

## **Sepsis in Buraidah Central Hospital, Qassim, Kingdom of Saudi Arabia**

**Gasim I. Gasim,<sup>1</sup> Imad R Musa,<sup>2</sup> Taha Yassin,<sup>2</sup> Hani A. Al Shobaili,<sup>1</sup> Ishag Adam<sup>1,3\*</sup>**

<sup>1</sup>Qassim College of Medicine, Qassim University, Kingdom of Saudi Arabia

<sup>2</sup>Buraidah Central Hospital, Kingdom of Saudi Arabia

<sup>3</sup> Faculty of Medicine, University of Khartoum, Sudan

### **Abstract**

**Objectives:** Severe sepsis is a major public health concern and a frequent cause of intensive care unit (ICU) admission with a high fatality rate. Higher (Sequential Organ Failure Assessment score) SOFA score and co-morbidity of acute renal failure (ARF) are risk factors contributing to fatal outcome. This work was meant to study the epidemiology of sepsis in Buraidah central hospital.

**Methods:** This is a descriptive study conducted in the period from January 1, 2012, to June 29, 2012 to determine the epidemiology (incidence, clinical characteristics) and the outcome of sepsis in Buraidah hospital, Saudi Arabia.

**Results:** Out of 387 patients admitted to ICU, 62 (16%) patients had sepsis, their mean (SD) age was 62.7 (21.3) years. Three quarters of them 47 (75.8%) presented with septic shock. The median APACHE II score was 26.5 (8 to 48) and SOFA score 11 (5 to 21). The mean of duration of hospital stay was 11.95 days. The most frequent infection site was the pulmonary (69.5%). There were 37 isolated organism, gram-negative organisms (13; 35.13%) were the predominant isolates. There were 25 (40.3%) deaths; the majority of the deaths were due to septic shock 20(80%). There was a significant difference between deaths and the survivors, in the APACHI II score, SOFA score), and whether ventilated or not.

**Conclusions:** There was a high incidence of septic shock (and higher mortality) among the patients admitted to the ICU of Buraidah central hospital, especially among the elderly patients with respiratory infections.

**Key words:** Sepsis; Shock; Saudi; APACHI II; SOFA

### **Correspondence**

**Gasim I. Gasim**

Qassim College of Medicine,  
Qassim University, Kingdom of Saudi Arabia

Mobile: 00966537285097

Email:gasimgsm@yahoo.com

## Introduction

Sepsis is a clinical syndrome featured by multi-system response to a microbial pathogenic insult encompassing conglomerate of related biochemical, cellular, and organ-organ interaction networks. A central link that connects these responses is inflammation, which, while trying to defend the body and prevent further harm, leads to further damage through the feed-forward, pro-inflammatory consequences of damage-associated molecular pattern molecules. <sup>(1)</sup> Sepsis is big health problem and can lead to high morbidity and mortality. <sup>(2-5)</sup> Data on sepsis in countries with less resource are scarce. <sup>(6)</sup> Yet algorithmic approaches to sepsis management such as early detection, use of antimicrobial treatment, prompt fluid resuscitation and concomitant invasive monitoring of parameters as central monitoring of venous pressure, and venous oxygen saturation, can reduce sepsis-related mortality. <sup>(7,8)</sup> Factors that contribute to unfavorable outcomes of severely ill patients in such settings include limitations due to cost, deficiency of diagnostic facilities including laboratories, microbiologic and imaging capabilities along with delayed presentation of severely sick patients. <sup>(9-13)</sup>

Severe sepsis and septic shock are recognized causes of admission, morbidity and mortality in intensive care units (ICUs). The sepsis syndromes are fatal, with hospital death rates for severe sepsis falling between 30% and 50%. <sup>(3,6)</sup> A consensus was developed to define the systemic inflammatory response to infection (sepsis). <sup>(14)</sup> The definition embraced sepsis-linked organ dysfunction, hypoperfusion or hypotension (severe sepsis), and septic-induced cardiovascular failure in spite of adequate fluid resuscitation (septic shock). The resultant consensus statement, issued in 1992, brought a new concept into clinical practice: the (SIRS). SIRS diagnosis was made when patients had two or more of the following clinical findings: body temperature over 38° C or under 36° C; heart rate higher than 90/ min; hyperventilation evidenced by a respiratory rate > 20/min or a PaCO<sub>2</sub> <32 mm Hg; and a total white blood cell count greater than 12,000 cells/ $\mu$ L or lower than 4000 cells/ $\mu$ L. <sup>(15)</sup> International experts reiterated the guidelines albeit making changes in 2001. <sup>(15)</sup> Along with the efforts made to improve the diagnostic criteria, criteria helping prediction of the

outcome were developed such APACHE II which was the result refinement of APACHE I in 1985 based on data extracted from 5815 ICU admissions at 13 different hospitals. The APACHE II score was formed of 12 routine physiologic measurements along with the patient's age and previous health status. <sup>(16)</sup> The maximum score is 71 points, while a score of 25 points gives a predicted mortality of 50% and a score exceeding 35 gives a predicted mortality of 80%. While APACHE II assess the severity of disease on admission (during the first 24 hours), <sup>(17)</sup> another scoring system namely "The Sequential Organ Failure Assessment" (SOFA) score was meant to assess the existence and extent of organ failure, characterized by being simple and objective, allowing for calculation of both the number dysfunctional organs involved and the severity of the involvement in six organ systems (pulmonary, coagulation, liver, cardiovascular, kidney, and the central nervous system), and it can assess individual or aggregate organ dysfunction. <sup>(18)</sup> It has been found that maximum total SOFA score exceeding 15 correlates with a mortality rate of 90%. <sup>(19)</sup> It was demonstrated that approximately 60% of an ICU budget was kept for sepsis and septic shock patients, albeit that those patients constituted less than a quarter of the ICU population. <sup>(20-22)</sup> The aim of this study was to determine the frequency and the clinical characteristics of sepsis in a hospital-based population in Al-Qassim region, Saudi Arabia.

## Patients and methods

A descriptive study was conducted in the period from the first of January 2012, to June 29, 2012 ICU of Buraidah Central Hospital which has a capacity of 10 beds. Convenient sampling method was used in the study where all subjects who fulfilled the inclusion criteria at the hospital were recruited in the study on daily basis until the total number of sample size was achieved. Sample size of 380 subjects was calculated based on a 2-sided hypothesis tests using Epiinfo with 80% power and confidence interval of 95%. The patients included adults (>18 years) with a diagnosis of sepsis (both community- and hospital-acquired infections) admitted to the ICU. Two or more of the following criteria were required: body temperature\* >38°C or <36°C, Heart rate over 90 beats per minute\*, Respiratory rate\* exceeding 20 breaths per minute or arterial CO<sub>2</sub>

tension < 32 mm Hg\* or a need for mechanical ventilation, White blood count >12,000/ mm<sup>3</sup> or < 4000/mm<sup>3</sup> or >10% immature forms reactive protein , procalcitonin > standard deviation of the normal altered mentation, presence of significant edema or hypervolemia defined as more than 20 ml/kg over 24 hours, hyperglycemia (blood glucose of more than 120mg/dl ) in the absence of diabetes mellitus, a blood pressure as follows; SBP<90 mm Hg, MAP <70, or an SBP decrease <40 mm Hg, arterial hypoxemia, cardiac index > 3.5L/min/m<sup>2</sup>, mixed venous saturation > 70%, oliguria, a rise in creatinine > 0.5 mg/dl, coagulopathy defined as INR >n 1.5 or aPTT >60 secs, thrombocytopenia (platelet< 100000/ $\mu$ L), hyperbilirubinaemia(bilirubin > 4 mg/dL), Hyperlactatemia ( $\geq$ 1 mmol/L), SIRS is defined by the presence of 2 or more of the criteria designated with an \*, Sepsis is defined by SIRS plus an evidence of infection, severe sepsis is defined by sepsis associated with organ dysfunction, while septic shock is defined as sepsis associated with hypotension that is not correctable to fluid therapy. Furthermore, data about the isolated organisms and their antibiotic sensitivity was obtained along with calculation of APACHI II and SOFA scores.

Decreased capillary refill or mottling.  
 (15) Participation was voluntary and thus if any of the patients refuses he will be automatically excluded, were discharged < 24 hours after hospitalization, noninfectious diagnoses took place of the diagnosis of sepsis during hospitalization, or were previously enlisted in the study. Hospital-acquired infections were described as infections which were neither present nor incubating on admission to the hospital, i.e., infections that become evident at 48 hours or more after admission. All participants signed a written informed consent before involvement in the study. Data demographic and clinical data was collected using a pre-tested questionnaire.

### **Ethical considerations**

Ethical approval was obtained from the Ethics and Research Committee at Ministry of

Health Qassim, KSA. A written consent was acquired from each participant/ guardian. Confidentiality of all participants was maintained and no names were requested in the questionnaires.

### **Statistical analysis**

Data were entered in computer using SPSS version 16.0 for windows. Results were expressed as mean (SD) or number (%). Student's t- test and chi-square test were used to compare the continuous and categorized data, respectively between the patients who died and the survivors. A *P* value < 0.05 was considered statistically significant.

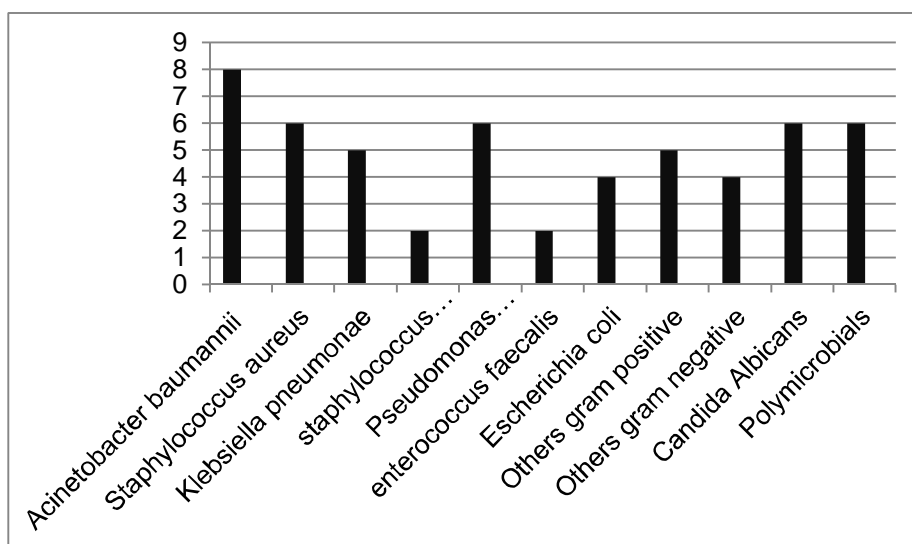
### **Results**

Out of 387 patients admitted to the ICU, 62 (16%) patients, with the males constituting 54.8%, mean (SD) of their age was 62.7(21.3) years. The patients presented with severe sepsis (4, 6.5%), septic shock (47, 75.8%), SIRS (5, 8.1%) and sepsis (6, 9.7%). Eleven (17.7%) were non Saudi's. Median APACHE II score was 26.5 (8 to 48) and SOFA score 11 (5 to 21). The mean (SD) of the duration of stay in hospital was 11.95 (14.57) days. Most of (57, 91.9%) the admissions were from the medical wards. The most frequent infection site was pulmonary (69.4%), the abdomen (8.1%), skin/ soft tissues (6.5%), blood, urinary system (1.6%), and others (12.9%) Table 1. Blood culture was positive for isolates in 37 (59.7 %) patients. Gram-negative organisms (13, 35.13%) such as *Acinetobacter baumannii* formed the most frequently isolated organisms while gram-positive organisms (*staph aureus*) were isolate in in 10 (27.03%) patients Figure 1. There were 25 (40.3%) deaths of these 3(12%) were due to severe sepsis and 20 (80%) due to septic shock, one (4%) was due to sepsis and one (4%) due to SIRS. There was a significant difference between the two groups in the APACHI II score (*p* value =0.008), SOFA score (*p* value <0.001), and whether ventilated or not (*p* value =0.012) see table. 1.

**Table 1: comparing the demographic and clinical features of survivors and non-survivors expressed as mean (SD) or n (%) as applicable**

Variable	Survivors (n=37)	Non-survivors n=25)	P value
Male Gender /	20 (54.0)	14 (56.0)	0.883
Age	60.0 (21.6)	67.0 (20)	0.201
APACHI II	24.0 (7)	29.0 (6.6)	0.008
SOFA	9.6 (3)	14.1 (3.6)	<0.001
Ventilation	25 (67.5)	23(92.0)	0.012
Culture Positive/Negative	20 (54.01)	17(68.0)	0.275
Hospital stay in days	12.7(12)	10.8 (18)	0.640

**Figure 1: showing the frequency of the commonly isolated organisms from culture in the study**



## Discussion

The current study showed that the incidence of severe sepsis was 16% of ICU admissions, and 47 (75.8%) of the admissions had evidence of infection, had septic shock. The incidence of severe sepsis was much less than what Venkata *et al.*, found (93.7%).<sup>(23)</sup> Lungs and urinary tract were the most frequent sites of infection in this study. The lung infection is followed by the abdomen in terms of frequency a finding that has been reported by other

researchers.<sup>(24, 25)</sup> In agreement with other studies,<sup>(23, 26)</sup> most isolated pathogens in the current study were Gram-negative bacilli, although some studies in developed countries reflected the other side of the coin with predominance of Gram-positive bacteria.<sup>(27, 28)</sup> Such finding could be explained by geographic variation, case mix, and antibiotic prescription manner. Moreover, clinical significance of the same pathogens may vary in different studies. *Acinetobacter baumannii* was the commonest

pathogen where it represented 16.3% of the infecting organisms, similarly, a group of other researcher found this pathogen to be the leading one in sepsis in ICU settings. <sup>(29, 30)</sup> Moreover, this study showed a significant difference between the survivors and non survivors in the APACHI II score, SOFA score and implementation of artificial ventilation. This goes with previous reports where Ogura et al found that the survivors have a lower APACHI II and SOFA scores and Forsblom et al found that mechanical ventilation is significantly associated with mortality among sepsis patients. <sup>(31, 32)</sup> The ICU mortality rates of severe sepsis, septic shock and sepsis was 40.3%, with the majority of the deaths occurring among those who have septic shock, this is slightly higher than the mortality rates in countries with lower compliance to sepsis resuscitation bundles as has been found by Levy et al. <sup>(33)</sup> The high mortality seen in this could well be explained by the fact the source of infection in most of our patients was the respiratory tract, along with the fact that they presented late where most of them were in septic shock on admission. Such determinants have been pointed to in the literature by some researchers. <sup>(34)</sup> There is scarcity in the data addressing the epidemiology of severe sepsis and septic shock in mixed ICU in Saudi Arabia. Our report might provide some valuable information in this context. However, it is not without limitations where the sample size is a small one. On the other hand, we have to acknowledge the weaknesses of the study which include; referral bias could not be excluded since Buraidah Central Hospital is one of the largest secondary level hospitals, secondly, the short duration of the study which coincides with winter and spring seasons, where the incidence of respiratory tract infection is higher which might lead to erroneously higher reported results.

### Conclusion

There was a high incidence of septic shock (and higher mortality) among the patients admitted to the ICU of Buraidah Central Hospital, especially among the elderly patients with respiratory infections.

### Recommendations

Future multi-center research of longer duration is required in order to insure early identification of high risk patient population,

timely implementation of approved treatment, in order to improve the clinical outcome. Findings demonstrated by the current study reflects the importance of prosecution of effective strategies to prevent both community-acquired pneumonia (e.g. public education, and immunization of the high risk groups against influenza and pneumococcus) and hospital-acquired pneumonia by implementing effective infection control guidelines.

### References:

1. Namas R, Zamora R, Namas R, An G, Doyle J, Dick TE et al. Sepsis: Something old, something new, and a systems view. *J Crit Care* 2012; 27:314.e1-11.
2. Bouza C, López-Cuadrado T, Saz-Parkinson Z, Amate-Blanco JM. Epidemiology and recent trends of severe sepsis in Spain: a nationwide population-based analysis (2006-2011). *BMC Infect Dis* 2014; 14:717.
3. Vincent JL, Marshall JC, Namendys-Silva SA, François B, Martin-Loeches I, Lipman J et al. Assessment of the worldwide burden of critical illness: the intensive care over nations (ICON) audit. *Lancet Respir Med* 2014; 2:380-6.
4. Baelani I, Jochberger S, Laimer T, Otieno D, Kabutu J, Wilson I, Baker T et al. Availability of critical care resources to treat patients with severe sepsis or septic shock in Africa: a self-reported, continent-wide survey of anaesthesia providers. *Crit Care* 2011; 15:R10.
5. Cerro G, Checkley W. Global analysis of critical care burden. *Lancet Respir Med* 2014; 2:343-4.
6. Becker JU, Theodosis C, Jacob ST, Wira CR, Groce NE. Surviving sepsis in low-income and middle-income countries: new directions for care and research. *Lancet Infect Dis* 2009; 9:577-82.
7. Westphal GA, Koenig Á, Caldeira Filho M, Feijó J, de Oliveira LT, Nunes F. Reduced mortality after the implementation of a protocol for the early detection of severe sepsis. *J Crit Care* 2011; 26:76-81.
8. Phua J, Ho BC, Tee A, Chan KP, Johan A, Loo S et al. The impact of clinical protocols in the management of severe sepsis: a prospective cohort study. *Anaesth Intensive Care* 2012; 40:663-74.

9. Girardis M, Rinaldi L, Donno L, Marietta M, Codeluppi M, Marchegiano P et al. Effects on management and outcome of severe sepsis and septic shock patients admitted to the intensive care unit after implementation of a sepsis program: a pilot study. *Crit Care* 2009; 13:R143.
10. Phua J, Koh Y, Du B, Tang YQ, Divatia JV, Tan CC et al. Management of severe sepsis in patients admitted to Asian intensive care units: prospective cohort study. *BMJ* 2011; 342:d3245.
11. Dunser MW, Baelani I, Ganbold L. A review and analysis of intensive care medicine in the least developed countries. *Crit Care Med* 2006; 34:1234-42.
12. Theodosis C, Brenner S. Framework and Rationale for Studying Sepsis in High HIV Seroincidence Resource Poor Settings: the Livingstone General Hospital Experience. International AIDS Conference Toronto 2006. Abstract no. CDB1279
13. Blomberg B, Manji KP, Urassa WK, Tamim BS, Mwakagile DS, Jureen R et al. Antimicrobial resistance predicts death in Tanzanian children with bloodstream infections: a prospective cohort study. *BMC Infect Dis* 2007; 7:43
14. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *Crit. Care Med* 1992; 20:864–874.
15. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med* 2003; 31:1250-6.
16. Knaus WA, William A, Draper EA, Elizabeth A, Wagner DP, Doughlas P, et al. APACHE II: a severity of disease classification system. *Crit Care Med*. 1985; 13:818–29.
17. Bouch DC, Thompson JP. Severity scoring systems in the critically ill. *Contin Educ Anaesth Crit Care Pain* 2008 8: 181-185.
18. Vincent JL, Moreno R. Clinical review: scoring systems in the critically ill. *Crit Care*. 2010; 14:207.
19. Vincent JL, de Mendonça A, Cantraine F, Moreno R, Takala J, Suter P, et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: Results of a multicentric, prospective study. *Crit Care Med* 1998; 26:1793-1800.
20. Bakker J, Rommes JH. Costs of ICU treatment in a general Dutch intensive care unit. *Intensive Care Med* 1996; 22:S302.
21. Bakker J, de Munck P, Rommes H, van Bussel H. Costs of severe sepsis in a multidisciplinary intensive care unit. *Crit Care Med* 1998; 26:A131.
22. Moerer O, Schmid A, Hofmann M, Herklotz A, Reinhart K, Werdan K, Schneider H et al. Direct costs of severe sepsis in three German intensive care units based on retrospective electronic patient record analysis of resource use. *Intensive Care Med* 2002; 28:1440-6.
23. Venkata C, Kashyap R, Farmer JC, Afessa B. Thrombocytopenia in adult patients with sepsis: incidence, risk factors, and its association with clinical outcome. *Journal of Intensive Care* 2013; 1:9
24. Karakoc C, Tekin R, Yeşilbağ Z, Cagatay A. Risk factors for mortality in patients with nosocomial Gram-negative rod bacteremia. *Eur Rev Med Pharmacol* 2013;17:951-7
25. Zhou J, Qian C, Zhao M, Yu X, Kang Y, Ma X et al. Epidemiology and outcome of severe sepsis and septic shock in intensive care units in mainland china. *PLoS One* 2014; 9:e107181.
26. León AL, Hoyos NA, Barrera LI, De La Rosa G, Dennis R, Dueñas C et al. Clinical course of sepsis, severe sepsis, and septic shock in a cohort of infected patients from ten Colombian hospitals. *BMC Infect Dis* 2013; 13: 345.
27. Finfer S, Bellomo R, Lipman J, French C, Dobb G, Myburgh J. Adult population incidence of severe sepsis in Australian and New Zealand intensive care units. *Intensive Care Med* 2004; 30:589-96.
28. Vincent JL, Sakr Y, Sprung CL, Ranieri VM, Reinhart K, Gerlach H et al. Sepsis in European intensive care units: results of the SOAP study. *Crit Care Med* 2006; 34:344-53.
29. Luna CM, Rodriguez-Noriega E, Bavestrello L, Guzmán-Blanco M. Gram-negative infections in adult intensive care units of Latin America and the Caribbean. *Crit Care Res Pract* 2014;2014:480463
30. Cheng B, Xie G, Yao S, Wu X, Guo Q, Gu M et al. Epidemiology of severe sepsis in

- critically ill surgical patients in ten university hospitals in China. *Crit Care Med* 2007; 35: 2538–2546.
31. Ogura H, Gando S, Saitoh D, Takeyama N, Kushimoto S, Fujishima S et al. Epidemiology of severe sepsis in Japanese intensive care units: a prospective multicenter study. *J Infect Chemother* 2014; 20:157-62.
  32. Forsblom E, Aittoniemi J, Ruotsalainen E, Helmijoki V, Huttunen R, Jylhävä J et al. High cell-free DNA predicts fatal outcome among *Staphylococcus aureus* bacteraemia patients with intensive care unit treatment. *PLoS One* 2014 10; 9:e87741.
  33. Levy MM, Rhodes A, Phillips GS, Townsend SR, Schorr CA, Beale R et al. Surviving sepsis campaign: association between performance metrics and outcomes in a 7.5-year study. *Crit Care Med* 2015; 43:3-12.
  34. Arturo Artero, Rafael Zaragoza and José Miguel Nogueira. *Epidemiology of Severe Sepsis and Septic Shock, Severe Sepsis and Septic Shock - Understanding a Serious Killer*, Dr Ricardo Fernandez (Ed.). InTech, 2012; 3-2