Abstract: Background: Sepsis is a common cause of morbidity and mortality among hospitalized patients. The prevalence of this condition has increased significantly in different parts of the world. Patients admitted to dermatology wards often have severe loss of skin barrier and use systemic corticosteroids, which favor the development of sepsis. Objectives: To evaluate the prevalence of sepsis among patients admitted to a dermatology ward compared to that among patients admitted to an internal medicine ward. Methods: It is a cross-sectional, observational, comparative study that was conducted at Hospital Santa Casa de Belo Horizonte. Data were collected from all patients admitted to four hospital beds at the dermatology and internal medicine wards between July 2008 and July 2009. Medical records were analyzed for the occurrence of sepsis, dermatologic diagnoses, comorbidities, types of pathogens and most commonly used antibiotics. Results: We analyzed 185 medical records. The prevalence of sepsis was 7.6% among patients admitted to the dermatology ward and 2.2% (p = 0.10) among those admitted to the internal medicine ward. Patients with comorbidities, diabetes mellitus and cancer did not show a higher incidence of sepsis. The main agent found was Staphylococcus aureus, and the most commonly used antibiotics were ciprofloxacin and oxacillin. There was a significant association between sepsis and the use of systemic corticosteroids (p <0.001). Conclusion: It becomes clear that epidemiological studies on sepsis should be performed more extensively and accurately in Brazil so that efforts to prevent and treat this serious disease can be made more effectively.

Keywords: Dermatology; Internal medicine; Sepsis; Systemic inflammatory response syndrome
INTRODUCTION

Sepsis is an important cause of morbidity and mortality among hospitalized patients, despite the recent advances in supportive care and the specific treatments for this disease. It is defined as an infection with concurrent systemic manifestations, which are the result of the host response. This response, known as Systemic Inflammatory Response Syndrome (SIRS), can be diagnosed based on the presence of two or more of the following variables, according to the consensus statement established by the American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM) in 1992:1

a) Fever (temperature above 38°C) or hypothermia (below 36°C);

b) Tachypnea (greater than 20 breaths per minute) or PaCO₂ (partial pressure of carbon dioxide) less than 32 mmHg;

c) Tachycardia (above 90 bpm);

d) Leukocytosis (above 12,000/µL), leukopenia (below 4,000/µL) or more than 10% immature neutrophils.

Thus, the presence of two or more criteria for SIRS in association with clinical and microbiological evidence of infection characterize sepsis.²

There are few and poor consistent data on the prevalence of sepsis among hospitalized patients in dermatology wards in Brazil. Brazil is a country of continental dimensions, with a heterogeneous population and unequal access to health care services. Private hospitals are usually better equipped and have more resources available than public hospitals, except for some public university hospitals. Measures to reduce the prevalence of sepsis and sepsis-related mortality must be addressed through reliable and consistent data on sepsis among the Brazilian population.

Inpatients in dermatology wards have often lost large areas of skin barrier, in addition to having impairment of the skin immune function. These patients, therefore, present conditions that are favorable to the development of sepsis. Frequent use of steroids and immunosuppressive drugs for prolonged periods of time accentuates the risk of sepsis in this group of patients. There is also a lack of data related to the epidemiological aspects and etiological profile of sepsis in this group.³

In this work, we used the 1992 SIRS definition, established by the ACCP and SCCM.¹ Sepsis, a systemic response to an infection, was defined by the presence of SIRS combined with a documented infection, being considered positive with the isolation of germs through blood culture or in gram-positive peripheral blood sample.¹

MATERIAL AND METHODS

This is an observational, cross-sectional, comparative analysis of medical records carried out at Santa Casa de Belo Horizonte in the period between 2010 and 2011.

The sample calculation was based on estimates of the prevalence of sepsis in dermatology wards and ITUs, according to reference work. Therefore, based on these estimates, the considered prevalence was approximately 7% with a margin of error of 5%.⁴, ⁵

We used a significance level of 5% (type I error) and power 80% (type II error). The final sample estimate was 141 patients (about 70 patients in each group).

All of the patients admitted to four beds (two female and two male) of the dermatology ward and four beds of the internal medicine ward (two female and two male) at Santa Casa de Belo Horizonte were randomly selected and included in the study carried out between July 2008 and July 2009, a total of 185 patients. From these, 93 (50.3%) patients were admitted to the internal medicine ward and 92 (49.7%) to the dermatology ward.

Patients younger than 12 years old were excluded, for it was a prerequisite for admission to the dermatology and internal medicine wards.

In this work, we used the 1992 SIRS definition, established by the ACCP and SCCM.¹ Sepsis, a systemic response to an infection, was defined by the presence of SIRS combined with a documented infection, being considered positive with the isolation of germs through blood culture or in gram-positive peripheral blood sample.¹

Data collection

Data were collected from April 2010 to March 2011 from the medical records of the patients included in the research and by filling out a form specially designed for the research.

This form showed the variables to be studied:

- Hospitalization Sector: Dermatology/Internal medicine ward.
- Date of birth, sex.
- Date of hospitalization, date of medical discharge.
- Reason for hospitalization, comorbidities.
- Medication in use; corticosteroids, type, dosage; immunosuppressor, type, dosage; others.
- Antibiotics, type, treatment period. This item was subdivided in A, B and C for patients using more
than one type of antibiotic or when any change was made to the original scheme firstly proposed.
- SIRS/SEPSIS.
- Fever (>38°C), hypothermia (<36°C), tachycardia (above 90 bpm), tachypnoea (above 20 bpm), complete blood count showing leukocytosis (>12,000) or leukopenia (<4,000), hypotension.
- Cultures: blood culture, isolated germ, sensitivity and resistance; urine culture, isolated germ, sensitivity and resistance; secretion culture, isolated germ, sensitivity and resistance; other cultures, isolated germ, sensitivity and resistance.

The collected data were organized in Excel spreadsheets to be analyzed through pertinent statistical methods.

Statistical Analysis

Descriptive analysis of all variables used in the study was carried out by means of frequency distribution tables and central tendency measures and variability.

To check the differences between patients hospitalized in the internal medicine and dermatology wards, we used the Pearson’s Chi-square test or Fisher’s exact test, when comparing proportions. To compare the continuous variables, we used the Mann-Whitney’s non-parametric test, suitable to the comparison between the two groups.

The same tests were used to evaluate the factors associated with the occurrence of sepsis in the univariate analysis. OR was also evaluated, with the respective CI of 95%.

The variables selected for the multivariate model of binary logistic regression were those with p-value below 0.20 in the univariate analysis. The forward method was used, with the variables being inserted one by one in the model, based on significance. For permanence of the variable in the final model, a 5% significance level (p value <0.05) was considered. The adjustment of the final model was evaluated through the Hosmer-Lemeshow statistical test. 6

The significance level of 5% was considered in all of the analysis, with the adoption of the Statistical Package for Social Sciences (SPSS) 15.0.

The study protocol was approved by the Ethics Committee of the hospital where the study was conducted.

RESULTS

The number of inpatients in the dermatology ward was 92 (49.7%), while it was 93 (50.3%) in the internal medicine ward. A little more than half of the patients studied (50.8%) were male.

Nine patients, that is, 4.9% of the total, presented sepsis. Diabetes was identified in 25 patients (13.5%); and 20 (10.8%) presented cancer at hospital admission; SIRS was reported in 65 patients (35.1%); community and nosocomial infections were detected in 88 (47.6%) patients. The average age was 54 years, and the median was 55 years. The average hospital stay was 15 days, with a median of 11 days.

Twenty-two (22) of the studied patients (11.9%) used systemic steroids during their hospital stay. Prednisone was used in almost the total number of cases (95.5%), and the most frequent dosage was 40 mg/day (30%). Three patients (1.6%) used an immunosuppressor, and only methotrexate was observed; the maximum dose was 15 mg/week (66.7%).

A hundred and ten (110) patients (59.4%) used antibiotics (ATB), and the maximum number was five antibiotics. A total of 25 different types of antibiotics were used, and the most frequently used one was ciprofloxacin (14.0%). In addition, in the 19 cases evaluated for the initial use of ATB, the antibiotic was not in accordance with culture in 10 cases (52.6%) and was changed after culture in seven cases (36.8%).

It is noteworthy that, out of the 12 cases which had no ATB change after culture, nine already belonged to the group whose antibiotic therapy had been introduced in accordance with culture. In the remaining three cases, the initial coverage, though empirical, was consistent with the desired coverage, and there was no need for changes in the antibiotic profile.

According to table 1, blood culture was performed in 22 patients (11.9%), with positive results and germ identification in seven (3.8%). Research for bacteria per gram of peripheral blood was positive in nine (40.9%) out of 22 cases. Urine culture and secretion culture were required in 22 patients (11.9%), with germ identification in seven (3.8%) urine cultures and in eight (4.2%) secretion cultures. In addition, the germs identified in each test were Escherichia coli, the most common germ found in the urine cultures, and S. aureus, the most common germ found in the secretion cultures.

According to the results showed in table 2, there was a statistically significant difference between inpatients from the internal medicine ward and those from the dermatology ward concerning prevalence of cancer, SIRS and age. Both cancer (neoplasia) and SIRS were more prevalent in the internal medicine ward (17.2% and 47.3%, respectively), compared with the dermatology ward (4.3 and 22.8%, respectively). In addition, we found a higher mean and median age among inpatients from the internal medicine ward.

Besides that, there was a statistically significant difference between inpatients from the internal medicine ward and those from the dermatology ward in...
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relation to use of systemic steroids. Among the inpa-
tients from the internal medicine ward, 2.2% used this
type of medication, while the percentage among der-
matology inpatients was 21.7%. There were no sta-
tistically significant differences between internal medi-
cine and dermatology patients regarding number of
antibiotics used.

Considering the univariate analysis, the factors
that showed statistically significant association with
the presence of sepsis were age and number of days in
hospital (p value <0.05). The prevalence of sepsis was
higher among inpatients from the dermatology (7.6%)
ward compared to that found among inpatients from
the internal medicine ward (2.2%); however, this asso-
ciation was not statistically significant (p=0.10).

After analyzing the association between sepsis
and use of corticosteroids, we observed that the
prevalence of sepsis among patients who did not use
corticosteroids was 1.8%, while it was 27.3% among
those who used this medication. We also noted the
association between occurrence of sepsis and amount
of ATBs. With the increase use of ATB, the chance of
occurrence of sepsis is 2.14 times higher. Blood culture
and urine culture were performed more frequently
among patients with sepsis, and this difference was
statistically significant (p<0.05).

The use of the immunosuppressor methotrexate
(MTX) did not show a statistically significant associa-
tion with sepsis (p=0.140). However, it is noteworthy
that one of the patients who had used MTX developed
sepsis.

In table 3, the patients were classified according
to age group, hospitalization place and associated
conditions. The use of corticosteroids was higher in all

|Blood Culture| No. | Percentage |
|-------------|-----|------------|
|No           | 163 | 88.1       |
|Yes          | 22  | 11.9       |

|Bacteria in peripheral blood|
|-----------------------------|
|Gram-negative | 13  | 59.1       |
|Gram-positive | 9   | 40.9       |

|Germ identified in blood culture|
|----------------------------------|
|Staphylococcus spp. | 1   | 14.3       |
|Staphylococcus aureus | 3   | 42.9       |
|Coagulase-negative Staphylococcus | 2 | 28.6       |
|Yeast | 1   | 14.3       |

|Uroculture| No. | Percentage |
|-----------|-----|------------|
|No         | 163 | 88.1       |
|Yes        | 22  | 11.9       |

|Bacteria in urine|
|------------------|
|Gram-negative | 19  | 90.5       |
|Gram-positive | 2   | 9.5        |

|Germ identified in uroculture|
|-------------------------------|
|Pseudomonas | 1   | 14.3       |
|Citrobacter freundii | 1 | 14.3       |
|Proteus mirabilis | 1   | 14.3       |
|Morganelia morgani | 1   | 14.3       |
|Escherichia coli | 3   | 42.9       |

|Secretion culture| No. | Percentage |
|-----------------|-----|------------|
|No               | 163 | 88.1       |
|Yes              | 22  | 11.9       |

|Bacteria in secretion culture|
|-----------------------------|
|Gram-negative | 14  | 63.6       |
|Gram-positive | 8   | 36.4       |

|Germ identified in secretion culture|
|-------------------------------------|
|Acinetobacter baumannii | 1 | 6.7        |
|Escherichia coli | 1   | 6.7        |
|Klebsiella | 1   | 6.7        |
|Proteus vulgaris | 4   | 26.7       |
|Pseudomonas aeruginosa | 1 | 6.7        |
|Pseudomonas spp. | 1   | 6.7        |
|Staphylococcus aureus | 6   | 40.0       |

|TABLE 1: Descriptive analysis of the variables related to blood culture, urine culture and secretion culture (n =185)| No. | Percentage |
|---|-----|------------|
|Blood Culture| No. | Percentage |
|---|-----|------------|
|No | 163 | 88.1       |
|Yes | 22  | 11.9       |

|Bacteria in peripheral blood|
|-----------------------------|
|Gram-negative | 13  | 59.1       |
|Gram-positive | 9   | 40.9       |

|Germ identified in blood culture|
|----------------------------------|
|Staphylococcus spp. | 1   | 14.3       |
|Staphylococcus aureus | 3   | 42.9       |
|Coagulase-negative Staphylococcus | 2 | 28.6       |
|Yeast | 1   | 14.3       |

|Uroculture| No. | Percentage |
|-----------|-----|------------|
|No         | 163 | 88.1       |
|Yes        | 22  | 11.9       |

|Bacteria in urine|
|------------------|
|Gram-negative | 19  | 90.5       |
|Gram-positive | 2   | 9.5        |

|Germ identified in uroculture|
|-------------------------------|
|Pseudomonas | 1   | 14.3       |
|Citrobacter freundii | 1 | 14.3       |
|Proteus mirabilis | 1   | 14.3       |
|Morganelia morgani | 1   | 14.3       |
|Escherichia coli | 3   | 42.9       |

|Secretion culture| No. | Percentage |
|-----------------|-----|------------|
|No               | 163 | 88.1       |
|Yes              | 22  | 11.9       |

|Bacteria in secretion culture|
|-----------------------------|
|Gram-negative | 14  | 63.6       |
|Gram-positive | 8   | 36.4       |

|Germ identified in secretion culture|
|-------------------------------------|
|Acinetobacter baumannii | 1 | 6.7        |
|Escherichia coli | 1   | 6.7        |
|Klebsiella | 1   | 6.7        |
|Proteus vulgaris | 4   | 26.7       |
|Pseudomonas aeruginosa | 1 | 6.7        |
|Pseudomonas spp. | 1   | 6.7        |
|Staphylococcus aureus | 6   | 40.0       |
Among the nine patients who had sepsis, two had diabetes and none had cancer (Table 4). Among the seven patients with a diagnosis of sepsis in the dermatology ward, five had bullous disease. The most frequently found germ in the blood cultures was S. aureus, which was found in three patients. Two cases were gram-positive, but there was no germ growth (confirming the diagnosis of sepsis, with no specific agent being isolated); and in one patient the found

### Table 2: Descriptive analysis of the variables place of admission, gender, sepsis, diabetes, SIRS, infection and neoplasm, age and number of days in hospital (n=195)

|                      | Internal Medicine | Dermatology | P value |
|----------------------|-------------------|-------------|---------|
| Gender               |                   |             |         |
| Male                 | 46                | 48          | 0.712*  |
| Female               | 47                | 44          |         |
| Sepsis               |                   |             |         |
| No                   | 91                | 85          | 0.100** |
| Yes                  | 2                 | 7           |         |
| Diabetes             |                   |             |         |
| No                   | 76                | 84          | 0.057*  |
| Yes                  | 17                | 8           |         |
| Neoplasm             |                   |             |         |
| No                   | 77                | 88          | 0.005*  |
| Yes                  | 16                | 4           |         |
| SIRS                 |                   |             |         |
| No                   | 49                | 71          | <0.001* |
| Yes                  | 44                | 21          |         |
| Infection            |                   |             |         |
| No                   | 51                | 46          | 0.510   |
| Yes                  | 42                | 46          |         |
| Type of infection    |                   |             |         |
| 1                    | 34                | 35          | 0.580   |
| 2                    | 8                 | 11          |         |

### Table 3: Descriptive analysis of the variables place of admission, gender, sepsis, diabetes, SIRS, infection and neoplasm, age and number of days in hospital (n=195)

|                      | Internal Medicine | Dermatology | P value |
|----------------------|-------------------|-------------|---------|
| Gender               |                   |             |         |
| Male                 | 46                | 48          | 0.008** |
| Female               | 47                | 44          |         |
| Sepsis               |                   |             |         |
| No                   | 91                | 85          |         |
| Yes                  | 2                 | 7           |         |
| Diabetes             |                   |             |         |
| No                   | 76                | 84          |         |
| Yes                  | 17                | 8           |         |
| Neoplasm             |                   |             |         |
| No                   | 77                | 88          |         |
| Yes                  | 16                | 4           |         |
| SIRS                 |                   |             |         |
| No                   | 49                | 71          |         |
| Yes                  | 44                | 21          |         |
| Infection            |                   |             |         |
| No                   | 51                | 46          |         |
| Yes                  | 42                | 46          |         |
| Age                  |                   |             |         |
| Average              | 57.9              | 50.6        |         |
| Standard Deviation   | 20.5              | 17.8        |         |
| Median               | 62.0              | 49.0        |         |
| Number of days in hospital |   |             |         |
| Average              | 16.9              | 12.6        |         |
| Standard Deviation   | 15.8              | 9.3         |         |
| Median               | 12.0              | 10.0        |         |

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**DISCUSSION**

The groups evaluated and compared in this study were homogeneous concerning sex and number of patients. However, the patients admitted to the dermatology ward were younger. The mean and median ages of dermatology inpatients are probably lower compared to internal medicine inpatients, as the diseases that justify hospitalization in the dermatology ward are associated with lower ages compared to the most prevalent diseases in internal medicine. Tumors, for example, arise at markedly higher ages and are significantly more associated with hospitalization in the internal medicine ward. Pemphigus, which accounts for most admissions to the dermatology ward, have higher incidence among young adults and non-elderly.

In the multivariate analysis, a higher chance of sepsis was found among younger patients, with reduction of 6% in the chance of sepsis with a one-year increase. This was due to sepsis being more prevalent in dermatology patients, who present lower average age at hospital admission. This factor is part of the multivariate analysis for its weight to be hierarchical and properly compensated.

One of the noteworthy aspects of the results was the complete absence of requests for skin secretion or respiratory cultures in the internal medicine ward, with only urine cultures being requested. In dermatology, it is routine to request skin (cutaneous) secretion cultures and antibiogram. This might be a study limitation, as the dermatological examination of the inpatients from the internal medicine ward might have been neglected or the request of cultures of any lesions or skin secretions may not be routine.

The prevalence of SIRS observed in the studied group was significantly higher among patients from the internal medicine ward (47.3%) when compared to the dermatology inpatients (22.8%). The literature available usually refers to lower values for SIRS in inpatients from dermatology wards, but with some differences. Thomas et al. (2010) underscore an incidence rate of SIRS of only 2.4% among 2,765 patients. These authors, however, evaluated patients admitted to a dermatology ward (721) and patients referred...
of SIRS among patients of internal medicine wards, the observed levels are around one third of the patients. These levels are below the findings in our sample, which had values similar to those of ITUs. It is possible that these data are due to the research being performed in a renowned tertiary care hospital to which the most severe cases are referred.14-15

The data confirm that the patients in the dermatology ward (21.7%) are around 10 times more likely to use corticosteroids than the patients in the internal medicine ward (2.2%). The association between sepsis and use of corticosteroids was also statistically positive, with p<0.001. The prevalence of sepsis among patients that had not used corticoids was just 1.8%, while it was 27.3% among those that used the medication. This factor (use of corticoids) was so closely associated with hospitalization in the dermatology ward that its permanence was avoided in the multivariate analysis model.

Many admissions to the dermatology ward are motivated by autoimmune bullous diseases that require, among other drugs, high doses of corticosteroids for prolonged periods of time. Despite immunossupression and consequent higher risk of sepsis (in addition to other important side effects), the use of these drugs dramatically reduced mortality from pemphigus after its introduction in the 50s.12 Ahmed and Moy (1982) investigated the death causes among patients with pemphigus between 1965 and 1980. All of them were using high doses of corticosteroids. The two patients with sepsis and whose main diagnosis was leprosy presented reactional effect, with large areas of skin ulcerations, and used corticosteroids. Other authors have also showed occurrence of sepsis in patients with leprosy.20

Of the nine patients that had sepsis, it was only possible to identify the agents in seven; in two, it was gram-positive, but there was no growth of germs. In our sample, the most frequently found germ in the blood cultures was \textit{S. aureus}, which was found in three out of seven patients. Coagulase-negative \textit{Staphylococcus} was isolated in two patients; and in one, the germ isolated was \textit{Staphylococcus spp}. There was, also, one case of sepsis by yeast (\textit{Candida spp}) in which the patient was under treatment for leprosy reaction. This patient presented loss of a large area of skin barrier and was under systemic corticotherapy.21

In the work by Ahmed and Moy (1982) on death causes among patients with pemphigus, sepsis was found in nine out of 13 patients. The germ most frequently found was \textit{S. aureus}, which was isolated in eight of the 13 patients.23

Studies on the antimicrobial susceptibility profile of \textit{S. aureus} to diverse antibiotics, performed in China between 2003 and 2007, analyzed 984 strains of \textit{S. aureus} isolated from pediatric patients with impetigo. The majority of the strains (94.5%) were resistant to penicillin, followed by erythromycin (86.2%) and clindamycin (69.6%). The incidence of methicillin-resistant \textit{Staphylococcus aureus} (MRSA) associated with the community was 1.1%, and all the strains were susceptible to ciprofloxacin.23

The most frequently used antibiotics in our study were ciprofloxacin and oxacillin, respectively, whose spectrum of coverage includes \textit{S. aureus}, the pathogen most frequently isolated in secretion and blood cultures. \textit{E. coli} was the most isolated bacteria in urine cultures and also presented sensitivity to ciprofloxacin. There are no data available in our country that contraindicate the use of ciprofloxacin or oxacillin as empirical antibiotic therapy for community-acquired infections. However, for patients presenting infections 48 hours after being hospitalized (hospital infections), starting the treatment with...
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ciprofloxacin or oxacillin would not be a good strategy, as the sample evaluated showed a significant chance of resistance to both types of antibiotics, which was also observed by Garner et al. (1988). There was antibiotic change after 36.8% of the requested cultures, emphasizing the need for research for more efficient coverage.

There are several studies in the literature reporting sepsis issues and their consequences in ITUs and other non-dermatological hospital areas. However, there are few studies on the subject in dermatology wards. A study including 1,826 hospital patients reported the highest incidence of nosocomial infections in dermatology wards (19.8%), compared with 13.1% inpatients of internal medicine wards.

In the univariate analysis of this study, a high prevalence of sepsis was found among the inpatients of the dermatology ward (7.6%), compared with that of the inpatients of the internal medicine ward. This higher prevalence, however, was not statistically significant (p=0.10). After the multivariate analysis, with the analysis of the main components and of hierarchical clustering, it was found that hospitalization in dermatology wards is related to a significant increase in the occurrence (OR 14.89) of sepsis. This was, possibly, due to factors previously assumed as premises, that is, large areas of skin loss, with impairment of the skin barrier and of the skin immune function, and the use of corticosteroids.

CONCLUSION
This study observed a higher prevalence of sepsis in patients hospitalized in the dermatology ward compared with those in the internal medicine ward. It also found that bullous diseases were the dermatological conditions most frequently associated with the development of sepsis. It did not find an association between sepsis and diabetes mellitus and cancer.

It is clear that there is a need for the close monitoring of patients hospitalized in dermatology wards, especially of those using corticosteroids and presenting extensive loss of the skin barrier, since this group is particularly vulnerable to the occurrence of sepsis. Early identification and prompt establishment of an appropriate course of action may be the differential response in the treatment of this severe complication.
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