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Assessment of Sepsis in a Developing Country: Where do We Stand?

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Abstract

Sepsis affects millions of people worldwide every year. The majority of sepsis research arises from developed countries. This large gap in medical advancement between the developed and developing world leaves us pondering over crucial questions that must be tackled: Are developing countries able to implement the standards of care set by the developed world? Do they have access to the ongoing medical innovations? Is there global equality of medical care? Is the burden and toll of sepsis heavier in the developing world?

To answer all these questions, the starting point is to assess the impact of sepsis on developing countries. Literature about Sepsis in Lebanon, a developing country in the Middle East Region, is scarce. This review article sheds light on the burden of sepsis in Lebanon and the Middle East as well as shares our personal research experiences.

Background

Sepsis is defined as a whole-body inflammatory response to an infection [1]. It occurs in millions of people yearly worldwide, with mortality rates up to 25 percent [2,3]. Sepsis carries the greatest burden on developing countries in terms of mortality, as compared to the developed world [4]. In the last few years, management modalities of sepsis were revolutionized in the developed world [1-5], but not in the developing world where resources are limited. Many efforts and suggestions have been made in order to improve the outcome of sepsis in underprivileged countries. A "three delays" model highlighting the importance of early-diagnosing and triage, adequate resuscitation, and monitoring and reassessment has been proposed recently when dealing with septic patients in resource limited countries [7]. There is a paucity of studies regarding sepsis in Lebanon. This review article aims at describing the burden of sepsis in Lebanon, as well as sharing our personal experience and research findings at the American University of Beirut Medical center (AUBMC), a tertiary care academic center in Beirut, Lebanon.

Sepsis in Lebanon and the Middle East

After a thorough literature review, it appears that data regarding the epidemiology, management, and outcomes of septic patients in Lebanon and the Middle East is very limited. This could be explained by many limitations in the health care system in the region, with the major one being lack of resources and funding [8]. In addition, the lack of National Patient Registries, active research, and health literacy impose more challenges. Many health care professionals in Lebanon argue that major limitations to health care are due to policy making, human resources and protocol implementation [9]. On the other hand, most of the research involving sepsis in Lebanon and the Middle East mainly revolves around the microbiology, the local antibiotic susceptibilities and resistances, and targeted patient populations [10-12]. Data regarding the toll of sepsis in numbers and outcomes is missing. Therefore, it is of significant clinical relevance to tackle this topic and assess the efficacy of sepsis management and outcomes.

Our Experience and Research

The grounds for research in Lebanon and the Middle East are extremely large, and the research opportunities and topics are endless.

It was an obvious choice to decide to study the impact of sepsis in this region, since septic patients are frequently encountered in the Emergency Department (ED) and on hospital floors. With estimates showing that numerous septic patients present to the Emergency Department [12], it was the perfect setting to conduct our study. The findings of our published study entitled: Descriptive Analysis of Sepsis in a Developing Country [13], can be best summarized as follows:

Methodology

After obtaining IRB approval, a sample of 97 adult patients with a confirmed diagnosis of sepsis, and presenting to our ED between January 2008 and June 2012, were retrospectively randomly selected as the study population. Data regarding their characteristics, management and treatment, laboratory findings, and mortality was recorded from their medical charts for analysis. Statistical analysis was performed using SPSS statistics for Windows version 21.0.

Patient characteristics

Most of our patients were elderly with a mean age of 70 years, and approximately equally divided between males and females. Most patients who presented in a state of shock and with a systolic blood pressure (SBP) under 90 mmHg were noticed to have significantly more co-morbidities such as hypertension, coronary artery disease, diabetes, malignancies, etc…

Microbiology

The most common sites of infections were the genitourinary system (40.2%), the respiratory system (19.6%), the integumentary (skin) system (10.3%), with 19.6% having an unidentified site of infection.

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A causative organism was isolated in 78.4% of the patients, and 42% of the patients had positive blood cultures upon admission. It was also noticeable that Gram negative organisms were far more likely the causative agent of the infection than Gram positive organisms, as *Escherichia Coli* was cultured from 38.1% of the isolates, followed by *Klebsiella pneumonia* (11.3%), and *Pseudomonas aeruginosa* (7.2%).

Management

The average amount of fluid administered to patients at 6 and 24 hours of presentation was 1.75 liters, and 3.37 liters respectively. Antibiotics were administered to 87% of patients in the Emergency Department with a mean time of administration of 3.43 hours. Norepinephrine was the most common vasoactive agent used (38.1%) to maintain perfusion, and the mean time to vasopressor use was 9.14 hours. Systemic Inflammatory Response Syndrome (SIRS) criteria of more than 2 were only fulfilled in 69% of patients at presentation.

Disposition

54.7% of patients were admitted to the General Practitioner Floor (GPU) as compared to 45.3% who were admitted to the Intensive care Unit (ICU). The average stay in the ED was around 13.35 hours.

Mortality

30.9 % percent of patients died in-hospital, and the 28-day mortality was 20.6%. Patients who expired in hospital had longer ICU stays and required longer durations of vasopressor therapy (p=0.001).

Discussion

Early recognition, adequate resuscitation and early antibiotic administration have been shown to be the most significant parameters in sepsis management [14, 16]. Delays in antibiotics, fluids and vasopressor therapy initiation directly correlate with increasing mortality and morbidity [17-19]. The Surviving sepsis campaign emphasizes on aggressive fluid resuscitation, and recommends that patients with severe sepsis receive a bolus of 30 ml/kg of fluids [1]. In our study, patients received a suboptimal average of 1.75 Liters in the first six hours. As mentioned earlier, early administration of antibiotics is essential especially in the first hour [1]. The time to antibiotics in our study was 3.43 hours, which represents a significant delay in therapy. In our study, the average ED length of stay until disposition for our septic patients was around 13.35 hours, compared to a US average of around 5 hours [14]. Our results can be explained by the lack of a protocol-based pathway for sepsis management that would have helped with the proper and timely management of such patients. We also had longer ED stays than what was described in the literature and this is mainly due to a suboptimal availability of critical care beds in our institution.

An interesting point to consider both in developed and developing countries is the concept of "care manager" (specially trained nurse) acting as the bridge between patients and their physicians, and helping in creating more awareness, and self-monitoring in chronic illnesses [20]. This concept, although initially piloted for chronic illnesses may potentially serve for earlier detection and management of acute illnesses such as sepsis.

Identifying the source of infection and addressing it promptly is essential in septic patients. The literature suggests that the most common sites of infection in sepsis are the respiratory and genitourinary system, as well as intra-abdominal surgical sites and indwelling catheters [2]. This goes hand in hand with our findings, as the three most common sites of infections harboring the causative organisms were the respiratory, genitourinary and integumentary systems. Data from the same center where this study was conducted and addressing blood stream infections in neutropenic patients demonstrated that Gram negative organisms are the more common pathogens [12]. Our results support this finding as Gram negative organisms were identified as the causative organisms in the majority of our septic population. Hence, it is essential to adjust antibiotic therapy when dealing with our Lebanese septic population in order to cover mainly for Gram negatives as well as local patterns of resistances.

SIRS criteria are used as a screening tool for possible septic patients; however, it appears that in the ED setting they are sensitive but not specific for sepsis identification [21]. Only 69% of our septic were found to have 2 or more SIRS Criteria at presentation; however, with further analysis, having less than 2 SIRS criteria had no correlation with mortality. Sepsis carries mortality rates between 20-30 % [2-3]; our data shows that sepsis carries a total mortality rate of 30.9, and a 28-day mortality rate of 20.6%. These finding suggest that mortality is slightly higher in Lebanon than the developed world.

Where are we Heading?

Having first hand exposure to health care training and research experience in leading US healthcare institutions, gaps and discrepancies in clinical medicine became obvious to our eyes in Lebanon. With sepsis being a global burden, and with the western world's intensive work on this topic, sepsis in Lebanon and the Middle East became our focus of interest. Currently, we have launched multiple research projects examining sepsis in Lebanon.

The implementation of sepsis treatment protocols in the developed world has been shown to reduce mortality, with the absence of such protocols in most developing countries impeding proper therapy [22]. Recently, the global paradigm has been shifting toward implementing sepsis protocols and bundles in the developing world. By stratifying points of care into tangible protocols, compliance with comprehensive resuscitation elements has significantly increased and resulted in sepsis related mortality reductions [23]. In fact, a multicenter study showed that implementation of sepsis management bundles was associated with a 25% relative risk reduction in mortality rates and in hospital mortality [24]. A Saudi Arabian 6-hour resuscitation bundle in the ICU showed a 10% reduction in sepsis related mortality [25]. Moreover, data from Uganda recently showed that early sepsis management and resuscitation also improved mortality drastically by 15% even in HIV infected patients [26]. At the time our study was conducted; our institution did not follow yet a standardized protocol-based approach to sepsis management. Recently this has changed as a sepsis bundle was implemented at our ED. Currently we are in the phase of data analysis for a study tackling the effect of this bundle introduction on sepsis management and mortality.

Other challenges that face the developing world are the limited exposure to acute and critical care medicine during training, little opportunities for higher medical education, under-developed triage systems reflecting weak health-disease literacy and lack of knowledge of sepsis best practice [7,27]. Moreover, the development of critical care in resource-limited regions is crucial and depends on care improvement, availability of qualified personnel and resources, adequate technology, and best practice exchange [28,29]. It is therefore of clinical relevance for future studies in Lebanon to assess health care workers and triage systems' knowledge of sepsis and its morbidity.

The management of sepsis is an ongoing process, requiring a team-

based approach and does not rely solely on early resuscitation efforts. Close monitoring, follow up and proper disposition are essential to achieve a decreased mortality [7]. Therefore, resources are essential to improve sepsis outcomes. Unfortunately, the developing world is always in shortage of vital commonly found resources in the developed world such as vital sign monitors as well as adequate infection control [7, 30]. A study conducted in Thailand stressed on the feasibility of modifying sepsis management guidelines and flexibility of care in accordance with the available resources in resource limited countries [31]. With limited resources at our hands in Lebanon, building a National Registry of Sepsis for future research and monitoring seems promising and vital.

Many conferences throughout the region were organized with the aim of spreading awareness about sepsis and shed the light on the most up-to-date evidence based management [32]. Global efforts have been done in order to quantify the mortality rates of sepsis and different diseases by region [33]. Experts in the field of sepsis management from developed countries have also taken the initiative and proposed recommendations for management modifications in developing countries [34]. In the last two decades, there has been a steady improvement in sepsis care; however, there still remain some areas of ambiguity in management, which should hopefully lay the ground for more innovative research approaches in the future [35].

Conclusion

Sepsis is a medical emergency, and a global public health concern. With the developed world having the luxury of having state of the art medical care, the developing one seems to struggle to achieve even basic care. There is a clear shortage of resources related to the inexperienced human element, lack of funding, and medical equipment. The critical care sector is underdeveloped, especially in rural areas of Lebanon and needs improvement with proper and constant medical training. A supervising body that monitors and ensures adequate treatment by constant assessment is critically missing and should be established.

Our interest in sepsis at AUBMC started recently, and research on this topic is a pioneering movement in the region. The initial step involves a basic description of the disease to assess it, followed by implementing protocols and assessing improvement in outcomes. We hope our interest and effort in sepsis research will stimulate further research in the field. We also hope our work would extrapolate benefits in the Middle East Region. At the end, the ultimate target is to design a nationwide comprehensive sepsis management approach that will provide not only the most up-to-date plan of care but also equity of care to the Lebanese population.

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