Characteristics and outcome of sepsis – A perspective from a tertiary care hospital in Pakistan

Shahla Siddiqui, Bushra Jamil, Nosheen Nasir, Najeeha Talat,

Fouzia A Khan, Philipe Frossard and Rabia Hussain

ABSTRACT

Objective:

Sepsis accounts for a high rate of mortality with significant impact on health care across the world. Our objective was to determine clinical determinants of outcome of sepsis in a tertiary care setting.

Design:

Prospective, observational study.

Place and Duration: A tertiary care University hospital catering to roughly 50,000 admissions per year with an intensive care unit [ICU] admitting around 1000 patients per year. The study was conducted from 2006-2007

Patients and Methods:

We studied 99 patients in one year with sepsis and/or septic shock as per SCCM definitions. Patients were enrolled after informed consent. Data on patient characteristics such as ethnicity, site of infection, type of infecting organisms, presence of co-morbidities and severity of sepsis was collected. Final outcome was recorded in terms of recovery from sepsis or mortality. Association between patient characteristics and outcome was done using chi square test.

Results:

Sepsis patients belonged to six ethnic groups; no significant difference was found in mortality between these groups. At the time of enrolment, 69% of patients had sepsis and 30% had septic shock. Mortality due to sepsis/septic shock was 36.36% and was significantly associated with male gender [p=0.04] and presence of septic shock [p< 0.001]. The commonest site of infection leading to sepsis was the respiratory tract [48%]. Forty nine patients were culture positive showing higher frequency of gram negative [59%] compared to gram positive organisms [28%].

Conclusions:

Majority of cases of sepsis arose from the respiratory tract infections; majority of culture-proven infections were due to gram negative bacteria and males were more likely to have a poor outcome in our cohort of sepsis patients. Outcome was not associated with ethnicity or presence or number of co-morbid conditions.

Key words:

Clinical characteristics, factors affecting sepsis outcomes, Pakistan

INTRODUCTION

Septic shock is the most common cause of mortality in the intensive care unit [ICU] in most countries [1],[2]. It is the leading cause of death overall and is the most common cause of shock in the United States [3],[4]. Despite recent advances in diagnosis and management, mortality from sepsis remains high, ranging from 15% in patients with sepsis to 40-50% in patients with septic shock with multi-organ dysfunction syndrome [MODS][5]. Preliminary data from Aga Khan University Hospital, a tertiary care referral center in Karachi, Pakistan, reveals that about 1.3% of all admissions are due to sepsis and the mortality rate in patients with sepsis or septic shock is 38%. Despite significant advances in the understanding of pathophysiology of sepsis, effective therapies are still lacking [6],[7].

There is a dearth of published data on the outcome of sepsis in Pakistan, as a nation-wide registry of sepsis does not exist [8],[9]. A database documenting the incidence, outcomes and distribution characteristics of sepsis patients can help in leading to measures designed to find etiological and associated factors as well as reduced incidence and improved outcomes of the disease [1],[10]. The objective of the current study was to identify factor/s contributing to a poor outcome in adult patients with sepsis. We conducted an observational study, comparing patients with sepsis who survived versus those who died in terms of age, gender, ethnicity, site of infection, type/s of infecting organisms and presence of other chronic conditions. As part of a larger controlled study looking at the cytokine levels and genetic predisposition of septic patients, we are describing the demographic data collected over a period of one year of such patients from a tertiary care hospital in Karachi, Pakistan.

METHODS

Study design: This was a prospective, observational study.

Setting: A tertiary care University hospital catering to roughly 50,000 admissions per year with an intensive care unit [ICU] admitting around 1000 patients per year.

Inclusion criteria: All patients over the age of 18 admitted to the hospital with a diagnosis of infection, sepsis or septic shock over a period of one year from August 2006 to 2007.

Exclusion criteria: Patients who developed shock due to a cardiogenic, hypovolemic or neurogenic cause.

Methodology**:** After obtaining approval for the Ethics Committee, all consecutive patients admitted to the hospital with sepsis were evaluated by a research assistant and enrolled in the study if they met the inclusion criteria. Informed consent was obtained in all patients. All consenting medical, surgical [including those with post-operative infections] and obstetrics and gynaecology patients with sepsis were recruited. Diagnostic criteria for categorization into sepsis and septic shock was as per the Society of Critical Care Medicine [SCCM] guidelines [10],[11] which state that patients with sepsis have a documented bacteraemia together with any 2 of the following signs or symptoms: a] white blood cell count <4000 and >10,000 b] respiratory rate of >35 b/min or a PaCO2 <32 mmHg and c] temperature >37.5 degrees Celsius or <34 degrees Celsius. Patients who developed septic shock were defined by a mean arterial pressure of < 60 mm Hg or hemodynamic instability.

All patients in the ward and special care units were followed by infectious diseases physicians throughout their hospital stay. All septic shock patients included in this study were managed in the ICU and were followed by intensive care physicians with daily assessment of vital signs and other parameters in accordance with APACHE II scoring systems [12],[13]. Patients underwent investigations in accordance with the standard protocol for sepsis work-up.

Ethics: Ethical approval for this study was obtained from The Aga Khan University Ethical Review Committee in 2006.

Statistical Analysis: Data was collected by a research officer on a Performa and entered into SPSS version 13.0. Student's t test was used for age and Chi square test was used for comparison of gender differences between patients with sepsis and septic shock.

RESULTS

A total of 99 cases of sepsis and septic shock were identified during the study period of one year, from 2006 -2007, from a largely representative ethnic distribution. Demographic characteristics of study population are shown in Table 1.

Table 1: Demographic characteristics and co-morbid conditions in patients with sepsis and septic shock

dy Groups	Age [Mean±SD]	M/F	Comorbids				Ethnicity					
			DM	HTN	IHD	CRF	Sindhi	Balochi	Punjabi	Pathan	Gujrati	Urdu
Sepsis	51.15942 ±16.27487	37/32	40%	50%	22%	26%	16%	13%	9%	12%	17%	33%
eptic Shock	52.46667 ±17.90344	16/14	37%	43%	23%	20%	27%	0	10%	10%	17%	37%

DM: Diabetes Mellitus; HTN:Hypertension; IHD: Ischemic Heart Disease; CRF: Chronic Renal Failure

There were 53 males and 46 females with a mean age of 51.8±17 years [table 1]. At the time of enrolment, 69 patients had sepsis and 30 had septic shock. Hypertension, diabetes mellitus, ischemic heart disease and chronic renal failure were the common commitment illnesses [table 1]. A small number of patients had chronic liver disease [6%] and pancreatitis when they developed sepsis. No significant association of mortality was found with any of the coexisting morbidities. Overall mortality due to sepsis and septic shock during the study period was 36.36%. Mortality was associated with male gender [p=0.04] [46% in males compared with 27% in females] and presence of septic shock [p<0.001]. Use of steroids was noted in 6% of patients and no association was found between dose and duration of steroids and outcome of sepsis.

The respiratory tract was the commonest site of infection associated with sepsis [48%] followed by the urinary tract [37.3%] and blood stream infections, including central line related infections and endocarditis [30.3%]. Infections at other sites were less common [Table 2].

Table 2: Sites of infection and types of organisms seen in patient groups according to outcome of sepsis

CHARACTERISTICS	ALL PATIENTS[N=99]	EXPIRED [N=36]	RECOVERED[N=61]
MEAN AGE	51.6	52.3	51.9
GENDER	M=56, F=46	M=24, F=12	M=28, F=33
SEPSIS	69	15	53
SEPTIC SHOCK	30	21	8
SITE OF INFECTION			
RESPIRATORY TRACT	48	22	25
URINARY TRACT	37	9	28
DEEP ABSCESSES*	11	4	7
CLABSI	14	7	7
BLOODSTREAM	14	5	9
ENDOCARDIUM	2	1	1
PERITONEUM	4	2	2
CNS	6	3	3
GENITAL	2	-	2
SKIN, SOFT TISSUES & BONE	9	2	7
MICRO DATA			
CULTURE POSITIVE	49	18	31
GRAM POSITIVE	14	7	7
GRAM NEGATIVE	29	8	21
POLYMICROBIAL	6	3	3

* e.g liver, spleen

CLABSI: central line associated blood stream infection

CNS: central nervous system

There was no significant difference in site of infection leading to sepsis in those who recovered and those who succumbed to sepsis.

Cultures from different sites were positive for pathogens in 49 patients. Patients who died of sepsis/septic shock had more culture-proven infections [31 vs. 18, table 2]. Overall, infections with gram negative organisms were more common [59%] as compared with gram positive bacteria.

Of the gram negative isolates, Escherichia coli was the most commonly isolated pathogen [22% of the cases] followed by Klebsiella spp, Acinetobacter and Enterobacter spp. Of the 12 isolates of *Staphylococcus aureus*, nine were methicillin resistant. No association was observed with outcome of sepsis and types of organisms which grew in respective cultures.

DISCUSSION

In this study, we looked at adult patients with sepsis and followed them for their entire duration of hospitalization. Our patients were younger, with a mean age of 51 +/- 16 years as compared with sepsis patients of European origin [median 64 years] [14], those from North America [mean 60.8 years] [15] and Brazil [median age 65.2 years] [16]. In the US, the average age of patients with sepsis has increased consistently over time, from 57.4 years to 60.8 years from 1979 to 2000. Sepsis developed later in life in female patients than in male patients: the mean age among women was 62.1 years, as compared with 56.9 years among men [difference, 5.2 years][17].

For this study, we did not specifically look for a gender association with development of sepsis or septic shock. However, we found a higher sepsis-related mortality in men.

Impact of racial variation on the incidence and outcome of severe sepsis has been the subject of many studies. In one study, whites were noted to have the lowest rates of sepsis, with both blacks and other nonwhites groups having a similarly elevated risk as compared with whites [mean annual relative risk, 1.89 and 1.90 respectively] [18]. In another study [19] after accounting for differences in poverty and geography, black race was found to be susceptible to a higher rate of severe sepsis—almost double that of whites. Sepsis has been noted to develop at a younger age in black men [mean age, 47.4 years], and has the highest mortality [23.3 percent] [17]. Hispanic ethnicity has been found to be protective, conditional on similar region and poverty [15]. Racially, Pakistanis are Caucasians. To look at further ethnic differences within our population, we categorized patients into six groups, which were largely representative of the population of Karachi. The groups were small and no significant association was found between ethnicity and susceptibility to severe sepsis and mortality in our population.

Potential mechanisms for heterogeneous susceptibility to sepsis observed in different populations include genetic differences, which have been explored according to sex [20] but not according to race, and other social and clinical factors. The underlying reasons for such disparities in the incidence, susceptibility and outcome of sepsis require further investigation.

As in other studies, not all cases of sepsis in our study had culture-proven infections; 60 percent of patients had positive cultures in the SOAP study on European patients [14] while specific organisms causing sepsis were recorded in 51 percent of all cases in a study conducted in the US [17]. In this study, cultures were positive in 49.4 percent of cases.

In the US, gram-negative bacteria were the predominant organisms causing sepsis in the 1980s, whereas gram-positive bacteria became common in subsequent years [17]. By the year 2000, gram-positive bacteria accounted for 52.1 percent of cases, with gram-negative bacteria accounting for 37.6 percent; polymicrobial, anaerobic and fungal infections were less common. Respiratory tract infections have been shown to be the most common infections associated with sepsis [16, 14] and we found a similar association in our patients.

Sepsis mortality is declining in the developed world, most likely as a consequence of early diagnosis, better diagnostic modalities and early institution of fluid and antibiotic therapy. Angus and co-workers [21] analyzed more than 6 million hospital discharge records from seven states in the USA and estimated that 751,000 cases of severe sepsis occur annually, with a mortality rate of 28.6%. In a large, prospective European epidemiological study [22], Alberti and colleagues evaluated 14,364 patients admitted to 28 ICUs. Their main findings were a crude infection incidence of 21.1percent. More recently, a multicenter French study [23] has shown a high incidence of septic shock [8.2 per 100 admissions] among critically ill patients associated with a high crude mortality rate [60.1%].

The total in-hospital mortality rate fell from 27.8 percent during the period from 1979 through 1984 to 17.9 percent during the period from 1995 through 2000 in the US [17].

Mortality from sepsis in our hospital has varied from a staggering 80% to 60 % prior to 2005 and from 55 % to around 36% over the last 4 years.

The reason for declining sepsis related mortality in our hospital remains unknown. It may be hypothesized that in the absence of bundled care for sepsis and early goal-directed therapy [which have only been recently introduced at our hospital] the main difference in management during these two time periods has been in the choice of empiric antibiotic for sepsis, which constitutes just one, albeit an extremely important component of sepsis management. With mounting resistance in gram negative organisms in the community [approx 50 percent resistance to 3rd generation Cephalosporins in community isolates and >75 percent resistance in isolates from in-patients] of E.coli and Klebsiella, and increasing prevalence of MRSA, [44 percent isolates from in-patients and 33 percent from outpatients] the empiric antibiotic of choice in a patient presenting with systemic infection or sepsis is either Piperacillin-Tazobactam or one of the Carbapenems with or without Vancomycin and/ or Amikacin for the first 48 to 72 hours at least, with subsequent modification according to culture and sensitivity results and the patients' condition. Early institution of appropriate antibiotic/s does impact outcome of sepsis. Whether this was the sole reason for relatively lower sepsis-related mortality during the study period as compared to previous years, remains a matter of conjecture.

A database documenting the incidence, outcomes and distribution characteristics of sepsis patients can provide information which may be useful for early recognition of factors associated with severe sepsis and timely institution of appropriate management, thereby improving the outcome of sepsis in our patients. To our knowledge, ours is the first study of its kind from Pakistan, describing the demographics, clinical and laboratory features and outcome of patients with sepsis who presented to our hospital in a third world setting. The findings presented here are a part of a study looking at association of cytokine profiles and cytokine gene polymorphisms with outcome in sepsis in our population.

In conclusion, sepsis in our hospital was most commonly seen in patients who had pneumonia and in those who were infected with gram negative organisms. Our patients were relatively young and sepsis-related mortality was similar to that noted internationally. We did not observe any association of outcome of sepsis with ethnicity or presence or number of concomitant chronic illnesses but males had poorer outcome.

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Author Information

Dr. Shahla Siddiqui
Khoo Teck Puat Hospital, Singapore,
tel: 006597966257
fax: 006566022137
add: 90 Yishun central
Singapore
79688

Corresponding Author:

Dr. Bushra Jamil
Department of Medicine
Aga Khan University,
Karachi, Pakistan.

Mailing Address:
Department of Medicine
Aga Khan University, Stadium Road
Karachi, 74800, Pakistan.
Tel: 9221-34930051, exr 4671
Fax:92-21-34934294
Mobile: 0300-2246132
Email: bushra.jamil@aku.edu
jamilbushra@yahoo.com

Dr. Nosheen Nasir
Department of Medicine
The Aga Khan University
Stadium Road P.O Box 3500
Karachi 74800, Pakistan

Dr. Najeeha Talat
JohnWayne Cancer Institute,
2200 Santa Monica Blvd CA 90404
tel: 3104495225,
talatn@jwci.org

Professor Fouzia A Khan
Department of Anaesthesia
The Aga Khan University
Stadium Road P.O Box 3500
Karachi 74800, Pakistan

Professor Philipe Frossard
Dean college of Arts and Sciences
Professor of Biological and Biomedical Sciences
Abu Dhabi University, Abu Dhabi Campus
P.O Box 59911, Abu Dhabi, UAE
800-ADYOU (800-23968)

Professor Rabia Hussain
Department of Pathology and Microbiology
The Aga Khan University
Stadium Road P.O Box 3500
Karachi 74800, Pakistan

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