# COMPARING THE TREATMENT RESULTS OF SEPSIS IN THE COMMUNITY CAUSED BY *STAPHYLOCOCCUS AUREUS* AND *ESCHERICHIA COLI* AT THE NATIONAL HOSPITAL FOR TROPICAL DISEASES

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*Objectives:* To evaluate and compare the treatment results of sepsis in the community caused by Staphylococcus aureus and Escherichia coli at the National Hospital of Tropical Diseases.

*Subjects and method:* Cross-sectional study was applied in this study and it was conducted on a total of 177 patients having treatment at the National Hospital of Tropical Diseases during period from July, 2021 to June, 2024.

*Results and conclusions:* The study results show 106 (59.89%) patients infected by *E. coli* bacteremia and 71 (40.11%) patients infected by *S. aureus* bacteremia. The mean age of the study group was 58.41 ± 17.09 years old (from 19 to 93 years old). The mean age of the group of patients with bacteremia caused by *E. coli* and *S. aureus* was 62.04 ± 15.82 years old, 53.0 ± 17.60 years old, respectively. The proportion of sepsis caused by *S. aureus* was 18.8% higher than that caused by *E. coli* in male patients, specifically accounted for *S. aureus* (66.2%) and *E. coli* accounted for 43.4%. *S. aureus* bacteremia is often caused by skin - soft tissue, musculoskeletal infections. *E. coli* bacteremia are often caused by digestive and urinary tract infections. The mortality rate due to *S. aureus* bacteremia is 36.6%, nearly 3 times higher than the mortality rate due to *E. coli* bacteremia. The treatment time of the S. aureus bacteremia group is longer than that of the *E. coli* bacteremia group.

**Keywords:** Sepsis, *S. aureus* bacteremia, *E. coli* bacteremia.

## INTRODUCTION

In 2016, the 3rd International Consensus Conference agreed and defined sepsis (SEPSIS-3) as follows: "Sepsis is a life-threatening organ dysfunction resulting from a dysregulation of the host response to infection"[1] . In 2017, an estimated of 11 million sepsis cases caused of deaths occurred worldwide, with the highest burden in sub-Saharan Africa, Oceania, South Asia, East Asia, and Southeast Asia[2]. *Staphylococcus aureus* and *Escherichia coli* are the two most common bacterial pathogens causing sepsis. *S. aureus* bacteremia and *E. coli* bacteremia are caused by different bacterial pathogens, but many symptoms overlap and develop together according to the pathophysiological mechanism of sepsis, so approaching patients with sepsis and finding the causes which face many challenges. In Vietnam, there are only separated studies on sepsis caused by *S. aureus* or *E. coli*, there is no specific study comparing the treatment results of sepsis between these two causes. Therefore, we conducted this study to evaluate and compare the treatment results of sepsis caused by *S. aureus* and sepsis caused by *E. coli* at the National Hospital of Tropical Diseases from 2021 - 2024.

## RESEARCH OBJECTS AND METHOD

### Research object

*Selection criteria:* Patients ≥ 18 years old who satisfy both of the following criteria:

• Have ≥ 2/4 criteria of Systemic Inflammatory Response Syndrome* or have two or more clinical symptoms suggestive of sepsis (fever, primary focus of infection, hepatomegaly, splenomegaly).

• Blood culture results show *S. aureus* or *E. coli* growth within the first 48 hours of admission to the National Hospital of Tropical Diseases or another hospital within the first 48 hours.

*Systemic inflammatory response syndrome includes:

- Temperature > 38°C or < 36°C.

- Heart rate > 90 cycles/minute.

- Respiratory rate > 20 times/minute or $PaCO_2$ < 32 mmHg (spontaneous breathing).

- White blood cells > 12000/mm$^3$ or < 4000/mm$^3$, or > 10% immature leukocytes.

*Exclusion criteria:* Pregnant women. HIV/AIDS patients. Patients with a history of chronic liver or kidney failure.

- The patient's blood culture tested positive for two different pathogens after 48 hours of hospitalization.

- Location and timing of the study: The study was conducted at the National Hospital of Tropical Diseases located in Ha Noi Viet Nam, collecting patients treated from July 1, 2021 - June 30, 2024.

**Research methods:** Cross - sectional study.

**Sample size and sampling technique:** Convenience sampling. All patients meeting the criteria were selected for the study.

**Techniques used in the study:** The tests used in the study were all routine tests, according to the Ministry of Health's guidelines for diagnosis and treatment of sepsis. Blood culture bottles were incubated using an automated blood culture system (BactecFX, USA and BacT/Alert Virtuo, Bio Mérieux, France). Bottles that were reported positive by the machine which were Gram stained, the specimen after culture is automatically identified by the Maldi-tof MS system (Bruker, Germany) and Vitek 2 COMPACT (BioMérieux, France). Antibiograms were performed using the Kirby Bauer antibiotic diffusion disc method and/or automated antibiograms on the Vitek 2 COMPACT system, with results interpreted according to the CLSI (Clinical and Laboratory Standards Institute) guidelines, version 2017, with annual updates. (CLSI).

**Data analysis and processing:** Research data were analyzed and processed using medical statistics using SPSS software version 20.0.

**Research ethics:** Data collection is approved by the National Hospital of Tropical Diseases. Patient information is kept confidential and is used for research purposes only. Research information is guaranteed to be reliable, accurate and never published before.

## RESULTS

### General characteristics of the research group

**Table 1.** General characteristics of the research group

| Age group/gender | | *S. aureus* bacteremia (%, n) | *E. coli* bacteremia (%, n) | After 6 months (n = 166) |
|---|---|---|---|---|
| **Sex** | Male | 66.2 (47) | 43.4 (46) | **0.003** |
| | Female | 33.8 (24) | 56.6 (60) | |
| **Age group (years)** | 18 - 35 | 19.7 (14) | 4.7 (5) | **0.005** |
| | 36 - 45 | 11 (15.5) | 12.3 (13) | |
| | 46 - 55 | 19.7 (14) | 15 (14.2) | |
| | 56 | - 65 | 19.7 (14) | |
| | | 25.4 (18) | 45.3 (48) | |
| **Age ± SD** | | 53.0 ± 17.60 | 62.04 ± 15.82 | **0.000** |

**Comments:** During the 3-years of study period, 177 patients met the selection criteria, including 106 (59.89%) patients with *E. coli* bacteremia, 71 (40.11%) patients with *S. aureus* bacteremia. The mean age of the study group was 58.41 ± 17.09 years old (from 19 to 93 years old). The mean age of the patients with *E. coli* and *S. aureus* bacteremia was 62.04 ± 15.82 years old, 53.0 ± 17.60 years old, respectively. The mean age of *E. coli* bacteremia was higher than the mean age of *S. aureus* bacteremia (p < 0.001). The proportion of patients over 65 years old with *E. coli* bacteremia was higher than that of *S. aureus* bacteremia (p < 0.001). The proportion of patients over 65 years old with *E. coli* bacteremia was higher than that of *S. aureus* bacteremia (p < 0.001). *E.coli* was nearly twice as high as that of *S. aureus* in the same age group (p = 0.005). The rate of *S. aureus* in men was higher than that of *E. coli* (p = 0.003). The rate of *S. aureus* in men was twice as high as that of S. aureus in women. The rate of *E. coli* in men was not different between men and women.

**Table 2.** Clinical manifestations upon admission to hospital

| Presenting clinical syndromes | S. aureus bacteremia (%, n) | E. coli bacteremia (%, n) | p |
|---|---|---|---|
| Asymptomatic | 5.6 (4) | 17 (18) | **0.025** |
| Skin and soft tissue | 64.8 (46) | 1.9 (2) | **0.000** |
| Digestive system | 4.2 (3) | 30.2 (32) | **0.000** |
| Urinary system | 1.4 (1) | 23.6 (25) | **0.000** |
| Respiratory system | 22.5 (16) | 23.6 (25) | **0.871** |
| Nervous system | 1.4 (1) | 3.8 (4) | **0.352** |

**Comments:** Clinical manifestations upon admission to hospital of the *S. aureus* bacteremia patients group were mainly in the skin - soft tissue, musculoskeletal system (64.8%). Clinical manifestations upon admission of the *E. coli* bacteremia patients group were mainly in the digestive system (30.2%), urinary system (23.6%), and respiratory system (23.6%). In particular, the proportion of patients with no initial symptoms when hospitalized caused by *E. coli* is than *S. aureus* bacteremia patients group (p = 0.025).

**Table 3.** Patient history

| Prehistoric | S. aureus bacteremia (%, n) | E. coli bacteremia (%, n) | p |
|---|---|---|---|
| Having underlying conditions | 57.7 (41) | 73.6 (78) | 0.028 |
| Hypertension | 18.3 (13) | 26.4 (28) | 0.21 |
| Diabetes | 21.1 (15) | 29.2 (31) | 0.227 |
| Cirrhosis, viral hepatitis | 12.7 (9) | 20.8 (22) | 0.166 |
| Short-term corticosteroid using within the past 3 months | 9.9 (7) | 7.5 (8) | 0.588 |
| Alcoholism | 12.7 | 13.2 | 0.918 |
| Gout | 9.9 (7) | 1.9 (2) | 0.031 |
| Cancer | 1.4 (1) | 3.8 (4) | 0.649 |
| Other | 21.1 (15) | 20.8 (22) | 0.952 |

**Comments:** The rate of underlying diseases in the *E. coli* bacteremia was 73.5%, higher than that in the *S. aureus* bacteremia (57.7%), a statistically significant difference with p = 0.028. The *E. coli* bacteremia

patient had a higher rate of underlying diseases such as hypertension (26.4%), diabetes (29.2%), cirrhosis, and viral hepatitis (20.8%) than the *S. aureus* bacteremia.

**Table 4.** Percentage of patients with septic shock, respiratory failure, impaired consciousness upon admission and procedural intervention during treatment by cause

| Signs/Operation | *S. aureus* bacteremia (%, n) | *E. coli* bacteremia (%, n) | p |
|---|---|---|---|
| Septic shock | 15.5 (11) | 22.6 (24) | 0.242 |
| Respiratory failure | 38 (27) | 36 (34) | 0.58 |
| Disorder of consciousness | 19.7 (14) | 15.1 (16) | 0.422 |
| Sepsis tube placement | 38 (27) | 17.9 (19) | 0.003 |
| Blood filtration | 25.4 (18) | 8.5 (9) | 0.002 |

**Comments:** The rate of sepsis patients with septic shock when hospitalized due to *E. coli* was higher than that of *S. aureus*. The rate of patients with respiratory failure and impaired consciousness when hospitalized due to *S. aureus* bacteremia was higher than that of *E. coli* bacteremia. However, the difference was not statistically significant. During treatment, the rate of patients with *S. aureus* bacteremia requiring septic intubation (38%) was higher than that of patients with *E. coli* bacteremia (17.9%), the difference was statistically significant with $p = 0.003$. The rate of patients requiring dialysis during treatment was also higher in the *S. aureus* bacteremia (25.4%) than in the *E. coli* bacteremia (8.5%) ($p = 0.002$).

**Table 5.** Comparison of treatment results between the two causes

| Result | *S. aureus* bacteremia (%, n) | *E. coli* bacteremia (%, n) | p |
|---|---|---|---|
| Get well soon | 63.4 (45) | 84 (89) | 0.002 |
| Death | 36.6 (26) | 16 (17) | |
| Length of hospital stay (days, median, IQR) | 19.18 (8 - 30) | 12.19 (7.75 - 15.25) | 0.000 |
| Length of hospital stay in mortality group (days) | 16.23 (4 - 30) | 6.94 (1 - 10.5) | 0.032 |

**Comments:** The mortality rate of sepsis caused by *S. aureus* (36.6%) was higher than that of *E. coli* (16%), $p = 0.002$. The average timing of hospital stay caused by *S. aureus* bacteremia patients group (19.18 (8 - 30) days) was higher than that of *E. coli* bacteremia patients group (12.19 (7.75 - 15.25) days), ($p < 0.001$). The length of hospital stays of death group caused by *S. aureus* sepsis (16.23 (4 - 30) days) was higher than that of the group that died due to *E. coli* sepsis (6.94 (1 - 10.5) days), ($p = 0.032$).

## DISCUSSIONS

During the 3-year study period, 177 patients met the selection criteria, including 106 (59.89%) patients with *E. coli* bacteremia and 71 (40.11%) patients with *S. aureus* bacteremia. The mean age of the study group was 58.41 ± 17.09 years old (from 19 to 93 years old). The mean age of the patients with *E. coli* and *S. aureus* bacteremia was 62.04 ± 15.82 years old and 53.0 ± 17.60 years old, respectively. At the same time, our study also showed that the rate of patients over 65 years old with *E. coli* bacteremia was 17.09 years old and 17.09 years old, respectively. *E. coli* bacteremia was nearly twice as high as that of *S. aureus* bacteremia in the same age group ($p = 0.005$), indicating that *E. coli* bacteremia often occurs in older people,

which also explains why the mean age of *E. coli* bacteremia was higher than that of *S. aureus* bacteremia. In our results, the mean age of the study groups was lower than that of Ranjani Somayaji et al. in Thailand[3]. However, the common point is that the mean age of *E. coli* bacteremia was higher than the mean age of *S. aureus* bacteremia (p < 0.001).

*S. aureus* bacteremia (66.2%) than in the group with *E. coli* bacteremia (43.4%) (p = 0.003). The proportion of males with *S. aureus* bacteremia was twice as high as that of females with *S. aureus* bacteremia. Our results are similar to those of Ranjani Somayaji[3] and another study on bacteremia in Central Norway by Arne Mehl et al.[4] Sarah A Alhunaif[5].

In our study, there were differences in clinical manifestations at organs upon admission between the study groups. The proportion of patients with skin-soft tissue and musculoskeletal infections upon admission was highest in the group of patients with S. aureus bacteremia (64.8%), followed by respiratory manifestations (22.5%). For the group of patients with *E. coli* bacteremia, clinical manifestations upon admission were mainly gastrointestinal infections (30.2%) (p < 0.001)), urinary tract (23.6%) (p < 0.001), and respiratory tract (23.6%). Although the proportion of infection manifestations at organs upon admission varied depending on the study, many studies have shown that skin-soft tissue and musculoskeletal infections are the most common causes of *S. aureus* bacteremia[6], gastrointestinal and urinary tract infections are common sources of *E. coli* bacteremia[7,8]. This result is similar to our study results. This result is consistent with the normal residence location of bacteria.

The rate of underlying conditions in the *E. coli* bacteremia patients group was 73.5%, higher than that in the *S. aureus* bacteremia patients group (57.7%), a statistically significant difference with p = 0.028. The *E. coli* bacteremia patients group had a higher rate of underlying conditions such as hypertension (26.4%), diabetes (29.2%), cirrhosis, and viral hepatitis (20.8%) than the *S. aureus* bacteremia group, however, the difference was not

statistically significant (p > 0.05), similar to the results of the research group conducted by Ranjani Somayaji[3].

Our study showed that the rate of patients with septic shock when hospitalized due to *E. coli* bacteremia was higher than that of *S. aureus* bacteremia. Studies have shown that gram-negative bacteria are more common causes of septic shock, of which *E. coli* is the leading gram-negative etiology[9,10]. The rate of patients with respiratory failure and impaired consciousness when hospitalized due to *S. aureus* bacteremia was higher than that of *E. coli* bacteremia, however, the differences were not statistically significant. During treatment, the rate of patients with *S. aureus* bacteremia requiring septic intubation (38%) was higher than that of patients with *E. coli* bacteremia (17.9%), a statistically significant difference with p = 0.003. The rate of patients requiring dialysis during treatment was also higher in the *S. aureus* bacteremia patients group (25.4%) than in the *E. coli* bacteremia patients group (8.5%) (p = 0.002). This explains the treatment results and treatment time of the study groups. The mortality rate of *S. aureus* bacteremia (36.6%) was higher than that of *E. coli* bacteremia (16%). In our study, the mortality rate of the study groups was lower than that of Ranjani Somayaji in Thailand[3]. *S. aureus* bacteremia was 43%, *E. coli* bacteremia was 19%). However, we found that the mortality rate of *S. aureus* bacteremia was much higher than that of *E. coli* bacteremia (p = 0.002), the ratio was approximately 3:1. The average length of hospital stay of the *S. aureus* bacteremia patients group (19.18 (8 - 30) days) was higher than that of the *E. coli* bacteremia patients group (12.19 (7.75 - 15.25) days), (p = 0.000). The hospital stay of the group that died due to *S. aureus* bacteremia (16.23 (4 - 30) days) was higher than that of the group that died due to *E. coli* bacteremia patients group (6.94 (1 - 10.5) days), (p = 0.032), our results are different from the results of the Ranjani Somayaji research group[3]. This shows the disease and economic burden of *S. aureus* bacteremia, so we need to predict the cause of *S. aureus* bacteremia

early, thereby building an initial empirical antibiotic strategy when approaching patients with sepsis in general, sepsis caused by *S. aureus*, *E. coli* in particular to improve survival rate, reduce mortality rate, and reduce treatment time for patients.

## CONCLUSIONS

- The average age of people with *E. coli* bacteremia (62.04 ± 15.82 years) was higher than the average age of people with *S. aureus* bacteremia (53.0 ± 17.60 years).

- *S. aureus* bacteremia is more common in men than in women, and the rate of men with *S. aureus* bacteremia is higher than that of *E. coli* bacteremia.

- *E. coli* bacteremia is more common in patients with underlying diseases than *S. aureus* bacteremia.

- *S. aureus* bacteremia is often caused by skin - soft tissue and musculoskeletal infections. *E. coli* bacteremia is often caused by digestive and urinary tract infections.

- The mortality rate due to *S. aureus* bacteremia is 36.6%, nearly 3 times higher than the mortality rate due to *E. coli* bacteremia. The treatment time of the *S. aureus* bacteremia patients group is longer than the treatment time of the *E. coli* bacteremia patients group. Therefore, we need to have a proper clinical approach to sepsis patients and develop an appropriate initial empirical antibiotic use strategy.

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