .....
2. U/E, Cr: .....

   LFT: .....
3. Urine culture: .....

   Stool culture:.....

   Blood Culture: .....

   Bone Marrow Culture: .....
4. Widal agglutination test: .....

   2/52 later: .....
5. Radiology: .....

   .....

D.	COMPLICATIONS	PERIOD OF
1.	.....	.....
2	.....	.....

3. ....

4. ....

5. Perforation:

Time: .....

Duration: .....

Perforation operation interval: .....

No. of perforations: .....

Distance from ileocecal valve: .....

Culture: peritoneal fluids: .....

Histology: Mesenteric node biopsy: .....

edge of perforation: .....

Serum: Urea...Na^+.....K^+.....Cl^-.....

HCO_3^-..... Cr.....

E. TREATMENT:

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Post op. complications:

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F. OUTCOME:

Recovery: .....

Relapse: .....

Death: .....

Cause of death: .....

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