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A study on Multiple organ failure in patients with septic shock

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Abstract

Introduction: Sepsis is an intricate, heterogeneous, and highly lethal syndrome that can be hard to identify and treat. Defined as a life-threatening organ dysfunction caused by a dysregulated host response to an infection, sepsis is one of the major and most urgent public health challenges worldwide. If not recognized early and managed promptly, it can lead to septic shock, multiple organ failure and death. In the community setting, sepsis often presents as the clinical deterioration of common and preventable infections. Sepsis also frequently results from infections acquired in health care settings.

Material and Methods: This is a retrospective study was conducted in the Department of Critical Care at NRI Medical College & General Hospital among patients with septic shock with multiple organ failure was conducted by reviewing the electronic medical records of adult patients, 18 years old and older, treated for septic shock. Patients were identified via the electronic medical record to include patients with the primary diagnosis of septic shock and a procedure code for apheresis. Patients with the primary diagnosis of shock plus each of the following flags were screened: 2 or more vasopressors, lactic acid > 2 mmol/L, platelet nadir < $200 \times 10^3/\mu L$, and pH < 7.3.

Result: None of the three patients 21 to 30 years old died, 2/9 patients age 31-40 years, and 51-60 years 19/31 died. Twenty eight patients were died. Death occurred in 1 of 12 patients with one organ failure, in 18/30 with 2 or 3 organ failures, and 9/18 with 4 or more organ failures. The mean value ± SD of APACHE II (mortality risk) for survivors was 19.25 ± 7.32.

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Conclusion: The incidence of sepsis has been increasing in recent years in our setting. However, hospital mortality has been significantly reduced. In septic patients, all organ failures except liver have shown a statistically significant reduction on associated mortality, with cardiovascular failure as the most relevant. Early source control and the simplification of algorithms to recover tissue perfusion could explain these results.
Keywords: Multiple organ failure, Septic Shock, Plasma.

Introduction

Sepsis is an intricate, heterogeneous, and highly lethal syndrome that can be hard to identify and treat. [1] Defined as a life-threatening organ dysfunction caused by a dysregulated host response to an infection, sepsis is one of the major and most urgent public health challenges worldwide. [2] It is estimated that more than 30 million people globally are diagnosed with sepsis each year, leading to 5 million deaths, with high economic burden and long-term morbidity among survivors. [3] Particularly, annually in the United States sepsis is present in 1.7 million hospitalized patients and contributes to 270,00 deaths. [4]

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. [5] If not recognized early and managed promptly, it can lead to septic shock, multiple organ failure and death. It is most frequently a serious complication of infection, particularly in low- and middle-income countries where it represents a major cause of maternal and neonatal morbidity and mortality. [6]

In the community setting, sepsis often presents as the clinical deterioration of common and preventable infections. Sepsis also frequently results from infections acquired in health care settings, which are one of the most frequent adverse events during care delivery and affect hundreds of millions of patients worldwide every year. [7]

Healthcare-associated infections are often resistant to antibiotics and can rapidly lead to deteriorating clinical conditions. Antimicrobial resistance is a major factor determining clinical unresponsiveness to treatment and rapid evolution to sepsis and septic shock. Sepsis patients with resistant pathogens have been found to have a higher risk of hospital mortality. [8] Implementing preventive measures against infections, such as good hygiene practices, ensuring access to vaccination programmes, improved sanitation and water quality and availability, and other infection prevention and control best practices both in the community and health care settings, are key steps in reducing the occurrence of sepsis. [9]

Prognosis in sepsis is influenced by characteristics of the patient (*e.g.* age, immunologic status, comorbidities, among others) and characteristics of the infection (*e.g.* pathogen type, virulence, site of infection, inoculum, among others). [10] Although combinations of such characteristics influence the clinical presentation and risk, sepsis is a common pathway from infection to death, in which progressive organ dysfunction is the mean. In this study, we present a comprehensive overview of the features found in patients with sepsis that lead to multiple organ failure and death. [11]

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Aim: The Aim of this study is to provide data from our teaching hospital ICU related to the incidence of septic patients, the distribution of Multiple organ failure and distribution of failure among each of the organs. The mortality rate, relationship between mortality and age, and mortality and types of organs affected was evaluated. The main bacterial causes of sepsis was also identified.

Material and Methods:

Study design

This is a retrospective study was conducted in the Department of Critical Care at NRI Medical College & General Hospital among septic shock with multiple organ failure was conducted by reviewing the electronic medical records of adult patients, 18 years old and older, treated for septic shock.

Study subjects

Patients were identified via the electronic medical record to include patients with the primary diagnosis of septic shock and a procedure code for apheresis. Patients with the primary diagnosis of shock plus each of the following flags were screened: 2 or more vasopressors, lactic acid > 2 mmol/L, platelet nadir < 200 × 10^3/μL, and pH < 7.3.

Intervention

All patients in both groups were treated for sepsis at the discretion of the attending intensivist. All patients were ordered to receive 30 cc/kg of IV fluids and timely administration of empiric antibiotics while in the emergency department, prior to admission to the hospital, per the hospital's sepsis protocol. While this sepsis treatment protocol was available, individualized treatment occurred in both groups based on physician preferences (e.g., adjunct steroids, ascorbic acid, thiamine).

All mechanically ventilated patients were managed with a lung-protective strategy according to the ARDSnet protocol. In cases of severe respiratory acidosis, adjustments to the ventilator were made according to ARDSnet recommendations, allowing for permissive hypercapnia when appropriate. In cases of severe, life-threatening acidosis, ventilator settings may have been adjusted outside this protocol by the attending physician.

Definition of variables

The primary study outcome was all-cause 28-day mortality. Secondary outcomes included hospital mortality, a new need for renal replacement therapy (RRT) during admission and at discharge, mortality associated with a new need for renal replacement therapy, ICU length of stay, hospital length of stay, daily fluid balance, and change in sequential organ failure assessment (SOFA) and cardiac SOFA scores 48 h after identification in patients surviving at least 48 h. "Time zero" for the intervention group was defined as the documented date and time of completion of the first plasma exchange treatment. "Time zero" for controls was defined as the first recorded vital signs in the intensive care unit. Patients were propensity-

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matched using age, gender, chronic co-morbidities (HTN, DM, CKD, COPD), APACHE II score, SOFA score, lactate level, and number of vasopressors at ICU admission, while all primary and secondary outcomes were measured and calculated based on time zero defined above.

Patient charts were reviewed through hospital discharge or death. For patients discharged prior to day 28, mortality was assessed by searching subsequent admissions and online obituaries. Values used for calculation of the 48-h SOFA scores were the most recent vital signs and labs to the exact hour of inclusion. Patients who expired prior to 48 h were excluded from the SOFA and fluid balance analyses.

Table 1: SOFA Scoring Criteria

System	**Score/Points**				
	0	**1**	**2**	**3**	**4**
Respiratory system PaO2/FiO2 ventilation /mmHg(kPa)	≥400(53.3)	≥400(53.3)	<300(40.0)	<200(26.7) + Mechanical ventilation	<100(13.3) + Mechanica ventilation
Coagulation system Blood platelet/ (103 •μL−1)	≥150	<150	<100	<50	<20
Liver Bilirubin / [mg•dl−1 (μmol•L−1)]	<1.2(20)	1.2–1.9(20–32)	2.0–5.9(33–101)	<6.0–11.9(102–204)	≥12.0(204)
Cardiovascular system	MAP≥70mmH	MAP<70mmHg	Dopamine	Dopamine 5.1–15.0 or epinephrine ≤0.1 or norepinephrine >0.1	Dopamine >15 or adrenaline >0.1 or norepinephrine >0.1
Central nerve system (GCS	15	13-14	10-12	6-9	<6
Kidney Creatinine / [mg•dl−1 (μmol•L−1)]	<1.2(110)	1.2–1.9(110–170)	2.0–3.4(171–299	3.5–4.9(300–400)	>4.9(440
Urine Volume (mL•d−1)	-	-	-	<500	<200

Computation and matching of propensity score

Patients were propensity-matched using age, gender, chronic co-morbidities (HTN, DM, CKD, COPD), APACHE II score, SOFA score, lactate level, and number of vasopressors at ICU admission to generate propensity scores.

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Patient characteristics

Patients had a high mortality risk with similar baseline APACHE II and SOFA scores. While baseline SOFA scores were similar, patients in the intervention arm had higher SOFA scores at time zero. All patients presented with septic shock requiring at least two vasopressors, and a majority required a new start of renal replacement therapy.

Statistical Methods

SPSS22.0 statistical software was used for univariable analysis. Measurement data were represented by ($\bar{X}$±s) and the differences between groups were analyzed by *t*-test. Enumeration data were expressed as n(%) and the differences between groups was analyzed by X^2 test. Logistic regression was used for multivariable analysis. $P < 0.05$ was considered statistically significant.

Results

Table 2: Distribution of Age

Age Group in years	**Number of patients**	**Died**
21-30	2	0
31-40	9	2
41-50	18	7
51-60	31	19
Total	60	28

In table 2, None of the three patients 21 to 30 years old died, 2/9 patients age 31-40 years, and 51-60 years 19/31 died.

Table 3: Distribution of Gender

Gender	**Number of patients**	**Percentage**
Male	41	68.3
Female	19	31.6
Total	60	100

Table 4: Number of systems in Multiple organ failure **and mortality**

Multiple organ failure	**Number of patients**	**Died**
1	12	1
2-3	30	18
>4	18	9
Total	60	28

In table 4, Twenty eight patients were died. Death occurred in 1 of 12 patients with one organ failure, in 18/30 with 2 or 3 organ failures, and 9/18 with 4 or more organ failures.

Table 5: Types of systems affected

System failure	N° patients with each organ type (n = 60)	Died
Respiratory	6	1/6
Renal	8	2/8
Hepatic	12	9/12

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Cardiovascular	20	11/20
CNS	2	1/2
Coagulation	3	1/3
Gastrointestinal	7	2/7
Metabolic	2	1/2

Table 6: Observation Index of various parameters

Observation Index	**Mean±SD**
Heart rate (times/min)	115.88±20.09
Respiration (times/min)	31.49±8.55
MAP (mmHg)	90.21±21.66
Arterial blood Ph value	8.55±0.55
WBC count (cells/mm^3**)**	19,813.93±1713.44
APACHE II Score (points)	19.25±7.32

The mean value ± SD of APACHE II (mortality risk) for survivors was 19.25 ± 7.32 in table 6.

Table 7: Distribution of Blood Investigation

Investigation	**Mean±SD**
Sodium (mEq/L**)**	140.99±10.78
Potassium (mEq/L**)**	3.44±0.99
Blood glucose (mg/dl)	271.55±21.35
Creatinine (mg/dl)	18.55±6.28

Table 8: Comparison of Enumeration Data Between the Two Groups [n (%)]

Observation Index	Multiple organ failure **(n = 60)**
History of chronic disease (Yes/No)	33/27
Surgery (Surgery/Non-surgery)	12/48
Bacteria culture growth (Yes/ No)	45/15
Ventilator usage (Applied/Not applied)	50/10

Table 7: Effect of objective measures of Multiple organ failure

Measure	**TPE (n = 60)**
Cards SOFA at time zero	3.0± 0.13
Cards SOFA at 48 h	2.7± 2.66
Lactate at time zero (mg/dl)	37.2 ± 8.5
Lactate at 24 h	6.9 ± 7.9 (n=30)
Platelet count at time zero (cells/mm^3**)**	1,03,923.8 ± 13270.6
Extubations	5
New intubations	0 (1 places on ECMO)
Deaths prior to 48 h	8

Discussion

This is study shows that the association of organ failure with mortality has changed over time depending on the affected organ. To our knowledge, there are no epidemiological studies that

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have analyzed the evolution of the behavior of mortality associated with the different organ failures in septic patients.

Protocols to increase the detection of sepsis, better antimicrobial stewardship and initiate early source control have led to an improvement in the vital prognosis of patients with multiorgan failure. [12] For this reason, an improvement in survival of all organ failures analyzed separately would be expected. Nevertheless, our study shows that this impact is not homogeneous. Although the nature of our study does not allow us to establish causal relationships, we suggest that the differences in the evolution of mortality associated with each organ failure could be related to an improvement in the care of some of them (cardiovascular failure) compared to those without specific treatment (liver failure).

In our opinion, the most relevant result in our analysis is the reduction in mortality in the cardiovascular failure group. Evolution in management protocols has greatly simplified the initial management of septic shock. Current protocols advocate for a lower positive fluid balance and an early use of norepinephrine, which allows an earlier recovery of tissue perfusion.

We do not believe that the reduction in mortality in renal failure could be due to an improvement in extrarenal clearance techniques, the lack of consensus on which is the best modality or the moment of initiation of the technique may hinder a greater impact. [13] However, the close relationship between the improvement in tissue perfusion and renal function is well known, which could explain the parallelism between improved cardiovascular and renal failure survival.

There is also a reduction in mortality in respiratory failure, although not so marked. Although non-invasive techniques (high-flow nasal cannulas, non-invasive mechanical ventilation) have failed to significantly impact the general prognosis of patients with sepsis, in some subpopulations they do appear to be useful. [14] The incorporation of recruitment maneuvers (prone position, PEEP,) and the use of extracorporeal techniques can also explain this better prognosis.

Improvement in each organ failure mortality rates results in a reduction in global mortality on septic patients. The general trend observed in our study is also present in other observational studies, both in the epidemiological characteristics of the patients and in the origin and impact of infections. [15] Liver failure, however, presents an opposite trend.

Sepsis is not considered in epidemiological studies as a major cause of acute liver failure. [16] However, when it appears, it defines a scenario of high mortality. Liver failure in sepsis does not have specific treatment or organ support measures. The use of extracorporeal techniques in sepsis for liver support is still anecdotic and cannot be considered a standardized technique. [17] Macrophage activation-like syndrome (MALS) in septic patients causes hepatic dysfunction and hematological alterations and, when present, significantly increases mortality

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in these patients. [18] MALS, which does not respond to standard sepsis treatment, could explain the high mortality of septic patients with liver failure and the lack of prognostic improvement that septic patients with hematological dysfunction have experienced over the years.

Knowing the dimensions of sepsis at the population level is essential for a rational use of economic and health resources. The incidence of sepsis increases year after year, and mortality has been decreasing in parallel. Our data are consistent with other epidemiological studies both in Europe and in other settings and also with clinical data from population studies in our territory. [19-21] The increase in incidence is attributed to a better control of other pathologies, increase in life expectancy and increase in patient's age, though it should be noted that an increase in diagnostic coding in recent years could have contributed to the progressive increase in the incidence of sepsis. [22]

Conclusion

The incidence of sepsis has been increasing in recent years in our setting. However, hospital mortality has been significantly reduced. In septic patients, all organ failures except liver have shown a statistically significant reduction on associated mortality, with cardiovascular failure as the most relevant. Early source control and the simplification of algorithms to recover tissue perfusion could explain these results. On the contrary, mortality associated with liver failure in sepsis is very high and has not changed, a fact that could be explained by the lack of specific treatment for the failure of this particular organ.

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