CLINICAL AND EPIDEMIOLOGICAL FEATURES OF *SALMONELLA* SEPTICAEMIA AT THE UNIVERSITY TEACHING HOSPITAL, LUSAKA

BY

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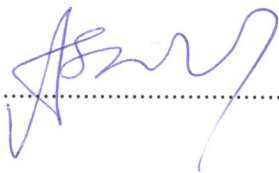
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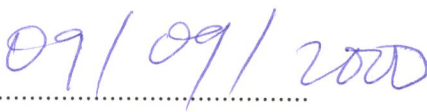## UNIVERSITY OF ZAMBIA
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DECLARATION

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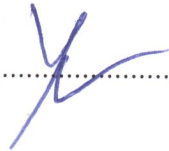
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APPROVAL

This dissertation of **ALI SALIM ALI** is approved as fulfilling the requirements for the award of the Degree of Master of Medicine in Internal Medicine of the University of Zambia.

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ABSTRACT

SETTINGS

Study was conducted at the University Teaching Hospital medical wards. 98 Patients with positive blood cultures for Salmonella *spp.* were studied.

OBJECTIVES

To describe clinical and epidemiological features of Salmonella septicaemia at the University Teaching Hospital, Lusaka.

METHODS

Consecutive patients who met the inclusion criteria were recruited into the study.

All patients were clinically evaluated. Bloods cultures, slides for malaria parasite, urea and electrolytes, HIV test and Haemoglobin, were done to all patients using approved routinely used methods at University Teaching Hospital. *Salmonella* serogrouping and antibiotic sensitivity test were done at the University of Colorado USA.

RESULTS

Greater number of the patients was between 23 years and 39 years of age, with median of 32 years. *Salmonella typhimurium* is the commonest isolate (60%). *Salmonella munchen* and *S.heidelberg, which were recently* isolated for the first time in Zambia, were also isolated in this study (2% each). *Salmonella* isolates are 100% sensitive to

Ceftazidime, Ciprofloxacin and Ceftriaxone. Chlromphenicol intermediate sensitive by 96%. The rate of HIV among *Salmonella* septicaemia patient was found to be 75.5%. 75% of these patients had major co-existing disease conditions such as, pulmonary tuberculosis (35.7%), Meningitis (20.4%), Kaposis sarcoma (7.1%), etc.

CONCLUSION

Clinical and epidemiological features of the *Salmonella* septicaemia in our patients could not be determined due to co-existence of major disease conditions, which confound the clinical manifestation of *Salmonella* septicaemia.

ACKNOWLEDGEMENTS

DEDICATION

I dedicate this work to my wife Lydia John Zungufya and my three beautiful daughters;

Nasrat, Gheda and Raya for their love and support.

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LIST OF ABBREVIATIONS

HIV   *Human Immune virus.*

UTH   University Teaching Hospital.

AIDS   Acquired Immune Deficiency Syndrome.

ZDHS   Zambia Demography and Health Survey.

Hb   Hemoglobin.

ELISA   Enzyme-Linked ImmunoSorbant assay.

CDC   Center for Disease Control.

FBC&ESR   Full blood count and erythrocytes sedimentation rate

Fig.   Figure.

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CHAPTER ONE

BACKGROUND

1:0:0. Zambia.

Zambia is a land locked country covering an area of 752,612 square kilometres and consisting of about 2.5 percent of the area of Africa. It shares borders with Democratic Republic of Congo and Tanzania in the north, Malawi and Mozambique in the east, Zimbabwe and Botswana in the south, Namibia in the southwest and Angola in the west. .

Zambia lies between 8 and 18 degrees south and between 20 and 35 degrees east. It has a tropical climate and vegetation with three distinct seasons: the cool dry season from May to August, a hot dry season during September and October and warm wet season from November to April.

Administratively, the country is divided into nine provinces and 67 districts. The 1990 national census reported a total population of 7.8 million, with growth rate of 2.7 percent per annum. Zambia's population is essentially a young one, approximately 50% of the population comprises children aged 15 years or younger.

Zambia is one of the three most urbanised countries in Africa, along with South Africa and Algeria. 45% of Zambians live in the urban areas, most of which are located along the line of rail, where the social amenities such as housing, sanitation and so on have been considerably over stretched. Moreover, poor economic performance has resulted in high employment especially in urban areas (ZDHS, 1996). As has been pointed out, Zambia's demographic and socio-economic situation is conducive to the spread of communicable

diseases such as *Salmonella* infections, including sexually transmissible infections and AIDS (Matondo, 1993).

1:1:0. Lusaka

Lusaka has been the capital city of Zambia since 1935; its population is now close to 2 million. As a result of urbanisation Lusaka has now attracted huge in-flows of intra-country migrants and migrants from the surrounding neighbouring countries, which has created tremendous pressure on Lusaka's employment prospects and social amenities including health care facilities (Matondo, 1997). The average population density in Lusaka ranges from 50 people or more per square kilometre. Life expectancy at birth in 1990 was 46 and 48 for male and female respectively (ZDHS, 1996).

Lusaka urban public health system is organised through a network of 22 urban clinics, which provide primary health care for the population close to where they live. In addition, there is a thriving private sector. There are several private clinics scattered all over the city. Lusaka has three public hospitals; Maina Soko Military Hospital, Chainama Hills Hospital and the University Teaching Hospital (UTH). University Teaching Hospital is the largest hospital in Lusaka, and in the whole country. In addition, there are also two small private hospitals in the city. However, apart from the western style health services, there are many traditional healers in practice, providing a wide variety of services all over the city (Matondo, 1997).

1:2:0. Salmonellosis.

Salmonellosis is a worldwide problem with an impact on the health and economy (Anderson, 1976), it has the potential for epidemic occurrence both in humans and animal population with high virulence and mortality (Gorbach, 1988).

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Salmonella typhi and other *non-typhi Salmonella* infections remain a major cause of morbidity and mortality in the tropics (Anderson, 1976). They are a constant threat and must be considered in the differential diagnosis of any febrile patient.

Studies done in the tropics reveal that the prevalence and incidence of salmonellosis are high and increasing (Anderson *et al.,* 1976; Wittler *et al.,* 1 989 and Pegues *et al.,* 1994).

Salmonella infection is not rare in Zambia (Dube, 1984). *Salmonella* bacteraemia cases at UTH have been on the increase since 1985. The rate of *Salmonella* isolation has dramatically increased to a level where it might be said to be an epidemic (Salim *et al.,* 1998). The actual incidence and prevalence of *Salmonella* septicaemia at UTH is not known, although the UTH board of infectious diseases control committee reported 322 cases of *salmonella* septicaemia from January to August 1997. This is the first study to address this problem, according to our knowledge.

Increase in the incidence of *Salmonella* infection may be due to the growing number of people with HIV infection, neglected sanitary facilities, lack of safe water and the problem of contamination in mass food processing industries (Gorbach, 1988).

The risk factors for *salmonella* infections include: Malaria, HIV, Schistosomiasis, malnutrition, sickle cell disease, malignancy, G6PD-deficiency etc (Christie, 1987).

The diagnosis of *salmonella* bacteraemia is difficult to make, as it is based entirely on blood cultures (Petit *et al.,* 1994; Hornick, 1985 and Edelman, 1986). In many hospitals in the developing countries blood cultures are not done due to lack of resources (Petit *et al.,* 1994; Wicks, 1971), indeed even with the availability of adequate microbiological facilities and

materials, a sizeable proportion can be negative due to the high rate of self administration of antibiotic medication (Wicks, 1971).

Clinically, it is difficult to differentiate *Salmonella* bacteraemia from other causes of septicaemia. Common febrile illness such as malaria and tuberculosis can present in a similar fashion and complicate the diagnosis by clinical criteria alone (Vugia *et al.*, 1993).

Treatment of *salmonella* septicaemia is difficult and expensive due to the worldwide circulation of multidrug resistant strains (Munoz, 1993), in part due to the indiscriminate use of antibiotics both in human and veterinary practice (Adeleye *et al.*, 1993).

CHAPTER TWO

LITERATURE REVIEW

2:0:0. Bacteriology.

More than 2500 serotypes of *Salmonella spp* have been identified, *Salmonella typhi* was the first member to be described and is the causative organism of typhoid fever. (Hornick *et al.*, 1979; Holt *et al.*, 1994).

Two classification systems are in use, one system (Kauffman-White) recognise each serotype as specie. The second system (Edwards-Ewing) recognises three species: *S. cholerasuis, S. typhi* and *S. enteritidis*. The remaining species in the Edward-Ewing system are biotype of *S. enteritidis*. *Salmonella* isolates can also be characterised according to susceptibility to antibiotic and various bacteriophages (Boyd *et al.*, 1951).

Salmonella are gram-negative flagellated, non-sporulating, facultative anaerobic bacilli, which ferment glucose. They grow well on ordinary media and form pale colourless colonies on Mac-conkey medium since they are non-lactose fermenters (Mandell, 1976).

They may be distinguished from each other by biochemical and serological tests. *Salmonella* have a somatic "O" antigen situated on the surface of organism, which is a lipopolysaccharide and is group specific. The flagella "H" antigen is a protein and species specific. The "Vi" capsular antigen is a polysaccharide, which is related to invasiveness and is the basis of a typhoid vaccine (Sadallah, 1990).

2:1:0. Epidemiology.

Salmonellosis exists throughout the world (Edelman, 1986). All age groups are vulnerable, but at the extremes of age, the disease can be more severe (Gorbach, 1988).

Salmonellae are primarily pathogens of lower animals. The reservoir of infection in animals constitutes the principal source of non-typhi *Salmonella* organisms that infect man, although infection may be transmitted from person to person.

Salmonellae have been isolated from almost all animal species, including poultry, cows, pigs, pets, lizards, snakes etc (Aserkoff *et al.*, 1970).

A few *Salmonella* serotype are highly host-adapted and tend to be virtually "species specific". For example, the only known reservoir for *S .typhi* is man, and infection with this organism strongly implies direct or indirect exposures to human source. Chimpanzees, mice and other animals have been infected with *Salmonella species* experimentally, but are not known to be infected in nature. *Salmonella paratyphi* A, B and C is thought also to have reservoir primarily in man, although animal infections are observed occasionally in nature (Rubin *et al.,* 1982).

Animal salmonellosis has been reported from all over the world including Africa and Zambia in particular (Sharma *et al.*, 1996). In Zambia, *Salmonella spp* has been isolated from dead, in shell chicken embryos (Kabilika, 1996) and other chicken specimens submitted for necropsy (Sharma *et al.*, 1991). It has also been isolated from table eggs and chicken carcasses ready to enter the market (Hang`ombe, 1998).

Meats and dairy products are often implicated in *Salmonella* outbreaks (Hornick, 1985). The most accurate information on sources of human salmonellosis is derived from studies of outbreaks. Poultry and poultry products are the most important source of human infection and are estimated to be responsible for about one-half of the common-vehicle epidemics (Sharma *et al.*, 1991). *Salmonellae* in faeces of infected hens may contaminate the surface of eggshells or penetrate into the interior of the egg through hairline cracks. In hens with ovarian infection, organism may gain access to the yolk (Kabilika, 1996).

Acquisition of non-typhi salmonellosis from contaminated water occurs, but this mode is more characteristic of *S. typhi*. Since humans are the only reservoir of *S. typhi*, direct or indirect contact with a person with typhoid fever or with a chronic carrier is necessary for infection (Aserkoff *et al.*, 1970).

Salmonella spp has been isolated more from males than females (Aserkoff *et al.*, 1970). Cross-infection with spread from person to person by contact, or by fomites is responsible for virtually all the outbreaks in neonatal nurseries and in paediatric wards and is important in many outbreaks among hospitalised adults. The vulnerability of hospitalised patients to *salmonella* infection is related in part to the presence of major underlying diseases and to chemotherapeutic agents that alters resistance to infection. Salmonellosis tends to be unusually severe in institutionalised patients, with overall case fatality ratio of 2.3 percent. The case fatality ratio is highest in nurseries 7.0 percent and nursing home 8.7 percent (Baine *et al.*, 1973).

In a study from the Kenyatta National Hospital in Nairobi, the risk factors for nosocomial salmonellosis were determined: These include recent use of antimicrobials (91%) and pre

existing health impairment such as malnutrition, multiple hospitalisation and HIV-infection (Paton et al., 1991).

2:2:0. Pathogenesis.

Studies show a large number of Salmonella must be swallowed in most instances to produce disease in healthy human beings. Limited studies with several serotypes, including S. typhi, show that in general, 10^6 - 10^9 organism must be ingested to produce symptomatic infection (Finlay, 1994a). However, in the event of infection with the unusual virulent organisms or in the patients with reduced resistance, symptomatic infection may result from extremely small number of organisms (Goldberg, 1996).

Low pH seems to make the stomach unsuitable for colonisation by Salmonella. Smaller doses of Salmonella can cause infections if the stomach pH is increased (Finlay, 1994b). In addition to low pH, other adverse conditions encountered by Salmonella in the stomach are digestive enzymes (Bliska et al., 1993). The small intestine provides other protective mechanism through motility and normal flora. Epithelial cells render the intestinal barrier impermeable to solutes and water. Although the exact site of entry is not definite, Salmonella preferentially pass through the intestinal barrier at the M cells (Kohbata et al., 1986). Alteration of normal flora by antibiotics markedly reduces the size of inoculum required to produce Salmonella infection in animals and humans and prolongs the convalescent carrier state. Prior antibiotic therapy also enhances the possibility of infection with antibiotic-resistant Salmonella strains (Pace et al., 1993).

Salmonella that survive the antibacterial mechanism in the stomach and upper bowel multiply in the small intestine. Infections do not progress beyond local lymph nodes unless in more intrusive serotype like Salmonella enteritidis (Finlay, 1994b).

Patients with impaired cellular and humoral immune mechanism are at increased risk of development of salmonellosis. Impairment of host defences caused by malnutrition, malignancies, infection with immunodeficiency viruses or therapeutic measures such as corticosteroid or immunosuppressive therapy also predispose to infection and disease (Christie, 1987; Goldberg, 1996).

Patients with sickle-cell haemoglobinopathies, malaria and bartonellosis, all associated with haemolysis, have an increased incidence of salmonellosis. The mechanism responsible for the alterations in susceptibility in these diverse states are multiple and complex. A defect in the alternative complement pathway has been demonstrated in patients with sickle cell anaemia. Haemolysis experimentally induced marked enhanced susceptibility to challenge with *S. typhimurium* in mice (Mahan, 1994).

The mechanism by which *Salmonella* organism causes invasive, bacteraemic disease as opposed to enterocolitis alone was the focus of several studies (Galan *et al.*, 1991; Miller, 1990). One invasive serotype, *S. dublin,* contains an 80-kb pair virulence plasmid with a highly conserved 8.2-kb pair region. The presence of this plasmid decreases the inoculum necessary to cause mortality in mice by more then 400 percent (Lester *et al.*, 1988; Gulig, 1990). The mechanism by which it confers increased virulence is not known. Possibilities include enhanced production of lipopolysacccharide, avoidance of microbicidal properties of host mononuclear cells, or production of toxins (Gulig, 1990). The property of invasion by *S. typhimurium* is associated with a group of "invasion" genes invA, invB, invC and invD (Galan *et al.*, 1991).

Another virulence factor is the ability of *Salmonella* organisms to survive within macrophages. *Salmonellae* are phagocytosed, but not killed by host cells such as macrophages and polymorphonuclear leukocytes, making them unamenable to antibiotic therapy. The participation of phagocytes explains the hyperplasia and hypertrophy of reticuloendothelial system (Goldberg and Rubin, 1996; Chinsembu 1996). *Salmonella* persist in phagocytes through inhibition of a respiratory burst that produces oxygen radicals, inhibition of phagosome-defensin formation persistence in or escape from the phagolysosome, resistance to anti-microbial peptides and nutrient limitation (Miller, 1990).

The role of IgA in immunity was also investigated, and the author postulate that this antibody inhibit an important gut adherence step (Michetti *et al.*, 1992).

The ability of *Salmonella* to acquire iron in the host is an essential adaptive component of the disease process (Litwin and Calderwood, 1993). For *Salmonella* to establish an infection, they must pirate iron from the host. Therefore, *Salmonella* species have evolved mechanism to secrete high-affinity iron-biding chelators that sequester iron from the host environment (Crosa 1989)

2:3:0. Clinical manifestation.

The relative prominence of certain clinical manifestation in person infected with *Salmonella* forms the basis for the designation of several clinical syndromes: like enterocolitis, enteric fever, bacteraemia, localised infection and chronic enteric and urinary carrier state.

2:3:1. Enterocolitis.

Acute enterocolitis is the most common clinical expression of *salmonella* infection. Incubation period is 6 to 48 hours and the illness begins with nausea and vomiting. Myalgia and headache are common. The cardinal manifestation is diarrhoea, which may vary from few loose motions to fulminant diarrhoea. In other instances stool may be associated with tenesmus and blood. Fever and chills are common. Abdominal cramps occur in about half of the patients, with increase in bowel sounds and abdominal tenderness is present

Electrolyte and water depletion may be severe during illness, leading to shock (Paton *et al.*, 1991). Toxic dilatation of the colon has been described as a rare complication and transient bacteraemia occurs in about 5 percent of the patients (Salyers and Whitt, 1994).

2:3:2. Enteric fever.

Enteric fever is a clinical syndrome produced classically by *S. typhi* and also at times by *S. paratyphi A, S. paratyphi B* and *S. paratyphi C.* Other serotypes occasionally produce the clinical picture of enteric fever. Enteric fever (typhoid) is a severe prolonged disease with a high rate of complications.

The incubation period is usually 10-14 days, but may vary from 7 to 21 days. The onset is insidious and the initial manifestations are non-specific and consist of fever, malaise, anorexia, headache and myalgia. Fever ranges from 38 to 40 degrees centigrade by the end of first week. Either constipation or diarrhoea may occur and respiratory symptoms including, cough and sore throat may be prominent. Neuropsychiatric manifestation, including confusion, dizziness, seizures or acute psychosis may be predominant in an occasional case.

The patient usually appears acutely ill. Fever is usually prominent and in many instances the pulse is slow relative to the temperature. Rose spots, 2-4 mm erythromatous maculopapular lesions that blanch on pressure, appear characteristically on the upper abdomen in crops of approximately 10 lesions. The lesions are transient and resolve in hours to days (Litwack, 1970). Cervical lymphadenopathy may be present. Examination of the chest may reveal moist rales. The abdomen is tender, especially in the lower quadrant. Abdominal distension is common and peristalsis is often hypoactive (Hornick, 1970). The sensation of displacing air and fluid filled loops of bowel is characteristic. Hepatomegaly is noted in about 25-50 percent of the patients and soft, tender spleen can be palpable in about 40-60 percent (Hornick, 1970). In about 10 percent of the patients, changes in the level of consciousness are present and consist of lethargy, delirium or coma (Litwack *et al.*, 1970).

Complications of typhoid fever can be classified as secondary to toxaemia (myocarditis, hepatic and bone marrow damage), secondary to local gastrointestinal lesions (haemorrhage and perforation), secondary to prolonged severe illness (suppurative parotiditis and pneumonia), secondary to growth and persistence of *Salmonella typhi* bacteraemia (relapse, meningitis, endocarditis, osteomyelitis, arthritis etc) and secondary to therapy (bone marrow suppression, hypersensitivity reaction and toxic crisis).

2:3:3. Bacteraemia.

Salmonella can produce an illness characterised by fever and sustained bacteraemia without manifestations of enterocolitis or typhoid fever. This syndrome may be caused by any *Salmonella* serotype.

Salmonella bacteraemia is characterised by hectic febrile course lasting for days or weeks. The organism is isolated from blood, but stool cultures are often negative. Localised suppurative infections develop in about 10 percent of the patients and may become apparent days, months or even years, after the initial bacteraemia (Mandal *et al.*, 1987).

The *salmonella* septicaemia syndrome is common in patients with HIV/AIDS. Organisms are difficult to eradicate from tissues even with strong antibiotics and repeated relapses of infection are common. *Salmonella* bacteraemia may be the initial clinical manifestation of AIDS (Jacobs, 1985; Sperber, 1987).

2:3:4. Local infection

Localisation of infection may occur at any site after *Salmonella* infection irrespective of the associated clinical syndrome, but more frequent in patients with *Salmonella* bacteraemia syndrome than in patients with enterocolitis. Localised infection has been reported in the thyroid, meninges, bone, heart, lungs, kidneys, adrenals, pancreas, spleen, liver, testes, pericardium etc (Mandal *et al.*, 1987).

The sites determine, to a large extent, the clinical manifestation. Although most patients have spiking temperatures and polymorphonuclear leucocytosis.

2:3:5. Carrier states.

Excretion of the organism in stool after enterocolitis or enteric fever persists for variable periods of time, usually a few weeks (acute carrier) or over a year (chronic carrier). The incidence of the chronic enteric carrier state after typhoid fever is 1 to 3 percent and about one percent in non-typhi salmonellosis (Litwack, 1970). Chronic carriers are asymptomatic.

Patients with *S.hematobium* involvement of the urinary tract have a propensity to become chronic urinary carriers after typhoid fever. Urinary carriers may continue to excrete large numbers of bacilli in urine for months or years (Gendrel *et al.*, 1994). *Salmonella* carriers have a major role in the epidemiology of the disease.

2:4:0. Major co-existing disease conditions.

2:4:1. Malaria.

Malaria is a protozoan disease transmitted by the bite of infected *Anopheles* mosquitoes, affecting more than 500 million people and causing between 1 and 3 million deaths each year (Herwald, 1995). Malaria occurs through out the tropical regions of the world, *Plasmodium falciparum* predominates in Africa. Endemicity is traditionally defined in terms of palpable-spleen rates in children 2 to 9 years of age as hypoendemic (<10 percent), mesoendemic (11 to 50 percent), hyperendemic (51 to 75 percent) and holoendemic (>75 percent) (Molineuax, 1980).

The first symptoms of malaria are non-specific: These include, the lack of sense of well being, headache, fatigue, abdominal discomfort and muscle aches followed by fever. In some instances a prominence of headache, chest pains, abdominal pains, arthralgia, myalgia or diarrhoea may suggest systemic infection like salmonella septicaemia (Petit *et al.*, 1994; Batler, 1991; Commey *et al.*, 1994; Gendrel *et al.*, 1994). Nausea, vomiting and orthostatic hypotension are common in the severe falciparum malaria. Many clinical abnormalities have been described in acute malaria, but most of the patients have few abnormal physical findings other than fever, malaise, mild anaemia and a palpable spleen. Spleen enlargement is very common among otherwise-healthy individuals in malaria-endemic areas and reflects repeated infection (White *et al.*, 1992). Slight enlargement of the liver is also common, particularly

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among young children, mild jaundice may develop and usually resolves over 1 to 3 weeks (Herwaldt, 1995).

2:4:2. Meningitis.

Meningitis may be defined as an inflammatory response to infection of the pia-arachnoid space and cerebrospinal fluid of the subarachnoid space.   Since the subarachnoid space is continuous over the brain, spinal cord and optic nerves, the infection in this space extends throughout the cerebrospinal axis unless there is obstruction of the subarachnoid space. Ventriculitis is uniformly present with meningitis.

The relative frequency of isolation of various bacteria species and fungus as a cause of meningitis varies with age and geographical location.   In Zambia, the overall incidence of meningitis is not known but in the United States of America during 1986, the incidence out of a population of 100,000 per year was (2.9) for *Hemophilus influenza*, (1.35) for *Nesseria meningitidis* and (1.0) for *streptococcus pneumonia*.   Data available at UTH for the year 1996, were *Cryptococcus neoformans (367), Streptococcus pneumonia (245), Nesseria meningidis (86), Hemophilus influenza (20), Escheria coli (22),* and *Salmonella spp (62)* (Mwaba 1997).

Mortality rate for meningitis is dependant on the cause, the highest being the *cryptococcus* meningitis (70%) (Mwaba, 1997), followed by *streptococcus pneumonia* meningitis (30%) (Townsend, 1995).

Meningitis due to the anaerobic bacteria is rare.   It accounts for less than one percent of pyogenic cases (Townsend, 1995).

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The classical clinical presentation of adults with meningitis includes headache, fever and meningismus, often with signs of cerebral dysfunction; these manifestations are found in more than 85 percent of patients. Nausea, vomiting, rigors, profuse sweating, weakness, myalgia and photophobia are also common. Cerebral dysfunction is manifested primarily by confusion, delirium or a declining level of consciousness ranging from lethargy to coma in those instances where it is difficult to differentiate from septicaemia like *Salmonella* etc (Petit *et al.*, 1994).

2:4:3. Pulmonary tuberculosis.

Tuberculosis is principally caused by *Mycobacterium tuberculosis*. Disease due to *Mycobacterium bovis* also occurs in some countries where cattle tuberculosis has not been eradicated. In equatorial Africa some cases are due to *Mycobacteria africanum* belonging to the *Mycobacterium avium complex* (Grange *et al.*, 1998). The disease usually affects the lungs, although in up to one-third of cases other organs are involved. Transmission usually takes place through air borne spread of droplet produced by patients with infectious pulmonary tuberculosis.

It is estimated that 8.8 million cases of tuberculosis occurred worldwide in 1995, 95 percent of them in the developing countries. It is also estimated that nearly 3 million deaths from tuberculosis occurred in 1995 of which 98 percent were in developing world (Rieder, 1995).

Pulmonary tuberculosis can be categorised as primary and post primary (secondary). Primary pulmonary tuberculosis results from the initial infection with *Mycobacterium bacilli*. Only 5 percent of infected patients develop pulmonary tuberculosis due to pulmonary or extra

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pulmonary lesions. Thus the overall chance of developing active tuberculosis is about 10 percent (Styblo, 1986).

Post primary disease, also called adult type or reactivation results from endogenous reactivation of latent infection and is usually localised in the apical and posterior segment of the upper lobes.

Early in the course of the disease, symptoms and signs are often non-specific and insidious, consisting mainly of fever and night sweats, weight loss, anorexia, general malaise, weakness and cough.

There is a strong correlation between HIV infection and pulmonary tuberculosis, in sub-Saharan Africa. Those that present with tuberculosis have a relative risk of being dual infected with HIV of between 5.4 percent and 7.1 percent (Chum et al., 1996). In Lusaka, Zambia 37 percent of children admitted in UTH were HIV positive in 1990, compared with 11 percent without tuberculosis (Chintu et al., 1993). In 1991 they were, 56 percent and in 1992, the figure rose to 68.9 percent (Luo et al., 1994).

2:4:4. Acquired ImmunoDeficiency Syndrome.

Acquired immunodeficiency syndrome (AIDS) is the most severe manifestation of a clinical spectrum of illness after infection with *Human immunodeficiency virus (HIV)*. The syndrome is defined by the development of serious opportunistic infections, neoplasm, or other life-threatening manifestation resulting from progressive HIV-induced immunosuppression.

AIDS was first recognised in mid 1981 when unusual clusters of *Pneumocystis carinii* pneumonia and Kaposi`s sarcoma were reported in young previously healthy homosexual men in New York city, Los Angeles, and San Francisco (Curran, 1983). In 1983, more than 2 years after the first report of AIDS, a cytopathic retrovirus was isolated from persons with AIDS and associated conditions such as chronic lymphadenopathy (Levy *et al.*, 1984). In 1985 a sensitive enzyme-linked immunosorbent assay (ELISA) was developed.

The current estimate of the number of cases of HIV infection among adults world-wide is approximately 22 million, and among children it is approximately 1 million. HIV sero prevalence in Zambia varies from one part to another part of the country, ranging from 2% in rural area to 32% in cities and big towns (Luo *et al.*, 1994).

HIV is transmitted by both homosexual and heterosexual contact, by blood, blood products and by infected mothers to infants, either intrapartum, perinatal or via breast milk. After more than 15 years of scrutiny, there is no evidence that HIV is transmitted by casual contact or that the virus can be spread by insects, such as a mosquito bite (Schacker, 1996).

Studies of homosexual and heterosexual men have demonstrated an association between HIV infection, sexually transmitted diseases such as; syphilis, gonorrhoea and genital herpes (Marmor *et al.*, 1982).

HIV-1 and HIV- 2 are genetically and immunologically distinct. HIV-2 has only 40% DNA homology with HIV-1. Most cases of HIV-2 infection have been reported from countries in West Africa, but several well documented cases have also been reported else where (Clavel *et al.*, 1987).

Clinical manifestation of HIV/AIDS is wide and complex. It depends on the stage of the

disease and the type of the opportunistic and non-opportunistic conditions present (Schacker,

1996).

CHAPTER THREE

3:0:0. Problem.

The diagnosis of *Salmonella* bacteraemia is difficult. Signs and symptoms are not specific (Hornick *et al.*, 1993), it is based on blood cultures (Petit *et al.*, 1994). In most rural hospitals and some times referral hospitals, blood cultures can not be performed due to the lack of material, equipment and expertise, and yet early diagnosis and timely treatment is crucial in order to reduce mortality and the spread of the infections.

HIV is the major problem in Zambia. Prevalence among adults is 32 percent (Luo, 1994). Its association with Salmonella infection is well documented in the west (Levy, 1994), but not in Zambia. Salmonella is the common opportunistic infection, hence recognition of the infection can be used as an early marker of HIV infection.

The existence of multi-durg resistant Salmonella strains, made treatment of Salmonella infections difficult and expensive (Paton *et al.*, 1991). It is important to know the antibiotic susceptibility of *Salmonella spp* in Zambia.

The studied, documented signs and symptoms of the patients with positive blood cultures for *Salmonella spp*, are to be used by clinicians to suspect the presence of *salmonella* bacteraemia.

3:1:0. Objectives.

1. To describe clinical symptoms and signs in *salmonella* septicaemia.

2. To describe epidemiological features of *salmonella* septicaemia

3. To describe prevalence of HIV-infection among *salmonella* septicaemia patients.

4. To describe antibiotic sensitivity of *Salmonella* isolates.

5. To describe common *Salmonella species* causing septicaemia.

3:2:0. Research methodology.

3:2:1. Study site

The study was conducted at the University Teaching Hospital (UTH) medical wards Lusaka for the following reasons: The UTH draws patients from 22 urban clinics, several private clinics and traditional healers. It has a functioning laboratory capable of performing blood cultures and other routine investigations.

3:2:2. Study design.

Descriptive of cross sectional type.

Descriptive design was chosen, because the study was intended to describe phenomena in the clinical presentation of *Salmonella* septicaemia.

3:2:3. Sampling procedure.

Patients were recruited consecutively. Consecutive sampling method was used because of the limited time and anticipated high exclusions.

3:2:4. Sample size.

98 consecutive patients who fulfilled the inclusion criteria were studied.

3:2:5. Inclusion criteria.

The following criteria were used for recruiting patients into the study:

a) Above the age of 15 years.

b) Positive blood cultures for *Salmonella spp*

c) Willing to participate in the study.

d) Alive at time of positive culture results.

e) In hospital at time of positive culture results.

3:2:6. Exclusion criteria.

The following criteria were applied to exclude patients from the study:

a) Age below 15 years.

b) Negative blood cultures results.

c) Dead, or otherwise not available for further evaluation when cultures were positive.

d) Unwilling to participate in the study.

3:2:7. Clinical examination.

Detailed medical and social history was taken and noted, in patients who fulfilled inclusion criteria after obtaining verbal consent.

The investigator (Salim) did physical examination to all patients. Particular attention was paid to the following;

- General condition.

- Pallor, jaundice, oedema, clubbing, cyanosis.

- Hydration status.

- Temperature, pulses, respiratory rate, blood pressure.

- Central nervous system signs.

- Chest signs.

- Cardiovascular signs.

- Abdominal signs.

- Stigma of HIV/AIDS (silk hairs, herpes zoster scars, Kaposis sarcoma etc).

The negative and positive findings were entered into the data sheets and EPI-INFO software programme.

Specimens of blood for full blood count, blood urea and electrolytes, retro viral test (about 10 mils) in their appropriate containers, blood slide for malaria parasites, urine and stool samples were collected by the investigator.

Patients were discharged, when they were apyretic for at least three days and showed improvement in general condition.

3:2:8. Laboratory methods.

1. Blood slide for malaria parasites.

Malaria parasites were looked for using routine methods at UTH (Gimsa's stain).

2. Full blood count.

Routine methods using automated (coulter T-660) machine.

3. Blood electrolytes and urea.

Routine methods using automated (cobas mirror-8) machine.

4. Blood cultures for Salmonella species, antibiotic sensitivity and serogrouping.

Blood cultures processed at UTH microbiology laboratory, serogrouping and antibiotic susceptibility test were done at the University of Colorado Centre of Health Science United States of America.

Blood cultures were done by adding 10 mls of blood to the 70-90 mls of thioglycolate and incubated overnight at 37 degrees centigrade. Every other day blind subcultures were done to chocolate, blood and Mac-conkey agar plates, any growth that was found, was evaluated biochemically to determine identification. *Salmonella* antiserum based on the "O"and "H" antigen was used for serogrouping.

The antibiotic sensitivity test was done by the disc diffusion method (Kirby-Bauer) which involve the use of a standard Muller-Hinton agar.

5. HIV test.

HIV serology was done in all cases, using two enzyme linked immunosorbant assays test (Wellcozyme: Wellcome diagnostics, Partford, Oxford).

CHAPTER FOUR

RESULTS

4:0:0. Demographic characteristic of the patients

4:1:0 Sex Distribution

The sex distribution was considered, of which the females were more than males as shown on fig. 1.

FIG.:1. SEX DISTRIBUTION
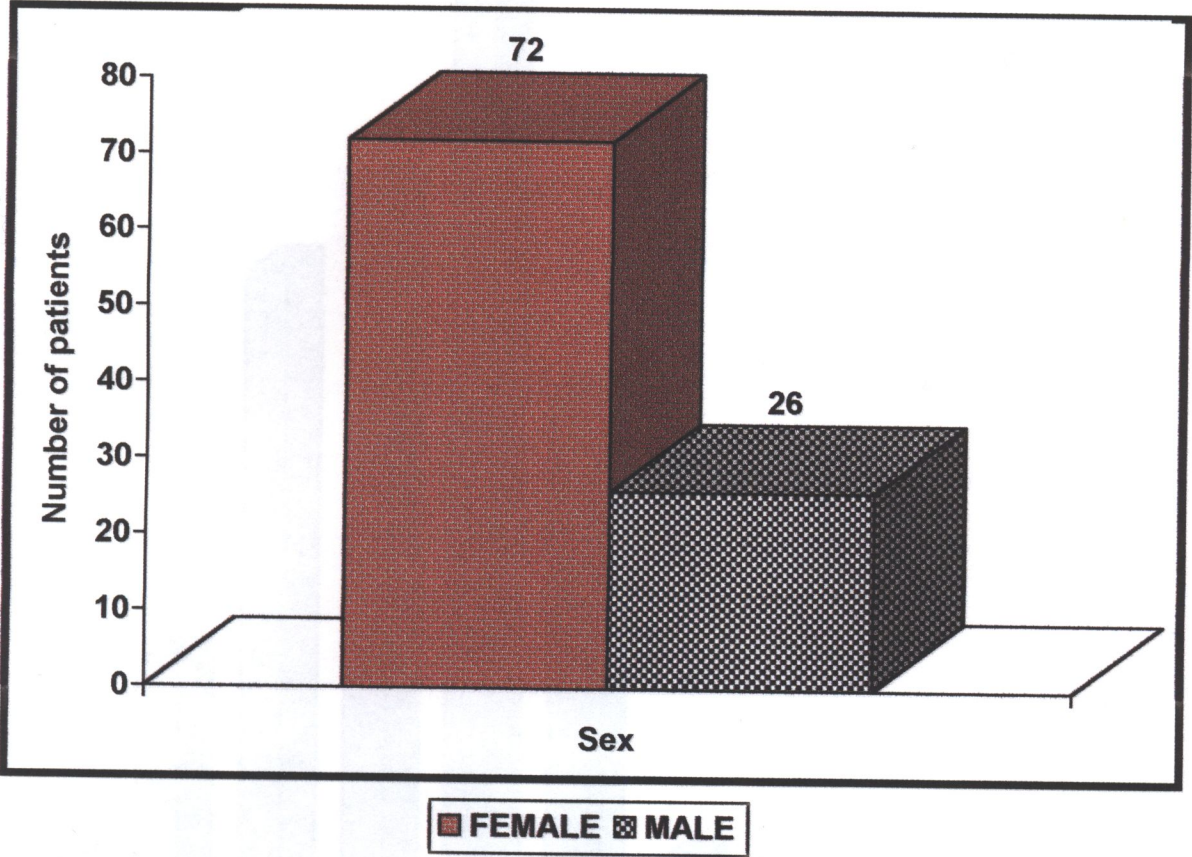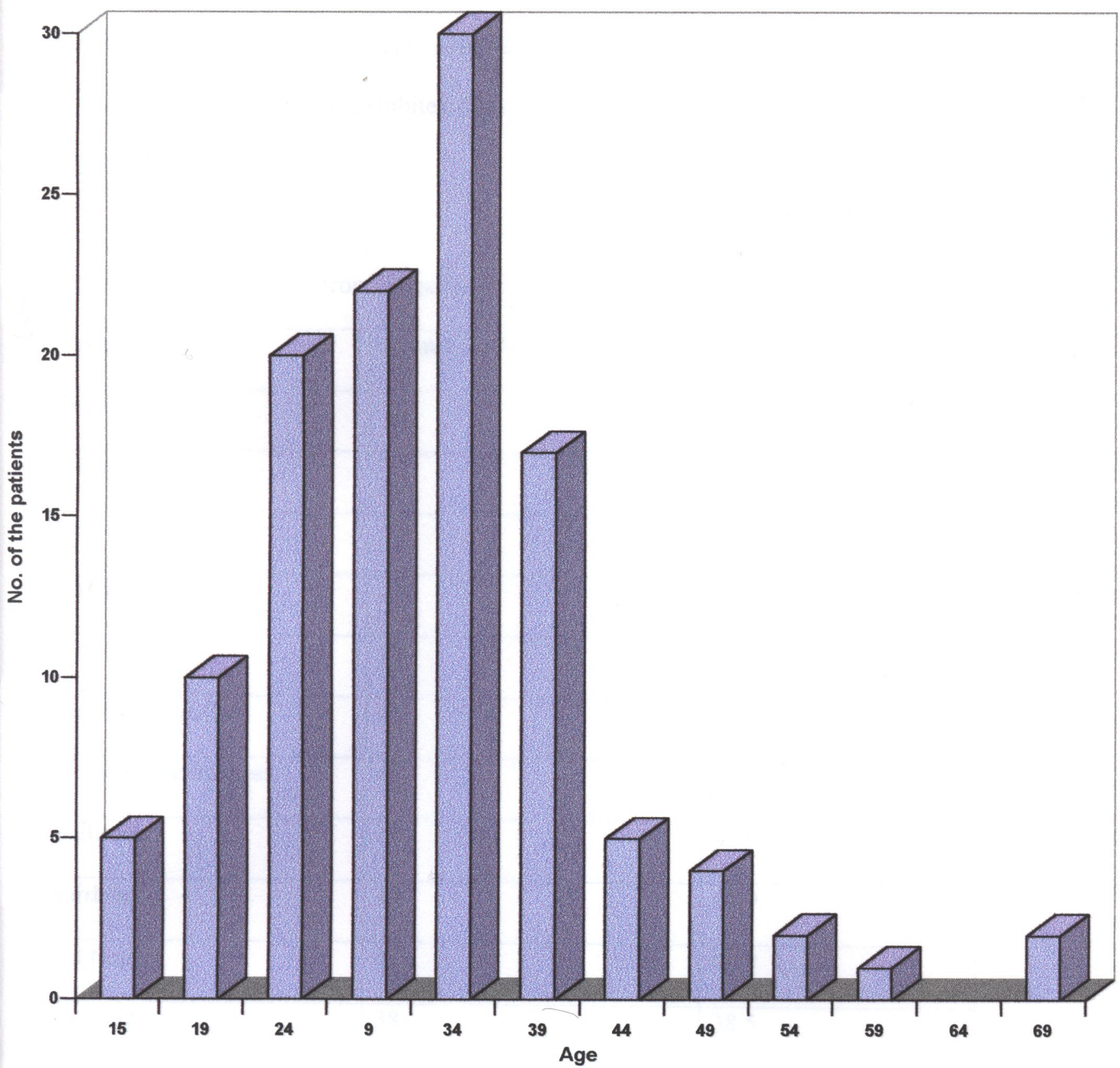
FIG.: 2. Age distribution.

4:2:0 Age distribution

The age range was between 16 and 68 years as shown on the graph above.

4:3:0 Clinical findings

The clinical findings of 98 patients with *Salmonella* septicaemia were observed as tabulated in table 1. Different patients exhibited different signs. More than one sign were observed to a majority of patients (75%).

Table 1: Clinical findings from 98 patients observed

Clinical finding	Number of the patients	Percentage
Fever	90	91.8
HIV +ve	74	75.5%
Coughing	73	74.5%
Anaemia (Hb>9g/dl)	71	74.0
Chest signs	58	59.2
Lymphadenopathy	45	45.9
Altered consciousness	45	45.9
Headache	45	45.9
Diarrhoea	44	44.9
Oral thrush	42	42.9
Vomiting	38	38.5
Hepatomegaly	34	34.7
Splenomegaly	27	27.6
Neck stiffness	27	27.6
Convulsion	23	23.5
Abdominal tenderness	14	14.3
Blood stool	11	11.2

4:4:0 Major Coexisting disease conditions

A number of major coexisting disease conditions were observed. More than one disease condition could occur in one patient. The major coexisting conditions are indicated in table 2 below.

Table 2: Major coexisting disease conditions observed

Coexisting disease/condition	Percentage
Pulmonary Tuberculosis	35.7
Meningitis	20.4
Herpes zoster	7.1
Kaposis sarcoma	7.1
Malaria	6.1
Pregnancy	5.1
Chronic renal failure	5.1
Arthritis	4.1
Bacterial endocarditis	1.0
Diabetes mellitus	1.0
Syphilis	1.0
Cerebra vascular accident	1.0

4:5:0 Antibiotic susceptibility of *Salmonella* Isolates

Antibiotic sensitivity tests were done on the 50 subset of the *Salmonella* isolates. The following are the results as indicated in table 3;

Table 3: Susceptibilities of isolates to the antibiotics

Drugs Used	Resistance (%)	Sensitive (%)	Intermediate (%)
Ampicillin	93	7	0
Chloramphenicol	0	4	96
Ceftazidime	0	100	0
Ciprofloxacin	0	100	0
Ceftriaxone	0	100	0
Cefazoline	57	7	36
Gentamicin	32	7	61
Co-trimoxazole	93	7	0

4:6:0 Serovariant of Salmonella Isolates

The 50 serovariant isolated from 98 patients with *Salmonella* septicaemia are indicated in the histogram on the following page.

FIG.: 3. Serovariant of *Salmonella* isolates.

SEROVARIANT OF SALMONELLA ISOLATES
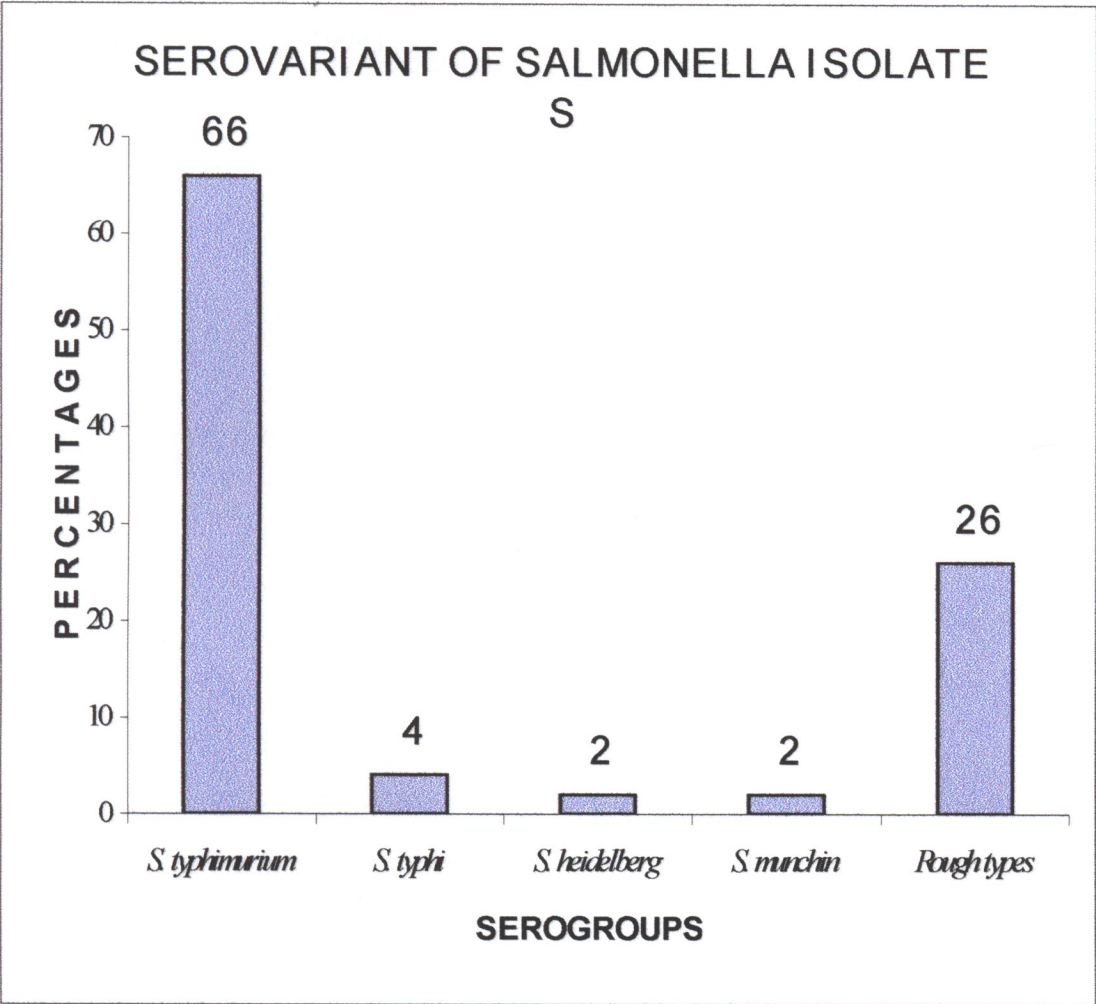
4:7:0. Data handling and analysis.

The data was stored and further analysed using the statistics database package "EPI-INFO" version 6.04 (WHO Geneva, 1994)

CHAPTER FIVE

DISCUSION

5:0:0. Limitation of the study.

This study has some limitations. Firstly, blood cultures were ordered by treating doctors, who are using different criteria. Ideally, cultures should be performed on all patients with the suspicion of bacteraemia, but as practised in most of the developing countries, blood cultures are performed on critically ill patients only due to the limited resources. This is the group of the patient likely to be HIV positive and have more than one major illness. The investigator had no authority over the investigating criteria employed by other doctors in the department.

Secondly, two thirds of the patients were not studied, because they were either discharged or died before the results of blood cultures are obtained. So our data represent patients who survived, and those who stayed longer in hospital.

Thirdly, a study from Tanzania (Lennox *et al.*, 1998) and Uganda (Ssali *et al.*, 1998), isolated a large number of mycobacteria and fungi from the blood, from the set of the patients similar to ours. We did not culture for those organisms, therefore, is a strong possibility some of the signs and symptoms are due to the mycobacterium and fungi.

Lastly, laboratory investigations were not done under ideal research conditions. Investigator had no capacity or authority to influence the sensitivity of the laboratory methods.

5:1:0. Age and sex distribution.

Within the period under review 98 patients of age between 16 and 68 were reviewed, median is 32. As expected the greater number of the patients studied were between 23 years and 39 years of age. These roughly reflect the distribution of AIDS patients in the population (Luo *et al.*, 1994; Chintu, 1993; Gruenewald *et al.*, 1994 and William, 1991), this is also a productive age group of the population, therefore *Salmonella* septicaemia will seriously affect the socio-economic well being of the community and the nation. Preponderance of this age bracket in our study is different from previous work of Cohen and William, which was done at different settings. The reason for this probably is due to the high prevalence of HIV/AIDS in this age group (Sai-cheong *et al.*, 1994; Morel, 1995). Also William (William *et al.*, 1991) found different *Salmonella* serotype to affect different age group. He found blood isolates percentages of *Salmonella heidelberg* were higher for younger age groups and lower for older age group, than blood isolates percentages of *Salmonella enteritidis* and *S.typhimurium*, observation that was not collaborated by this study. There were no infected subjects between 59 and 64 years age group for the same reason above.

Our study shows female predominance (72.4%) over the male (27.6%), which is different from other studies (Sai-cheong *et al.*, 1994; Ruben, 1994).

Married individuals (66.3%) are more affected then single (31.6%) and widowed (2.0%), this could point to the magnitude of the heterogeneous sexual route of transmission of the HIV which is the confounding factor, in the increase of the incidence of *salmonella* bacteraemia

(Blaser and Cohn, 1986). However, it is difficult to account for this from our study.

Salmonella septicaemia remains the major cause of mortality in the world and UTH in particular (Salim *et al.*, 1998). Mortality in our study is 52% out of 98 patients.

5:2:0. Serovariant.

50 *Salmonella* isolates, their serogroup and antibiotic sensitivity were determined as shown in the results. *Salmonella typhimurium* is the commonest isolate 33 (60%), *Salmonella typhi* isolated only 2 (4%), *S.heidelberg* and *S.munchen* 1(2%) each, rough type 13 (26%).

Salmonella typhimurium is the predominant isolate isolated, which correspond with the findings of other studies in other parts of Africa (Wamola, 1993; Kariuki, 1993). *Salmonella enteritidis* was not isolated. Studies done in Europe (Binkin, 1993) and America (Pegues, 1994; Gruenewald, 1994), *Salmonella enteretidis* is the commonest species.

Unlike *Salmonella typhi* and *paratyphi, non-typhi Salmonellae* are widely disseminated in nature and are intimately associated with animal reservoirs. There is no data for outbreak of non-typhi salmonellosis in Zambia, but in the USA for example 40, 912 cases have been reported (David *et al.*, 1994).

Non-typhi Salmonella, especially *Salmonella enteritidis* are important etiologic agents of food borne disease. Grade A shell eggs, have become the most important source of outbreaks of *S. enteritidis* worldwide (Sharma, 1991).

Why is *Salmonella* septicaemia mostly caused by *S. typhimurium* in sub-Saharan Africa, while in Europe and America is caused by *S. enteritidis* is an interesting question. *Salmonella enteritidis* in Zambia has been isolated from table eggs (Hang'ombe, 1998) and poultry as far back as 1991 (Sharma, 1991), but none from human studies (Salim, 1998). This observation can be explained by the difference in the virulence and invasiveness of the *Salmonella* of the same serotype from country to country (Sai-cheong, 1994; Wittler, 1989; Cohen 1987). In addition, these variations appear to be important factors in regard to the occurrence of bacteraemia (Wittler *et al.*, 1989). However, further work is required to explain this interesting finding.

Salmonella heidelberg and *munchen* have been isolated for the first time in Zambia (Salim, 1998). Previous work has shown that *S. heidelberg* is often a cause of gastroenteritis, but there is an association with neonatal sepsis (Levine, 1991). Also Levine (Levine, 1991) noted that *S. heidelberg* is not associated with septicaemia among individuals with AIDS.

5:3:0. Antibiotic susceptibility.

In the past three decades world-wide circulation of multiple resistant enteric pathogens have attracted intense interest because it poses serious problems in the treatment of infectious diseases. In Africa, there have been reports on the incidence of multiple drug resistance in *Salmonella* (Adeleye *et al.*, 1993).

The increased prevalence of resistant bacteria, is the direct result of antibiotic misuse and overuse in the human and animal environment (Kariuki *et al.*, 1993). There is convincing evidence that both sub-therapeutic and therapeutic dose of antibiotics cause increased

antibiotic resistance in the intestinal flora of the patients (Lambert *et al.*, 1985).

The pattern of antibiotic sensitivity in this study is elaborated in the results above. *Salmonella* isolates are 100% sensitive to Ceftazidime, Ciprofloxacin and Ceftriaxone probably because they are not widely used in Zambia. It is important to note that Chloramphenicol remains an effective agent in vitro. This is important because it is cheap, available and it can be taken orally as well as parentally, however, continuous surveillance is needed to be done as 96% of isolates showed intermediate sensitivity to Chloramphenicol. Gentamicin, Ampicillin, Co-trimoxazole and Cefazoline cannot be considered effective emperic antimicrobial agents for *non-typhi Salmonella* infections due to the high degree of resistance.

It is interesting to look at the findings of Dube (Dube, 1984), which were compiled 15 years ago on stool isolates of *Salmonella*. In that study, Chloramphenicol was resistant in the majority of isolates 60% and Gentamicin was sensitive in 60% of isolates, while Co-trimoxazole and Ampicillin showed resistance approximately by the same margins. The reason for this may be Chloramphenicol being less prescribed in the past 10 years and Gentamicin widely used. A comparable study of stool isolates during our study period was not done.

Since the present study was a cross sectional one, analysis of the data does not offer any information of value on the comparative efficacy of different antibiotic treatments.

A recent study conducted in Kenya (Kariuki and Gilks, 1996), shows a high resistance to most readily available drugs like Ampicillin, Cefuroxine, Chloramphenicol, and Co-trimoxazole.

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The 4-fluoroquinolone antibiotics have been an important addition for the therapy of all forms of salmonellosis including enterocolitis, enteric fever, and the chronic carrier state (Asperilla et al., 1990). Advantages of this class are their oral route of administration, their effectiveness against multiple-resistant strains of *Salmonella spp*, their high level of tissue penetration, and their excellent efficacy rates. Their disadvantages are on there toxicity to children and there are reports of resistance to certain strains of *Salmonella spp.* (Dupont, 1991; Aspperilla et al., 1990; Piddock et al., 1990).

Two Spanish hospital based reviews (Munoz et al., 1993; Reina et al., 1993), and a study in the United Kingdom (Threlfa et al., 1993), document the recent emergence of plasmid-encoded multidrug-resistant *non-typhi Salmonella* strains and the role of antimicrobial therapy in food animals in promoting the emergence of multidrug resistance.

Quinolones and third generation cephalosporins remain the drugs of choice for the treatment of multidrug-resistant salmonellosis. A third generation cephalosporin is preferred for the treatment of complicated *Salmonella* infections, such as endocarditis. Seriously ill patients with non-typhi Salmonellosis should be treated with more than one class of antimicrobial agents until susceptibilities are known.

In view of reported development of resistance to quinolones, there is a need for regular antibiotic sensitivity surveillance at UTH.

5:4:0. HIV status of the *Salmonella* septicaemia patients.

The isolation of pathogens normally regarded as non-opportunistic from HIV-infected patients in industrialised countries has been well documented (Schrager, 1988).

Gilks (Gilks *et al.*, 1990), in Nairobi was the first to describe the importance of blood stream infections in African adults infected with HIV-1. Two subsequent studies that investigated bacteraemia in HIV-positive patients in Rwanda (Taelman *et al.*, 1990) and the Ivory Coast (Vugia *et al.*, 1993) suggested that infections due to *non-typhi* species were an important cause of mortality and morbidity in this patient population.

Human immunodeficiency virus-infected patients are well-recognised, immunocompromised group at risk for severe, persistent bacteraemic salmonellosis (David, 1993).

In a study assessing the overall impact of HIV epidemic on bacteraemic salmonellosis, the centres for disease control (CDC), showed that in 25- to 49-year old men in the United States of America, the proportion of *Salmonella* isolates reported from blood increased from 2.8% in 1978 to 1982 to 14.2% in 1983 to 1987. The increase was due to the incidence in acquired immunodeficiency syndrome-AIDS (Levine *et al.*, 1991). In addition, those adolescents and adults with AIDS had 0.5% recurrent *salmonella* septicaemia. A similar observation was reported by Castilla (Castilla *et al.*, 1996) in Spain.

Thus, it appears that the AIDS epidemic is contributing to a changing epidemiology of salmonellosis.

In our study the rate of HIV infection among *Salmonella* septicaemic patients was 75.5% which is similar to the reviews of German (German *et al.*, 1998) in Bangui, Central Africa and Ssali (Ssali *et al.*, 1998) in Uganda. Other studies show a lower prevalence of about 48% (William, 1991; Odempsey, 1994; Morel, 1995; Petit, 1994). This difference is probably due to the different criteria involved in doing blood cultures.

The data available indicate that the immunological defence mechanisms that were able to maintain the function in these patients still afforded much protection against the dissemination to the blood of a number of common pathogens. However, there seems to be less protection afforded against the spread of *Salmonella typhimurium* (Gruenwald, 1994).

The high correlation between HIV infection and salmonellosis strongly suggests that testing for antibodies to HIV should be carried out when *salmonella* septicaemia, multiple site infection, or even gastroenteritis and urinary tract infections are diagnosed. Salmonellosis can be used as a maker that leads to an earlier diagnosis of HIV infection in some patients.

5:5:0. Diagnosis of *Salmonella* septicaemia.

Diagnosis of *Salmonella* septicaemia is very difficult, as it is based entirely on the blood and bone marrow cultures (Petit, 1994). Clinically it is difficult to differentiate from other causes of septicaemia (Vugia, 1993).

Contrary to the typhoid fever where the symptoms are typical (Petit, 1994), the *non-typhi Salmonella* septicaemia presents a vast range of symptoms (Lester, 1991).

The severity and variety of symptoms vary widely with the geographical areas and age

(Batler, 1991), and receiving strong interference from coexisting malaria, schistosomiasis and HIV infection (Petit, 1994; Battler, 1991; Commey, 1994; Gendrel, 1994).

To our knowledge there has been no attempt to study the clinical diagnosis for *non-typhi Salmonella* bacteraemia. Several new methods for the rapid detection of *Salmonella* from primary culture plates have been reported, however, these methods are not sufficient and specific enough for clinical use as they are also expensive (Orden *et al.*, 1993).

The incidence rate of signs and symptoms are; fever 91.8%, diarrhoea 44.9%, headache 45.9%, cough 74.5%, lymphadenopathy 45.9%, chest signs 59.2%, altered consciousness 45.9% and anaemia 75.5%.

The above signs do not give real clues, nor allow proper differential diagnosis e.g. fever present in about 70% of patients admitted in the hospital (Petit, 1994), diarrhoea occurs in 68% of HIV infected patients (Khumalo-ngwenya, 1994). In areas of endemic to malaria, most people have splenomegaly.

The clinical signs mentioned above, are not specific, and their sensitivity is not known, however, it seems prudent to include salmonellosis in the differential diagnosis of fever in our setting and give blind treatment with *Salmonella* sensitive antibiotic in order to reduce morbidity and mortality.

About 75% of our patients have major co-existing disease conditions; pulmonary tuberculosis 35.7%, meningitis 20.4%, which produce interference in the clinical manifestation of our patients with *Salmonella bacteraemia*. Therefore salmonellosis should be considered in the differential diagnosis, or as a co-existing condition in-patients with tuberculosis, meningitis and other HIV-related conditions at UTH.

CHAPTER SIX

CONCLUSION AND RECOMENDATIONS

6:0:0. Conclusions.

1. HIV infection was found in the majority of the *Salmonella* septicaemic patients.

2. *Salmonella typhimurium* is the predominant causative agent of *Salmonella* septicaemia in UTH.

3. Patients with *Salmonella* septicaemia are likely to have other major co-existing HIV-related diseases such as pulmonary tuberculosis and Kaposi`s sarcoma.

4. *Salmonella* isolates are resistant to commonly used antibiotics in UTH such as Co-trimoxazole, Ampicillin, Gentamicin and Cefazoline.   Drugs that should be used for treatment of suspected *Salmonella* septicaemia are Ciprofloxacin, Ceftazidime and Ceftriaxone.

6:1:0. Recommendations.

1. Patients with signs of immunosuppression and fever should be screened for *Salmonella* infection.

2. Patients with *Salmonella* bacteraemia should be counselled and offered HIV test.

3. Co-trimoxazole, Ampicillin and Nitrofuranton should not be used as empirical treatment for *Salmonella* infection at UTH; instead quinolones and third generation cephalosporins are preferable.

4. UTH should review its antibiotic treatment policy and guidelines in respect of these findings.

5. Further research is required on the epidemiology, drug sensitivity, and clinical criteria for

suspecting *Salmonella* sepsis and use of salmonellosis as an HIV/AIDS related or defining

opportunistic condition

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APPENDICES

Appendix 1.

PATIENT CONSENT FORM

I..have understood objective of the study which has been

explained to me by Dr Ali Salim.

The explanation include:

1. A patient information sheet and a verbal explanation of the study.

2. The purpose and length of study.

3. Study requirements.

I further understood that I am free to withdraw from this study at any time after giving

Consent, without any reason to be given, and that if I do, this will in no way affect my

treatment or care by doctor. I am aware that my personal information may be scrutinized by

competent authorities and authorized persons, but it will be treated as strictly confidential and

will not be publicly available.

I consent to participate in the study. I understand that I will not receive any benefit from

participating in the study.

Signature of the patient...................

Signature of the witness.................

Date....................

Appendix. 2.

DATA RECORDING SHEET UNIVERSITY TEACHING HOSPITAL
DEPARTMENT OF MEDICINE

IP No☐☐☐   Date☐☐.☐☐.☐☐

Name…………………………..   Age☐☐☐   Address……………………………………

Sex☐ (F/M)   Ward……..   Date of Admission☐☐.☐☐.☐☐

Date of discharge☐☐.☐☐.☐☐   Marital status☐ (M/W/S)
……………………………………………………………………………………………………

Wt☐☐☐.☐☐ Kg.   Ht☐☐☐ Cm. Bp☐☐☐/☐☐☐. Temp☐☐.☐ C.   Ps☐☐☐Beats /min
……………………………………………………………………………………………………

Principal complains:

Fever☐ (Y/N).   Diarrhea. ☐ (Y/N). If Yes how many times/day? ☐, what type?

Others…………………………………………………………………………………………..

Past medical history……………………………………………………………………………

Where is the source of food, poultry and water……………………………………………………...

……………………………………………………………………………………………………

Physical examination.

General examination……………………………………………………………………………..

Head……………………………………………………………………………………………

Respiratory system……………………………………………………………………………

Cardiovascular system………………………………………………………………………….

Abdomen………………………………………………………………………………………

Nervous system………………………………………………………………………………..

Muscular skeletal system……………………………………………………………………..

Others…………………………………………………………………………………………

……………………………………………………………………………………………………

56

Laboratory findings:

1. Mps ☐ (+/-)

2. FBC&ESR...

3. Blood urea and createnin...

4. Urine culture..

5. Stool culture...

6. HIV test...

7. Others..