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Bacteremia Predictive Factors among Inpatients of Internal Medicine Department. A Prospective Cross- Sectional Survey in Aswan University Hospital

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ABSTRACT

Background: bacteremia is the presence of bacteria in the blood stream that are alive and capable of reproducing. It is a type of blood stream infection

Aim of the Work: was to identify bacteremia predictive factors among inpatients at Internal Medicine Department in Aswan University Hospital and to improve the management and decrease mortality among inpatients through clinical parameters.

Patients and Methods: we estimated blood cultures of one hundred patients at our department from April 2017 to April 2018.

Results: The final diagnosis and univariate analysis have shown use of central venous line ($p<0.001$), high axillary body temperature ($p<0.001$), greater pulse rate ($p<0.001$), leucocytosis ($p<0.001$), neutrophilia ($p<0.0001$), and creatinine ($p<0.002$) were associated with bacteremia. Positive blood cultures patients have shown in our study that temp >38^{O}C, leucocytosis, neutrophillia >85%, tachycardia>90 and serum creatinine >1.3% were independent risk factors of bacteremia.

Conclusion: The presence of bacteremia can be highly predicted by fundamental clinical information such as high pulse rate, leucocytosis, high grade temperature and neutrophilia.

Keywords: Bacteremia Predictive Factors

INTRODUCTION

Bacteremia is the presence of bacteria in the blood stream that are alive and capable of reproducing. It is a type of blood stream infection **(1).**

Bacteremia is defined as either a primary or secondary process. In primary bacteremia, bacteria have been directly introduced into the bloodstream **(2).** Injection drug use may lead to primary bacteremia **(2).** In the hospital setting, use of blood vessel catheters contaminated with bacteria may also lead to primary bacteremia. Secondary bacteremia occurs when bacteria have entered the body at another site, such as the cuts in the skin, or the mucous membranes of the lungs (respiratory tract), mouth or intestines (gastrointestinal tract), bladder (urinary tract), or genitals. Bacteria that have infected the body at these sites may then spread into the lymphatic system and gain access to the bloodstream, where further spread can occur **(3).**

Bacteremia may also be defined by the timing of bacteria presence in the bloodstream: transient, intermittent, or persistent. In transient bacteremia, bacteria are present in the bloodstream for minutes to a few hours before being cleared from the body and the result is typically harmless in healthy people. This can occur after manipulation of parts of the body normally colonized by bacteria, such as the mucosal surfaces of the mouth during teeth brushing, flossing, or dental procedures, or instrumentation of the bladder or colon **(3).**

Intermittent bacteremia is characterized by periodic seeding of the same bacteria into the bloodstream by an existing infection elsewhere in the body, such as an abscess, pneumonia, or bone infection, followed by clearing of that bacteria from the blood stream. This cycle will often repeat until the existing infection is successfully treated. Persistent bacteremia is characterized by the continuous presence of bacteria in the bloodstream **(1)**.

It is usually the result of an infected heart valve, a central line-associated bloodstream infection (CLABSI), an infected blood clot (suppurative thrombophlebitis), or an infected blood vessel graft **(1).**

Persistent bacteremia can also occur as part of the infection process of typhoid fever, brucellosis, and bacterial meningitis. Left untreated, conditions causing persistent bacteremia can be potentially fatal **(4).**

Bacteremia is clinically distinct from sepsis, which is a condition where the blood stream infection is associated with an inflammatory response from the body, often causing abnormalities in body temperature, heart rate, breathing rate, blood pressure, and white blood cell count **(4)**.

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Bacteremia is related to the leading causes of inpatient mortality in spite of the introduction of new antimicrobial agents and aggressive therapy [5]. Needless to say, it is very important to take blood cultures both from patients in whom severe infection is suspected and from those patients in whom severe infections should be suspected.

However, the precise criteria for obtaining blood cultures have not been established; the decision depends on the physician's judgment [6].

Moreover, it is often difficult to estimate the probability of bacteremia based on clinical findings, for example, elderly. patients often fail to show the usual clinical features indicative of bloodstream infection [6].

A study to evaluate the incidence and clinical impact of bacteremia on patients' outcomes in the USA revealed that centralvenous catheter use, other infections, mechanical ventilation, trauma, haemodialysis and malnutrition were independent risk factors [6].

Another prospective study showed that mortality due to bactaeremia was related significantly to age, rapidly fatal diseases, septic shock, multiple organ failure, previous use of antimicrobials, infection from Enterobacteriaceae species that produced extended-spectrum β-lactamases and inadequate empirical treatment [7].

There are only a few previous reports of studies designed to identify predictive risk factors through direct comparison of patients with bacteremia with those with negative blood culture results.

One report identified predictive factors among elderly patients as male sex, obesity, low McCabe score on admission, gastrostomyat admission, recent surgery and urinary incontinence [8].

Another retrospective study, which examined risk factors of bacteremia among patients in an intensive care unit (ICU) for 5 months, determined that long ICU stays and hospitalisation for trauma were risk factors of bactereamia [9].

To the best of our knowledge, no reports that contain hospitalized patients from whom blood cultures were taken in a general internal medicine unit are present.

Aim of the Work

The aim of the current work was to analyze predictive factors of bacteremia to establish when blood cultures should be taken, in order to improve management and decrease mortality due to bacteremia among patients at Internal Medicine Department of Aswan University Hospital.

RESULTS

PATIENTS AND METHODS

This prospective, cross-sectional study included a total of one hundred patients who were subjected to blood cultures at the Department of internal Medicine in Aswan University Hospital, in Aswan, Egypt. Approval of the ethical committee and a written informed consent from all the subjects were obtained.

The blood culture results were collected prospectively from the clinical laboratory data base from all internal medicine inpatients who had blood cultures taken from 1 April 2017 to 1 April 2018. If blood cultures were taken repeatedly to check treatment effects or to rule out bloodstream infection, only the first culture results for each patient were used for analysis.

Positive blood culture results of skin commensals accompanied by no additional antimicrobial treatment were recognized as contaminants and such patients were included in the culture-negative group.

This and other clinical information at or just before blood culture sampling was extracted by chart review: age, female sex, artificial devices placed when blood cultures were taken, preceding antimicrobial use within 2 weeks, recent surgical procedures within a month, use of immunosuppressive drugs, history of malignant diseases and HIV infection. We also extracted axillary body temperature, systolic and diastolic blood pressure, pulse rate, white cell count with percentages of neutrophils and lymphocytes, blood urea nitrogen (BUN), creatinine, estimated glomerular filtration rate (eGFR), C reactive protein(CRP), body mass index, and albumin levels from the medical charts.

Univariate comparison of each variable between patient groups with and without bacteremia was performed by Fisher's exact test. Differences with a p value <0.05 were defined as statistically significant.

Variables with a p value <0.10 in univariate analysis were entered into univariate and multivariable logistic regression models to determine factors predictive of bacteremia.

We did not enter diagnoses into multivariable analysis because of the small number of patients in each diagnosis.

The accuracy of the logistic regression model was assessed by the area under the receiver-operator characteristic curve (ROC-AUC).

Table 1: Descriptive of sex regarding final diagnosis

Final diagnosis	Blood culture (+) patients' diagnoses				
	Male (n=19)		Female (n=22)		Total
ACUTE CHOLECYSTITIS	1	5.3	0	0.0	1
ACUTE PYELONEHRITIS	3	15.8	4	18.2	7
ASCENDING CHOLANGITIS	2	10.5	0	0.0	2
CELLULITIS AKI	3	15.8	0	0.0	3
Infected central catheter	3	15.8	10	45.5	13
Lobar PNEUMONIA	4	21.1	0	0.0	4
Chronic PYELONEPHRITIS	3	15.8	0	0.0	3
BROCHO PNEUMONIA	0	0.0	3	13.6	3
HYPO GLYCAEMIC COMA AND UTI	0	0.0	1	4.5	1
Hepato cellular failure	0	0.0	1	4.5	1
SBP	0	0.0	3	13.6	3

This table showing 41 (41%) patients with true positive blood culture, the most prevalent diagnosis among patients was infected central catheter with percentage (31.7%) followed by pyelonephritis with percentage (24.4%), so analysis of table (1) showing patients with infected central catheter and pyelonephritis with high percentage of bacteremia and patient with acute cholecystitis had a low percentage of bacteremia.

Table 2: Extracted patient variables and results of univariate analysis

Variables Demographic data of patients	Total	Blood culture				P. value
		Negative (n=59)		Positive (n=41)		
		No.	%	No.	%	
Age	54.03+17.06	54.41±17.41		53.49±16.75		0.793
Female Sex	55(55%)	33	55.9	22	53.7	0.990
Preceding use of antimicrobial use of antibiotic 2wks	43(43%)	42	71.2	1	2.4	0.000
History of malignancy OR HIV	3(3%)	0	0.0	3	7.3	0.131
Use of immune suppressive drugs	8(8%)	3	5.1	5	12.2	0.362
Recent surgical procedures	26(26%)	14	23.7	12	29.3	0.692
FINAL DIAGNOSIS						
ACUTE CHOLECYSTITIS	1(1%)	0	0.0	1	2.4	0.001
acute on top of ckd	1(1%)	1	1.7	0	0.0	
ACUTE ON TOP OF CKD	2(2%)	2	3.4	0	0.0	
ACUTE PYELONEHRITIS	8(8%)	1	1.7	7	17.1	
ASCENDING CHOLANGITIS	2(2%)	0	0.0	2	4.9	
BROCHO PNEUMONIA	3(3%)	0	0.0	3	7.3	
CELLULITIS	1(1%)	1	1.7	0	0.0	
CELLULITIS AKI	5(5%)	2	3.4	3	7.3	
DIABETIC NEPHROPATHY	3(3%)	3	5.1	0	0.0	
DKA	8(8%)	8	13.6	0	0.0	
DKA UTI	7(7%)	7	11.9	0	0.0	
HEART FAILURE	3(3%)	3	5.1	0	0.0	
HEPATIC ENCEPHALOPATHY	6(6%)	6	10.2	0	0.0	
HYPO GLYCAEMIC COMA AND UTI	1(1%)	0	0.0	1	2.4	
Hepato cellular failure	1(1%)	0	0.0	1	2.4	
HYPOKALAEMIA	3(3%)	3	5.1	0	0.0	
infected central catheter	18(18%)	5	8.5	13	31.7	
PNEUMONIA	8(8%)	4	6.8	4	9.8	
PYELONEPHRITIS	4(4%)	1	1.7	3	7.3	
PYONEPHROSIS	3(3%)	3	5.1	0	0.0	
AKI	3(3%)	3	5.1	0	0.0	
SBP	3(3%)	0	0.0	3	7.3	
SLE	5(5%)	5	8.5	0	0.0	
UTI	1(1%)	1	1.7	0	0.0	
Clinical and laboratory finding						
SBP	109.8+17.64	112.88±15.43		105.37±19.76		0.035
DBP	66.6+15.84	67.29±15.18		65.61±16.89		0.605
Pulse	97.21+11.96	92.36±10.92		104.2±9.81		0.001
Temp	38.32+0.98	37.74±0.73		39.16±0.62		0.001
RR	20.08+2.75	19.27±2.69		21.24±2.44		0.001
RBS	232.16+136.73	264.97±148.17		184.95±102.77		0.002
BMI	27.1+2.47	27.61±2.23		26.37±2.64		0.016
HB	10.19+1.51	10.3±1.51		10.02±1.52		0.376
MCV	86.9+5.54	88.22±5.63		85±4.87		0.004
WBC	14.58+6.98	11.24±5.61		19.37±5.92		0.000
NEUTROPHILES	78.67+11.88	71.73±9.38		88.66±6.96		0.000
PLT	213.89+86.86	204.68±89.37		227.15±82.38		0.205

Variables Demographic data of patients	Total	Blood culture				P. value
		Negative (n=59)		Positive (n=41)		
		No.	%	No.	%	
SERUM ALBUMIN	46.48+32.19	3.7±0.87		4.03±0.61		0.034
ALT	2.51+1.87	38.14±26.15		32.15±11.74		0.126
AST	3.84+0.79	30.31±22.34		27.58±10.8		0.420
BUN	35.72+21.64	43.49±37.87		50.78±21.28		0.223
Creatinine	29.2+18.54	2.01±1.48		3.24±2.14		0.002

Table (2) shows extracted patients variables with positive and negative blood culture and result of univariate analysis.

Table 3: Univariate and Multivariate analysis of studied parameters

	Univariate analysis			Multivariate analysis		
	OR	**95% CI**	**P. value**	**OR**	**95% CI**	**P. value**
Female sex	1.096	0.492-2.441	0.822	0.111	0.010-1.185	0.069
Age >60 years	0.700	0.314-1.560	0.383	0.828	0.122-5.604	0.846
Pulse rate >90 bpm	**0.060**	**0.019-0.191**	**<0.001****	0.309	0.036-2.657	0.285
Axillary body temperature >38.0°C	**76.375**	**16.114-361.998**	**<0.001****	**0.005**	**0.000-0.114**	**0.001****
Neutrophils >80%	**25.477**	**8.314-78.069**	**<0.001****	**0.023**	**0.002-0.307**	**0.004****
Creatinine mg/dL	**1.455**	**1.142-1.853**	**0.002****	2.044	0.886-4.717	0.094

Blood culture (dependent variable); **Boldface** is a good predictor

We conducted univariate logistic regression analysis and, based on the univariate analysis summarised in table (2), multivariable logistic regression analysis. Variables considered for the multivariable regression analysis were female sex, age, pulse rate, axillary body temperature, central venous line, per cent neutrophils, creatinine in table (3).

Table 4: ROC curve analysis

	AUC	Cutoff	Sensitive	Specificity	+PV	-PV	Accuracy
Pulse	0.808	>90	90.24	64.41	63.8	90.5	77.33
Temp.	0.913	>37.9	95.12	79.66	76.5	95.9	87.39
NEUTROPHILES	0.940	>85	78.05	100.0	100.0	86.8	89.03
Creatinine	0.719	>1.3	98.0	45.76	56.2	100.0	72.88

We evaluated the quality of this model using the discrimination of ROC-AUC; the ROC curve analysis as follow was pulse rate >90 had sensitivity 90.24 and specificity 64.41 with accuracy 77.33, temperature>38 had sensitivity 95.12 and specificity 79.66 with accuracy 87.39, neutrophills >85% with sensitivity 78.05 and specificity 100 with accuracy 89.03, serum creatinine >1.3 with sensitivity 100 and specificity 45.76 with accuracy 72.88. (Note: This article contains no figures)

DISCUSSION

This is a study of direct comparison of patients with positive and negative blood cultures, in order to identify predictive factors of bacteremia.

We took blood cultures of 100 patients at Internal Medicine Department in Aswan University Hospital from April 2017 to April 2018. 41 Patients of 100 patients had a positive blood culture.

Positive blood cultures patients have shown in our study that temp >38*c, leucocytosis, neutrophillia >85%, tachycardia>90 and serum creatinine >1.3% were independent risk factors of bacteremia.

Our study revealed that tachycardia was independent risk factor of bacteremia as tachycardia has been indicator of sepsis new guide lines didn't include tachycardia in sepsis def guidelines [(10)].

As shown in table (1) and (2) most prevalent diagnosis among patients with bacteremia was infected central catheter and pyelonephritis.

Several authors have reported that a positive blood culture was relatively low among patients with pneumonia. The percentage of bacteremia was high in infected central catheter with (31.7%) and patients with pyelonephritis with (24.4%) and in pneumonia with percentage (17%). White cell count with differential and CRP levels are frequently used as a marker of a systemic inflammatory reaction, but CRP wasn't associated with bacteremia in our study. Several studies have shown the usefulness of CRP for estimating the risk of bacteremia in patients with sign of sepsis. Our study results suggest that increase neutrophils percentage was timely and reliable response to bacteremia, it is very important to consider obtaining blood cultures when patients have a higher percentage even CRP is not high. On the basis of multivariable analysis and the ROC analysis, the model in this study showed sufficient power to predict bacteremia in an inpatient ward.

Our model could be used for the establishment of minimum criteria for obtaining blood cultures, as well as for instituting an automatic alert system for detection of bacteremia among inpatients. A recent publication reported that a computerized clinical decision support intervention for reducing the duration of urinary tract catheterizations \was successfully integrated within a hospital's healthcare system. Similarly, it would be possible to develop an

automatic alert system for bacteremia using patients' fundamental clinical information. Several studies have shown that the presence of chills is a powerful single predictor of bacteremia **(11).** In Japanese emergency rooms, it was reported that the severity of chill was correlated with the risk of bacteremia**(12).**

Since we did not evaluate patients subjective and objective symptoms. In this study, a future study should analyses physical findings and symptoms, including chill, in addition to the items we used in this study.

Our study revealed that high-grade temperature, high pulse rate, leucocytosis, absolute neutrophilia and elevated serum creatinine are independent risk factors of bacteremia. Many other studies revealed different results as in USA revealed that central venous catheter.

Other infections, mechanical ventilation, trauma, haemodialysis, and malnutrition were independent risk factors **(6).**

Another prospective study showed that mortality due to bacteremia was related significantly to age, rapidly fatal distress, septic shock, multible organ failure previous use of antimicrobials, infection from enterobacteriacea species that produced extended _spectrum B _lactamases and in adequate empirical treatment **(7).**

There are only a few previous reports of studies designed to identify predictive risk factors through direct comparison of patients with bacteremia with those with negative blood cultures.

Our study helps in determining predictive factors of bacteremia that improve the management and decrease mortality among inpatients of internal me divine department.

CONCLUSION

In conclusion, the presence of bacteremia can be highly predicted by fundamental clinical information such as pulse rate, leucocytosis, high grade temperature and neutrophil percentage. In particular, neutrophils

>85%, pulse rate >90 bpm and body temperature >38 were found to be associated with greater risk for bacteremia Our results emphasize the importance of taking blood cultures if the pulse rate is >90 bpm, high grade temperature and for ordering a differential white cell count in addition to the total count to predict bacteremia.

To confirm our results, a future multicenter prospective study with a sufficient number of patients should be carried out using standardized criteria for obtaining blood cultures based on the results of this.

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