Sepsis – Retrospective Observational Study of Sepsis and Septic Shock treated in internal medicine wards

Sepsis – Estudo Observacional Retrospectivo de Sépsis e Choque Séptico na enfermaria de medicina interna

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ABSTRACT

Introduction: Sepsis and septic shock are very relevant in clinical practice. Most studies focus on the treatment in Intensive Care Units. Outside these units, the reality is largely unknown. The aim of this study is to epidemiologically characterize sepsis and septic shock patients admitted at internal medicine wards.

Material and Methods: Retrospective observational study, involving patients admitted to internal medicine wards with the diagnosis of sepsis/septic shock during a year

Results: A total of 308 patients were included in the study. 53% were female, with higher levels of comorbidities. Almost 40% were in septic shock, at admittance. Mortality rate was 29,87%. Overall, microbiologic documentation was possible in 92.2% of the cases, with higher prevalence of infection in the urinary (52.6%) and respiratory (34.8%) systems. Initial antibiotic therapy was appropriate in 50% of cases.

Previous antibiotic therapy (OR 3.84; IC95% 2.4-6.2; p<0.0001) and bedridden status (OR 3.15; IC95% 1.7-5.8; p<0.0002) were independent risk factors to antimicrobial resistance.

Discussion: Sepsis outside intensive care units is an escalating reality with high rates of morbidity and mortality. Timely diagnosis and collecting cultures to appropriate treat are primordial to best results.

Conclusion: This study provides data regarding sepsis/septic shock treated outside intensive care units, that allow a better knowledge of this reality so that it is possible to plan strategies to best attend these patients. Prospective analysis to consolidate criteria for diagnosis, follow-up and prognosis of these patients, as well as review of protocols of action are needed.

Keywords: Infection; Sepsis; Septic Shock; Internal Medicine Ward; Portugal

RESUMO

Introdução: A sépsis e o choque séptico apresentam grande relevância na prática clínica. A maioria dos estudos abordam o tratamento em Unidades de Cuidados Intensivos. A realidade fora destas unidades é amplamente desconhecida. O objectivo deste estudo é caracterizar epidemiologicamente doentes com sépsis/choque séptico internados na enfermaria de medicina interna.

Material e Métodos: Estudo observacional, retrospectivo, dos doentes admitidos no serviço de Medicina Interna com o diagnóstico de sépsis/choque séptico durante um ano

Resultados: Foram incluídos 308 doentes, 53% do sexo feminino, com maior grau de comorbilidades. Cerca de 40% apresentavam choque séptico à admissão. A taxa de mortalidade foi de 29,87%.

Globalmente, foi possível documentação microbiológica em 92.2% dos casos, sendo as infecções dos aparelhos urinário (52.6%) e respiratório (34.8%) as mais prevalentes. A antibioterapia inicial foi adequada em 50% dos doentes.

Antibioterapia prévia (OR 3.84; IC95% 2.4-6.2; p<0.0001) e o estado de dependência (OR 3.15; IC95% 1.7-5.8; p<0.0002) foram factores de risco independentes para a presença de resistência antimicrobiana.

Discussão: A sépsis fora das unidades de cuidados intensivos constitui uma realidade crescente com elevada morbimortalidade. O diagnóstico precoce e a colheita de exames culturais para tratar de forma dirigida são primordiais para melhores resultados.

Conclusão: Este estudo fornece dados de sépsis/choque séptico tratados fora de unidades de cuidados intensivos, que permitem um melhor conhecimento desta realidade para planear estratégias para melhor tratar estes doentes. Análises prospectivas para consolidar critérios de diagnóstico, seguimento e prognóstico destes doentes, bem como a revisão de protocolos de actuação são necessárias.

Palavras-chave: Choque Séptico; Enfermaria Medicina Interna, Infecção, Portugal, Sépsis

INTRODUCTION

Sepsis can be defined as the systemic response to an infectious disease, caused by bacteria, virus, fungus or protozoa. Its incidence is increasing[1] due to best emergency attendance, larger elderly population and larger number of immunosuppressed patients. More, the growing of bacterial resistance has also contributed to that increase[2]. Although the real numbers aren't known and probably are underestimated, it is estimated 17 million cases all over the world[3].

According to the *Center for Disease Control and Prevention*, sepsis incidence has duplicated from 2000 to 2008, and the number of hospitalizations has raised 70%[4]. Additionally, elevated mortality rates are observed, between 18% and 40%[4] in patients with sepsis and septic shock. SOAP study (The European Sepsis Occurrence in Acutely Ill Patients), that included patients admitted with sepsis and septic shock in 198 intensive care units from different countries, estimates mortality rates from 32% for sepsis and 54% for septic shock[5].

In Portugal, hospital mortality for sepsis after a community acquired infection was estimated to be 38% in the SACiUCI study (community-acquired sepsis in intensive care unit). National data available at INFAUCI study (Impact of infection on admission and of the process of care on mortality of patients admitted to the Intensive Care Unit) indicate high mortality rates as 48,8% in septic shock patients[6].

Sepsis can be associated with any infectious focus, with the

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Cómo citar este artículo: Santos S, Ponciano A, Monteiro JR, Pinhal F, Leite J, Fernandes C
Sepsis – Retrospective Observational Study of Sepsis and Septic Shock treated in internal medicine wards. Galicia Clin 2020; 81 (3): 70-74

Recibido: 03/05/2019; Aceptado: 13/07/2019 // http://doi.org/10.22546/57/2317

most common infections being pneumonia, intra-abdominal infection and urinary tract infections. Pneumonia, in most epidemiologic studies is the responsible focus for half of all cases. Other frequent focus are catheter infection related, soft tissue abscess, meningitis, endocarditis among others[7].

Not all patients with sepsis or septic shock are admitted to intensive care units. According to guidelines[8], admission to intensive care units should be evaluated according to curability of the disease and effective utility of intensive care. It is important to recognize that overloading of hospital beds, makes its management difficult, and in the real world severe patients may stay in medicine wards or emergency department[9,10].

The reality of sepsis treated outside intensive care units is widely unknown, so this study aims to ascertain sepsis/septic shock data at internal medicine wards of a non-tertiary hospital by quantifying and epidemiology characterize patients admitted during a year. This study also aims to identify and characterize antibiotics used, most common infections and microorganisms associated with these patients.

MATERIAL AND METHODS

This is retrospective observational study, using a selection of patients that were discharged from internal medicine wards at a non-tertiary hospital, with sepsis and/or septic shock diagnosis between January and December 2015.

During the study period, were included all patients over 18 years old that were discharged from internal medicine wards. Patients transferred from other hospitals were excluded. Discharge notes that were codified with the diagnostic sepsis and/or septic shock in accordance with International Statistical Classification of Diseases and Related Health Problems, 9th Revision (ICD-9) were selected and sepsis/septic shock criteria were confirmed according to sepsis-2 definitions[11] (the definition in force when the patients were admitted to hospital).

Nosocomial and community acquired infections were defined according to the Center for Disease Control and Prevention (CDC) definitions for nosocomial infections[12].

Organisms were defined as multiresistant if resistant to three or more antimicrobial classes[13].

All the patients were evaluated taking in account its clinical files from the emergency department and hospital admission. Demographic data, diagnosis at admission, comorbidities present, as clinical and laboratorial data, including microbiologic data. Microbiologic product where agent was isolated was registered, initial antibiotic therapy and its appropriation (according sensibility tests). Length of stay and discharge status were also collected data.

General descriptive statistical analysis was realized for each study variable. Continuous variables are presented as medium ± standard deviation according to its distribution. Groups comparison was realized using chi square (categorical variables) and Student's T or Mann-Whitney (continuous variables).

For independent risk factors associated with infection was elaborated a model of logistic regression. Was evaluated appropriated antibiotic therapeutics with bacteria resistance, length of stay and hospitality mortality.

A p values inferior to 0.05 was considered as sufficiently low so that a significant difference is considered. Statistical analysis was done with software SPSS, version 22, IBM, New York, USA.

RESULTS

During the study period, 308 patients were included. Mean age was 79.6±12 years old, 53% were female. 26% of the patients were resident in nursing home and 24.7% had a high grade of dependence (17% bedridden). 105 patients had been in a hospital ward the 3 months before the index case.

Female population presented more prevalence of diabetes *mellitus* (58.3% vs. 41.7%, p=0.004), heart failure (53.3% vs. 46.7%, p= 0.25) and dementia (56.8% vs. 43.2%, p=0.02). Global mortality rate was 30%, and the mean length of stay was 12±11 days.

Population characteristics are presented at Table 1.

Urinary tract infection (52.6%) and respiratory infection (34.8%) were the most common. 0.6% (2 patients) had catheter-related infection and 1 patient (0.3%) had a central nervous system infection. In 5.2% was not possible to identify the infection focus (Graphic 1).

Globally, it was possible to document microbiology agent in 92.2% of the cases. 50% by urine culture, 27.4% by blood culture and around 17% by sputum culture. The other 2 cases (0.6%) concern catheter culture and wound exudate culture.

Gram negative agents were the ones more prevalent (80.1%), mostly *Escherichia coli* (92.3%), followed by gram positive (14.5%). Almost 5.4% *Candida* spp was isolated.

When microorganism was isolated in catheter culture or wound exudate culture, 56% was *S. aureus* and it was also registered one case of fungal infection by *Candida* spp.

The prevalence of multiresistance[14] was of 43.2%, in which *Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Staphylococcus aureus* methicillin-resistant and *Acinectobacter* spp were the most widely found.

Graphic 2 presents agents distribution by sample.

Initial empiric antibiotic therapy was proper in 50% of the patients, being the most frequent antibacterial used a beta lactam with beta lactamase inhibitor (71.1%). Length of antibacterial therapy was of 5.86±3 days. Inappropriate antibiotic therapy was due in 84.7% of all cases to the presence of antibiotic resistance.

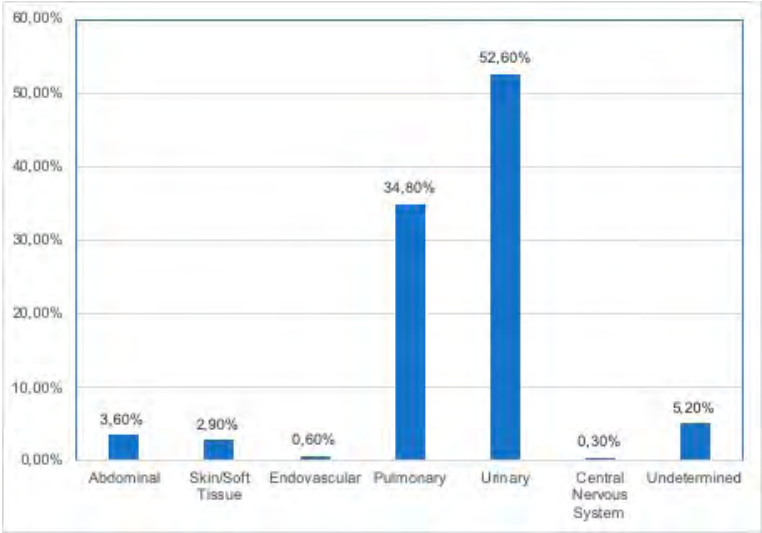
Multivariate analysis, after adjusting for comorbidities, mortality was associated with illness severity (OR 1.95, IC95% 1.2-3.2, p 0.008) and functional status (OR 4.74, IC95% 2.7-8.2, p <0.0001). Early introduction of antibiotic therapy

Table 1. Population demographic characteristics

	Female (n=162; 53%)	Male (n=146; 47%)	Total (n=308)	*p*
Age (years), min-max	79±12	80±12	79.6±12	0.4658
Length of stay (days) medium	12±11	13±11	12±11	0.4263
Functional status Dependent Bedridden	 61.8% 60.4%	 38.2% 39.6%	 24.7% 17.2%	 <0.0001 0.0003
Mortality	58.7%	41.3%	92 (29.9%)	0.0023
Septic shock at admission	90 (54.1%)	56(45.9%)	122(39.6%)	0.1513
Diabetes *mellitus*	58.3%	41.7%	33.4%	0.0037
Chronic Kidney Disease	48.9%	51.1%	30.5%	0.7003
Heart failure	53.3%	46.7%	14.6%	0.2481
Chronic pulmonary Disease obstructive disease	45.2%	54.8%	13.6%	0.0930
Dementia	56.8%	43.2%	24%	0.0173

Community acquired infection was identified in 74,03% of the patients.

Graphic 1: Source of infection



Graphic 2. Multiresistant agents distribution

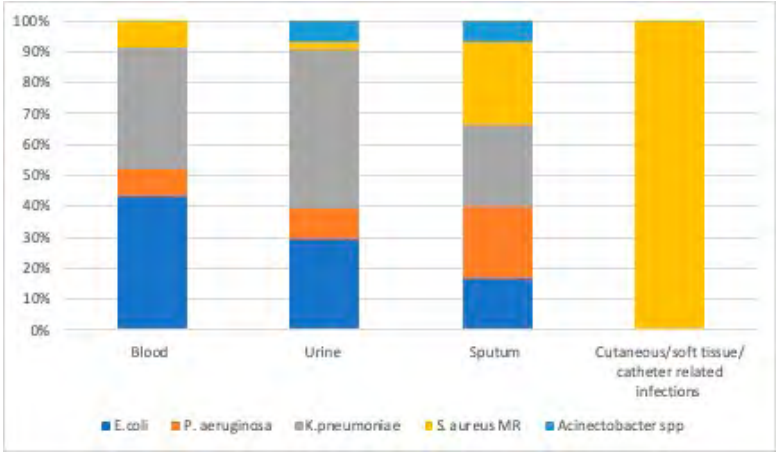


Table 2. Risk factors at admission and mortality – multivariate analysis

	Total	Survival	Non – survival	Odds ratio	Confidence Interval 95%	p
Functional Status Dependent Bedridden	 24.7% 17.2%	 21.6% 33.5%	 56.6% 54.7%	 4.74 3.61	 2.7335-8.2298 1.9585-6.6399	 p<0.0001 p<0.0001
Multiresistant agent	32.1%	39.5%	15.1%	0.27	0.1443-0.5093	p<0.0001
Previous antibiotic therapy (AT)	51.6%	22.8%	37.1%	1.99	1.2105 – 3.2899	p 0.007
Inappropriate initial AT	34.1%	27.9%	30.5%	1.13	0.6241 – 2.0594	p 0.68
Beginning AT <3hours	38.3%	31.6%	27.9%	0.14	0.6195-1.2659	p 0.5
AT changed	33.4%	33.9%	23.3%	0.59	0.3242 – 1.0795	p 0.085

was considered a protective factor with a 86% reduction in mortality. Table 2 presents mortality risk factors in our cohort.

Previous antibiotic therapy (OR 3.84, IC95% 2.4-6.2, p <0.001) and extreme dependence status (OR 3.15, IC95% 1.7-5.8, p 0.0002) were independent risk factors to the presence of antibiotic resistance. (Table 3)

DISCUSSION

This study presents a contemporary analysis of the epidemiology and prognosis of sepsis patients admitted to internal medicine wards. So far, we do not have knowledge of other national studies with this population, so it is a pioneer study regarding the population that doesn't gather criteria to admission in intensive care units.

Almost a quarter of patients presented septic shock at admission with higher mortality associated as well as comorbidities in accordance with national reality[6].

Community-acquired infections and Gram-negative bacteria predominated. This study also presents high prevalence in microbiological documentation in line with international epidemiological studies[14].

The urinary tract has been identified as the main source of infection in more than half of the cases, contrary to the tendency of previous national series in which respiratory tract infections predominate, which we associate with the increasing use of invasive devices and urological procedures.

There is an elevated number of sputum cultures without microbiology isolation and an elevated number of urine cultures positive with microbiology documented which explains the high rate of gram negative isolated.

In this study, it was not possible to determine the focus of infection in 5.2%, stressing the risk of antimicrobial resistance by the use of broad spectrum empirical antibiotics. A multidisciplinary and cooperative approach between emergency and inpatient services can contribute to an improvement not only in the procurement of biological products but also in microbiological documentation, which are crucial for the rational use of antimicrobials.

The presence of multiple risk factors is significantly associated with the presence of bacterial resistance to antimicrobials. Among them, the use of antibiotics in the previous 3 months was the most significant risk factor.

This retrospective analysis allowed to establish the general characteristics of patients with sepsis in the internal medicine wards as well as prognostic analysis. However, because it is a retrospective analysis, there are some limitations, namely the selection of patients diagnosed with sepsis/septic shock based only in medical records and the methodology of product harvesting. These limitations imply a prospective analysis to consolidate criteria for diagnosis, follow-up and prognosis of these patients, as well as review of protocols of action, with a view to reducing mortality.

Table 3. Multivariate analysis – antimicrobial resistance

	Odds ratio	Confidence interval 95%	p
Functional status Dependent Bedridden	 3.12 3.15	 1.7946 – 5.3804 1.7165 – 5.8093	 p 0.0001 p 0.0002
Age (per year)	0.99	0.99-0.99	p 0.9
Previous antibiotic therapy	3.84	2.3900 – 6.1592	p<0.0001

CONCLUSION

This study calls to attention the significant prevalence of sepsis/septic shock treated in internal medicine wards, particularly in specific high-risk populations, with marked prevalence in elderly, dependent and with many comorbidities patients. It also serves to highlight the importance of soon diagnose and the value of collection of cultures to appropriately treat.

These records would also be useful in providing reliable, quantifiable data regarding sepsis/septic shock treated outside intensive care units numbers in regards to plan strategies to best attend these patients.

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