**Advances in**
**Clinical and Medical Sciences**
Volume 1, Issue 1

Research article

# Clinical Presentation of Bacteremia in Anorexia Nervosa

Kristin Sterrett[1,2], Leah Puckett[1,2], Ashlie Watters[1,2], David Wyles[2,3], Philip S. Mehler[1,2,3,4] and Dennis Gibson[1,2*]

[1]ACUTE Center for Eating Disorders and Severe Malnutrition at Denver Health, Denver, USA

[2]Department of Medicine, University of Colorado School of Medicine, Aurora, USA

[3]Department of Infectious Disease at Denver Health, Denver, USA

[4]Eating Recovery Center, Denver, USA

***Corresponding author:** Dennis Gibson, ACUTE Center for Eating Disorders and Severe Malnutrition at Denver Health, Denver, USA and Department of Medicine, University of Colorado School of Medicine, Aurora, USA

## Abstract

**Objective:** To better understand the presentation of bacteremia in patients with anorexia nervosa (AN).

**Method:** In this retrospective study, 10 patients with AN and bacteremia were compared to 10 AN patients without bacteremia.

**Results:** Patients with bacteremia had significantly elevated tachycardia and fever compared to the control group but respiratory rate, white blood cell count, and blood pressure remained similar between the two groups. Systemic inflammatory response syndrome criteria (SIRS) and quick sequential organ failure assessment (qSOFA) were not useful tools in predicting severe infection in the studied population.

**Conclusions:** Patients with AN may not manifest the typical physiologic changes associated with a severe infection, and current scoring assessments may be unhelpful in clinical decision-making.

## Introduction

Eating disorders (EDs) affect up to 17.9 % of young women and 2.4% of young men by early adulthood and are associated with one of the highest mortalities of all psychiatric disorders [1,2]. The medical complications associated with EDs are myriad [3], although life-threatening infection in this population has not previously been studied.

Historically, people with EDs have been presumed to be at lower risk for infection [4,5]. However, it remains unclear as to whether risk is truly reduced or whether the diagnosis is delayed due to lower clinical suspicion or immunologic changes of AN [6,7,8]. Indeed, many of the physiologic changes seen in patients with severe anorexia nervosa may confound the clinical presentation of an infection. These changes can include bradycardia, leukopenia, and hypothermia among other findings [3,5,9]. Leukopenia is a result of gelatinous marrow transformation. It is present in 40.4% of patients with AN admitted to the residential level of care (average BMI 15.5) [18]. Bradycardia is thought to be the result of increased vagal tone. It's important to note that many patients with severe AN present with hypotension thought also to be the result of increased vagal tone. Hypothermia results from several physiologic changes: reduced brown adipose tissue, sarcopenia, reduced sympathetic tone, and reduced resting metabolic rate. Prior studies have noted a decreased fever response in people with AN with bacterial infections [6,10].

Systemic inflammatory response syndrome (SIRS) criteria, the quick sequential organ failure assessment (qSOFA), and the national early warning score 2 (NEWS2) aid in diagnostic decision-making and prognostication of infection-related illnesses, including sepsis. While these criteria have shown prognostic accuracy for in-hospital mortality in the general population, they have not been examined in the ED population [11].

The primary aim of this retrospective case series is to describe the clinical presentation of bacteremia in people with AN. It is hypothesized that these individuals will not present with the typical clinical parameters associated with infection, and the SIRS criteria, qSOFA, and NEWS2 will be ineffective decision-making tools.

**Methods**

ACUTE Center for Eating Disorders and Severe Malnutrition (ACUTE) is an inpatient hospital unit that specializes in medical stabilization of patients with severe EDs and other forms of malnutrition. In this retrospective cohort study, all patients aged 18-65 years old who were admitted to ACUTE between May 1, 2016, and September 30, 2022, were eligible if they were diagnosed with bacteremia, using the search terms "bacteremia" and "sepsis". There were 1,672 electronic medical charts that were screened, and 29 patients met the inclusion criteria. Patients were included in the case group only if diagnosed with bacteremia during their hospitalization (n=10). Patients with only a single blood culture growing gram-positive organisms were excluded. The bacteremia cohort was age-, gender-, and admission percent

ideal body weight (%IBW)-matched to a control group who were randomly selected from patients admitted to ACUTE without a diagnosis of bacteremia.

Manual chart review was conducted for clinical variables of interest. Percent IBW was calculated using the Hamwi method[12], and body mass index (BMI) was calculated as weight in kilograms over height in meters squared. Vitals and lab values used for analysis were recorded within 24 hours of bacteremia diagnosis and were day-matched with the case group from the day the bacteremia was diagnosed.

SIRS is defined as two or more of the following: temperature >38°C or <36°C, tachycardia >90 beats per minute (BPM), tachypnea >20 breaths per minute (BPM), leukocytosis >12 k/uL or leukopenia <4 k/uL.13 The qSOFA is calculated by the following: glascow coma scale (GCS) 15 (zero points) vs <15 (one point), systolic blood pressure (BP) </=100 (one point) and zero points for higher BPs, respiratory rate >/=22 BPM (one point) and zero points for lower rates. Two to three points indicates organ dysfunction and increased risk for in-hospital mortality[14]. The NEWS2 is based on six physiologic parameters (respiratory rate, oxygen saturation, systolic BP, pulse rate, level of consciousness, and temperature). A score of 0-4 is considered low risk (a score of 3 in any one individual parameter is low-medium risk), 5-6 is considered medium risk, and 7 or more is considered high risk for adverse outcomes[15].

Baseline demographics and anthropometric statistics are presented in tabular form. Univariate statistics were used to describe the cohort. The distributions of continuous variables were determined by the Shapiro-Wilks test. Scores for SIRS, qSOFA, and NEWS2 were compared between the case and control groups using independent t-tests or Wilcoxon signed rank tests. P values of <0.05 were considered statistically significant, and all analyses were completed using SAS Enterprise Guide software version7.1 (SAS Institute, Cary, NC).

**Results**

The majority of the cases were female (80%) and all were White or Caucasian. The average age of the cases was 38.4 years old (SD: 11.8), and the admission %IBW was 57.2% (SD: 12.7). On the day of bacteremia diagnosis, cases had a higher maximum pulse (M: 113.2 BPM [SD: 22.6] compared to 86.5 BPM [SD: 16.5], t(18) =-3.02, p=.007) and a higher maximum body temperature (M: 38.0°C [SD: 0.9] vs 36.9°C [SD: 0.9], t(18)=-3.76, p=.001); respiratory rate approached significance, with faster rates noted in the bacteremia cohort (M: 19.7 BPM [SD: 4.1] vs M: 16.9 BPM [SD: 1.0], t(18)=-2.9, p=0.05).

There were no significant differences in %IBW, O2 saturation, minimum systolic BP, and white blood cell (WBC) count between patients diagnosed with bacteremia and the matched control patients. Mean WBC counts and respiratory rates remained within normal limits for patients with bacteremia (Table 1). All patients in the case and control groups had GCS scores of 15, and no patients were in respiratory failure.

Mean SIRS and qSOFA scores were 1.9 and 1.0, respectively, for patients with bacteremia, and they did not differ significantly from the control cohort (Table 1). Mean NEWS2 scores were 6.1 for the bacteremia group and did differ significantly from the NEWS2 score for the control group (3.5, p=0.02). Six of the patients in the bacteremia group had high SIRS scores, two individuals had elevated qSOFA scores, and six individuals had elevated NEWS2 scores while two patients in the control group had high SIRS scores, and four individuals had high NEWS2 scores. A significant number of points for qSOFA and NEWS2 were awarded for oxygen levels (SpO2) and hypotension (Table 2). There were no deaths secondary to the bacteremia, with all patients recovered and without transfer to a higher level of care.

**Discussion**

This retrospective case series investigated the presentation of individuals with AN and bacteremia. The results of this study suggest that a high clinical suspicion is necessary when considering an infectious etiology in individuals with severe malnutrition due to the more atypical presentation. Patients with bacteremia and severe malnutrition related to AN manifested tachycardia and fever, with significant increases in these vital signs compared to the control group, although respiratory rate, WBC count, O2 saturation, and BP remained similar between the case and control groups. Furthermore, the mean respiratory rate, WBC count, and O2 saturation remained within normal limits for the bacteremia group, suggesting these parameters are less helpful in decision-making in this regard.

Following on these observations it is not surprising that the qSOFA score, which does not include pulse or temperature, was ineffective in discriminating bacteremia in our population. While the simplicity of qSOFA makes it attractive, studies in other hospitalized populations have also shown poor sensitivity for early detection of severe infections[15,16]. SIRS criteria and NEWS2 include more components (including pulse and temperature) and trended toward or showed a significant difference, respectively, between the bacteremic and control patients in our cohort. Based on these findings, fever, tachypnea, hypoxia, and tachycardia, when present, should all increase the clinical suspicion for an infectious process, while leukocyte count and blood pressure are unhelpful in these decision-making algorithms for this patient population, over-estimating the severity of illness.

Normal WBC counts and pulses can still be concerning for an underlying infection, reflecting a relative "tachycardia" or relative "leukocytosis". Ultimately the entire clinical picture needs to be assessed, and a low threshold to evaluate for infection should always be considered. It remains unclear as to whether mortality is increased in those with bacteremia and malnutrition secondary to AN, given the highly specialized care provided at ACUTE.

One limitation of this study is the retrospective character of the research, which has inherent limitations. The individuals in this study were extremely malnourished, with a mean %IBW less than 60%, and thus these findings may not apply to higher-weighted patients with EDs. Finally, this study consisted of a very small sample size with all bacteremia patients experiencing good outcomes (ie no infection related mortality or need for higher level of care). This likely contributed to the lack of difference in some scoring systems (qSOFA) between groups and limited the statistical analysis. Future studies should continue to investigate clinical predictors of infection in individuals with AN.

**Conclusion**

Due to the compensatory physiologic changes associated with malnutrition in AN, a high clinical suspicion is necessary when considering an infectious diagnosis. This study found that AN patients with bacteremia tended to develop tachycardia and fevers, while WBC count, respiratory rate, and hypotension were less helpful in decision-making. In another recent study reviewing the cause of death in patients with severe AN, infection was listed on the death certificates of 29% of the studied population.19 It is unclear if the atypical presentation of sepsis-bacteremia in this patient population is causative of the overall high mortality of AN and it is imperative that the threshold to evaluate for infection in this population be adjusted to not miss a life-threatening infection, particularly when other aspects of the clinical presentation are not as expected. Future studies are needed to best define clinical predictors to help diagnose infection in individuals with eating disorders.

| Patients with Bacteremia (n=10) | | | | Patients without Bacteremia (n=10) | | | | |
|---|---|---|---|---|---|---|---|---|
| **Variable** | **Mean (SD)** | **Minimum** | **Maximum** | **Mean (SD)** | **Minimum** | **Maximum** | **t-stat (18)** | **p value** |
| Age | 38.4 (11.8) | 20 | 64 | 37.8 (11.1) | 20 | 62 | 0.12 | 0.91 |
| Admit IBW | 57.2 (12.7) | 38.0 | 82.0 | 56.7 (12.6) | 34.8 | 80.2 | 0.1 | 0.9 |
| IBW on day of diagnosis of bacteremia | 62.4 (14.1) | 45.2 | 88.8 | 60.8 (11.5) | 35.6 | 74.5 | 0.28 | 0.78 |
| **Maximum heart rate** | **113.2 (22.6)** | **82** | **154** | **86.5 (16.5)** | **64** | **118** | **3.02** | **0.007** |
| **Maximum temperature** | **38.0 (0.9)** | **36.7** | **39.6** | **36.9 (0.2)** | **36.4** | **37.2** | **3.77** | **0.001** |
| Minimum temperature | 35.8 (3.2) | 26.8 | 38.2 | 36.4 (0.2) | 36.1 | 36.7 | 0.59 | 0.56 |
| Respiratory rate | 19.7 (4.1) | 16 | 30 | 16.9 (1.0) | 16 | 18 | 2.9 | 0.05 |
| White blood cell count | 6.4 (4.5) | 2.6 | 17.3 | 5.24 (3.1) | 2.9 | 13 | 0.67 | 0.51 |
| Oxygen saturation minimum | 94.6 (3.0) | 91 | 97 | 94.1 (2.7) | 90 | 98 | 0.93 | 0.36 |
| Minimum SBP | 97.2 (8.8) | 85 | 117 | 97.3 (13.4) | | | 0.02 | 0.98 |
| | | | | | | | | |
| SIRS | 1.9 (1.4) | 0 | 4 | 0.9 (0.7) | 0 | 2 | 2.02 | 0.06 |
| qSOFA | 1.0 (0.7) | 0 | 2 | 0.6 (0.5) | 0 | 1 | 1.47 | 0.16 |
| **NEWS2** | **6.1 (2.6)** | **2** | **10** | **3.5 (1.8)** | **0** | **5** | **2.6** | **0.02** |

**Table 1. Patient demographics, vital sign abnormalities, and scores on assessment**

Abbreviations

IBW: Ideal body weight; SBP: systolic blood pressure; SIRS: systemic inflammatory response syndrome; qSOFA: quick sequential organ failure assessment; NEWS2: national early warning score 2; SD: standard deviation

**Patients with Bacteremia**

| Patient Number | Bacterial Species | SIRS | Criteria met | qSOFA | Criteria met | NEWS2 | Criteria met (points) |
|---|---|---|---|---|---|---|---|
| 1 | Klebsiella | 2 | Hyperthermia, leukopenia with elevated bands (21%) | 1 | Hypotension | 9 | $SpO_2$ (1), Need for oxygen (2), Hypotension (2), Tachycardia (3), Hyperthermia (1) |
| 2 | Bacteroides | 2 | Hyperthermia, tachycardia | 1 | Hypotension | 10 | $SpO_2$ (3), Hypotension (3), Tachycardia (2), Hyperthermia (2) |
| 3 | MSSA | 3 | Leukopenia, Hyperthermia, Tachycardia | 0 | | 4 | $SpO_2$ (1), Hypotension (1), Tachycardia (1), Hyperthermia (1) |
| 4 | Staphylococcus Epidermidis/Enterobacter | 0 | | 1 | Hypotension | 4 | $SpO_2$ (2), Hypotension (2) |
| 5 | Serratia/Klebsiella/ Enterobacter | 0 | | 1 | Hypotension | 2 | Hypotension (2) |
| 6 | MSSA | 3 | Leukopenia, Hyperthermia, Tachycardia | 0 | | 7 | $SpO_2$ (1), Need for oxygen (2), Tachycardia (3), Hyperthermia (1) |
| 7 | MSSA | 1 | Tachycardia | 1 | Hypotension | 5 | $SpO_2$ (1), Hypotension (2), Tachycardia (2) |
| 8 | MSSA | 3 | Hyperthermia, Tachycardia, Tachypnea | 2 | Hypotension, Tachypnea | 8 | Tachypnea (2), Hypotension (2), Tachycardia (2), Hyperthermia (2) |
| 9 | Salmonella | 1 | Tachycardia | 1 | Hypotension | 4 | $SpO_2$ (1), Hypotension (2), Tachycardia (1) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 10 | Klebsiella | 4 | Hyperthermia, Leukocytosis, Tachycardia, Tachypnea | 2 | Hypotension, Tachypnea | 8 | Tachypnea (3), Hypotension (2), Tachycardia (2), Hyperthermia (1) |
| **Patients without Bacteremia** | | | | | | | |
| 1 | | 1 | Tachycardia | 0 | | 3 | $SpO_2$ (1), Hypotension (1), Tachycardia (1) |
| 2 | | 2 | Tachycardia, Leukopenia | 1 | Hypotension | 5 | $SpO_2$ (1), Hypotension (2), Tachycardia (2) |
| 3 | | 1 | Tachycardia | 1 | Hypotension | 4 | Hypotension (3), Tachycardia (1) |
| 4 | | 0 | | 0 | | 3 | $SpO_2$ (2), Hypotension (1) |
| 5 | | 1 | Leukopenia | 0 | | 0 | |
| 6 | | 1 | Leukopenia | 1 | Hypotension | 4 | $SpO_2$ (2), Hypotension (2) |
| 7 | | 2 | Tachycardia, Leukocytosis | 1 | Hypotension | 4 | $SpO_2$ (2), Hypotension(2), Tachycardia (1) |
| 8 | | 0 | | 0 | | 1 | Hypotension (1) |
| 9 | | 0 | | 1 | Hypotension | 5 | $SpO_2$ (3), Hypotension (2) |
| 10 | | 1 | Leukopenia | 1 | Hypotension | 5 | $SpO_2$ (3), Hypotension (2) |

**Table 2. Breakdown of points given for scoring systems**

Abbreviations: MSSA: Methicillin sensitive *Staphylococcus aureus*

Key words: bacteremia, infection, eating disorders, anorexia nervosa, tachycardia, fever

References


1. Silen Y and Keski-Rahkonen A. Worldwide prevalence of DSM-5 eating disorders among young people. Current Opinions in Psychiatry. 2022;35:362-371.
2. Auger N, Potter B, Ukah UV, et al. Anorexia nervosa and the long-term risk of mortality in women. World Psychiatry. 2021;20(3):448-9.
3. Gibson D, Workman C, Mehler PS. Medical complications of anorexia nervosa and bulimia nervosa. Psychiatric Clinics of North America. 2019;42:263-74.
4. Bowers TK and Eckert E. Leukopenia in anorexia nervosa. Lack of increased risk of infection. Archives of Internal Medicine. 1978;138(10):1520-3.
5. Palla B and Litt IF. Medical Complications of Eating Disorders in Adolescents. Pediatrics. 1988;81(5):613-623.
6. Brown RF, Bartrop R, Beumont P, Birmingham CL. Bacterial Infections in Anorexia Nervosa: Delayed Recognition Increases Complications. International Journal of Eating Disorders. 2005;37(3):261-265.
7. Fink S, Eckert E, Mitchell J, et al. T-Lymphocyte Subsets in Patients with Abnormal Body Weight: Longitudinal Studies in Anorexia Nervosa and Obesity. International Journal of Eating Disorders. 1996;20(3):295-305.
8. Gibson D and Mehler PS. Anorexia Nervosa and the Immune System-A Narrative Review. Journal of Clinical Medicine. 2019;8(11):1915.
9. Nishita JK, Ellinwood EH, Rockwell WJK. Hypothermia in anorexia nervosa: Increase in nonshivering thermogenesis. International Journal of Eating Disorders. 1985;4(3):307-19.
10. Birmingham CL, Hodgson DM, Fung J, et al. Reduced febrile response to bacterial infection in anorexia nervosa patients. International Journal of Eating Disorders. 2003;34:269-72.
11. Raith EP, Udy AA, Bailey M, et al. Prognostic Accuracy of the SOFA Score, SIRS Criteria, and qSOFA Score for In-Hospital Mortality Among Adults with Suspected Infection Admitted to the Intensive Care Unit. JAMA. 2017;317(2):290-300.
12. Hamwi GJ. Therapy: changing dietary concepts. In: Danowski TS eds. Diabetes Mellitus: Diagnosis and Treatment. New York, NY: American Diabetes Association; 1964:73-8.
13. Bone RC, Balk RA, Cerra FB, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM consensus conference committee. American College of Chest physicians/society of critical care medicine. Chest. 1992;101(6):1644-55.
14. Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA. 2016;315(8):801-10.
15. Physicians RCo. National early warning score (NEWS) 2: Standardising the assessment of acute-illness severity in the NSH; RCP: London, UK, 2017.
16. Williams JM, Greenslade JH, McKenzie JV, et al. SIRS, qSOFA and organ dysfunction: insights from a prospective database of emergency department patients with infection. Chest 2017;151:586-596
17. Giamarellos-Bourboulis EJ, Tsaganos T, Tsangaris I, et al. Validation of the new Sepsis-3 definitions: proposal for improvement in early risk identification. Clin Microbiol Infect 2017;23:104-9.

18. Walsh K, Blalock DV, Mehler PS. Hematologic findings in a large sample of patients with anorexia nervosa and bulimia nervosa. Am J Hematol. 2020 Apr;95(4):E98-E101.
19. Westmoreland P, Duffy A, Rienecke R, Le Grange D, Joiner T, Manwaring J, Watters A, Mehler P. Causes of death in patients with a history of severe anorexia nervosa. J Eat Disord. 2022 Dec 24;10(1):200.

Citation: Kristin Sterrett, Leah Puckett, Ashlie Watters, David Wyles, Philip S. Mehler and Dennis Gibson, Adv Clin Med Sci, "Clinical Presentation of Bacteremia in Anorexia Nervosa". 2023; 1(1): 101

Received Date: October 16, 2023; Published Date: October 31, 2023