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Original Contribution

Clinical outcomes of ED patients with bandemia

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ABSTRACT

Background: Although an elevated white blood cell count is a widely utilized measure for evidence of infection and an important criterion for evaluation of systemic inflammatory response syndrome, its component band count occupies a more contested position within clinical emergency medicine. Recent studies indicate that bandemia is highly predictive of a serious infection, suggesting that clinicians who do not appreciate the value of band counts may delay diagnosis or overlook severe infections.

Objectives: Whereas previous studies focused on determining the quantitative value of the band count (ie, determining sensitivity, threshold for bandemia, etc.), this study directs attention to patient-centered outcomes, hypothesizing that the degree of bandemia predisposes patients to subsequent negative clinical outcomes associated with underappreciated severe infections.

Methods: This retrospective study of electronic medical records includes patients who initially presented to the emergency department (ED) with bandemia and were subsequently discharged from the ED. These patients were screened for repeat ED visits within 7 days and death within 30 days.

Results: In patients with severe bandemia who were discharged from the ED, there was a 20.9% revisit rate at 7 days and a 4.9% mortality rate at 30 days, placing severely bandemic patients at 5 times significantly greater mortality compared to nonbandemic patients ($P = .032$).

Conclusion: Our review of patient outcomes suggests that the degree of bandemia, especially in the setting of concurrent tachycardia or fever, is associated with greater likelihood of negative clinical outcomes.

1. Introduction

Infectious disease represents the third leading cause of death in the United States and second worldwide [1], underscoring the importance not only of timely treatment but also of timely identification via efficient and accurate clinical diagnostic tests. The objective measure most commonly utilized in a clinical setting for suspected infections is the white blood cell count (WBC).

Although an elevated WBC is a widely acknowledged and utilized measure for infection [2–5] and criteria for systemic inflammatory response syndrome (SIRS) or sepsis [6], the standard breakdown of the WBC does not include the band count, or immature neutrophil count, unless specifically requested by the physician. This is partially because the utility in adult patients is contested and highly variable. Furthermore, the band count is often subject to variability in technique and experience of the technician performing the count [7,8].

However, more recent studies suggest that an elevated band count is significantly associated with bacteremia and other infectious processes, specifically with gram-negative bacteremia, pneumococcal infections, and *Clostridium difficile* infections [9,10]. Some studies go further to suggest that bandemia is a superior indicator of infection relative to both WBC and temperature as bandemia was initially present in 80% of patients who did not present with elevated WBC or temperatures and were later found to be bacteremic [11]. Another study reports that the sensitivity of band counts was greater than that of either WBC or absolute neutrophil count (ANC) specifically for at-risk populations such as infants and elderly patients [12,13]. This suggests that clinicians who do not appreciate the value of band counts may have a delayed diagnosis or overlook a severe infection and thereby negatively impact patient outcomes.

This reported correlation between bandemia and severe infections underscores the importance of clarifying the significance of band counts in a clinical setting. However, there are currently no clinical standards by which otherwise healthy-appearing patients with isolated bandemia should be treated with antibiotics, let alone admitted to the hospital. Previous studies have focused mainly on determining whether the band count is of quantitative value; however, there is inconsistency in defining a single standard to determine what constitutes an elevated band count, with thresholds ranging from ≥5% to ≥20% [9–12].

The primary objective of this study is to determine whether the degree of bandemia, in patients who presented to the emergency

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Table 1
Group demographics

Band counts	Normal ≤10	Mildly elevated 11-20	Moderately elevated 21-30	Severely elevated >30
Mean age (y)[a]	47.8 ± 18.1	46.1 ± 18.4	50.4 ± 19.5	50.4 ± 17.3
Females	54.8% (708)	56.6% (107)	47.4% (36)	48.1% (39)

[a] Reported as age during initial presentation to ED.

department (ED) and who were ultimately discharged from the ED, is an important predictor of subsequent negative patient outcomes (repeat visit within 7 days or death within 30 days). Patients with negative outcomes will be assessed for any unifying characteristics that should have been considered more thoroughly in the setting of bandemia. We hypothesize that patients with increasing degrees of bandemia—who otherwise did not present with symptoms suggesting serious infection (ie, did not meet SIRS or sepsis criteria)—would experience greater rates of return visits or death related to undiagnosed infectious processes.

2. Materials and methods

2.1. Study design

We conducted a multicenter 3-year retrospective cohort study using records from the EDs associated with the University of California San Diego (UCSD) Health System with a combined annual census of 65 000. One hospital is an urban, academic teaching hospital (level 1 trauma center), and the other is a suburban community hospital.

The scope of the study was limited to patients who presented to the ED between January 1, 2010, and December 31, 2012. The UCSD Human Subjects Protections Program approved the study.

2.2. Population and data collection

Patient data were abstracted from the hospital's internal shared electronic medical record (EMR) EPIC (Epic Systems Corp., Verona, Wis). Patients were included in this study if they were 18 years or older at the time of initial presentation, had a WBC with manual band count, and were discharged from the ED after their initial presentation. Any patient with multiple ED visits during the study period that were greater than 7 days apart was accounted separately for each visit. Other data collected included patient age, gender, vital signs, past medical history, medications, and, if available, culture results. Patient records were also evaluated for any subsequent visits and clinical outcomes consistent with a negative health outcome.

In cases where the EMR was insufficient to determine whether the patient revisited a hospital within 7 days, the outcome was listed as "Unknown" and the patient was excluded from population totals in analyses concerning revisits. In cases where the EMR was insufficient to determine whether the patient died, San Diego County Medical Examiner records were searched for matching death records. If no matching record was found, the patient was assumed to be alive at 30 days and included in population totals for analyses concerning mortality.

Evaluation of records also included assessing past medical histories for any systemic condition that primarily manifests in elevated ANCs or band counts, including hereditary neutrophilia, myelodysplastic syndromes, myeloproliferative disorders, and familial cold autoinflammatory syndrome [14]; any chronic conditions that cause a reactive, secondary manifestation of elevated ANC or band counts, including smoking (at least 20 pack years, habitually smoked a half-pack per day, or quit smoking less than 5 years ago) [15,16], chronic inflammatory conditions (such as rheumatoid arthritis, inflammatory bowel diseases, chronic hepatitis), asplenia [17], and any neoplastic infiltration into bone marrow [18]. We also evaluated for any active medications with leukocytosis as a known side effect, including glucocorticoids [19], lithium [20], and recombinant colony-stimulating factors rG-CSF and rGM-CSF. Patients with any of the above conditions or medications were excluded.

2.3. Data analysis

Elevated band count, or bandemia, is defined as greater than 10%, as in the SIRS criteria [6]. Band counts were categorized as less than 10 (normal), 11 to 20 (mildly elevated), 21 to 30 (moderately elevated), and greater than 30 (severely elevated). A negative clinical outcome was defined as any revisit (including redischarge or admission) to a UCSD ED within 7 days or death within 30 days of the initial visit with

Table 2
Comparing lack of negative outcomes amongst patients with SIRS

Band counts	Mildly elevated 11-20	Moderately elevated 21-30	Severely elevated >30	*P*[a]
Total visits[b]	113	46	48	
No revisit	92.1% (106)	100% (46)	87.5% (42)	.081
Total visits[c]	143	61	59	
No death	97.9% (140)	98.4% (60)	96.6% (57)	.619

[a] Comparisons are between severely elevated and mildly elevated/moderately elevated.
[b] Only includes patients with a known outcome at 7 days and 2 or more SIRS criteria at initial presentation. Patients without known outcome at 7 days were excluded from total.
[c] Includes all patients without who had 2 or more SIRS criteria at initial presentation, assuming all patients alive at 30 days in absence of records suggesting otherwise.

Table 3
Comparing proportion of negative clinical outcomes between patient groups

Band counts	Normal ≤10	Mildly elevated 11-20	Moderately elevated 21-30	Severely elevated >30	*P*[a]
Total visits[b]	961	145	60	67	
Revisits w/in 7 d[c]	17.6% (169)	20.7% (30)	13.3% (8)	20.9% (14)	.138
Discharged	9.3% (89)	13.8% (20)	8.3% (5)	10.4% (7)	.785
Admitted	8.3% (80)	6.9% (10)	5.0% (3)	10.4% (7)	
Total visits	1292	188	76	81	
Deaths w/in 30 d	0.9% (11)	3.7% (7)	3.9% (3)	4.9% (4)	.032

[a] Comparisons are between severely elevated and normal/mildly elevated/moderately elevated.
[b] Total revisits excludes patients without known outcome at 7 days. Total deaths include all patients with initial presentation on assumption that all patients were alive at 30 days in absence of records suggesting otherwise.
[c] Includes only bacterial infectious processes. Other diagnoses/causes of death were primarily attributed to an underlying chronic and/or systemic condition, adverse drug reaction, and/or to an acute cardiovascular, pulmonary, gastrointestinal, neurological, etc., event.

Table 4
Patient profiles of negative outcomes

Age and sex	Vital signs during initial presentation[a]				Band count/ WBC	SIRS	Relevant[b] PMH/ meds	History/diagnosis of initial presentation	History/diagnosis of return within 7 d	Cause of death within 30 d	Notes on laboratory[c] results
	Temp.	HR	BP	RR							
Mildly elevated											
25 M	36.7-36.9	98-**113**	111/79-120/80	16-20	15/**32.7**	2	None	1. Brought in from jail with vertigo, dizziness s/p fall 2. Pneumonia on x-ray, given moxifloxacin	*Admission (day 1)* 1. Worsening vertigo, due to phenytoin toxicity 2. Hemoptysis, x-ray improved, stable O_2 saturation	N/A	"Marked leukocytosis"
61 F	37.1-37.7	**106-113**	111/64-117/78	16-18	11/4.1	2	Marrow transplant (1 mo prior) Hodgkin disease (on chemotherapy)	Fever, throat pain On nitrofurantoin for previous UTI Pt declined further evaluation	*Admission (day 3)* Fever, 7/10 painful throat mucositis, pharyngitis	N/A	None
61 F	36.7-37.4	**102-126**	84/62-106/60	15-18	13/5.6	2	Marrow transplant (2.5 mon prior) Hodgkin disease (on chemotherapy)	1. Fever and diarrhea, resolved since morning 2. Thrombocytopenia	*Admission (day 4)* 1. Continuing fever, cough, soft stool with hematochezia 2. Anemia, worsening thrombocytopenia 3. Suspected fungal pneumonia	*Death (day 12)* Septic shock	Stool: *C. difficile* Urine: *E. coli* Blood: *MAC* "WBC normal, platelets improved"
56 F	36.7	66-**95**	117/74-145/72	16	17/11.4	2	Sirolimus, racrolimus (for liver transplant 3 y prior)	General weakness, no localized sx's, admitted and treated for SIRS 2 weeks prior Pt. declined further evaluation	N/A	*Death (day 27)* SIRS and advanced leiomyosarcoma	Bandemia reviewed with pt.
82 M	36	51	115/61	**22**	13/**33.8**	2	None	Nausea, severe abdominal and chest pain (with extensive cardiovascular history) Pt. desires hospice care	N/A	*Death (day 16)* Sepsis causing atrial fibrillation, worsening mental status	Leukocytosis attributed to dexamethasone (terminated 1 wk prior)
71 F	37.1-**39.1**	**101-108**	116/71-127/85	16-18	18/**3.6**	3	Metastatic colon cancer (on chemotherapy)	Fever and diarrhea, treated for *C. difficile* colitis 1 mo prior Pt. requests discharge	*Discharged (day 1)* Continued fever and diarrhea	N/A	Stool: *C. difficile* Bandemia noted
32 F	36.8-**38.4**	89-**118**	123/67-149/78	15-20	17/9.5	3	None	1. Fever, cough, congestion suggesting URI 2. Abdominal cramps, diarrhea, suspect colitis, given ciprofloxacin for coverage	*Discharged (day 2)* Vomiting, bloody diarrhea suggesting infectious colitis, continued cramping	N/A	Bandemia noted
30 M	37.8-**38.6**	63-**99**	107/61-131/73	16-18	18/8.9	3	None	Headache, neck pain, cough and congestion suggesting URI	*Discharged (day 2)* Worsening productive cough, pneumonia on CXR	N/A	"Labs ok"
46 M	36.6-37.2	76-**92**	98/52-114/63	16-18	13/**14.3**	2	None	Nonexertional chest pain, general malaise Given azithromycin	*Discharged (day 1)* Continued chest pain, exertional SOB, suspect atypical pneumonia	N/A	"WBC elevation"

Moderately elevated											
28 M	37	58-67	133/68-147/75	18-20	29/8.4	1	None	Headache, lightheadedness s/p assault (1 wk), sutures on forehead, hand, wrist Suspect post-concussive syndrome	*Discharged (day 5)* Pt. presented for suture removal, mild erythema, purulent drainage Suspect simple wound infection	N/A	None
96 F	36.8-**38.3**	82-**110**	78/41-114/56	18-**28**	26/**27.8**	4	None	Fever, altered mental status, norexia, suspect sepsis Pt. requests palliative care at home	N/A	*Death (day 6)* Suspected bacteremia	"High WBC"
Severely elevated											
47 F	37.1-**39**	**107-108**	110/58-121/73	16	33/4.0	3	None	Fever, nonproductive cough, aches Atypical pneumonia on x-ray, + Flu PCR, given ceftriaxone, azithromycin, oseltamivir	*Admission (day 2)* Worsening fever, aches, cough after initial improvement suggesting superimposed bacterial infection	N/A	Sputum: *MSSA* "CBC unremarkable"
52 M	36.9	**92-99**	116/71-133/83	18-20	61/16.5	2	Uncontrolled Type 2 diabetes	Productive cough, chest discomfort x-ray shows pneumonia, pt. refused admission, given azithromycin Noted hyperglycemia, well-healing ulcer on left toe with no evidence of cellulitis	*Admission (Day 2)* Left leg swollen, tender, erythematous with open, draining blister Dyspnea, pneumonia complicated with loculated pleural effusion Suspected sepsis, ellulitis	N/A	Sputum: *Mycobacterium* (not TB, rapid-growing, or MAC) Bandemia noted
52 M	37.2-37.4	**95-102**	114/72-129/87	16-18	33/4.3	2	Metastatic esophageal cancer (on chemotherapy)	Fever, nonproductive cough Pneumonia diagnosis, given levofloxacin 2 d prior Pt. declines admission, given moxifloxacin	*Admission (day 2)* Increased SOB, productive cough, pleuritic chest pain, suspect nosocomial pneumonia and sepsis	N/A	Bandemia noted
51 F	37.2	**136-137**	109/81-122/78	14-18	41/8.6	2	Metastatic ovarian cancer (on salvage chemotherapy) Baseline tachycardia, hypoxemia	SOB with no home O_2, admitted 2 wk prior for symptomatic pleural effusions Stable on x-ray	*Admission (day 1)* Nausea and vomiting, 5/10 abdominal pain, continuing SOB	*Death (day 4)* Nosocomial pneumonia and bacteremia	Blood: *B. cereus* "Labs noted"
61 M	37.4-**39.2**	82-**112**	118/78-128/53	16-20	31/5.6	3	None	Acute idiopathic febrile illness Pt. feels better after IV fluids	*Admission (day 2)* Fever returned, generalized muscle weakness, urinary incontinence/urgency Suspect UTI, early SIRS	*Death (day 10)* Septic shock, unknown source	"WBC WNL"
37 F	37.2-37.7	**98-126**	117/71-132/72	18	45/7.9	2	None	Urinary "pressure" and frequency, urinalysis suggesting UTI, given cephalexin prescription	*Discharged (day 2)* Nausea and vomiting, flank pain, pt. did not fill prescription Suspect acute pyelonephritis	N/A	Urine and blood: *E. coli* "WBC normal"

[a] Reported as a range from minimum to maximum, taking into account all recorded vitals measurements taken during the initial visit to the ED. Any vitals or lab results meeting SIRS criteria are bolded and underlined.
[b] Only includes any PMH that may have increased patient's susceptibility to bacterial infections.
[c] Indicates notes made on electronic record about WBC lab results obtained from the initial visit to the ED.

a suspected or confirmed infectious process. Negative clinical outcomes are described by band count categories with a general breakdown of etiology. Clinical information and patient history by outcome is presented for cases of death within 30 days. Comparisons between clinical outcome and band group were made using a Fisher exact test due to small cell sizes overall. The same was done for patients meeting SIRS criteria. For clinical outcome comparisons, severely elevated was compared to normal/mildly/elevated/moderately elevated groups. For SIRS criteria comparisons, severely elevated was compared to mildly/moderately elevated. Data were analyzed with Excel (Microsoft, Redmond, Wash).

3. Results

Eligible patients were categorized according to their band counts in increments of 10%. Group demographics are recorded in Table 1.

3.1. Negative health outcomes

The overall proportion of patients who met at least 2 SIRS criteria at initial presentation and did not experience a negative clinical outcome is presented in Table 2. There were no significant differences between deaths and revisits among patients meeting SIRS criteria (P's > .05).

The number of patients who had a negative clinical outcome from each band count group is presented in Table 3. The proportion of patients with revisits is roughly equivalent across all groups and did not achieve significance (P's > .05). When comparing revisits due to infectious etiologies only, the mildly elevated patients (2.8%, 4 patients) had nearly 3 times as many revisits without admission compared to normal (1.1%, 11 patients); the severely elevated patients (5 patients, 7.5%) had about 2 times as many revisits with admission compared to normal (3.2%, 31 patients). Other groups were comparable in proportion of revisits. Statistics were not performed on infectious etiologies alone due to very small sample sizes.

The proportion of patients with death at 30 days is almost directly correlated with the degree of bandemia: mildly and moderately elevated groups were roughly equivalent with over 4 times the amount of deaths compared to the normal group, whereas patients who initially presented as part of the severely elevated group had nearly 1.5 times the mortality compared to both mildly and moderately elevated groups ($P = .032$). These differences were preserved after isolating infectious etiologies, with mildly elevated (1.6%, 3 patients) and moderately elevated (1.3%, 1 patient) having over 6 times the number of deaths compared to normal (0.2%, 2 patients), and severely elevated (2.5%, 2 patients) having about 2 times the mortality compared to mildly and moderately elevated groups. Statistics were not performed on mortality associated with infectious etiologies due to very small sample sizes.

3.2. Clinical profiles

Table 4 summarizes relevant clinical information and patient history surrounding initial discharge and subsequent representation. The most common SIRS criteria met across all bandemic categories was tachycardia (>90 bpm) and fever (>38 °C). These results, along with other clinical details and progression of patient care, are discussed below.

4. Discussion

This study demonstrates that negative outcomes after initial ED discharge occur more frequently as the severity of bandemia increases: although no significant correlation with revisits was observed, there was a significant correlation with mortality at 30 days, suggesting bandemia to be a negative prognostic marker. Furthermore, patients with negative outcomes tend to have at least one episode of recorded tachycardia or fever (as defined by accepted SIRS criteria) in conjunction with their bandemia.

Assuming that most physicians recognize bandemia as an indicator of infection, it seems unlikely that it would simply be a failure to identify bandemia that would lead to a greater proportion of negative outcomes after bandemic patients are discharged. This raises the question of whether there were additional factors that contributed to these negative outcomes, sparing lapse in clinical judgment.

4.1. Severely elevated profiles

Of those patients with bandemia who had negative outcomes, just under half of the patients received antibiotics upon initial discharge. This seems counterintuitive, given that bandemia is a known surrogate marker for infection. Those patients from the severely elevated group received the greatest proportion of antibiotic coverage (4 of 6), with 2 of these patients (both 52 M) preferring outpatient treatment over the physician's recommended admission. This increased proportion of antibiotic use may be a consequence of these patients having objective findings on diagnostic tests (chest x-rays, urinalysis) that revealed an infectious etiology, thus supplementing bandemia with more concrete etiology of the infection.

The two patients (51 F and 61 M) who did not receive antibiotics both died from an infectious process within 30 days. On initial discharge, there were no alternative diagnoses noted to rule out infectious processes; however, it was noted that both patients were subjectively better and considered stable after preliminary workup. Although past medical history may account for increased susceptibility in 51 F (on chemotherapy), there was no other known contributing factor for 61 M. This case may reflect a case where the bandemia was unrecognized or not considered appropriately (stated “WBC within normal limits” in physician note), especially in the context of febrile and tachycardic episodes.

4.2. Moderately elevated profiles

Both patients in this group did not receive antibiotics initially; however, the rationale behind these decisions was clear. Records indicate that patient 96 F was highly suspicious for sepsis, but family resistance to substantial treatment and personal wishes for palliative care after physician counseling were respected. Patient 28 M was the only patient in the entire study with a negative outcome who did not meet two or more SIRS criteria. Furthermore, this patient's presenting symptoms were possibly unrelated to an infectious process and were more likely due to his recent head trauma.

4.3. Mildly elevated profiles

Less than half of the patients in the mildly elevated category received antibiotics (4 of 9), with two of these patients having objective evidence of infection (chest x-ray, prior diagnosis) and the other two having suspected infectious diagnoses based on clinical pictures that were likely most concerning for fever/tachycardia and leukocytosis, respectively.

Of the remaining 5 patients in the mildly elevated category, 3 (56 F, 82 M, and 71 F) were offered admission but refused or requested palliative care. These three patients account for 2 (56 F and 82 M) of the deaths within 30 days. Notably, they all had areas of susceptibility to infection due to immunosuppressants, age, and other systemic complications. In all three cases, bandemia or leukocytosis was explicitly noted or reviewed with the patient as part of the rationale for recommending admission and further treatment.

The remaining two patients (61 F and 30 M) are very contrasting cases. An upper respiratory illness of viral etiology was highest on the differential for patient 30 M, which combined with young age and lack of existing medical conditions, may account for the decision to discharge without antibiotics. Despite a mild bandemia, physician notes indicate a failure to recognize and acknowledge this abnormal

laboratory value ("Labs ok"). This may have contributed to this patient's negative outcome.

The other remaining patient (61 F) had a complicated medical history with conditions suggesting an immunosuppressed state. It is clear that the patient's clinical course progressively declined, where an admission after her initial ED visit may have safeguarded against subsequent death from septic shock. Although it was noted that this patient had a history of baseline tachycardia and was afebrile and stable at 102 bpm before initial discharge, it is unusual to dismiss an episode of tachycardia at 126 bpm in a patient who has also been on carvedilol for 2 months. Furthermore, laboratory notes indicate dismissal of bandemia as well. Given the patient's immunocompromised past medical history, bandemia, and tachycardia, the decision to discharge may represent a failure to recognize or acknowledge this abnormal laboratory value or possibly even a lapse in clinical judgment.

Although the above negative outcomes may be concerning, it is notable that most of the bandemic patients who initially presented with at least two SIRS criteria did not have any negative outcome. This may indicate that bandemia or SIRS criteria are not necessarily highly sensitive or specific measures of the severity of infection. One must consider these values in conjunction with contextual evidence and clinician judgment to guide patient care [21,22]. Perhaps, these measures could be of added use if applied using modified, risk-stratified, weighted screening tools [23,24].

However, the relative lack of negative outcomes may also be an indicator of successful efforts to raise awareness and educate physicians on the mortality of SIRS/sepsis. These collaborative efforts to create and publicize more uniform definitions and management guidelines for SIRS/sepsis started at the turn of the century, with the Surviving Sepsis Campaign publishing thorough evidence-based guidelines in 2004 [25]. Its success has been reflected in various international institutions [25]. This may be reflected here in the low percentage of negative outcomes seen at the UCSD ED, although a more encompassing, comparative retrospective study would be needed to confirm this.

4.4. Limitations

This study was limited to a 3-year period and revealed overall correlations between mortality and increasing degree of bandemia. Although limited statistical analyses were performed, more advanced analysis that would have allowed controlling for potential confounders could not be performed due to the small sample size for the outcomes of interest. This study was performed at two hospitals with a shared EMR. Subsequent follow-up ED visits or hospital admission at other hospitals would not have been captured. Analysis of patient records and subsequent conclusions drawn about clinical decision making are limited to the quality and thoroughness of the physician's notes.

5. Conclusion

Because infectious diseases are a significant problem with potentially high mortality, it is important to minimize negative outcomes and optimize identification of clinical characteristics that would indicate further evaluation. This study shows that degree of bandemia significantly correlates with an increased likelihood of a negative clinical outcome, specifically death within 30 days. In patients with severe bandemia who were discharged from the ER, the 30-day mortality rate was nearly 5%, approximately 5 times that of patients without bandemia.

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