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Original Article

Association of Central Venous Oxygen Saturation ($ScvO_2$) with Intensive Care Unit Mortality in Patients with Sepsis and Septic Shock in Bangladesh

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Abstract:

Background: *Sepsis and septic shock are deadly conditions and leading causes of ICU admission. Early identification of sepsis and aggressive interventions for sepsis can have impact on outcome. This study examined the association between central venous oxygen saturation ($S_{CV}O_2$) and intensive care unit (ICU) mortality in patients with sepsis and septic shock.*

Methods: *This is an observational study that had taken place in ICU of BIRDEM General Hospital, Shahbag, Dhaka for a period of one year from July 2017 to June 2018. Around 147 adult patients with sepsis and septic shock were consecutively enrolled as study subjects during this time period, excluding patients with age < 18 years, pregnant patients, patients readmitting to ICU during the same hospitalization period or patients with the diagnosis of acute myocardial infarction, acute left ventricular failure and decompensated heart failure. $S_{CV}O_2$ was measured at the time of diagnosis of sepsis or septic shock. The patients who were discharged or transferred from ICU were classified as survivors and those who died during ICU stay were categorized as non-survivors.*

Results: *In this study, a total 147 patients were enrolled as a case of sepsis or septic shock. In a group of 114 hypoxic patients (ScvO2 ≤ 70%), 10.5% (n=12) were survivors and 89.5% (n=102) were non-survivors (p=0.001). Among 28 normoxic patients (ScvO2 = 71-89%), 89.3% (n=25) were survivors and 10.7% (n=3) were non-survivors (p=0.001). In case of 58 hyperoxic patients (ScvO2 ≥ 90%), 20% (n=1) was survivor and 80% (n=4) were non-survivors (p=0.761). The overall ICU mortality rate was 74.1%.*

Conclusion: *Sepsis or septic shock patients with hypoxia had significantly higher mortality while those with normal $S_{CV}O_2$ had significantly lower mortality. Although hyperoxic patients with sepsis or septic shock reported higher mortality, the data was not statistically significant.*

Keywords: *Central venous oxygen saturation, Mortality, $S_{CV}O_2$, Sepsis, Septic shock.*

Introduction

Sepsis is life threatening organ dysfunction caused by a dysregulated host response to infection.[1] It affects millions of people around the world each year and kills as many as one in four (and often more).[2] An extremely complex chain of events like inflammatory and anti-inflammatory processes, hormonal and cellular reactions together with circulatory derangement occurs in sepsis.[3] Early identification of sepsis and aggressive interventions for sepsis can have impact on outcome.[4] If sepsis is not recognized early and promptly, it can lead to septic shock, multiple organ failure and death.

The central venous oxygen saturation ($ScvO_2$) value is obtained by measuring the oxygen saturation in venous blood returning to the heart by placing a central venous catheter in internal jugular or subclavian vein to observe the level of tissue oxygenation in septic patient.[5] The normal value of $ScvO_2$ is 71% to 89%, called normoxia.[6] It represents the balance between oxygen delivery and consumption. A low $ScvO_2$ (≤ 70%) or hypoxia may indicate a decrease in oxygen delivery, an increase in oxygen extraction or combination of both, whereas an elevated $ScvO_2$ (≥ 90%) or hyperoxia may indicate failure to utilize oxygen at tissue level.[6]

Oxygen exchange deficiency can be categorized in three types of failure: (1) macrocirculatory failure (2) microcirculatory failure and (3) mitochondrial failure. Macrocirculatory failure is assessed by parameters like central venous pressure, mean arterial pressure cardiac index and $ScvO_2$.[7] A deficiency in any of these parameters can result in an inadequacy in oxygen delivery to the tissue. The causes of microcirculatory failure is multi factorial and include physiologic shunt, increased microvascular permeability and microvascular thrombosis. In some instances, in spite of adequate macrocirculatory flow, microcirculatory failure prevents the oxygen to reach at tissue level.[8] Finally in mitochondrial failure, oxygen is present at cellular level but the mitochondria are dysfunctional and unable to process the oxygen.[9] In latter two cases, the $ScvO_2$ may actually be elevated (≥ 90%) - a condition refer to as tissue dysoxia. In these cases, increasing oxygen supply will not ameliorate the problem. Global tissue hypoxia is one of the most important factor in the development of multi-organ dysfunction syndrome. In septic patients $ScvO_2$ monitoring is a better indicator of global tissue hypoxia than vital signs and other clinical parameters.[10]

Previous works found that abnormal level of $ScvO_2$ was associated

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with higher rate of mortality in septic patients.[11, 12] However, no data exist regarding level of $ScvO_2$ and its consequences in septic patients in Bangladesh. So the current study was designed to look at the association of $ScvO_2$ and intensive care unit (ICU) mortality among septic and septic shock patients.

Methods

Study design and procedure

Prior to this study, ethical clearance was obtained from institutional review board of Bangladesh Diabetes Association (BADAS). This was a cross-sectional, observational study carried out in ICU of BIRDEM General Hospital, Dhaka, Bangladesh over a period of 12 months from July 2017 to June 2018. All adult patients admitted to ICU with the features of sepsis or septic shock or developed sepsis or septic shock in the course of ICU stay were included in the study, excluding young patients (age < 18 years), pregnant patients, patients readmitting to ICU during the same hospitalization period or patients with the diagnosis of acute myocardial infarction, acute left ventricular failure and decompensated heart failure. Based on these criteria around 147 patients were consecutively selected for the study as shown in figure 1. With all asceptic precaution, a central venous catheter was introduced into the jugular vein by an expert doctor after admission and the $ScvO_2$ was measured. Appropriate investigations were sent and patient management was done according to the treating doctor and hospital protocol. The patients who were discharged or transferred from ICU were classified as survivors and those who died during ICU stay were categorized as non-survivors. Data regarding age, sex, comorbidity, $ScvO_2$ and mortality were recorded in a case record form after taking informed written consent from each patients or guardians. The participants were assured of confidentiality and anonymity, emphasizing that all the information acquired was used for academic purpose and data analysis only.

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Statistical analysis

Data were input into statistical software and rechecked. Analysis was done using Statistical Package for Social Sciences (SPSS) software (version 23.0). Categorical data such as age groups, gender, comorbidities, ScvO2, mortality and diagnosis were presented as frequencies and percentages while continuous variable like age (in years) was summarized using mean and standard deviation in a table. The patients were subdivided according to $ScvO_2$ thresholds (provided in operational definition) into two groups, survivor and non-survivor. Chi-square test was used to show the association between $ScvO_2$ and mortality (survivors and non-survivors) in patients with sepsis or septic shock. A p-value of less than 0.05 was considered statistically significant.

Operational definition

Sepsis:

Sepsis is life threatening organ dysfunction caused by dysregulated host response to infection.[13] Patients were diagnosed as sepsis when there was acute change in total sequential/sepsis related organ failure assessment (SOFA) score ≥ 2 points secondary to infection.

Septic shock:

Patients were considered to be in septic shock when septic patients developed persistent hypotension requiring vasopressors therapy to maintain mean arterial pressure (MAP) ≥65 mmHg and having a serum lactate level >2 mmol/L (18 mg/dl) despite adequate fluid resuscitation.[14]

$ScvO_2$ thresholds:

$ScvO_2$ thresholds were classified into clinically meaningful groups according to Pope et al.[6]

- Hypoxia: ScvO2 ≤ 70%
- Normoxia: ScvO2 70-89%
- Hyperoxia: ScvO2 ≥ 90%

Mortality:

Mortality was categorized into survivors and non-survivors group.

Results

This study included a total of 147 patients in the study population and among them 29 (19.7%) patients were found to be in sepsis and 118 (80.3%) patients were in septic shock. Table I shows the distribution of study population according to sociodemographic and clinical characteristics. Majority (58.5%) of the patients belonged to 51-70 years age group. The mean age of the study population was found 65.0±11.1 years, ranging from 22 to 86 years. The male to female ratio was 1:1.1. The most common comorbidity was diabetes mellitus (100%), followed by hypertension (85%), chronic kidney disease (57.1%), cerebrovascular disorder (20.4%), bronchial asthma (8.8%) and chronic obstructive pulmonary disease (7.5%). Around 114 (77.6%) of the patients had hypoxia while 28 (19.0%) had normoxia and 5 (3.4%) had

hyperoxia. Overall mortality of the study population was 74.1% (n=109). Table II shows the association of $ScvO_2$ with mortality in patients with sepsis and septic shock. Mortality was found to be significantly higher in hypoxic patients (10.5% survivors versus 89.5% non-survivors; p 0.001) and significantly lower in normoxic patients (89.3% survivors versus 10.7% non-survivors; p 0.001). Even though the mortality was also seen higher in hyperoxic patients, the results were not statistically significant (20% survivor versus 80% non-survivors; p 0.761).

Table I: Distribution of study population according to sociodemographic and clinical characteristics (N=147)

Characteristics	Frequency (n)	Percentage (%)
Age (in years)		
≤30	5	3.4
31-50	6	4.1
51-70	86	58.5
>70	50	34.0
Mean±SD	65.0±11.1	
Gender		
Male	68	46.3
Female	79	53.7
Comorbidities		
Diabetes mellitus	147	100
Hypertension	125	85
Ischaemic heart disease	7	4.8
Chronic kidney disease	84	57.1
Chronic obstructive pulmonary disease	11	7.5
Bronchial asthma	13	8.8
Thyroid disorder	8	5.4
Cerebrovascular disorder	30	20.4
Chronic pancreatitis	1	0.7
History of tuberculosis	3	2
Central venous oxygen saturation ($S_{CV}O_2$)		
Hypoxia ($ScvO_2 \leq 70\%$)	114	77.6
Normoxia ($ScvO_2$ = 71% - 89%)	28	19
Hyperoxia ($ScvO_2 \geq 90\%$)	5	3.4
Mortality		
Survivors	38	25.9
Non-survivors	109	74.1
Diagnosis		
Sepsis	29	19.7
Septic shock	118	80.3

Table II: Association between central venous oxygen saturation with mortality (N=147)

Central venous oxygen saturation (%)	Survivors (n=38)		Non-survivors (n=109)		p value*
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)	
≤70% (Hypoxia)	12	10.5	102	89.5	0.001
71% - 89% (Normoxia)	25	89.3	3	10.7	0.001
≥90% (Hyperoxia)	1	20.0	4	80.0	0.761

*p value < 0.05 is considered significant

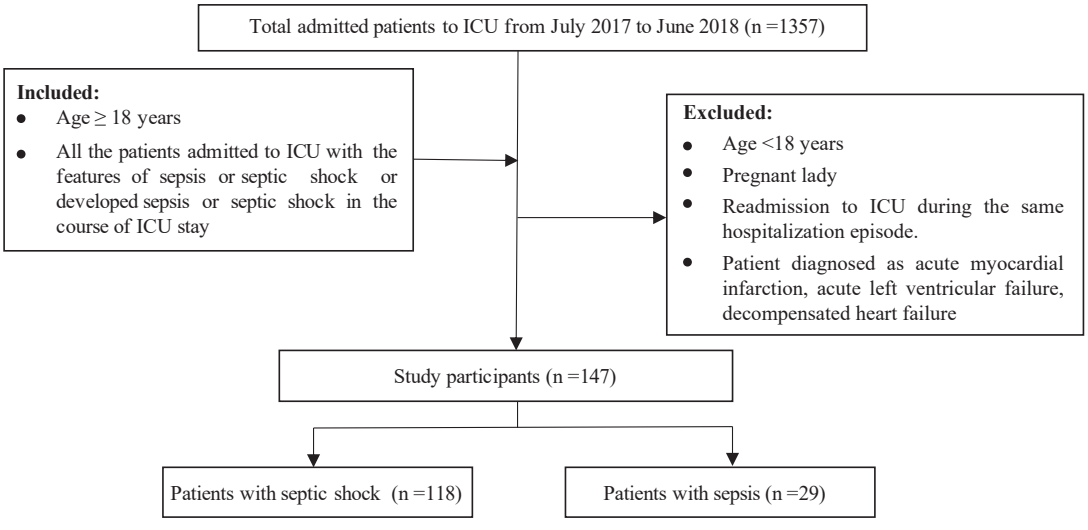

Figure 1: Method of selection of study population

Discussion

Sepsis and septic shock are commonly seen in critically in patients and these are one of leading causes of death in patients admitted in ICU. In this study, a total 147 patients were enrolled in final analysis.

Majority of the patients belonged to age group of 51-70 years and the mean age was 65.0+11.1 years, which was similar to study by Boulain et al.[12] It may be due to ageing being a strong independent risk factor for both sepsis and septic shock.[15] The current study showed similar male to female ratio but Boulain et al. and Shalaby et al. showed male predominance.[12, 16] Hu et al. stated in their epidemiologic study on sepsis that demographic characteristics were highly variable in septic patients.[17]

Boulain et al reported that most common comorbidities among septic patients were hypertension, diabetes mellitus and chronic obstructive pulmonary disease.[12] Lee et al found hypertension, diabetes, chronic lung disease, cardiovascular disease, chronic renal failure are common comorbidities in septic patients.[14] As this study was done in the largest diabetes hospital of the country so most common co-morbidities were diabetes mellitus (100%), then hypertension (85.0%), chronic kidney disease (57.1%) and cerebrovascular disorder (20.4%). In this study septic shock was diagnosed in 80.3% patients and remaining 19.7% were in sepsis, the results of which were similar to study by Pope et al.[6] Mohammadien et al observed that in hospital mortality was 72.6%.[18] This finding was similar to this study.

The current study observed that majority (77.6%) of the patients suffered from hypoxia and mortality rate was high (89.5%), which was consistent with Sturm et al. study.[19] It may be due to hypoxia induced cell injury. In normoxic patients, mortality rate was lower (10.7%). The finding was similar to Pope et al. study, where mortality rate was reported to be 12% that may be due to inadequate tissue oxygenation.[6] Mortality rate (80%) was higher in hyperoxic patients that was similar to study by Park et al.[20] It may be due to failure to utilize oxygen by the cell. Therefore, it can be concluded that there is an association between $ScvO_2$ and ICU mortality in patients with sepsis and septic shock.

Like any other scientific study, the present study is not without limitations. This was a single center study with small sample size. Multicenter study with a greater sample size would provide a better result. The authors could not track antibiotic usage in study subjects that might affect the outcome.

Conclusion

Septic and septic shock patients with hypoxia had significantly higher mortality while those patients with normoxia has significantly lower mortality. Although hyperoxic patients with sepsis or septic shock reported higher mortality, the data was not statistically significant. Therefore, it is imperative to maintain and monitor oxygen levels within the normal range in septic and septic shock patients to reduce mortality. Further study is recommended to establish central venous oxygen saturation as a predictor of ICU mortality in septic patients.

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