ORIGINAL ARTICLE

INCIDENCE, OUTCOME AND RISK FACTORS FOR SEPSIS - A TWO YEAR RETROSPECTIVE STUDY AT SURGICAL INTENSIVE CARE UNIT OF A TEACHING HOSPITAL IN PAKISTAN

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Background: Sepsis is amongst the leading causes of admission to the intensive care units and is associated with a high mortality. However, data from developing countries is scares. Aim of conducting this study was to determine the incidence, outcome and risk factors for sepsis on admission to surgical intensive care unit (SICU) of a teaching hospital in Pakistan. **Methods:** Two year retrospective observational study included all consecutive adult admissions to the surgical intensive care unit (SICU) of a University Hospital, from January 2012 to December 2013. **Results:** Two hundred and twenty-nine patients met the inclusion criteria. Average age of the patients was 46.35±18.23 years (16–85), mean Acute Physiology and Chronic Health Evaluation II (APACHE II) score was 15.92±8.13 and males were 67.6%. Median length of ICU stay was 4 [IQR 5]. 43% patients fulfilled the criteria of sepsis at the time of admission to the SICU and incidence of severe sepsis/septic shock was 35%. Abdominal sepsis was the most frequent source of infection (57.5%). The overall intensive care unit mortality was 32.31% but the mortality of sepsis-group was 51.15% as compared to 17.7% of the non-sepsis group. Stepwise logistic regression model showed that increasing age, female gender, non-operative admission, admission under general surgery and co-morbidities like ischaemic heart disease and chronic kidney disease were significant predictors of sepsis. **Conclusion:** The incidence of sepsis and severe sepsis/septic shock, on admission to SICU is high and mortality of the sepsis group is nearly three times the mortality of the non-sepsis group.

Keywords: Sepsis, severe sepsis, septic shock, intensive care units, incidence

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INTRODUCTION

Sepsis represents a significant socioeconomic burden worldwide. Extrapolating data from high-income countries, approximately 31 million cases of sepsis are reported globally with about 6 million deaths per year.[1] The incidence and rate of hospitalization for severe sepsis increases annually and sepsis is amongst the leading causes of admission to the intensive care units (ICUs) in the United States.[2–4] The incidence of sepsis in studies reported in the last decade ranges from 9–37% for all patients admitted to the ICUs and severe sepsis remains a leading cause of death. Mortality rates for severe sepsis in patients admitted to intensive care units vary from 30 to 50%.[2,4–6]

The largest part of the global sepsis burden occurs in low and middle -income countries. 90% of the worldwide deaths from pneumonia, meningitis or other infections occur in less developed countries and majority of deaths in neonates and infants attributable to sepsis occur in Asia and sub-Saharan Africa.[7,8] Statistics from developing countries however are limited to sepsis in under-five children and maternal sepsis.

The prevalence and outcome of sepsis in intensive care units in Pakistan is largely unknown. The primary objective of this study was to estimate the incidence of sepsis on admission to the surgical intensive care unit (SICU) of a tertiary care hospital and compare the characteristics and outcome of patients with and without sepsis in order to identify risk factors of sepsis in this cohort of patients. The secondary objective was to document the frequency of use of Surviving Sepsis Campaign (SSC)[9] recommended interventions in the sepsis group.

MATERIAL AND METHODS

This 2 year retrospective observational study was exempted for review from the institutional ethical review committee. Files of all consecutive adult (non-cardiac) admissions to the surgical intensive care unit (SICU), from January 2012 to December 2013 were reviewed. Cases with an incomplete record, death or discharge from ICU earlier than 24 hours and documentation of do not resuscitate orders within 24 hours of admission were excluded from the study. In case of re-admission, only the first admission was considered. Data was collected on predesigned forms by the team of primary investigators. Department data entry officer entered and stored all the data on SPSS. Data was reviewed periodically by the primary investigators and ambiguities resolved by a re-review of the patients medical record. The demographic information (age and gender), admitting department, primary diagnosis, presence of co-morbidities (i.e., diabetes mellitus (DM), hypertension (HTN), ischaemic heart disease (IHD), chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), malignancy or history of

alcohol abuse), type of admission (elective surgery, emergency surgery or non-operative), APACHE II score, length of ICU stay and outcome (discharge or death in ICU and hospital) were documented on the study Performa. Cases were assigned to the sepsis group if they fulfilled the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference criteria of defining sepsis10, i.e., presence of two or more systemic inflammatory response syndrome (SIRS) criteria along with suspected or documented source of infection, either in the surgeon's notes, nursing notes, positive culture report or radiological evidence. The most likely source of infection was classified as lungs, urinary tract, abdomen, musculoskeletal, central nervous system, or peripartum. In case of more than one likely source of infection, the source of most severe infection at the time of presentation was considered. The sepsis and non-sepsis groups were compared for mean age, gender, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, type of admission, co morbidities, admitting departments, ICU mortality and length of ICU stay. In the sepsis group compliance with the SSC-recommended-interventions carried out after admission to SICU were recorded. Key interventions recorded included serum lactate, blood cultures, broad spectrum antibiotic cover, central venous access, ScvO2, fluid challenge, and vasopressor use.

All statistical analyses were performed with the software SPSS-19. Statistical analysis results were expressed as mean±standard deviations for continuous variables and numbers and percentages for categorical variables. Independent sample t-test and Mann-Whitney U test were used as per condition of normality checked by Kolmogorov-smirnov and histogram for quantitative observations and chi-square test was applied to compare categorical observation between sepsis and non-sepsis groups. Unadjusted odd ratio were computed by logistic regression and for adjusted Odd ratio step wise multiple logistic regression was applied to build model to predict sepsis. $p \leq 0.05$ was considered as significant

RESULTS

Five hundred and forty seven surgical admissions in two years, from January, 2011 till December, 2012 were evaluated. Three hundred and eighteen (58%) patients were excluded from the study due to missing files or incomplete data recorded or not meeting the inclusion criteria. The study group, therefore, consisted of 229 patients. Patients admitted to the SICU were predominantly male (67.6%), average age was 46.35±18.23 years (16–85) and the mean APACHE II score was 15.92. One hundred and fifty-six patients were received from the operating rooms (68%) and seventy-three non-operative (32%) patients were received from emergency room and surgical wards. In the operative group 85% patients underwent emergency surgical procedures and 15% had elective surgeries. Admissions under various departments are as shown in the figure-1. The overall intensive care unit mortality was 32.31% and the hospital mortality was 34%. The median length of ICU stay was 4 [IQR 5] 2–45 days (min-max).

A total of 99 (43%) patients fulfilled the criteria of sepsis at the time of admission and 81% of these patients were in severe sepsis or septic shock. Presence of SIRS criteria in both septic and non-septic patients is shown in table-1.

Abdominal sepsis was the most frequent source of infection (57.5%) in this cohort of SICU patients, rest are shown in figure-2. The characteristics of patients with and without sepsis are compared in table-2.

The incidence of sepsis was highest in the non-operated group (52%), followed by emergency surgery group (43%) and elective surgery group (16%). The incidence of sepsis was highest in the patients admitted under the care of departments of orthopaedics (9/10) and urology (7/10) followed by general surgery (63/97) and it was the lowest in the neurosurgical patients (11/84). The sepsis group was associated with a higher incidence of comorbid as shown in figure-3.

In univariate analysis, age, APACHE II score, type of admission, DM, IHD and CKD and general surgery were significant independent predictor of sepsis while in multivariate analysis, stepwise logistic regression model showed that increasing age, female gender, non-operative admission, admission under general surgery and co-morbidities like IHD and CKD were significant predictor of sepsis in the final model as shown in table-3.

Except for measuring central venous oxygen saturation (34/99), compliance with most of the interventions recommended by the SSC guidelines in the patients diagnosed with sepsis on admission or during the SICU stay was more than 90%, i.e., serum lactate (93%), blood cultures (93%), antibiotics (100%), fluid boluses (96%), CVP (96%), and vasopressors (78%).

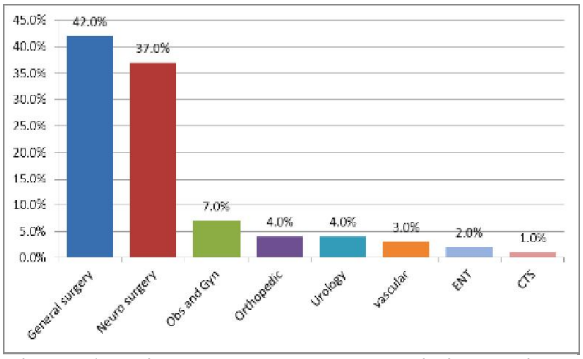

Figure-1: Primary departments admitting patients to SICU

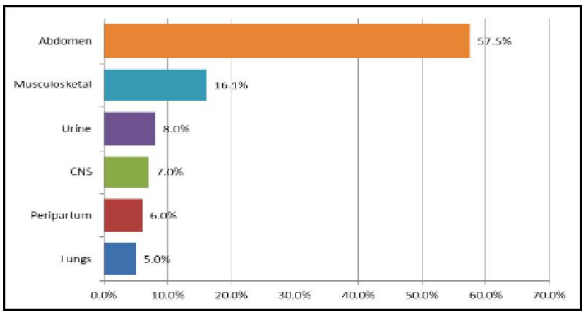

Figure-2: Source of infection on admission to SICU

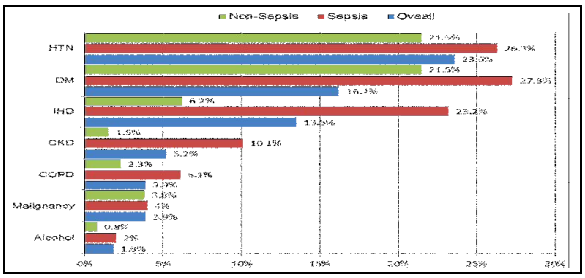

Figure-3: Comorbidities in SICU admissions, sepsis, non-sepsis and overall

Table-1: SIRS criteria in sepsis and non-sepsis groups on admission to SICU, n=229

SIRS Criteria	Sepsis n=99	Non-sepsis n=130	*p*-value
Temperature >38 or <36 C	93 (93%)	14 (10.8%)	0.0005
Heart rate >100/min	91 (91.1%)	33 (25.6%)	0.0005
Respiratory rate >28/min	81 (81.8%)	18 (14%)	0.0005
WCC >14,000 OR <4,000/min	76 (76.8%)	4 (3%)	0.0005

Table-2: Comparison of characteristics of patients with and without sepsis n=229

Variables	**Overall**	**Sepsis n=99**	**Non-Sepsis n=130**	***p*-Value**
APACHE II score	15.92±8.13	19.47±8.40	13.13±6.43	0.005
Average age	46.35±18.23	52.81±18.87	41.44±16.14	0.0005
Male	155 (67.7%)	62 (62.6%)	93 (71.5%)	0.15
Female	74 (32.3%)	37 (34.7%)	37 (28.5%)	
Non-Operative	73 (31.9%)	38 (38.4%)	35 (26.9%)	0.01
OR-Emergency	132 (57.6%)	57 (57.6%)	75 (57.7%)	
OR-Elective	24 (10.5%)	4 (4%)	20 (15.4%)	
Co-morbidities	85 (37.1%)	49 (49.5%)	36 (27.7%)	0.001
DM	37 (16.2%)	27 (27.3%)	10 (7.7%)	0.005
HTN	54 (23.6%)	26 (26.3%)	28 (21.5%)	0.404
IHD	31 (13.5%)	23 (23.2%)	8 (6.2%)	0.005
CKD	12 (5.2%)	10 (10.1%)	2 (1.5%)	0.004
COPD	09 (3.9%)	6 (6.1%)	3 (2.3%)	0.18
Malignancy	9 (3.9%)	4 (4%)	5 (3.8%)	0.99
Alcohol	3 (1.3%)	2 (2%)	1 (0.8%)	0.41
Admitting Departments				
Neuro Surgery	84 (36.7%)	11 (11.1%)	73 (56.2%)	0.0005
General Surgery	97 (42.4%)	63 (63.6%)	34 (26.2%)	0.0005
Obs and Gynae	14 (6.1%)	6 (6.1%)	8 (6.2%)	0.977
Ortho	10 (4.4%)	9 (9.1%)	1 (0.8%)	0.003
Urology	10 (4.4%)	7 (7.1%)	3 (2.3%)	0.106
CTS	3 (1.3%)	1 (1%)	2 (1.5%)	0.990
ENT	5 (2.2%)	0 (0%)	5 (3.8%)	0.070
Vascular	6 (2.6%)	2 (2%)	4 (3.1%)	0.701
ICU Stay				0.023
Median [IQR]	4 [5]	5 [4]	3 [4]	
Min-Max	2–45	2–42	2–38	
Mortality in ICU	74 (32.3%)	51 (51.5%)	23 (17.7%)	0.0005

Table-3: Factors associated with sepsis, univariate and multivariate stepwise logistic regression analysis model

Predictors	**Univariate**			**Multivariate**		
	OR	95%CI	*p*-Value	**Crud OR**	**95%CI**	***p*-Value**
Age (Per years increase))	1.037	1.02–1.05	<0.001	1.04	1.02–1.06	<0.001
APACHE Score	1.06	1.03–1.10	<0.001			
Male	0.66	0.38–1.16	0.15	0.35	0.16–0.79	0.012
Female	1			1.00		
Type of admission						
Non-Operative	5.42	1.68–17.44	<0.01	38.42	5.35–275.63	<0.001
OR-E	3.8	1.23–11.73	0.02	13.06	2.07–82.12	0.006
OR-Elect	1			1.00		
Co-Morbidities						
DM	4.5	2.05–9.83	<0.001			
HTN	0.41	0.70–2.39	0.41	0.198	0.065–0.602	0.004
IHD	4.62	1.96–10.84	<0.001	3.7	1.00–13.97	0.05
CKD	7.19	1.53–33.61	0.012	56.16	6.89–457.2	<0.001
Admitting Departments						
Neuro Surgery	0.098	0.048–0.20	<0.001	0.125	0.041–0.384	<0.001
General Surgery	4.94	2.81–8.71	<0.001	3.54	1.40–8.97	0.008
Obs & Gyn	0.98	0.33–0.29	0.97			
Ortho	6.86	0.78–59.70	0.081			
Multivariate, forward step wise logistic regression applied to predict sepsis						

DISCUSSION

Nearly 43% (99/229) patients presenting to SICU during the study period fulfilled the sepsis criteria on admission. It is difficult to compare the sepsis rate with other studies due to variation in definitions used to identify 'sepsis' cases and the different patient populations in medical, surgical or mixed ICUs. The SOAP study[11], which is a large pan-European study also used ACCP/SCCM definition of sepsis and described that 37% of adult patients admitted to predominantly medical ICUs, had sepsis. However, there was considerable variation in the rates of sepsis reported from the participating countries. For example higher rates were reported from Portugal (73%), UK and Ireland (52%) and Eastern Europe (48%), a nearly similar rate from Greece (43%) and France (41%) and lower rates of sepsis as compared to this study were reported from countries like Netherlands (39%), Italy (38%), Spain (35%) and Switzerland (18%). The EPIC II study[12] included predominantly surgical patients from Western Europe, Central and South America, Asia, Eastern Europe, North America, Oceania and Africa and considered 51% patients to be infected on the day of the study, but infection rate was 32% in those patients where the pre-study duration of ICU stay was 0-1 day. However in the EPIC II study 'infection' was defined according to the International Sepsis Forum definition[11]. The incidence of severe sepsis in this study was 35%, which is comparable to the incidence of severe sepsis reported in the SOAP study[11] from countries like Italy (32%), Netherlands (34%), Eastern Europe (43%), UK and Ireland (45%), but is very high as compared to 10.9% incidence of severe sepsis in Asian intensive care units (Phua)[14] and 11.8% in Australian and New Zealand intensive care units (Finfer)[15]. A delay in recognition of sepsis and inadequate resuscitation prior to admission to the SICU in the non-operative group, along with underlying disease severity in the emergency surgery group could explain the high incidence of severe sepsis/septic shock at the time of presentation to the SICU. The most common source of infection in this study was abdominal sepsis (57.5%), followed by musculoskeletal infections (16%). This reflects the unique case-mix of the SICU that predominantly admits emergency post-operative cases with highest admissions under general surgery. Admitting diagnoses of these patients were intestinal perforations, intestinal obstruction, abdominal gun-shot injuries, pancreatitis, bowel ischaemia, obstructed hernias, abdominal malignancies, abdominal tuberculosis, blunt trauma and blast injuries and necrotizing fasciitis.

The non-operative group included patients who had no surgical intervention in the preceding 48 hours and showed a very high incidence of sepsis (52%). Most of the patients in this group belonged to orthopaedics and urology with infected fractures, urinary tract infections and wound infections, admitted either directly from the emergency department or surgical floors after undergoing surgery more than 48 hours prior to SICU admission. The incidence of infection was very low in the neurosurgical (13%) and elective post-operative cases (4%). The most common source of infection described in the previously quoted studies is lung/respiratory tract, i.e., SOAP[11] (64%), EPIC II[12] (63.5), Finfer[15] (50.3%), MOSAIC[14] (37.4%). In this study lungs were considered as primary reason for admission only in 5% of cases. The reason could be that we considered the most severe infection at the time of admission, patients could have a respiratory tract infection in addition to the most obvious surgical source or may have developed pneumonia during the course of ICU stay but it was not captured in this study.

The ICU mortality in this study was 32% which is less than the mortality reported from Asian intensive care units[14] (36.7%). However, the mean APACHE II score of predominantly medical/non-operated patients in that study was higher (22.8) as compared to the mean APACHE II score of our study (15.92). The mortality of the sepsis-group in this study was nearly three times (51%) as compared to the non-sepsis group (17.7%). Alberti and co-workers[16] reported a similar mortality in non-infected (16.9%) and infected cases (53.6%) in 2002. Mortality of septic patients in this study was twice as high as the mortality of infected surgical patients in the EPIC II study[12] (25%), the predominantly medical septic patients in the SOAP study[11] (27%), Finfer's study[15] (26.5%) and a study from US[4] (28.6%). One reason could be that excluding 19 patients, the rest of the patients in the sepsis-group had severe sepsis or septic shock (81%) on admission to SICU, whereas the proportion of patients in severe sepsis varies from 10–64% in the other studies. The hospital where this study is was conducted is a tertiary referral centre for complicated general surgical patients from other hospitals of the city as well as far-flung areas and is one of the few trauma centres in the city. Highest admissions were for surgical emergencies like gut perforations, gunshot injuries and blunt trauma, necrotizing fasciitis and necrotizing pancreatitis associated with a high mortality. High mortality could also be due to the presence of comorbidities like diabetes, ischaemic heart disease and chronic kidney diseases in the sepsis group.

The SSC[9] recommended interventions for early recognition and management of sepsis and compliance with the bundles has shown to improve survivor[17]. To qualify as compliance with the resuscitation bundles, predefined targets of mean arterial pressure (MAP), central venous pressure (CVP) or lactate clearance should be met. As this was a retrospective study it was not possible to determine the

time of diagnosis of sepsis, study the effect of using the interventions in achieving the specific targets, account for confounding factors like lead-time bias or standardize treatment received prior to admission to SICU. Therefore like a few other authors[18,19] we also considered any attempt to measure lactate, central venous pressure, central venous oxygen saturation, send blood cultures, given antibiotics, give fluids for resuscitation, or use vasopressors as compliance. This explains the high compliance shown in this study with the SSC recommendations in addition to the fact that the study was done in a university hospital where facilities for measuring lactate, arterial blood gas analysis, central venous oxygen saturation, blood cultures etc. are readily available along with institutional protocols to manage sepsis. The major limitation of this study was the retrospective study design which resulted in exclusion of a large number of cases admitted to the SICU during the study period, due to incomplete information. This study also reflects the incidence of sepsis in surgical patients in one hospital and may not reflect the incidence in other types of intensive care units and other hospitals. Multi centre hospital based studies and population studies are required to determine the true prevalence of sepsis at a national level.

CONCLUSION

This study shows a high incidence of sepsis (43.23%) in patients admitted to the SICU of a teaching hospital in Karachi associated with a very high mortality (51.1%), as compared to the non-sepsis group. Stepwise logistic regression model showed that increasing age, female gender, non-operative admission to SICU, admission under general surgery and co-morbidities like IHD and CKD were significant predictor of sepsis in this cohort of patients.

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AUTHOR'S CONTRIBUTION

All the authors contributed equally.

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