A STUDY TO DETERMINE THE ETIOLOGY AND OUTCOME OF ADULT PATIENTS PRESENTING WITH SEPSIS TO UTH.

by

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DECLARATION

I declare that this dissertation is my own work. It is being submitted for the master's degree in internal medicine at the University of Zambia, Lusaka. It has not been submitted before for any degree or examination at this or any other university.

Signed:.....

Student

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Supervisor

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Head of department

ABSTRACT

BACKGROUND

Sepsis accounts for a significant burden of morbidity and mortality. In developed countries, it has been implicated as the second leading cause of non-cardiac death. Mortality from sepsis is on the increase with mortality rate of 33-61%. In spite of the high burden of sepsis in sub-Saharan African, data regarding the etiology and outcome of septic patients is limited. We conducted a prospective cohort study to look at the etiology and outcome of patients presenting with sepsis to UTH, in Lusaka, Zambia.

OBJECTIVES

To describe the aetiology, characteristics and outcomes of patients presenting with sepsis to the department of medicine.

METHODS/ RESULTS

Patients who met the inclusion criteria for sepsis were recruited into the study. Vital signs and management details were recorded and bloods were drawn for urea, Creatinine, full blood count and culture. A total of 161 patients were enrolled. 110 (68 %) of the patients were HIV positive with 23 (14%) who had unknown status. Mortality in our cohort of septic patients was at 40.4. Important predictors for in-patient mortality were: low GCS on admission [OR 11.2(3.5-36.4)] and Blood culture being positive [OR 2.38(1.14-4.95)].

CONCLUSION

Most of the septic patients presenting to UTH had advanced immunosuppression (WHO stage 3 or 4) and had a high mortality rate. *Staphylococcus aureus* and streptococcus *pneumoniae* were the highest isolates in our study. Identified predictors of in-patient mortality could be used to try and improve outcome of septic patients admitted to UTH.

DEDICATION

To my husband Jonathan, you have always supported me through this ragged terrain and given me confidence to carry on.

To my dad and mum, Reverend Julius and Mrs Jane Chimese, my sisters Chushi, Chisha, Mulubwa and Mwaba, thank you for the roles that you played in my life to make me the person

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LIST OF ABREVIATIONS

AIDS	**-**	Acquired immunodeficiency syndrome
CD4	**-**	Cluster of differentiation 4+
CI	-	Confidence interval
DBP	**-**	Diastolic blood pressure
HIV	-	Human immunodeficiency virus
HB	**-**	Haemoglobin
HAART	-	Highly Active Antiretroviral Therapy
IL	**-**	Interleukin
OR	**-**	Odds ratio
SD	-	Standard deviation
SIRS	-	Systemic Inflammatory Response Syndrome
SBP	**-**	Systolic blood pressure
TNF	**-**	Tumour necrosis factor
UTH	**-**	University Teaching Hospital
WHO	**-**	World Health Organization
WBCC	**-**	White blood cell count
U	-	Unknown HIV status

CHAPTER 1

1.0 INTRODUCTION

Sepsis is said to be the result of the body's response to invading microbes. When the counterregularory mechanisms fail such that there is organ dysfunction it is termed as severe sepsis. When there is hypotension with organ dysfunction that is termed as septic shock. Sepsis can be caused by any microorganism but bacteria account for most cases. Approximately 30 to 60 percent of patients with sepsis and 60 to 80 percent of patients with septic shock have blood cultures that are positive for bacteria or fungi and gram negative bacteria account for two thirds of these isolates (Munford,1994). Factors that predispose to gram negative bacteraemia include diabetes mellitus, lymphoprolipherative disease, cirrhosis of the liver and burns. Risk factors for gram positive bacteraemia include vascular catheters and other indwelling mechanical devices.

Sepsis accounts for a significant burden of morbidity and mortality and has been implicated as the second leading cause of non-cardiac death in developed countries.

In developing countries the situation is worse. This is due to a number of factors. Firstly the high HIV/AIDS prevalence has contributed greatly to the increase in the number of septic patients. Other factor include limitation of drugs and other items that should be used in the treatment of such patients, deficiency of man power and late presentation of the very sick patients to the hospital. For instance, a retrospective chart review at Livingstone General hospital, in Zambia revealed that 79 (86%) of 92 hypotensive septic

patients received no intravenous fluids for resuscitation(Theodosis 2006). In another study done in Kampala Uganda described limitation in terms of supplies. Oxygen, drugs and intravenous fluids were all in short supply (Jacobs 2009).

Guidelines have been formulated in developed countries which encourage early diagnosis, antimicrobial treatment and aggressive fluid resuscitation (Jacob 2009). These measures have been shown to improve outcome. Some of these measures are too costly to be implemented in resource limited countries like Zambia, therefore there is need to come up with cost effective measures to improve outcome. This study seeks to determine the aetiology and outcome of patients presenting with sepsis in the department of medicine.

CHAPTER 2

2.0 LITERATURE REVIEW

Bacteraemia is the presence of bacteria in the blood. Release of toxins in the blood by bacteria leading to shock and vascular collapse is teamed as septicaemia. Epidemiological data regarding the management and outcome of the sepsis syndrome is limited in low and medium income countries such as Zambia (Jacob 2009).

Sepsis has been described as uncontrolled inflammatory response to the presence of microorganisms. Also described as an infection plus two or more features of systemic inflammatory response syndrome (SIRS) criteria. Systemic inflammatory response syndrome is described as consequences of a dysregulated immune system and may have an infectious or non-infectious aetiology. It can result from conditions such as autoimmune disorders, pancreatitis, thromboembolism, burns or surgery. Clinically it is recognized by the presence of two or more of the following:

- temperature greater than 38°C or less than 36°C,
- Heart rate greater than 90beats/min.
- Respiration greater than 20/min,
- WBC count greater than $12000x10^9$ or less than $4000x10^9$ or greater than 10 percent immature neutrophils (Levy 2009).

Septic shock is defined as sepsis induced hypotension despite adequate fluid resuscitation including the presence of organ perfusion abnormalities such as lactic acidosis, oliguria and acute alteration in mental status (Bone 1992).

The physiological response to infection includes activation of host defence mechanisms that result in influx of activated neutrophils and monocytes, the release of inflammatory mediators, local vasodilatation and increase endothelial permeability and activation of coagulation pathways. In sepsis the mechanism is the same although it's on a systemic level resulting in diffuse endothelial dysfunction. In bacterial infection the features of sepsis are brought about by the interaction between the host immune cells and the endotoxin contained in the cell wall of gram negative organisms. For gram positive organisms, the interaction occurs either with components of the cell wall or with the exotoxin released by the organism. These interactions results in release of inflammatory mediators, the most notorious of which are tumour necrosis factor alpha (TNF), Interleukin 1 and 6 (IL 1 and 6).

Worldwide, there is an increase in the incidence of septicaemia, probably due to the increased burden of immunosuppression due to HIV and other immunosuppressive therapies. It is also disproportionally increased in the elderly and age is an independent predictor of mortality. Mortality from sepsis is also on the increase with a death rate of 33 to 61 percent (Sprung 2008). In the United States, it is a major cause of morbidity and mortality and has been implicated as the second leading cause of non-cardiac death

(Martin 1979). Mortality from septic shock is 28 % to 50%. About 750,000 are affected annually and more than 210,000 die (Angus 2001).

The Brazilian Sepsis Epidemiological study enrolled 1383 patients admitted in 5 different intensive care units and found mortality rates of 34.7% for sepsis, 47.3% for severe sepsis and 52% for septic shock (Silva E 2004).

Pneumonia was the commonest cause of sepsis in a study done in Saudi Arabia and blood cultures were positive in 88% of the patients. 48% of the isolates were gram negative of which *Klebsiella pneumoniae* was the highest isolate, *Streptococcus pneumoniae* was the leading gram positive organism isolated. Mortality due to sepsis /septic shock was 54%. These were patients with no history of prior use of antibiotics (Salim B 2009).

In a study done in Nigeria by Meremikwu M. Martin in 2005, 49% of the study population had positive blood cultures. *Staphylococcus aureus* and coliforms were the leading cause of septicaemia in children in that region and they were shown to be sensitive to cephalosporins and azithromycin.

Bacteraemia, particularly by *Streptococcus pneumoniae* and *non -typhi Salmonella* are a major cause of morbidity in HIV infected patients (Gilly 2001). A study done in Tanzania found blood stream infection in 28 percent of patients in the study population.

Mycobacterium tuberculosis was the highest isolate, followed by *non- typhi Salmonella*. The third isolate was *Staphylococcus aureus.* All the *mycobacteria* isolated in this study were sensitive to isoniazid and rifampicin but one isolate was resistant to streptomycin and another one was pyrazinamide resistant (Archibald 1998).

HIV infection is an important risk factor for blood stream infections in adult patients admitted with fever. Therefore if the HIV status of a patient is known, initiation of empirical antimicrobial therapy would be the right way to go (Archibald). In a study done in Malawi by Archibald and friends, 74% of the study population was HIV positive. Blood stream infection was found in 35% of HIV positive patients against 13% in HIV negative patients. The most commonly isolated organism was *Streptococcus pneumoniae* followed by *Mycobacteria tuberculosis*. Ugandan study done in 1998 by Ssali et al had 24% bacteraemia, with bacteraemia being more frequent in HIV infected than uninfected individuals. 76% of the study populations were HIV positive. The most commonly isolated organism was *Mycobacteria tuberculosis* which was found mostly in HIV positive patients. This was followed by *Streptococcus pneumoniae*. Studies have shown that in areas of high HIV prevalence sepsis contributes significantly to mortality and the causative organisms of the sepsis varies depending upon regional and population characteristics.

CHAPTER 3

3.0 STATEMENT OF THE PROBLEM

Septicaemia is an important cause of mortality and morbidity in the developing world.

Patients with septicaemia make up a significant proportion of admissions to the department of medicine. At UTH mortality has been persistently high with a case fatality rate of 65% in 2007 and 76% in 2008. Physical signs and symptoms are important and useful in identifying possible causes but their specificity is limited.

Definitive diagnosis is by culture of body fluids to identify the microorganisms and establish antimicrobial susceptibility pattern so that an antibiogram is created for use in the procurement of antimicrobials. Furthermore knowing the type of organisms responsible for the sepsis and the outcome of septic patients will help us put in place prevention and treatment measures to reduce the mortality and morbidity due to sepsis at UTH.

3.1 STUDY JUSTIFICATION

Although sepsis is a major problem in sub-Saharan Africa, very few studies have described the burden of sepsis in this area (Angus,1998). UTH in Lusaka had a mortality rate from sepsis of 65% and 76% in 2007 and 2008 respectively. This study was conducted in order to describe the burden of sepsis, management and the outcome of septic patients admitted to the University Teaching Hospital and its addition to the knowledge bank can be used as a basis for future studies on sepsis.

3.2 GENERAL OBJECTIVES

To describe the aetiology, characteristic and outcome of patients presenting with sepsis to the department of medicine at UTH.

3.3 SPECIFIC OBJECTIVES

I. To determine the outcome of patients presenting with sepsis.

II. To identify the different micro-organisms responsible for sepsis and their antimicrobial susceptibility patterns.

III. To determine the proportion of patients admitted with sepsis who have laboratory proven bacteraemia

IV. To describe the clinical characteristic of patients presenting with sepsis.

V. To identify clinical predictors for in-patient mortality in patients presenting sepsis.

CHAPTER 4

4.0 RESEARCH METHODOLOGY

We conducted a descriptive in-patient cohort study of all septic patient admitted to UTH from August to December, 2010. The study was conducted at the University Teaching Hospital, which is the largest referral hospital in Zambia. It is located in Lusaka which is the capital city of Zambia and has a population of just over 2 million according to the 2000 census. Patients were enrolled from the Adult Filter Clinic, where medical patients first present to the UTH. Enrolled patients were then followed up through the medical wards till they were either discharged or died.

The Sample size was calculated online using the Open-Epi program. We assumed a culture positivity rate of 19%, mortality rate of 40% bactereamic patients and mortality rate of 20% in non bacteraemic patients. Using 95% confidence interval and 80% power we arrived at 288 patients. However due to financial constraints only 165 patients were recruited.

4.1 Study Procedure

We enrolled a total of 165 out 315adult septic patients admitted to UTH over the study period. The 150 were not enrolled due to logistical problems and some of them had received many dosages of antibiotics prior to there being seen by the research team. All enrolled patients had the SIRS criteria which is a source of infection plus two or more of the following

- Axillary temperature greater than 38° C or less than 35° C.
- Heart rate greater than 90 beats/ min
- Respiratory rate greater than 20 breaths/min
- WBCC greater than $12000X10^9$ or less than $4000X10^9$ or 10% immature neutrophils

Those with gastrointestinal bleeding and those who failed to give informed consent were excluded from the study.

Informed consent was obtained from the study participants or their next of kin (guardian, spouse). Information obtained from the participants was treated with utmost confidentiality and all participants were assured of that. Patients who refused to take part in the study continued to receive the usual standard of care for septic patients. Approval was sought from the University of Zambia Research and Ethics Committee and the managing director UTH through the head of the department of medicine. Detailed history including demographic details such as age, sex, marital status, residential address, level of education and employment status were taken and entered on the data entry sheet. Parameters measured on admission such as temperature, blood pressure, respiratory rate were also entered on the data entry sheet.

Blood for culture was collected using aseptic techniques. Vene puncture sites were disinfected using iodine solution followed by methylated spirit .Initially we had planned to use Bactec™ blood culture bottles but due to financial constraints the bottles finished just after culturing 137 specimens. The remaining 24 cultures were performed using

manual blood culture bottles which were locally made by the UTH microbiology lab. About 10mls of blood was put into each blood culture bottle and immediately transported to the laboratory. The Bactec^{TM} bottles were put in a BD BACTEC^{TM} 9050 blood culture system. Upon detection of any growth in any of the culture bottles, specimens were then sub cultured on blood , chocolate and McConkey agars. Full identification of organisms was done using the standard operating procedure of the University Teaching Hospital microbiology laboratory. The antibiotic sensitivity of the bacteriological isolates was determined by agar diffusion method using antibiotic discs.

Cerebral spinal fluid was inoculated onto chocolate , blood, MacConkey and Sabararoud agars Media was then incubated at 35° C in 5% $C0_2$ for up to 72 hours. Identification of species was carried out using the UTH microbiology standard operating procedure. Other bloods were drawn for full blood count, urea and electrolytes, liver function test, HIV test and CD4 count. Patient's clinical details including management details were recorded until they died or were discharged. These included amount of intravenous fluids given in the first 6 and 24hours type of empirical antimicrobial given and any other investigations done. Outcome was documented as mortality or discharge

Data was collected on a data entry sheet. Each participant was assigned an identification number. It this number that was used to enter data into an excel spread sheet electronically.

4.2 Data analysis

Data collected on a hard copy was entered into and analysed using EPI INFO version 3.5.1. Overall prevalence of bacteraemia in adult septic patients at UTH was determined. Descriptive statistics were reported as means and standard deviations for those which were normally distributed. Odds ratios at 95 confidence interval were calculated. Statistical significance was defined as $P< 0.05$. Variables with clinically relevant cut off points were dichotomised. Various variables were assessed in order to determine independent predictors for in patient mortality. These included age, sex, HIV status, bacteraemia or not, admission Glasgow coma scale, level of haemoglobin, whether patient received empirical antibiotics and intravenous fluids. Stepwise backward logistic regression was used to determine the predictors of in-patient mortality.

CHAPTER 5

5.0 RESULTS

Table 1. Clinical characteristics

Clinical Characteristics	Total **n (SD)**	HIV+ **n (SD)**	HIV- **n (SD)**	Unknown HIV status **n (SD)**
Age, mean(SD)	39.0(15.6)	37.5(12.4)	37.3(19.4)	48.3(21.1)
Sex*				
Male	79(49.1)	54(50.9)	14(50)	11(47.8)
Female	82(50.9)	56(49.1)	14(50)	12(52.2)
Inclusion criteria (mean (SD))				
Admit temp ° C,	37.5(1.7)	37.3(1.7)	37.3(1.8)	37.7(1.4)
Admit RR, Breaths/min,	27.9(8.2)	28.1(8.4)	25.3(5.7)	29.7(9.5)
Admit pulse rate	99.7(17.3)	100.3(17.7)	96.2(12.9)	101.5(19)
Admit SBP, mmhg, mean	106.1(22)	103(17.5)	109(31.9)	117.4(23.5)
Admit DBP, mmhg, mean	65.8(15.4)	64.7(15.1)	63.5(14.6)	73.9(16.2)
Admit WBCC in cells/ml	9.0(5.8)	7.8(5.2)	10(5.2)	13.7(6)
Complaint				
Headache	54(33.5)	37(33.6)	9(32.1)	8(34.9)
Cough	49(30.4)	36(32.7)	4(14.3)	9(39.1)
Fever	12(7.5)	5(4.5)	5(17.9)	2(8.2)
Diarrhea	28(17.4)	21(19.1)	6(21.4)	1(4.3)
Convulsions	7(4.3)	3(2.7)	3(10.7)	1(1)
Abdominal pain	2(1.2)	6(5.4)	0(0)	0(0)
Vomiting	7(4.3)	6(8.7)	6(3.6)	2(8.7)
Type of infection				
Meningoencephalitis	47(29.2)	35(31.8)	6(21.7)	6(26.1)
Gastroenteritis	22(13.7)	19(17.3)	3(10.7)	0(0)
Tuberculosis	3(1.9)	3(2.7)	0(0)	0(0)
Pneumonia	37(23)	27(24.5)	3(10.7)	7(30.4)
others	52(32.3)	26(23.6)	16(57.1)	10(43.5)

**All figures are frequency and (%) unless otherwise stated

A total of 165 patients were enrolled, one patient was excluded because of transfer to a surgical unit and three were lost to follow up. The mean age of the study participants was 39(range16-88). Males made up 49.1 of the study population. 110 patients were HIV positive with 31.85% of these being in WHO stage IV and 43.3% being on HAART. Most of the means for the total number of patients number of patients do meet the SIRS criteria when we consider the standard deviation. The clinical characteristics of all study patients are summarised in table 1

5.1 Microbiology

Table 2. Sensitivity patterns.

	n	Chloramphenicol.	Ciproflox acin	Cefotaxime.	Septrin	Penicillin.	Erythromycin
Gram +							
S. aureus	10	3/8 (38)	7/10 (70)	2/2 (100)	1/6(16.7)	3/8 (38)	0/4(0)
S.pneumoniae[c]	4	0/3(0)	2/2(100)	1(100)	0/2(0)	2/2(100)	4/4(100)
Other Strep%	2	0/1(0)	1(100)	1(100)	0/1(0)	1(100)	½(50)
Micrococcus	3	0/2(0)	3/3(100)	-	0/2(0)	0/1(0)	
bacillus	2	-	-	-	-	-	-
Gram -							
*Salmonella**	5	1/3(33.3)	5/5(100)	3/3(100)	4/4(100)	-	
Non-salmonella^	8	4/8(50)	5/8(63)	½(50)	2/6(33)	0/3(0)	2/2(100)

**( ) indicate % of Numbers in tested specimens that were susceptible to listed antibiotic

5 samples were mixed growth suggestive of contaminants

% Includes 1 Group B beta-haemolytic streptococcus

^ Includes 4 Klebsiella, 1 citrobacter, 2 acinetobacter, 1 haemophilus influenza.

c strep and 1 untyped strep

* Includes 3 S. typhi and 2 non-typhi species

39 (24.2%) had bacteraemia. Only aerobic cultures were used to grow the organisms which were both gram negative and positive. The most commonly isolated organism was *Staphylococcus aureus* (25 %), followed by *Streptococcus pneumoniae* (10%) and *Salmonella typhi*. There were 5 cultures yielded mixed growth and these were regarded as contaminants and so bringing the number of total bacteraemia to 21 % .The above table is a summary of the sensitivity patterns of the various isolated organisms.

5.2 Mortality

Forty percent (65)of our cohort of septic patient died during admission. Median length of in hospital stay was 15.5 days. Predictors for in-patient mortality were low GCS on admission [OR 11.2, (CI 3.5-36.4)], HIV status, those with unknown HIV status were more likely to die than the HIV negative patients [OR 8.38(CI 2.36-29.7)]. other predictors of in-patient mortality included the presence of laboratory proven bacteremia.

Table 3. Unadjusted risk factors for in hospital death

Variable	*Total n (%)*	*Survived n (%)*	*Died n (%)*	*Odds ratio (95% CI)*
Age	39(15.6)	37.1(14.5)	41.8(16.8)	
Hb				
≥9	83(51.6)	50(52.1)	33(50.8)	
<9	78(48.4)	46(47.9)	32(49.2)	1.05(0.56-1.8)
HIV status				
-ve	28(17.4)	22(22.9)	6(9.2)	1
+ve	110(68.3)	67(69.8)	43(66.2)	2.35(0.88-6.28)
U	23(14.3)	7(7.3)	16(24.6)	8.38(2.36-29.7)
CD4 count*				
<200	60(71.4)	35(67.3)	25(78.1)	1.73(0.62-4.80)
≥200	24(28.6)	17(32.1)	7(21.9)	
Bacteremia				
Yes	39(24.9)	17(17.7)	22(33.8)	2.38(1.14-4.95)
No	122(75.8)	79(82.3)	43(66.2)	
GCS				
13-14	106(66.3)	77(81.1)	29(44.6)	1
9-12	33(20.6)	14(14.7)	19(29.2)	3.60(1.60-8.11)
<9	22(13.1)	4(4.2)	17(26.2)	11,2(3.5-36.4)
Type of infection				
Gastroenteritis	22(13.7)	15(15.5)	7(19.8)	1
Meningitis	47(29.2)	25(26.5)	22(33.8)	1.89(0.65-5.47)
Pneumonia	40(24.8)	23(24)	17(26.2)	1.58(0.53-4.73)
Other	52(32.3)	32(34.2)	19(29.2)	1.23(0.43-3.56)
Creatinine				
>180	25 (15)	15(15.6)	10 (15.6)	0.98(0.41-2.34)
≤180	136(85)	81(84.6)	55(84.6)	
MAP				
<65	132(78.1)	52(80)	80(83.3)	1.25(0.56-2.81)
≥65	29(21.9)	13(20)	16(16.7)	

Table 4: Management details

	Total ***n (%)***	Survived ***n (%)***	Death ***n (%)***	OR **(95% CI)**
Time to antibiotics				
<1 hour	46(28.6)	31(32.3)	15(23.1)	0.58 (0.27-1.25)
≥1 hour	115(71.4)	65(67.7)	50(76.9)	
Time to first IVFs				
<1 hour	47(29.2)	29(30.2)	18(27.7)	0.86 (0.43-1.72)
≥1 hour	114(70.8)	67(69.8)	47(72.3)	
IVFs in first 6 hours (L)				
0	66(41.8)	37(56.1)	29(46)	1.3(0.7-2.5)
1	67(42.4)	41(43.1)	26(41.3)	
2 or more	25(15.8)	17(17.9)	8(12.7)	
IVFs in first 24 hours (L)				
0-1	88(54.7)	53(55.2)	35(53.8)	0.86(0.53-1.4)
2-3	58(36)	31(32.3)	27(41.5)	
4 or more	15(9.3)	12(12.5)	3(4.6)	

Only 28% of patients received antibiotics within the first one hour of admission. 76% of the people who died did not receive any antibiotics in the first one hour of admission. For intravenous fluids, the more fluids a patient received, the higher the chances of survival.

Table 5 Adjusted Odds of death for selected risk factors

Variable	Odds ratio	95% CI
Anemia	0.91	0.74 -4.93
Blood culture (positive /negative)	4.8	1.50-15.0
GCS 13-14 9-12 <9	1 5.50 16.00	 1.90-16.20 2.90-87.10
HIV negative Positive unknown	1 4.20 7.70	 1.00-17.00 1.20-47.70
Hour to IVF yes/no	0.40	0.10-1.10
MAP >65 <65	1 2.10	 0.70-6.80
IVF in first 6 hours 0 1 2 or more	 1 0.80 0.30	 0.30-2.00 0.10-1.10

Identified predictors for in patient mortality were positive blood culture, low GCS on admission and HIV status. Patients who presented with low GCS on admission were 16 times more likely to die than those with normal GCS.

CHAPTER 6

DISCUSSION

This study was a prospective cohort evaluation of septic patients admitted to UTH, which is the largest hospital in Zambia. The result from this study showed that the prevalence of bacteraemia in septic patients admitted to UTH was 21% with the commonest isolate being *Staphylococcus aureus* .*Streptococcus pneumoniae* was the second most isolated organism followed by *Salmonella typhi*. Our results are similar to those of the Ugandan study where the prevalence of bacteraemia was 18.9 with non-typhoid *Salmonella* being the highest isolate, followed by *Staphylococcus aureus* and *Streptococcus pneumoniae* being the least isolated organism (Jacobs 2009). However our results are different from those found in a Tanzanian study. Firstly they had a higher yield of 28% bacteraemia with mycobacteria being the highest isolate. This finding was unexpected as most of the studies done in sub-Saharan Africa have shown non-typhoid *Salmonella* and with *Streptococcus pneumoniae* as the commonest causes of sepsis (Archibald 2000). This difference could be explained by the methodology used as most of these studies including ours did not culture for mycobacteria.

The percentage of confirmed HIV infection in our study population was 68 with 14 % having there HIV status unknown or undetermined at the time of demise or discharge. These were patients who spent very few hours or days in the hospital such that by the time they died or were discharged an HIV test had not have been done.

Mortality in our cohort of septic patient was 40.4 % with a majority of them having laboratory proven bacteraemia. The mortality rate in this study was comparable to other studies on sepsis in the region (Jacobs, Salim). Identified predictors for inpatient mortality were HIV status, being bacteriaemic and low Glasgow coma scale on admission. For those whose HIV status was unknown the odds of dying were higher than those who were HIV negative. Probably because there were too sick such that they died before the HIV test could be done. We observed delays in giving fluid resuscitation and antibiotics. For instance 77 % and 70% of the patients who died received antibiotics and intravenous fluids respectively more than one hour after admission. Probably this was due to overcrowding and deficiencies of antibiotics and intravenous fluids.

Our antimicrobial susceptibility testing revealed that salmonella typhi was 100% susceptible to ciprofloxacin but other gram negatives were just about 63% susceptible. Most the organisms were 100% susceptible to cefotaxime. The two antimicrobial would be good for empirical treatment in view of the sensitivity in our setting.

The overall rate of blood culture contamination in this study was low. This was so because of the aseptic techniques that were maintained throughout the process of blood collection. The skin was cleaned using povidine iodine and alcohol

Study limitations

Only one blood culture specimen was collected from each patient. Probably if we had collected two blood culture specimens per patient our yield would have been much higher.

Two types of blood culture bottles were used, that is the bactec^{TM} and the manual ones. If we had used the bactec^{TM} bottles only probably the yield would have been higher.

Secondly those blood culture that yielded mixed growth could not be repeated as the patients had either dead or where discharged by the time the results came out from the lab.

Due to limitations of funds, we did not culture other body fluids apart from blood and we did not culture for mycobacteria.

Antibiotic disc for sensitivity testing were not readily available so it was difficult to tell which antibiotic the organisms were susceptible to.

CHAPTER 7

CONCLUSION

Most of the septic patients presenting to UTH had advanced immunosuppression (WHO stages 3 or 4) .Mortality in our cohort of septic patients was found to be approximately 40% and this was higher than similar studies in the sub-region. The organisms identified are *Staphylococcus aureas*, *streptococcus pneumoniae* and *Salmonella typhi*. Major predictors for in patient mortality were being HIV reactive, low GCS on admission and positive blood culture.

RECOMMENDATIONS

Patients presenting with the identified predictors for mortality (low GCS, positive blood culture) should be nursed in a high dependence ward with intensive monitoring.

There is a need for regular antimicrobial sensitivity patterns (antibiogram) to be made available to the clinicians to help with prescription/ choice of empirical antibiotics.

Blood culture bottles should be made available in all emergency rooms and samples collected in all septic patients in order to improve our management.

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APPENDIX

A study to determine the aetiology and outcome of septic patients presenting to UTH

UNIVERSITY TEACHING HOSPITAL
DEPARTMENT OF MEDICINE

DATA ENTRY SHEET

1	**File Number:**	_____
	Demographics	
2	**Physical Address**	_____
3	**Phone Number**	_____
	Date Of Enrolment:	☐ ____/____/_____
	Age:	_____
	Sex:	☐ Male
		☐ Female
	Marital Status:	☐ Single
		☐ Married
		☐ Divorced
		☐ Widowed
	Occupation:	_____
	Education:	☐ None
		☐ Primary School
		☐ Secondary School
		☐ College/ University
	Inclusion Criteria	
	Temperature on Admission	_____
	Admission respiratory Rate	_____
	WBCC	_____
	Systolic BP	_____
	Diastolic BP	_____
	Pulse Rate	_____
	HIV Description	
	HIV Status:	☐ Negative
		☐ Positive
	CD4 Count	_____
	On HAART?	☐ Yes
		☐ No
	Regimen:	☐ Zidovudine ☐ Didanosine ☐ Indivavir
		☐ Stavudine ☐ Emtricebine ☐ Nelfinavir
		☐ Lamivudine ☐ Neveraoine
		☐ Abacavir ☐ Efev
		☐ Tenofovir ☐ Lopinavir
	WHO Staging:	☐ 1
		☐ 2
		☐ 3
		☐ 4
	Presenting Complaint	☐ Fever
		☐ Diarrhoea
		☐ Headache
		☐ Cough
		☐ Others
	Duration Of Complaint:	_____ Weeks
	Prior use of Antimicrobials	☐ Yes
		☐ No
	Duration:	_____
	Type of Antibiotic:	☐ Amoxyl
		☐ Septrin
		☐ Pen V
		☐ Others
	Co Morbidy Condition	☐ Heart Failure
		☐ Chronic Kidney Disease
		☐ Diabates Mellitus
		☐ Hypertension
		☐ Others
	Clinical Findings	☐ Neck Stiffness
		☐ Altered Mentation
		☐ Crepitations
		☐ Dehydrated
		☐ Others
	Laboratory Investigations	
	Blood Culture:	☐ Negative
		☐ Positive
	Organism	_____
	Sensitivity	_____
	Urine Culture:	☐ Negative
		☐ Positive
	Organism	_____
	Sensitivity	_____
	CSF: Microscopy: Indian Ink	☐ Negative
		☐ Positive
	Organism	_____
	Culture:	☐ Negative
		☐ Positive
	CSF: Microscopy: Gram Stain	☐ Negative
		☐ Positive
	Organism	_____
	Culture:	☐ Negative
		☐ Positive
	Sensitivity	_____
	Stool: Microscopy	☐ Negative
		☐ Positive
	Organism	_____
	Culture:	☐ Negative
		☐ Positive

RESEARCH CONSENT FORM EFFECT OF ETIOLOGY ON OUTCOME OF PATIENTS PRESENTING WITH SEPTICEAMIA TO THE DEPARTMENT OF MEDICINE, UNIVERSITY TEACHING HOSPITAL.

1. INTRODUCTION

The faculty of the department of medicine with Dr Mwinsa Chimese as the principal investigator are carrying out a research on an infection called sepsis. The study is trying to find out the commonest germs that cause this infection and what happens to the patients who come to UTH with this infection. This will be made possible by your agreeing to participate in the study. Your participation will help us get the information that we need to make important policies and interventions for this problem. Planning for effective policies and interventions is very difficult if we don't know the extent of the problem. Therefore your participation in this study will be very helpful.

2. WHAT HAPPENS IN THIS RESEARCH STUDY?

You will be interviewed now and may be followed up for further information as the study progresses. Bloods and other body fluids will be collected for investigations such HIV test, CD4 count, culture, u/e, creatinine and liver function test

(this test will look at how your liver and the kidneys are working) The information collected will be kept confidential.

Blood will be drawn from a vein in one of your arms using a needle into a syringe. This will be after cleaning the skin with methylated spirit.

3. POSSIBLE PROBLEMS

We believe that the processes being used will not be harmful. However if we notice anything peculiar to you during or after information is collected, we will let you know so that it helps you on whether you want to continue taking part or not.

4. BENEFITS

Patients taking part in this study will be fully investigated

5. YOUR RIGHTS TO PARTICIPATE, NOT PARTICIPATE, OR TO WITHDRAW FROM THE STUDY

Taking part in this study is voluntary. You do not need to take part in this study - it is up to you. You may choose to either participate or not. If you want to take part in the study, you can later change your mind and stop participating in the study. You are not obliged to give reasons but if you give reasons they will be treated with utmost confidence because they are very useful to us. You will suffer no penalty and lose no benefits that you may be entitled to if you do not take part in this study. Your present or future medical care in Zambia will be the same whether or not you take part in the study.

6. CONFIDENTIALITY

Your name will never be made public by the investigators. The medical record will be treated the same as all medical records at the health centres. A code number that makes it very difficult for anyone to identify you will identify the research information gathered during this study from you. All information will be stored in a secure place. Information from this study may be used for research purposes and may be published; however, your name will not be made public by the investigators**.** It is possible that, after the study is over, we may want to look again at the laboratory and interview record data collected during this study to help us answer another question. If this happens, still your name will not be made public by the investigators.

If you have any questions concerning this study or your rights as a research participant, you can contact the following:

A study to determine the aetiology and outcome of septic patients presenting to UTH

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A study to determine the aetiology and outcome of septic patients presenting to UTH

THE UNIVERSITY OF ZAMBIA

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23 November, 2010
Our Ref: 002-10-10

Dr Sophie Mwinsa Chimese
Department of Internal Medicine
University Teaching Hospital
P/Bag RW1X
LUSAKA

Dear Dr Chimese,

RE: SUBMITTED RESEARCH PROPOSAL: **"EFFECT OF ETIOLOGY ON OUTCOME OF ADULT PATIENTS PRESENTING WITH SEPSIS TO UTH"**

The above-mentioned research proposal was presented to the Biomedical Research Ethics Committee on 8 September, 2010 where changes/clarifications were recommended. We would like to acknowledge receipt of the corrected version with clarifications. The proposal is approved.

CONDITIONS:

- This approval is based strictly on your submitted proposal. Should there be need for you to modify or change the study design or methodology, you will need to seek clearance from the Research Ethics Committee.
- If you have need for further clarification please consult this office. Please note that it is mandatory that you submit a detailed progress report of your study to this Committee every six months and a final copy of your report at the end of the study.
- Any serious adverse events must be reported at once to this Committee.
- Please note that when your approval expires you may need to request for renewal. The request should be accompanied by a Progress Report (Progress Report Forms can be obtained from the Secretariat).
- **Ensure that a final copy of the results is submitted to this Committee.**

Yours sincerely,

Dr E. M. Nkandu
CHAIRPERSON

Date of approval: 23 November, 2010 **Date of expiry:** 22 November, 2011