ORIGINAL PAPER

The Etiology And Outcome Of Adult Patients Presenting With Sepsis To The University Teaching Hospital, Lusaka, Zambia

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ABSTRACT

Background: Sepsis accounts for a significant burden of morbidity and mortality.

In developed world, it is implicated as the second leading cause of non-cardiac death. Mortality from sepsis is on the increase with a mortality rate of 33-61%. In spite of the high burden of sepsis in sub Saharan Africa, data regarding the etiology and outcome of septic patients is limited. We conducted a prospective cohort study to describe the etiology, characteristic and outcome of patients presenting with sepsis to the University Teaching Hospital in Lusaka, Zambia.

***Methods*:** Patients who met the inclusion criteria were enrolled into the study and after a thorough examination, bloods were drawn for full blood count, urea and electrolytes, liver function testsand for culture. Samples for culture were collected under aseptic techniques and cultured for aerobic organisms. Biochemical and bacteriological methods were used to identify the isolates and antibiotic sensitivity patterns were determined using agar diffusion methods. Patients were then followed up until they either demised or were discharge

***Results*:** A total of 161 patients were enrolled of which 110(68%) were HIV positive and 23(14%) had unknown HIV status. Bacteremia was found in 39 (24%) with the most isolated organism being staphylococcus aureus. Mortality in our cohort of septic patients was determinedat 40%. Identified predictors for in patient mortality were low admission Glasgow coma scale[OR 11.2(CI 3.5-36.4)], positive blood culture[OR 2.38(CI 1.14-4.95)] and HIV status, those with unknown HIV status were more likely to die than those who were HIV negative[OR 8.38(CI2.36-29.7)]

***Conclusion*:** Most of the septic patients presenting to UTH had advanced immunosuppression (WHO stage 3 and 4) and had a high mortality rate. *Staphylococcus aureus* and *streptococcus pneumoniae* were the highest isolates. Identified predictors for in patient mortality couldbe used to try and improve outcome in septic patients at UTH.

INTRODUCTION

Sepsis is a clinical syndrome that results from the body's response to invading microorganisms. Systemic inflammatory response syndrome (SIRS) is having two or more of the following:(1) Body temperature greater than 38^0 C or less than36^0C; (2) Heart rate greater than 90 beats per minute; (3) Respiratory rate greater than 20breaths per minute; (4) White blood cell count greater than 12000 $X10^9$ or less than 4000 $X10^9$ or greater than 10% immature neutrophils[1]. When SIRS results from a suspected or confirmed infection, the syndrome is called sepsis.

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.[1] In developing countries, the situation is worse. This is due to a number of factors. Firstly, the HIV/AIDS prevalence has greatly contributed to the increase in the number of patients at risk for sepsis. Other factors include limited availability of antimicrobial agents and limitations in diagnostic capacity in developing countries. Deficiency in man power and late presentation to the hospital of the very sick patients contributes to increased morbidity and mortality from sepsis[2].Even on a global scale, the incidence of sepsis is on the increase probably due to the increased burden of immunosuppression due to HIV and

other immunosuppressive therapies. Mortality from sepsis is on the increase with a mortality rate of 33-61%[3]. In the United States sepsis is one of the leading causes of morbidity and mortality and has been implicated as the second leading cause of non-cardiac death.[4] Mortality from septic shock is 28- 50%. About 750 000 people are affected annually and 210 000 die[5].

Guidelines have been formulated in developed countries which encourage early diagnosis, antimicrobial treatment and early fluid resuscitation[6]. There is need to find cost effective measures to improve outcome in resource limited countries like Zambia. Even though sepsis is such a high burden in sub-Saharan Africa very few studies have been done .We conducted a prospective cohort study of septic patients with a view to determine the etiology and outcome of septic patients.

RESEARCH DESIGN AND METHODOLOGY

This wasa prospective in patient cohort study conducted at the University Teaching Hospital, Lusaka, Zambia from august to December 2010. Ethical approval was obtained from the University of Zambia Biomedical Ethics Committee. Patients were enrolled from emergency room after obtaining consent. All enrolled patients were aged 16 years and above and had a source of infection plus two or more of the SIRS criteria.

Demographic information was collected on each patient and a brief clinical examination was performed by the study physician to assess any source of sepsis. Bloods were collected for HIV test, complete blood count. Liver function tests, urea, Creatinine and for culture. Specimens were collected using aseptic techniques. Venipuncture sites were disinfected using iodine solution followed by methylated spirit. About 10mls of blood was put in each blood culture bottle and immediately transported to the laboratory. The bactec blood culture bottles were then put in an automated blood culture machine. Upon detection of any growth in any of the blood culture bottles specimen were then sub cultured into blood, chocolate and McKonkey agars. Identification of the organisms was done by standard bacteriological and biochemical means. The antibiotic sensitivity patterns of the isolates were determined by agar diffusion method using antibiotic discs. Data collected was then entered into *epi info* version 3.5.1 dataset.

Statisticalanalysis

Data collected on hard copies was entered and analyzed using EPI INFO. Overall prevalence of bacteraemia in adult septic patients was determined. Descriptive statistics were reported as means and standard deviation for those which were normally distributed. Odds ratio at 95% confidence intervals were also calculated. Statistical significance was defined as $P<0.05$. Variables with clinically relevant cut of points were dichotomized. Stepwise backward logistic regressionwas used was used to determine the predictors of inpatient mortality.

RESULTS

A total of 161 were included in the final analysis. The mean age of the study population was 39 (range 16 – 88). Males made up 49.1% of the study population and 110 (68.3%) were HIV positive. The baseline characteristics are shown in the table below.

Table 1. Clinical characteristics

Clinical Characteristics	Total **n=161**	HIV+ **n =110**	HIV - **n =28**	Unknown HIV status **n=23**
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 ^{0}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)
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)

MICROBIOLOGY

34(21%) of the patients had significant bacteraemia with 5(3.2%) growing contaminants. The most commonly isolated organism was *StaphylococcusAureus* (25%), followed by *StreptococcusPneumoniae(10%) and Salmonella Typhi.*

Table 2: Sensitivity patterns

Organism	n
Gram positive	
Staphylococcus Aureus	10
Streptococcus Pneumoniae	4
Other *Streptococcus*	2
Micrococcus	3
Bacillus	2
Gram negative	
Salmonella	5
Klebsiella	4
Acinetobacter	2
citobacter	1
Haemophilusinfluenzae	1

MORTALITY

Overall in-hospital mortality of our cohort of septic patients was 40.4% (65/161). For severe sepsis the in-hospital mortality was 54.9%(50/91). Median length of 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 statuswere more likely to die than those who were HIV negative[OR 8.38,(CI 2.36- 29.7)].Laboratory proven bacteremia was also an important predictor of in-hospital mortality [OR 2.38, (CI 1.14-4.95)].

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				
.	83(51.6)	50(52.1)	33(50.8)	
.	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.
<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: 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	1	
9-12	5.50	1.90-16.20
<9	16.00	2.90-87.10
HIV negative	1	
Positive	4.20	1.00-17.00
unknown	7.70	1.20-47.70
Hour to IVF yes/no	0.40	0.10-1.10
MAP >65	1	
<65	2.10	0.70-6.80
IVF in first 6 hours		
0	1	
1	0.80	0.30-2.00
2 or more	0.30	0.10-1.10

DISCUSSION

The study was a prospective cohort evaluation of septic patients admitted to the University Teaching Hospital, which is the largest hospital in Zambia.

Mortality in our study was 40.4% and this was higher than most studies in the region. Fluid and antibiotic resuscitation were suboptimal in our cohort of patients. This was consistent with a retrospective chart review which was done in Livingstone where 86% of hypotensive septic patients had intravenous fluid resuscitation[10]. Probably this was due to overcrowding resulting in high nurse- patient ratio. There were also limitations in terms of antibiotics, fluid and oxygen cylinders, for those who were in respiratory distress and needed oxygen supplementation.

Identified predictors for in patient mortality were positive or unknown HIV Status, positive blood culture and low Glasgow coma scale on admission. For those with unknown HIV status, the odds of dying were higher than those who were HIV negative. Probably because they were too sick and so died before an HIV test could be done. The identified predictors for in patient mortality could be used for evaluating critically ill patients presenting with sepsis.

Our study had limitations; firstly only one blood culture specimen was collected per patient. Probably the yield would have been higher if we had collected two or more specimens per patient. Secondly blood cultures that

yielded mixed growth could not be repeated as most of the patients had either died or were discharged by the time the results came out. Due to limitations in terms of funds, other body fluids and mycobacteria were not cultured for.

In conclusion, most of the septic patients presenting to UTH had advanced immunosuppression (WHO stages 3 or 4). Mortality in our cohort of septic patient was 40% and was comparable to similar studies in the region and so were the isolated organisms. Patients with identified predictors for in patient mortality should be nursed in high dependence ward.

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