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# Clinical aspects and the origin of sepsis patients treated at a university hospital

Aspectos clínicos e procedência de pacientes sépticos atendidos em um hospital universitário  
Aspectos clínicos y procedencia de pacientes sépticos atendidos en un hospital universitario

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## Keywords

Sepsis; Protocols; Health services; Emergency service; hospital; Mortality

## Descritores

Sepse; Protocolos; Serviços de saúde; Serviço hospitalar de emergência; Mortalidade

## Descriptores

Sepsis; Protocolos; Servicios de salud; Servicio de urgencia en hospital; Mortalidad

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## Abstract

**Objective:** To characterize the clinical aspects, severity and mortality of sepsis patients treated in the urgency and emergency departments of a tertiary hospital, relating them to the health services of origin, where initial care was performed.

**Methods:** Cross-sectional, quantitative study with sepsis patients, treated in the urgency and emergency departments of a tertiary university hospital.

**Results:** Of the 225 eligible patients, 115 (51.1%) were hospitalized with sepsis; of these, 63.5% were referred from other services. Among patients from other services, the development of septic shock and the need for mechanical ventilation was significantly more frequent. Patients admitted to the sepsis study hospital had greater adherence to the 3-hour package of the Surviving Sepsis Campaigning-2016. There was no difference between the mortality of those admitted for having sepsis and those who developed sepsis in the study hospital. However, 60.4% of the patients died, 63.2% of whom came from other services.

**Conclusion:** More than half of the patients hospitalized with sepsis come from other health services. they presented a greater degree of severity and required more therapeutic interventions. However, there was no difference in mortality rates.

## Resumo

**Objetivo:** Caracterizar os aspectos clínicos, gravidade e mortalidade de pacientes com sepse atendidos em setor de urgência e emergência de um hospital terciário, relacionando-os aos serviços de saúde de origem, onde foi feito o atendimento inicial.

**Métodos:** Trata-se de um estudo transversal, quantitativo, realizado com pacientes sépticos atendidos em setor de urgência e emergência de um hospital universitário terciário.

**Resultados:** Dos 225 pacientes elegíveis, 115 (51,1%) foram admitidos com sepse, e destes, 63,5% foram encaminhados de outros serviços. Entre os pacientes procedentes de outros serviços o desenvolvimento do choque séptico e necessidade de ventilação mecânica foi significativamente mais frequente. Os pacientes admitidos no hospital do estudo por sepse tiveram maior aderência ao pacote de 3 horas da Surviving Sepsis Campaigning-2016. Não houve diferença entre a mortalidade dos admitidos por sepse ou aqueles que desenvolveram sepse no hospital do estudo, entretanto, evoluíram a óbito 60,4% dos pacientes, destes, 63,2% procedentes de outros serviços.

**Conclusão:** Mais da metade dos pacientes admitidos por sepse provém de outros serviços de saúde. Estes apresentaram maior grau de gravidade e requereram mais intervenções terapêuticas. Entretanto, não houve diferença nas taxas de mortalidade.

## Resumen

**Objetivo:** Caracterizar los aspectos clínicos, gravedad y mortalidad de pacientes con sepsis atendidos en sector de urgencia y emergencia de un hospital terciario, relacionándolos con los servicios de salud de origen, donde se realizó la atención inicial.

**Métodos:** Se trata de un estudio transversal, cuantitativo, realizado con pacientes sépticos atendidos en sector de urgencia y emergencia de un hospital universitario terciario.

**Resultados:** De los 225 pacientes elegibles, 115 (51,1%) fueron admitidos con sepsis, y de éstos, el 63,5% fueron encaminados de otros servicios. Entre los pacientes procedentes de otros servicios el desarrollo del shock séptico y la necesidad de ventilación mecánica fue significativamente más frecuente. Los pacientes admitidos en el hospital del estudio por sepsis tuvieron mayor adherencia al paquete de 3 horas de la Surviving Sepsis Campaigning-2016. No hubo diferencia entre la mortalidad de los admitidos por sepsis o aquellos que desarrollaron sepsis en el hospital del estudio, sin embargo, evolucionaron a muerte el 60,4% de los pacientes, de éstos, el 63,2% procedentes de otros servicios.

**Conclusión:** Más de la mitad de los pacientes admitidos por sepsis provienen de otros servicios de salud. Estos presentaron mayor grado de gravedad y requirieron más intervenciones terapéuticas. Sin embargo, no hubo diferencia en las tasas de mortalidad.

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Conflicts of interest: none.

## Introduction

Sepsis is defined as the presence of a potentially fatal organic dysfunction caused by the host's dysregulated response to an infectious process, which can progress to a septic shock.<sup>(1)</sup> This disease has a worldwide impact on human health and causes about 6 million deaths per year.<sup>(2)</sup> In addition to being the leading cause of mortality in hospitals,<sup>(2)</sup> it reaches expenditures of \$ 23.7 billion per year for treatment in American hospitals.

In Brazil, data from the Latin American Sepsis Institute (ILAS), referring to the years 2005–2016, indicated that 52,045 patients were diagnosed with sepsis or septic shocks in registered hospitals. Regarding sepsis lethality, this report showed that the overall mortality reached 44.8% of patients hospitalized in public institutions. Among the 2,758 patients admitted with sepsis, coming from other services, 33% died. This proportion rises to 53.2% in public hospitals.<sup>(4)</sup>

Recognition and early diagnosis, accompanied by an effective treatment, are directly related to the patient's prognosis. After the sepsis diagnosis, treatment approaches are a priority and should be instituted immediately after identifying and guided by the goals recommended by the Surviving Sepsis Campaign (SSC).<sup>(5)</sup>

Studies on sepsis are concentrated in highly complex tertiary services, with emphasis on intensive care units. However, its treatment permeates the three levels of health care, organized to meet the different levels of complexity, classified in primary, secondary and tertiary according to the unique technological density.<sup>(6)</sup>

Septic patient care is effective when there is availability of staff and resources for the treatment of individuals in severe situations. The presence of intensivist and emergency professionals in services of less complexity is scarce. In addition, broad-spectrum antimicrobials and substitutive therapies are not always available at the primary and secondary health care levels.<sup>(7)</sup> In this sense, there is a need for studies that explore the treatment in institutions of lesser complexity until referral to services to promote the survival of these patients.

The objective of this study was to characterize the clinical aspects, severity and mortality of sepsis patients, treated in an urgency and emergency department of a tertiary hospital, considering the weaknesses of the services of less complexity and the demand for the care of sepsis patients in these institutions. They are related to the home health services, where the initial care was performed and compared to those patients diagnosed and treated at the study hospital.

## Methods

### Design

Cross-sectional, quantitative approach, carried out in the city of Londrina-PR, between August 2013 and October 2015.

### Place

The University Hospital of Londrina (*Hospital Universitário de Londrina*) is a supplementary body of the State University of Londrina (HU-UEL), a non-profit organization dedicated to teaching, researching and extending services to the community, for providing universal care. It is a tertiary hospital, with 303 beds distributed among hospitalization units, first aid and intensive care units (ICU). Moreover, it is a reference center in high complexity cases for the Unified Health System (SUS) in the northern region of the state of Paraná, Brazil. The Urgency and Emergency Departments serve patients from about 250 municipalities in Paraná and more than 100 cities in other states, a population estimated at 825,000. Londrina's 17th regional health service covers 21 municipalities and has 140 primary, 31 secondary and 5 tertiary services.

### Sample

Non-probabilistic sampling for convenience, obtained through reaching 225 patients immediately available after admission with a sepsis diagnosis or diagnosed in the urgency and emergency departments. Patients aged 14 and over were excluded, as well as palliative care patients, with no possibility of therapy.

## Variables and data collection

The variable sepsis was defined by means of the elements in force at the time of the study: a history suggestive of current infection and a sign or symptom of the Systemic Inflammatory Response Syndrome (SIRS). The sepsis associated with an organic dysfunction characterized as severe sepsis,<sup>(8)</sup> was described in this study as sepsis, considering the update in the diagnostic criteria.

The characterization of patients included the clinical-epidemiological and demographic variables: age; sex; origin and referral; SOFA score (Sequential Organ Failure Assessment); signs defining septic shock,<sup>(8)</sup> hospitalization period and clinical outcome.

Regarding sepsis therapy, the recommendations of SSC-2016<sup>(9)</sup> in force during the study period were adopted to care for patients as of the first 3 hours after diagnosis. For patients admitted for having sepsis, the initial three hours of sepsis were counted considering a zero-time admission. It was not possible to evaluate the treatment within the first hour of the sepsis diagnosis, currently recommended by the SSC,<sup>(5)</sup> given it was recommended after finishing the current study.

The origin of the patients was subdivided into a primary service, composed of basic health units (BHU) and secondary units, outpatient clinics and emergency care units (UPA). In these services in the municipality of the study setting, patients remain for a limited time and tend not to exceed 24 hours. Hospitals were subdivided according to their degree of complexity in secondary and tertiary services.

Data were collected in an audit instrument of the cases of sepsis treated in the urgency and emergency departments of the HU-UEL, based on the records of the managed protocol for sepsis and the medical records of patients. The data of origin were extracted from the documents of referral, referencing and the Rescue Service Report (RSR).

## Statistical analysis

The descriptive analysis was performed through the distribution of frequencies of categorical variables and, for continuous variables, measures of central tendency (mean and median), dispersion

(standard deviation - SD) and interquartile range were obtained. The Student's T-test, or nonparametric equivalent test (Mann-Whitney) when with non-Gaussian distribution, was used to compare the continuous variables. Pearson's Chi-squared test or Fisher's exact test was used to compare categorical variables, when indicated. Data were analyzed using the Epi Info™ program, version 7.2.2.6 (Centers for Disease Control and Prevention, Atlanta, USA). Statistical significance was set at  $p < 0.05$  for all analyzes.

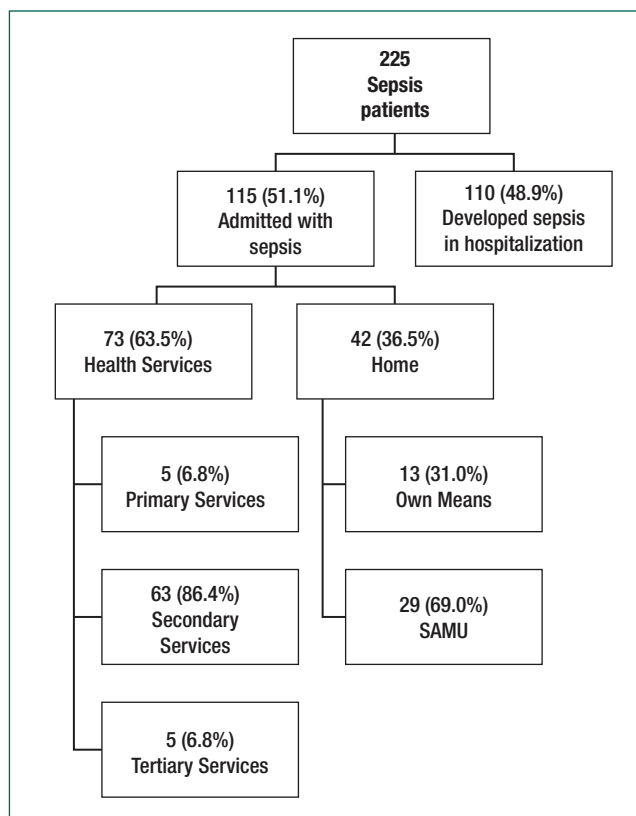
## Ethical aspects

This study is linked to the project "Adequacy and Implementation of a Managed Care Protocol for Sepsis patients in a University Hospital" (*Adequação e Implantação de um Protocolo Assistencial Gerenciado de Tratamento de Pacientes com Sepse em um Hospital Universitário*), authorized by the institution of the study and approved by the Research Ethics Committee involving Human Subjects of the *Universidade Estadual de Londrina* (State University of Londrina) with Certificate Presentation for Ethical Assessment (CAAE) No. 38733014.9.0000.5231, opinion No. 884.268.

## Results

The study sample consisted of 225 patients, admitted with sepsis or who developed this complication in the urgency and emergency departments of the study institution, according to the distribution presented in figure 1.

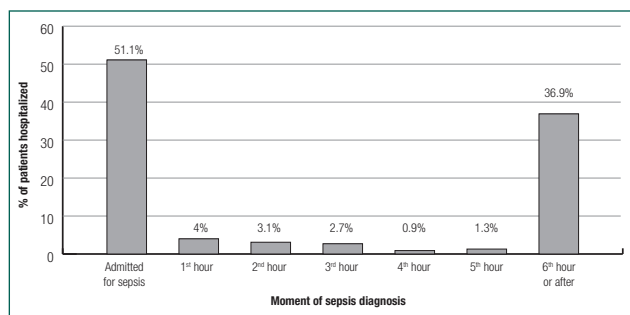
The sample had a predominance of individuals aged 60 or older (64.9%), average age 63.8 (SD 18.7), ranging from 14 to 98 years old. There was no difference in this variable among the categories of patients admitted with sepsis or who developed this complication in the study hospital. Regarding the time interval between admission and identification of sepsis, it 51.1% were admitted for sepsis, and 48.9% had sepsis identified after the admission in the corresponding department, more frequently after 6 hours of hospitalization. This is shown in figure 2.



**Figure 1.** Distribution of the study sample regarding the admission condition related to sepsis, origin and services of origin of sepsis patients

The most frequent focus of infection of sepsis was pneumonia (77.8%), followed by urinary tract infection (11.1%), surgical wound infection (1.2%), osteomyelitis (1.6%), cutaneous infection (0.8%), pericarditis (0.8%), meningitis (0.8%), infected sebaceous cyst (0.8%), encephalitis (0.7%), and focus without definition (3.6%). Pneumonia also prevailed among categories of patients coming from health services (90.4%), coming from their homes (71.4%) or those who identified sepsis in the study institution (71.8%).

Regarding statistical analysis, this study showed that patients admitted with sepsis had a higher occurrence of septic shocks (63.7%,  $p=0.003$ ) and a need for mechanical ventilation (57.3%,  $p=0.020$ ). As for the severe conditions of the studied patients, the SOFA and APACHE II severity scores had a median of 7 and 25, respectively, and were higher ( $p<0.05$ ) among patients admitted for having sepsis (median 9 and 27).



**Figure 2.** Distribution of sepsis patients assisted in the urgency and emergency departments as for the moment of sepsis diagnosis

Among those coming from other services, 37.0% had a complete report, including diagnostic, screening and therapeutic information, prepared by the referral service and sent to the study hospital. However, 63.0% had only partial information in the referral report. Among the reports analyzed, 47.9% had two or more SIRS criteria, totaling 81 reported changes. Of these, tachycardia was the most frequent (30.9%), followed by tachypnea (28.4%), leukocytosis (22.2%), hyperthermia (16.0%) and hypothermia (2.5%).

Organic dysfunctions were reported by the services of origin in 82.2% of the cases, and most of them (88.3%) had two or more organ dysfunctions due to sepsis. The most frequent was the decrease in the level of consciousness (30.7%), followed by the recent or increased need for oxygen to maintain oxygen saturation above 90% (30.1%), platelets below 100,000 (15.7%), creatinine above 2.0mg/dL or diuresis below 0.5ml/kg/h in the last two hours (9.8%), systolic blood pressure lower than 90mmHg or mean arterial pressure lower than 65mmHg (7.2%), blood pressure drop above 40 mmHg (4.6%) and international normalized ratio above 1.5 or partially active thromboplastin time over 60 seconds (0.7%).

Moreover, in relation to patients referred from health services, 87.7% had reports from the institutions of origin regarding therapeutic behaviors, of which 51.6% received antimicrobials, totaling 49 antimicrobials administered, considering that some patients received more than one class of antimicrobial. The most frequent were ceftriaxone (32.8%), followed by azithromycin (10.2%), cipro-



floxacin (10.2%), piperacillin/tazobactam (10.2%), cefepime (8.2%), clindamycin 6.1%), vancomycin (6.1%) and others (16.2%).

As for the patients coming from their homes, 30.9% used their own means. Among those transported by mobile emergency services (69.0%), 44.8% presented criteria for SIRS reported on screening in the prehospital care. Of the 32 alterations, the most frequent were tachycardia (37.5%) and tachypnea (37.5%), followed by hyperthermia (21.9%) and hypothermia (3.1%). Concerning organic dysfunctions, changes in blood pressure were detected in 20.6% of cases, decrease in the consciousness level by 51.7% and respiratory dysfunction requiring ventilatory support in 58.6% of the cases.

Regarding sepsis therapy, performed in the study hospital, except for antimicrobial therapy, patients admitted for sepsis had greater adherence to the 3-hour packet of SSC-2016, when compared to those who developed sepsis in the study hospital, considering that time zero was the time of admission for patients admitted for sepsis (Table 1).

**Table 1.** Distribution of sepsis patients regarding adherence to the treatment package during the first 3 hours (SSC-2016) in the urgency and emergency departments

Distribution of patients	Total	Admitted for sepsis		p-value*
		Yes n(%)	No n(%)	
Blood culture	99	61 (61.62)	38 (38.38)	0.003
Hemodynamic resuscitation	44	31 (70.45)	13 (29.55)	0.011
Collection of lactate	148	87 (58.78)	61 (41.22)	0.001
Antimicrobial therapy	163	82 (50.31)	81 (49.69)	0.400

\*Fisher's exact test

There was no difference between the mortality rate of those admitted for sepsis and those who developed sepsis at the study hospital. Of the total number of deaths (60.4%), 63.2% came from health services, with a prevalence of 90.7% of those who came from secondary levels.

## Discussion

The results of this study showed that there is an important demand of sepsis patients referred to the urgency and emergency services of tertiary hospitals,

especially secondary and primary services, and that require the use of complex emergency transportation, such as the Mobile Emergency Care Service (SAMU). Although research does not cite sepsis as one of the main causes of admission to emergency rooms, respiratory problems, including infections, are the focus of sepsis, and are among the first in admissions in Brazilian emergency departments.<sup>(10)</sup>

The direct search for sepsis was also expressive. This movement may indicate problems to access services of low complexity for treating infections prior to the sepsis. The literature points to difficulties related to the structural, operational and relational process, which imply access to the primary level.<sup>(11)</sup> Nonetheless, there are also difficulties at the secondary level, which result in restricted access to this service.<sup>(12)</sup>

Pneumonia was the most frequent focus of infection in the study sample, considering that this infection represented the majority among sepsis patients admitted from other services or home, as well as among those who developed sepsis at the institution of the study. The respiratory site is commonly affected by infectious processes, thus justifying pneumonia as the focus of sepsis. Medical records of hospitalized patients in four US institutions have identified pneumonia as the most prevalent (35.0%).<sup>(13)</sup> The study carried out in emergency units and clinics of a Spanish hospital shows a prevalence above 47.0% for respiratory infectious focus.<sup>(14)</sup> Brazilian public hospitals present a very similar reality, showing pneumonia as the most reported infectious focus (57.3%).<sup>(15)</sup>

In the more severe patients (APACHE II and SOFA severity scores), the use of mechanical ventilation and the evolution to septic shock were significantly more frequent among those admitted for sepsis. All the frequencies presented in this study were above those indicated in the ILAS report of 2017 for Brazilian public institutions,<sup>(4)</sup> demonstrating the severity of the situation of sepsis patients admitted in the studied department.

SIRS records were present in approximately half of reports of prehospital care or sepsis patients coming from health services, proving to be an important screening criterion, especially for services that

do not rely on diagnostic technologies. Although SIRS has been excluded from the diagnostic criteria for sepsis because of its low specificity, its manifestation can still be used as screening for severe patients. Tachycardia and tachypnea were changes reported more frequently in this study, corroborating with a survey in Spanish hospitals, which maintained high prevalence for the two categories cited, with the addition of hyperthermia or hypothermia.<sup>(14)</sup>

Regarding therapies for sepsis, the antimicrobial therapy, strongly recommended to increase survival,<sup>(5)</sup> was reported in roughly half of the reports from the health services that referred sepsis patients. This fact can be related both to the failures in the registries of the reference services and to the lack of knowledge about the therapeutic measures for sepsis by professionals of the services of origin of patients.

As of 2018, therapies that treat sepsis should start in the first hour after its diagnosis.<sup>(5)</sup> However, the recommendation in force during the study period, referring to the 3-hour pack, recommended by SSC-2016 was used.<sup>(9)</sup> Among the conducts are: collection of lactate and blood cultures, antimicrobial administration and volume replacement when indicated.<sup>(9)</sup> In this study, the therapeutic procedures for the 3-hour package were performed in more than half of patients admitted for sepsis, considering zero time the time of admission for sepsis. Adherence to the treatment package was significantly more frequent among patients admitted for sepsis when compared to adherence of these measures in patients whose diagnoses were made at the study institution. This reflects that it may be difficult to diagnose sepsis at the study institution, considering that patients admitted with suspicion or sepsis diagnosis from other institutions had greater access to therapies.

Even though most of the patients admitted for sepsis were given quick access to the recommended treatment, most of deaths occurred among this sample of patients. This result corroborates the need for early diagnosis and rapid therapy onset,<sup>(5)</sup> right in the institutions of origin of patients, especially the secondary services, which had a higher frequency of deaths. Evidence that delayed treatment package measures in these services, including administering antibiotics, decreases the survival of sepsis patients.

This study showed that among sepsis patients seen in the urgency and emergency departments of a tertiary hospital there is an important representation of patients referred by other services with this diagnosis, especially by secondary services. Data justify the need for these services to establish protocols to identify and treat sepsis, highlighting the importance of early diagnosis and effective treatment in this service, which may contribute to patient survival. A retrospective Australian study showed that if immediate treatment measures were instituted for the sepsis diagnosis, the mortality of these patients significantly reduced, from 35.0% to 18.4%, with an absolute reduction in the risk of death by 16.7%.<sup>(16)</sup>

Research does not allow establishing a chronological causal relationship between the variables and the outcome because this is a cross-sectional study. Although it has this characteristic, it also contributes to the clinical practice when exploring behaviors adopted for the treatment of patient with sepsis at the different levels of complexity.

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## Collaborations

Santos MCS, Sanches CT, Moraes URO, Albanase SPR, Carrilho CMDM, Volpato MP, Grion CMC and Kerbaux G declare that they contributed to project design, data analysis and interpretation, article writing, relevant critical review of intellectual content and approval of the final version to be published.

## Conclusion

Research showed that more than half of patients admitted for sepsis were referred with this diagnosis

from other health services. They were in a more serious condition and required more interventions. Even with access to the recommended treatment package, after admission to the study institution, mortality among patients admitted for sepsis was higher for those referred from other services. This result indicates that identifying and treating sepsis should be a priority in health services, to promote the survival of these patients. Therefore, it is necessary that all levels of health care be trained to diagnose sepsis early and adequately conduct cases until transfer patients to a more complex service, contributing to the quality of care and, consequently, to patient survival.

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