There is no association between weekend admissions and delays in antibiotic administration for patients admitted to the emergency department with suspicion of sepsis

A retrospective cohort study

Bruno V. B. Fahel, MSb,∗, Marina Manciola, MSb, Gabriel Lima, MSc, Manoel H. Barbosa, MSc, Chuva Starteri, MSc, João Gabriel Rosa Ramos, MD, PHDd, Juliana R. Caldas, MD, PHDab,d, Rogério da Hora Passos, MD, PHDa

Abstract

Admission to the emergency department (ED) on weekends has been associated with an increase in mortality and poor outcomes, but the associated findings are not consistent. It has been hypothesized that this association may be due to lower adherence to standards of care.

This study was conducted to evaluate whether weekend admissions to the ED increases the time to antibiotic administration in septic patients.

A retrospective cohort study of adult patients who were included in the sepsis protocol at a tertiary ED between January 2015 and December 2107 was performed. The sepsis protocol was activated for all patients with suspected severe infection.

A total of 831 patients with a mean age of 59±21 years were evaluated, of whom 217 (26.1%) were admitted on weekends. In addition, 391 (47.1%) patients were male, and 84 (10.1%) died in the hospital. Overall, the mean sequential organ failure assessment score was 2±1.9, and the mean Charlson comorbidity index was 3.7±3. The time to antibiotic administration was similar between patients admitted on weekends (36.29±50 minutes CI 95%) and patients admitted on weekdays (44.44±69 minutes CI 95%), P = 0.06; U = 60174.0. Additionally, mortality was similar in both groups of patients, with a 10.3% mortality rate on weekdays and a 9.8% mortality rate on weekends, P = 821.

In this cohort of patients with suspicion of sepsis in the ED, admission on weekends was not associated with increased delays in antibiotic therapy or higher mortality rates.

Abbreviations: CGI = Charlson comorbidity index, ED = emergency department, ICU = intensive care unit, SOFA = sequential organ failure assessment.

Keywords: prognostic, sepsis, weekend effect

1. Introduction

It is of great scientific interest to determine the prognostic factors for patients admitted to the emergency department, thus enabling the identification of death predictors and the development of measures to improve outcomes.[1] It has been hypothesized that weekday admission is associated with an increased risk of death. This association has been named the weekend effect and is described as an increase in mortality for patients admitted to the ED on weekends.[1] Its possible causes include reduced staff, less-qualified staff, and the admission of patients with more severe illness on weekends.[1] Although some studies have identified the weekend effect in their facilities,[1–6] others have obtained negative results,[7–10] which makes the validation of weekday admission as a prognostic factor uncertain. In this context of disparity, there is no consensus about the appropriate methodological approach among studies regarding the weekend effect. The existing literature is extremely heterogeneous regarding the analysis of medical care quality.

Sepsis is one of the greatest challenges in the emergency context. Mortality rates are high, and prompt diagnosis and measures are crucial for treatment.[11] There is evidence that early
Empiric antibiotic therapy is associated with lower mortality rates. Therefore, sepsis treatment can be an important measure for evaluating hospital staff efficiency.

In the present study, we aimed to assess the association between weekend admissions and an increased delay in antibiotic administration in patients with suspicion of sepsis at the emergency department. Additionally, we aimed to evaluate whether there is an increase in mortality among patients admitted on weekends.

2. Methods

2.1. Study design

A retrospective cohort was implemented to evaluate the data from patients who underwent the institutional sepsis protocol at the emergency department of Hospital São Rafael.

2.2. Setting

Hospital São Rafael is a private, tertiary hospital in Salvador, Brazil, with 352 beds, including 22 beds in the emergency department and 69 beds in the intensive care unit (ICU). The hospital serves patients with health insurance and private patients. In 2008, a sepsis protocol was created for this institution, aiming to recognize possible septic patients and standardize the therapy and measures for the care of these individuals. When activated, the emergency department, ICU, laboratory, and pharmacy medical staff begin the following measures: arterial blood analysis within 15 minutes, collection of material for cultures as well as antibiotic therapy within 1 hour, and decisions regarding ICU admission are carried out. Data were collected from patients admitted to the emergency department between January 2015 and December 2017.

2.3. Participants

The inclusion criteria were patients admitted to the emergency department who underwent the sepsis protocol. This protocol was initiated for every patient with suspected infection and a calculated quick sequential organ failure assessment (qSOFA) score ≥2. A combination of interventions as already mentioned in the setting subsection of this article was then initiated. The exclusion criteria were patients under the age of 18.

2.4. Variables

The exposition variable in this study was weekend admissions (Saturday at midnight to Sunday at 11:59 pm), a qualitative binary variable of “yes” or “no”.

The outcome variables included qualitative delay of antibiotic administration (a binary variable of “yes” or “no”); quantitative delay of antibiotic administration (measured in minutes) – for both of the aforementioned variables, delay was defined as a time from activation of the sepsis protocol to antibiotic administration greater than 60 minutes; and in-hospital mortality (absolute and relative).

| Table 1 | Association between clinical features and weekend admission. |
|---------|------------------------------------------------------------|
| Variable | Weekday (n=614) | Weekend (n=217) | P-value |
| Age (yr), median | 61.0 (41.0–76.0) | 64.0 (42.5–79.5) | .262 |
| Sex | | | .444 |
| Female | 324 (52.7%) | 116 (53.4%) | | |
| Male | 290 (47.3%) | 101 (46.6%) | | |
| Mortality | 63 (10.3) | 21 (9.8) | .821 |
| Charlson Comorbidity index | 3 (1–6) | 4 (1–6) | .315 |
| UCI admission | 235 (38.5%) | 88 (40.9%) | .523 |
| SOFA | 2 (1–3) | 2 (1–3) | .707 |
| Primary site of infection | | | |
| Abdominal | 117 (19.1%) | 52 (24.1%) | .061 |
| SSTIs | 48 (7.8%) | 10 (4.6%) | .055 |
| Nervous system | 8 (1.3%) | 4 (1.9%) | .284 |
| Urinary | 142 (23.1%) | 47 (21.8%) | .329 |
| Pulmonary | 192 (31.3%) | 72 (33.3%) | .301 |
| Not established | 92 (15.0%) | 25 (11.6%) | .103 |
| Others | 15 (2.4%) | 6 (2.8%) | .907 |
| Antibiotic delay (>1h) | 101 (16.4%) | 33 (15.4%) | .725 |
| Antibiotic delay (min) (median IQR) | 28 (10.0–48.25) | 25 (2.75–45.0) | .066 |
| Lactate delay (min) (median IQR) | 28 (21.0–38.0) | 27 (21.0–35.0) | .303 |
| Use of vasoactive drug | 27 (4.4%) | 3 (1.4%) | .041 |
| Medium arterial pressure, median (IQR) | 93 (78.3–105.3) | 93 (80.15–106.45) | .620 |
| Glasgow coma Scale | 15 (15–15) | 15 (15–15) | .165 |
| Shift turnover | 82 (13.4%) | 33 (15.2%) | .497 |
| Night shift | 184 (30.0%) | 71 (32.7%) | .450 |
| Laboratory values on admission, median IQR | | | |
| PaO2/FiO2 | 403.5 (341.0–500.0) | 391 (331.5–478.0) | .124 |
| Bilirubin | 0.5 (0.1–1.1) | 0.5 (0.1–1.2) | .857 |
| Creatinine | 0.9 (0.6–1.2) | 0.9 (0.7–1.25) | .275 |
| Platelets | 224.5 (159.0–308.0) | 214 (165.0–296.5) | .790 |

Values represent n (%), mean and median (IQR).

SOFA = sequential organ failure assessment, SSTIs = skin and soft tissue infections.
The covariates included age (in years), sex (male/female), Charlson comorbidity index (CCI) on admission, sequential organ failure assessment (SOFA) score on admission, primary site of infection (abdomen, skin and soft tissue, nervous system, urinary tract, lung, not established, and other), lactate measurement delay (time in minutes from protocol activation to serum lactate measurement), use of vasoactive drugs, medium arterial pressure, Glasgow Coma Scale, shift turnover admission (6 am–7:59 am and 6 pm–7:59 pm), night shift admission (7 pm–7 am) and laboratory results on admission (PaO2/FiO2, bilirubin, creatinine, and platelets).

2.5. Data sources/measurements

All data for all variables were obtained from electronic medical records. For the CCI, MedCalc Statistical Software version 16.4.3 was used.

2.6. Data availability

The data that support the findings of this study are available from the corresponding author, B.V.B.F, upon reasonable request.

2.7. Statistical methods

Statistical analysis was conducted using “IBM SPSS Statistics 21.0”. We tested for associations between weekend admissions and the time to antibiotic administration by applying 2 statistical methods: a Chi-squared test, using the categorical variables “weekend admission” and “delay to antibiotic administration”; and a Mann–Whitney U test, in which the categorical variable “weekend admission” and the continuous variable “time to antibiotic administration” were used. Additionally, the correlation between weekend admissions and time to serum lactate measurement was tested using the Mann–Whitney U test.

To assess the associations between the other variables and weekend admissions, Chi-squared tests and Mann–Whitney U tests were conducted for categorical and noncategorical variables, respectively (Table 2).

Finally, 2 multivariable models were used to identify independent predictors for mortality and antibiotic delay. These models included age, sex, weekend admissions, and severity scores. Logistic regression was conducted. The choice of these variables was based on a theoretical rationale. Crude and adjusted odds ratio (OR) values were calculated. P-values <.05 were considered significant.

2.8. BIAS analysis

We conducted, through theoretical rationale, the variables that could be possible biases of our analysis. In this way, we constructed 2 logistic regression models that included the following independent variables: weekend admissions, sex, age, CCI, and SOFA.

2.9. Ethical considerations

This study was approved by Hospital São Rafael Research Ethics Committee number 2.200.054 on August 3, 2017. (CAAE number 71553417.2.0000.0048). Research Ethics Committee number 2.200.054 on August 3, 2017.

3. Results

In the study period, 850 patients were eligible for activation of the sepsis protocol. Among them, 19 were excluded because they fulfilled the exclusion criteria (2.47%). Thus, data from 831 patients were evaluated. A total of 614 patients were admitted on weekdays (73.9%), and 217 were admitted on weekends (26.1%). All patients were followed until discharge.

Among these patients, 391 (47.1%) were male, and the mean age of the sample was 59 ± 21 (Table 1). The overall hospital mortality rate was 10.1% (84 deaths). Figures 1 and 2.

There was no significant difference between the number of delayed antibiotic administrations (more than 60 minutes) on weekdays (16.4%) and weekends (15.4%) (P = .725). Additionally, there was no statistically significant difference between the mean time, in minutes, of antibiotic administration on weekends (36.29 ± 50 minutes) and weekdays (44.44 ± 69 minutes), P = .06; U = 60174.0. There was no association between weekend admissions and delay in lactate, P = .303, U = 62984. In addition, no difference was observed between the mortality of patients...
admitted on weekends (9.8%) and weekdays (10.3%) [OR (95% CI) = 0.95 (0.56–1.58)].

Among the other variables used in our univariate model, only “use of vasoactive drugs” had statistical significance (P = .04), but with a low rate of association (Phi: -0.071 Cramer’s V: 0.071).

A logistic regression model analysis showed age [OR (95% CI) = 1.020 (1.002–1.039)], the SOFA score [OR (95% CI) = 1.336 (1.180–1.513)] and the CCI [OR (95% CI) = 1.202 (1.076–1.344)] as independent mortality predictors (Table 2). There was no impact of patient sex or weekend admission on mortality.

A second logistic regression model analysis (Table 3) showed that none of the variables chosen based on our theoretical rationale were independent predictors of antibiotic delay.

4. Discussion

In this cohort of patients with a suspicion of sepsis in the ER, admission on weekends was not associated with higher delays in antibiotic therapy or higher mortality. These findings suggest that this sepsis protocol helps to ensure consistency of care and therefore represents a potentially improved model for septic patients.

This is the first Brazilian study to assess the weekend effect in septic patients. In the present study, there was no significant difference in the time to administration of antibiotics between patients admitted to the hospital on weekdays and those admitted on weekends. Furthermore, there was no significant difference in mortality. In lieu of these results, it is important to highlight that the hospital where this study took place is an infection control reference hospital, with a well-established protocol to address every suspected case of infectious disease.

Results of most of the existing literature on this theme are inconsistent with our results, reporting the existence of the weekend effect[1–6,13] either in septic patients[3,13] or patients with other diseases (e.g., congestive heart failure, stroke, peptic ulcer hemorrhage, and cranioencephalic trauma).[1,2,4,5] Nevertheless, all these previous studies were conducted with a population from multicentric studies, therefore making it impossible to analyze standardized protocols that guarantee quality of care. With that in mind, multicentric studies regarding this theme must be criticized, as their results include heterogeneous groups from hospitals with differences in staff, diagnostic methods, and therapeutic resources. One of these multicentric studies[5] reported that most of the ICUs in Finland did not have 24 hours of coverage with intensive care specialists on weekends.

On the other hand, the studies that showed consistent results regarding the absence of the weekend effect[7–10] were conducted in unicentric populations. Three of them[7–9] which had a significantly larger population than ours, included patients regardless of disease, and only 1 study[10] had a similar population and included patients with a specific condition (cranioencephalic trauma). These studies had a trained (or in training) team of intensive care physicians 24 hours a day, every day, as did our study. In one of the studies,[10] the hospital also had an institutional protocol for the specific disease assessed. Therefore, we suggest that the use of specific protocols and trained teams 24 hours a day, 7 days a week, produces similar results in terms of mortality outcomes.

Notably, most of the studies about this theme analyzed mortality as the main outcome. Our study goes beyond this outcome by using the antibiotic administration time as the main outcome for the weekend effect in septic patients, as it has already been established in the literature as the main factor for changing the prognosis in septic patients,[11] especially when administered in the first hour.[12,16]

Additionally, delays in procedures, such as antibiotic therapy, have already been reported by several studies with other populations[17–19] as the main factor related to the weekend effect, despite other possible theories, such as the reduced or limited experience of healthcare teams on weekends.

Therefore, we concluded that the absence of the weekend effect in our study could be explained by our effective protocol, which endorses antibiotic administration within 1 hour. A similar conclusion was reached by Seymour et al.[16] who showed better outcomes among septic patients who received antibiotics within the first hour. Nevertheless, due the high mortality of sepsis around the world, especially in developing countries, the constant evaluation of the results of the protocol is needed and may improve prognosis in this group of patients.

Table 3

| Variable                          | B     | OR    | IC 95%   | P-value |
|----------------------------------|-------|-------|----------|---------|
| Weekend admission                | -0.069| 0.933 | 0.607    | 1.434   | .753   |
| Sex                              | 0.145 | 1.156 | 0.793    | 1.684   | .451   |
| Age                              | -0.003| 0.997 | 0.985    | 1.010   | .687   |
| Charlson Comorbidity Index       | -0.020| 0.980 | 0.890    | 1.076   | .674   |
| SOFA                             | 0.000 | 1.000 | 0.901    | 1.110   | .999   |
| Constant                         | -1.470|       |          |         |        |
It is important to emphasize that in the period this study was conducted, the Sepsis-3[11] diagnosis criteria had not been established for patients whose hospital stay occurred in 2015. Most mortality rates, absolute and relative, were higher in that year. This evidence supports the importance of continuously developing research that amplifies our knowledge about sepsis syndrome and allows improvements in management protocols.

The limitation of this study is the small sample size, as other similar studies[2–5] had a larger population. In addition, in this study, we only assessed some of the possible poor outcomes, not considering other possible markers that may denote worse outcomes, such as length of stay in the ICU. Therefore, we did not consider all possible signs of the weekend effect.

Author contributions

Conceptualization: Bruno Vilas Boas Fahel, Rogério da Hora Passos.

Data curation: Bruno Vilas Boas Fahel, Marina Santana Manciola, Gabriel Lima Silva, Manoel Henrique Fonseca Barbosa, Chhua Castro Starteri, Juliana Ribeiro Caldas, João Gabriel Rosa Ramos, Rogério da Hora Passos.

Formal analysis: Bruno Vilas Boas Fahel, Marina Santana Manciola, Gabriel Lima Silva, Manoel Henrique Fonseca Barbosa, Chhua Castro Starteri, Juliana Ribeiro Caldas, João Gabriel Rosa Ramos, Rogério da Hora Passos.

Funding acquisition: Juliana Ribeiro Caldas, Rogério da Hora Passos.

Investigation: Bruno Vilas Boas Fahel, Marina Santana Manciola, Gabriel Lima Silva, Manoel Henrique Fonseca Barbosa, Chhua Castro Starteri, Juliana Ribeiro Caldas, João Gabriel Rosa Ramos, Rogério da Hora Passos.

Methodology: Bruno Vilas Boas Fahel, Marina Santana Manciola, Gabriel Lima Silva, Manoel Henrique Fonseca Barbosa, Chhua Castro Starteri, Juliana Ribeiro Caldas, João Gabriel Rosa Ramos, Rogério da Hora Passos.

Project administration: Bruno Vilas Boas Fahel, Marina Santana Manciola, Gabriel Lima Silva, Manoel Henrique Fonseca Barbosa, Chhua Castro Starteri, Juliana Ribeiro Caldas, João Gabriel Rosa Ramos, Rogério da Hora Passos.

Resources: Bruno Vilas Boas Fahel, Marina Santana Manciola, Gabriel Lima Silva, Manoel Henrique Fonseca Barbosa, Chhua Castro Starteri, Juliana Ribeiro Caldas, João Gabriel Rosa Ramos, Rogério da Hora Passos.

Software: Bruno Vilas Boas Fahel, Marina Santana Manciola, Gabriel Lima Silva, Manoel Henrique Fonseca Barbosa, Chhua Castro Starteri, Juliana Ribeiro Caldas, João Gabriel Rosa Ramos, Rogério da Hora Passos.

Supervision: Juliana Ribeiro Caldas, João Gabriel Rosa Ramos, Rogério da Hora Passos.

Validation: Bruno Vilas Boas Fahel, Marina Santana Manciola, Gabriel Lima Silva, Manoel Henrique Fonseca Barbosa, Chhua Castro Starteri, Juliana Ribeiro Caldas, João Gabriel Rosa Ramos, Rogério da Hora Passos.

Visualization: Bruno Vilas Boas Fahel, Marina Santana Manciola, Gabriel Lima Silva, Manoel Henrique Fonseca Barbosa, Chhua Castro Starteri, Juliana Ribeiro Caldas, João Gabriel Rosa Ramos, Rogério da Hora Passos.

Writing – original draft: Bruno Vilas Boas Fahel, Marina Santana Manciola, Gabriel Lima Silva, Manoel Henrique Fonseca Barbosa, Chhua Castro Starteri, Juliana Ribeiro Caldas, João Gabriel Rosa Ramos, Rogério da Hora Passos.

Writing – review & editing: Bruno Vilas Boas Fahel, Marina Santana Manciola, Gabriel Lima Silva, Manoel Henrique Fonseca Barbosa, Chhua Castro Starteri, Juliana Ribeiro Caldas, João Gabriel Rosa Ramos, Rogério da Hora Passos.

References

[1] Zajic P, Bauer P, Rhodes A, et al. Weekends affect mortality risk and chance of discharge in critically ill patients: a retrospective study in the Austrian registry for intensive care. Crit Care 2017;21:223–30.
[2] Pauls LA, Johnson-Paben R, McGready J, et al. The weekend effect in hospitalized patients: a meta-analysis. J Hosp Med 2017;12:760–6.
[3] Shih YN, Chen YT, Shih CJ, et al. Association of weekend effect with early mortality in severe sepsis patients over time. J Infect 2017;74:343–51.
[4] Barnett MJ, Kaboli PJ, Sinro CA, et al. Day of the week of intensive care admission and patient outcomes: a multisite regional evaluation. Med Care 2002;40:530–9.
[5] Uusaro A, Kari A, Ruokonen E. The effects of ICU admission and discharge times on mortality in Finland. Intensive Care Med 2003; 29:2144–8.
[6] Blonagiri D, Plicher DV, Bailey MJ. Increased mortality associated with after-hours and weekend admission to the intensive care unit: a retrospective analysis. Med J Aust 2011;194:287–92.
[7] Ensinger SA, Morales JJ, Peters SC, et al. The hospital mortality of patients admitted to the ICU on weekends. Chest 2004;126:1292–8.
[8] Arabi Y, Alshimemeri A, Taher S. Weekend and weeknight admissions have the same outcome of weekday admissions to an intensive care unit with onsite intensivist coverage. Crit Care Med 2006;34:605–11.
[9] Laupland KB, Shapouri R, Kirkpatrick AW, et al. Hospital mortality among adults admitted to and discharged from intensive care on weekends and evenings. J Crit Care 2008;23:317–24.
[10] Lee KK, Ng I, Ang BT. Outcome of severe head injured patients admitted to intensive care during weekday shifts compared to nights and weekends. Ann Acad Med Singap 2008;37:390–6.
[11] Singer M, Deutschman CS, Seymour C, et al. The third international consensus definitions for sepsis and septic shock (sepsis-3). JAMA 2016;315:801–10.
[12] Ferrer R, Martin-Lloeches I, Phillips G, et al. Empircic antibiotic treatment reduces mortality in severe sepsis and septic shock from the first hour: results from a guideline-based performance improvement program. Crit Care Med 2014;42:1749–55.
[13] Charlson M, Szatrowski TP, Peterson J, et al. Validation of a combined comorbidity index. J Clin Epidemiol 1994;47:1245–51.
[14] Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974;2:81–4.
[15] Powell ES, Khare RK, Courtimey DM, et al. The weekend effect for patients with sepsis presenting to the emergency department. J Emerg Med 2013;45:641–8.
[16] Seymour CW, Gheesel F, Prescott HC, et al. Time to treatment and mortality during mandated emergency care for sepsis. N Engl J Med 2017;376:2235–44.
[17] Hoh BL, Chi YY, Waters MF, et al. The weekend effect compared with weekday stroke admission on thrombolytic use, in-hospital mortality, discharge disposition, hospital charges, and length of stay in the nationwide inpatient sample database, 2002 to 2007. Stroke 2010;41:2323–8.
[18] Myers RP, Kaplan GG, Shaheen AAM. The effect of weekend versus weekday admission on outcomes of esophageal variceal hemorrhage. Can J Gastroenterol 2009;23:495–501.
[19] MedCalc Statistical Software version 16.4.3 (MedCalc Software bv, Ostend, Belgium; https://www.medcalc.org; 2016). [Accessed 04 December 2018].