

## Original article

# Blood stream infection in an intensive care unit, a comparative study on the impact of infection control trained versus untrained nursing staff

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## ABSTRACT

**Background:** Blood stream infection (BSI) is characterized by high morbidity and mortality between patients. Procalcitonin (PCT) is released by thyroid gland in response to such infection. Adherence to infection control is fundamental to decrease blood stream infection rates. **The aim:** Observing role of infection control program on the prevalence of blood stream infection. Evaluating PCT as rapid marker for infection and sepsis. **Methods:** Patients were divided into group one, 33 patients cared by 20 infection control trained nurses and group two of 33 patients cared by 20 non-trained nurses. Incidence of BSI was calculated in both groups by blood culture. Procalcitonin was evaluated as rapid marker diagnosing infection earlier than blood culture and differentiating between causative bacteria. **Results:** Prevalence of BSI in group two was 51.5% vs 9.1% in group one. Procalcitonin highest levels were significantly associated with severity of infection and sepsis. **Conclusion:** Prevalence of BSI was significantly higher among patients in group two; cared by infection control trained nurses. Procalcitonin can be used as a rapid diagnostic marker for BSI. **Recommendations:** The study recommends application of frequent infection control training and using PCT as early diagnostic marker for blood stream infection.

## Introduction

Blood stream infection (BSI) is a severe disease characterized by high morbidity and mortality, directly linked to the delay in the first adequate antimicrobial administration, however, accuracy of antimicrobial treatment cannot be assured without microbiological documentation by blood culture result, due to the prevalence of emerging multidrug-resistant organisms [1]. Blood stream infection can be identified by positive one or more blood culture in association with certain symptoms and according to the causative

microorganism either pathogenic or skin microorganism [2].

“Sepsis occurs when microbes invade the blood stream from local source leading to signs of systemic illness in remote organs,” this was the first scientific definition for sepsis by Dr. Schottmuller in 1914. So, bloodstream infection or bacteremia was a condition describing how to diagnose sepsis. Over years this definition has not been changed. Sepsis, septicemia, and bloodstream infections (bacteremia). So, in clinical practice the terms are used interchangeably. Recently, we know that about one-

half of the patients with signs and symptoms of sepsis have positive blood culture or any other microbiological evidence of an infectious focus [3].

Quick sequential organ failure assessment score (qSOFA) is a quick bedside test that identifies patients with organ dysfunction and sepsis resulting from infection [4].

Procalcitonin (PCT) is the calcitonin prohormone naturally released by the thyroid glands. All PCT is cleaved to calcitonin in healthy humans, and only < 0.1 ng / ml of procalcitonin is found in the blood. During infection PCT control becomes modified. It results in a large release of PCT into the bloodstream that depends on the intensity of the sepsis [5]. It has been concluded that PCT in both medical and surgical patients is a helpful marker for early detection of sepsis as sepsis was best detected by PCT than c-reactive protein (CRP) [6].

Adherence to infection control preventive strategies as hand hygiene and infection control bundles are reasonable ways to avoid colonization of the health care workers' hands and contamination of equipment used for patient care and the environment surrounding the patient by pathogenic organisms [7].

As data concerning these issues are very vital for prevention and early diagnosis of blood stream infection and sepsis, this study aims to observe the role of infection control program on the prevalence of blood stream infection and evaluate PCT as a rapid marker for infection and sepsis.

## Subjects and methods

### Study design

Cross-sectional comparative study that was conducted in Medical Microbiology and Immunology Department Faculty of Medicine Zagazig University and Intensive Care Units (ICUs) Zagazig University Hospitals. Sixty-six patients admitted to the intensive care units were included in the study and divided according to the care providing nurse into group one of 33 patients served with 20 infection control trained nurses and group two of 33 patients served with 20 infection control non-trained nurses. Prevalence of blood stream infection was calculated and compared between the two groups. Approval for performing the study was obtained from Institutional Review Board (IRB), Medical Microbiology and Immunology Department, Intensive Care Units Zagazig University hospitals. Informed written consents were gathered from patients or their relatives.

### Infection control program assessment

Nurses from different ICU wards were divided into two groups; group 1: trained nurse group and group 2: non-trained nurse group according to the documented infection control training they received by the hospital.

To prove the difference between trained and non-trained, the infection control practice of the care providing nurses was evaluated according to the following parameters; the first parameter of comparison was baseline assessment including administrative policies, hand washing stations, available towels and suitable discard bins, availability of suitable personal protective equipment, availability of guiding posters, processing of reusable items, waste management protocol and unit sanitation.

The second parameter was process observation according to CDC checklist, concerned with the knowledge and proper procedures of hand hygiene, the use of personal protective equipments and different infection control bundles, upon which nurses were divided into group one (trained) and group two (non-trained), to evaluate rate of blood stream infection in the two groups of the patients treated by these different groups of care providing nurses [8-13].

### Patient selection and scoring

#### *Blood stream infection confirmation*

Blood stream infection was identified by one of two ways, the first way is by one or more positive blood cultures, and the positive recovered pathogens are defined as either primarily causing blood infection directly or confirmed to be transmitted secondarily from other site of infection in addition to having at least one of these clinical findings: fever (>38°C), shivering or hypotension. While the other way is by the presence of only one of: twice positive blood cultures for common skin microorganism twice or more than twice at different times, positive blood culture for common skin microorganism only once and the same microorganism isolated by venous culture catheter or positive blood antigen test for several microorganisms with no detected infections in any part of the body [2,14].

*Patients admitted to the ICU* and confirmed to have blood stream infection were further subclassified clinically according to qSOFA, with detected CRP and lactate serum levels.

Quick sequential organ failure assessment score identifies patients according to having two or more of the following criteria: respiratory rate  $\geq$  22/ min,

altered attention and systolic blood pressure  $\leq 100$  MmHg [15].

Septic shock is defined as serum lactate levels rising above 2 mmol/L despite adequate volume resuscitation, persisting hypotension requiring vasopressor to keep mean arterial pressure above 65 mmHg [16].

#### Specimen collection and blood culture

Blood samples were used to diagnose blood stream infection through cultivation on signal blood culture bottle (Oxoid,UK).

Wearing gloves, the venipuncture site was selected and disinfected by 70% alcohol. The area of needle entry was swabbed by 2% iodine in a circular motion and allowed to dry for about one minute. The protective cover was removed from the top of the bottle, then the top of the bottle was wiped by ethanol ether swab. Twenty millimeters of blood were withdrawn using a sterile syringe and withdrawn in the blood culture bottle. Using a new ethanol ether swab the top of the bottles was swabbed and covered. Each bottle was labeled by the name, date and time of collection. The inoculated bottle was incubated at 37 °C. Aerobic subculture was performed on appearance of the signal on signal blood culture bottles.

Conventional identification of the bacteria was performed and further confirmation of the Gram-negative isolates was done using API 20 E (Bio-Mérieux, USA) [17].

#### Procalcitonin assay

Measuring procalcitonin serum level (Elecsys BRAHMS PCT, Roche) was performed as follows; Two milliliters of blood sample were taken under complete aseptic conditions. The blood was left for 30-60 minutes. Then it was centrifuged for separation of the serum for 20 minutes at 4000xg's ( $\approx 6500$  rpm). Serum was immediately separated and stored at -20 °C until time of examination.

Then, Cooled reagents were brought to approximately 20°C. The reagents in the kit (M,R<sub>1</sub>,R<sub>2</sub>) are ready for use. Calibrators and controls were dissolved by adding 4 ml of distilled water and allowed to stand for 15 minutes. First incubation was performed between antigen in the sample (30 ug), a biotinylated monoclonal PCT-specific test antibody and monoclonal PCT specific antibody labelled with ruthenium complex to form a sandwich complex. Streptavidin coated microparticles were added for the second incubation, the complex became bound to a solid phase via interaction of biotin and streptavidin. The reaction mixture was aspirated into the

measuring cell where the microparticles were magnetically captured onto the surface of the electrodes. Unbound substances were then removed with ProCell/ProCellM. Application of a voltage of the electrode then induced chemiluminescent emission which was measured by a photomultiplier.

**C-reactive protein (CRP) assay:** results were obtained from patients reports.

#### Statistical analysis

Microsoft Excel software was used to analyze the collected data; primary clinical examinations, lab investigation and outcome measures. After that the data was introduced into Statistical Package for Social Sciences (SPSS version 20.0) software for further analysis. According to the type of data qualitative data was represented by numbers and percentages. While, quantitative data continues group was represented by mean  $\pm$  SD, the upcoming tests were used to examine differences for significance; difference and association of qualitative variable by Chi square test ( $X^2$ ). Differences detected between the quantitative independent groups by t test or Mann Whitney and multiple by Kruskal Wallis. P value was set at  $<0.05$  for significant results &  $<0.001$  for the high significant result. A receiver operating characteristic (ROC) was used to conclude different marker cutoff values.

#### Results

The first step performed in the study was comparison between the two ICU units involved in the study as regarding base line infection control assessment. As regarding administrative policies, both units fulfilled the required criteria except for regular availability of at least one infection control trained person. This point was missing in the second (non-trained ICU) group.

As for hand hygiene; both ICU units were deficient in suitable number of hand washing stations per ward as only a hand washing station was available for nine beds and single alcohol based hand rub station was available for every five beds while, the optimum number of alcohol based hand rub station is one for every bed. Available towels and suitable discard pins for used towels were inadequate only in the second group (non-trained). About personal protective equipment the first (trained ICU group) fulfilled all the required criteria while, (non-trained group) showed defect in presence of both sterile and clean gowns and masks and N95 respirators. Guiding posters were available in both ICU groups, but posters of infection control bundles

were deficient in group two (non-trained group). Processing of reusable items was properly performed in both groups, except for autoclaves that were not found in the non-trained group. Waste management protocol was applied properly in both groups. Specimen handling protocol wasn't performed in group two (non-trained group). Sanitation of the unit was performed properly, the point of defect was in the non-suitable number of cleaning workers in both groups.

The second step in the study was the comparison of the observation process. The first two processes observed were hand hygiene accuracy and proper personal protective equipment use. Results showed significant difference in proper performance between the two groups. Also, different infection bundles were observed. And significant difference in knowledge and performance was observed in specific points. The results of process observation comparison between trained and non-trained nurse groups were illustrated in **table (1)**.

Prevalence of blood stream infection in group one served by infection control trained nurses was only 3 (9.1%) blood stream infection cases, while in the second group served by non-trained nurse group the rate was 17 (51.5%) cases in the second group, This observation was statistically significant ( $P < 0.01$ \*). The most frequently isolated organism was *Staphylococcus epidermidis* followed by *klebsiella pneumoniae*, followed by *E. coli*, then *Staphylococcus aureus* and finally *Proteus* and *pseudomonas* by the same percentage (**Table 2**), (**Figure 1**).

Patients were further subdivided according to qSOFA score into negative group, sepsis and septic shock regardless of the care providing nurse group. Forty-six (69.6%) were with negative blood culture results. Fourteen (21.2%) met sepsis criteria and 6 (9.1%) met septic shock criteria.

Procalcitonin highest level was detected in septic shock cases  $61.31 \pm 32.25$  ng/ml followed by sepsis  $40.83 \pm 29.57$  ng/ml with statistically significant difference and  $P$  value  $0.00$ \*\* . As regarding CRP levels; highest CRP level was associated with septic shock  $157.66 \pm 79.97$  mg/l followed by sepsis  $102.64 \pm 63.88$  mg/l with statistically significant difference and  $P$  value  $0.00$ \*\* (**Table 3**).

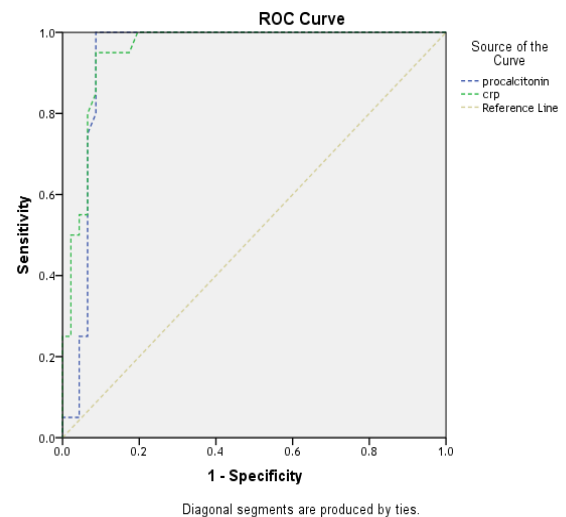
**According to ROC curve analysis PCT cut off**  $>48.2$  ng/ml was concluded for septic shock with sensitivity and specificity 98% and 95% (**Figure 2**). Another ROC curve was concluded for sepsis with cut off  $>22.5$  ng/ml for sepsis with sensitivity and

specificity 85% and 73% (**Figure 3**). While CRP cut off for septic shock was  $>150$  mg/l with sensitivity and specificity 98% and 96%. Cut off level of CRP for sepsis cases was  $>32.8$  mg/l with sensitivity and specificity 78% and 75% (**Table 4**).

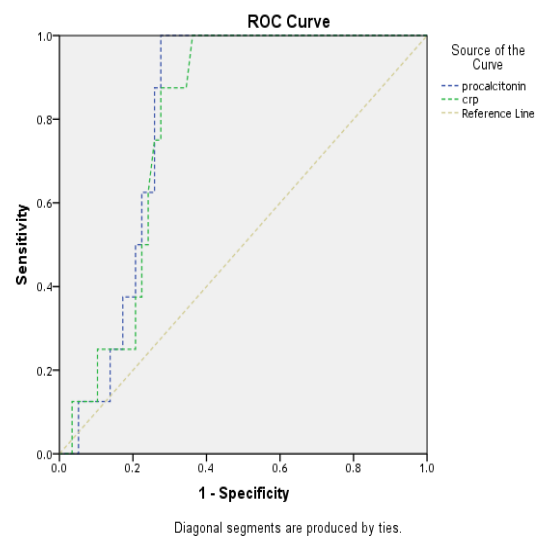
**Figure 1.** API strip of *Klebsiella.pneumoniae* isolate.



**Figure 2.** ROC curve regard cutoff of septic shock.



**Figure 3.** ROC curve regard cutoff of sepsis.



**Table 1:** Infection control practice assessment between group 1 and group 2 nurses.

	<b>Group I (No.=20)</b>	<b>Group II (No.=20)</b>	<b>X<sup>2</sup></b>	<b>p.value</b>
<b>1)Hand hygiene:</b>	No. %	No. %		
Proper hand hygiene procedure	18 (90.0%)	7 (35.0%)	12.906	<0.001**
<b>2)PPE:</b>				
Proper PPE usage.	17 (85.0%)	5 (25.0%)	14.545	<0.001**
<b>3)Ventilator associated pneumonia bundle:</b>				
General strategies.	20 (100.0%)	6 (30.0%)	21.538	<0.001**
Strategies to prevent aspiration.	20 (100.0%)	17 (85.0%)	3.243	0.071
Strategies to reduce colonization of digestive and respiratory tracts.	16 (80.0%)	13 (65.0%)	1.128	0.288
Strategies to minimize contamination of equipment used to care for patient receiving mechanical ventilation.	20 (100.0%)	20 (100.0%)	0.0	1.0
<b>4)Catheter associated urinary tract infection bundle:</b>				
Avoid unnecessary catheterization.	18 (90.0%)	13 (65.0%)	3.584	0.058
Insert using aseptic techniques.	20 (100.0%)	11 (55.0%)	11.612	<0.001**
Maintain sterile closed drainage system.	16 (80.0%)	13 (65.0%)	1.128	0.288
Review catheter necessity daily.	20 (100.0%)	20 (100.0%)	0.0	1.0
<b>5) Central line associated blood stream infection bundle:</b>				
Hand hygiene.	20 (100.0%)	19 (95.0%)	1.025	0.311
Maximum barrier precautions.	17 (85.0%)	18 (90.0%)	0.228	0.632
Chlorhexidine skin antiseptis.	20 (100.0%)	18 (90.0%)	2.105	0.146
Optimal site selection.	20 (100.0%)	20 (100.0%)	0.0	1.0
Daily review for necessity.	19 (95.0%)	14 (70.0%)	4.329	0.037*

**Table 2.** Blood culture result distribution between group 1 (n=33) and group 2 (n=33).

<b>Patient group Blood culture results</b>	<b>Group 1</b>	<b>Group 2</b>	<b>Total</b>	<b>X<sup>2</sup></b>	<b>P</b>	
-ve N %	30 (90.0%)	16 (48.5%)		14.06	0.00**	
+ve N%	3 (9.1%)	17 (51.5%)				
<b>Microorganisms isolate</b>	<b>-VE N%</b>	30 (90.9%)	16 (48.5%)	46 (69.7%)	16.7	0.01*
	<i>E.coli</i> N%	1(3.0%)	2 (6.1%)	3 (4.5%)		
	<i>Klebsiella</i> N%	2 (6.1%)	3 (9.1%)	5 (7.6%)		
	<i>Proteus</i> N%	0 (0.0%)	1 (3.0%)	1 (1.5%)		
	<i>Pseudomonas</i> N%	0 (0.0%)	1 (3.0%)	1 (1.5%)		
	<i>S.epidermidis</i> N%	0 (0.0%)	8 (24.2%)	8 (12.1%)		
	<i>S.aureus</i> N%	0 (0.0%)	2 (6.1%)	2 (3.0%)		
<b>Total N%</b>	100.0%	100.0%	100.0%			

**Table 3.** Procalcitonin level according to qSOFA classification.

	Negative blood culture	Sepsis	Septic shock	Kruskal walis	<i>P</i>
<b>Procalcitonin ng/ml</b>	15.81±22.74 19.9 (0.5-104.0)	40.83±29.57 41.0 (10.9-86.30)	61.31±32.25 65.7 (15.4-109.9)	<b>58.66</b>	<b>0.00**</b>
<b>CRP Mg/l</b>	16.46±35.87 35.0 (7.0-205.5)	102.64±63.88 105.0(16.0-219.0)	157.66±79.97 195.0(42.0-222.0)	<b>41.254</b>	<b>0.00**</b>

**Table 4.** Septic shock and sepsis cutoff levels of PCT and CRP.

	Area Under the Curve						Sensitivity	Specificity
	Test result variable(s)	Area	Cut off	<i>P</i>	95% Confidence Interval			
					Lower Bound	Upper Bound		
<b>Cut off septic shock</b>	<b>PCT ng/ml</b>	0.938	>48.2	0.00**	0.873	0.995	98.0%	95.0%
	<b>CRP mg/l</b>	0.954	>150	0.00**	0.907	0.998	98.0%	96.0%
<b>Cut off sepsis</b>	<b>PCT ng/ml</b>	0.802	>22.5	0.006*	0.6925	0.9051	85.0%	73.3%
	<b>CRP mg/l</b>	0.789	>31.8	0.008*	0.6754	0.8999	78.8%	75.0%

## Discussion

Sepsis is a life-threatening disorder characterised by acute organ dysfunction that occurs in response to infection. It can be prevented by appropriate infection prevention and control measures as hand hygiene, these measures will also help decrease the need for antibiotics consumption [18].

One of the infection control procedures compared between the two nurse groups in the current study was hand hygiene that was significantly different between the two groups as 100% of nurses serving the first group used correct decontamination hand procedures in addition to their knowledge about proper use of alcohol hand rub and ordinary hand wash; in comparison to the second nurse group only 65% used correct decontamination procedure and 75% only showed appropriate knowledge about when to use alcohol hand rub or

ordinary wash. Another infection control point compared between the two groups that showed significant difference was the proper knowledge and application of infection control bundles.

In this study prevalence of blood stream infection in group one served by infection control trained nurses was only 3 (9.1%) blood stream infection cases, while in the second group cared by non-trained nurse group the prevalence was 17 (51.5%) cases with *P value* 0.01\* (**Table 1**). These results were compatible with several studies [19-21].

**Ista and colleagues** in their study about the effect of infection control bundles reported decrease the prevalence of infections significantly from median 6.4 per 1000 to 2.5 per 1000 after implementation of bundles. Health professionals' compliance with bundle protocols was evaluated and was stated suboptimum in all of them. For that reason, protocol and guideline compliance is a global hand hygiene practice and other different

implementations, but the most effective implementation was when nurses had the authority to problem in health care [19]. They also explained to discontinue the procedure if a physician broke the protocol [20].

Also, **Ershova and colleagues** reported that Health care associated infections' cumulative prevalence decreased significantly for blood stream infection from 16% to 7.8% after implementing an infection control program. The hypothesis that implementing infection control program acted in a double fold way with initial decrease in nosocomial patient to patient transmission which subsequently lead to a decrease in nosocomial infection level. Implementing contact precautions including proper personal protective equipment usage in addition to cohorting patients with *Acinetobacter* or *Klebsiella* were the most critical interventions they depended on. These efforts were paired with intensive environmental disinfection measures and skin antisepsis for indwelling devices [20].

**Phan and colleagues** in their study concerned with role of infection control training in reducing blood stream infections reported that infection control training reduced the blood stream infection rate significantly from 6.31 infections per 1000 catheter days in the pre-intervention period to 3.84 in the post-intervention period after application of the training [21].

Over the past decades there has been a continuous research for a supreme biomarker diagnosing sepsis. A marker that must have an elevated diagnostic accuracy (high sensitivity and specificity). Procalcitonin has shown to be a promising marker in the diagnosis and management of sepsis [22]. So, the current study was aiming to detect role of PCT as rapid marker diagnosing blood stream infection. According to the current study PCT highest level was detected in septic shock cases 61.31±32.25 ng/ml followed by sepsis 40.83±29.57 ng/ml with statistically significant difference and *P value* 0.00\*\*. C-reactive protein levels also were analyzed; highest CRP level was associated with septic shock 157.66±79.97 mg/l followed by sepsis 102.64±63.88 mg/l with statistically significant difference and *P value* 0.00\*\*. That was in consistent with **Yunus and colleagues**, **Ahmed and colleagues**, **Kim and colleagues**, **Tambo and colleagues** and **Alju-Beita and colleagues**, who also showed points of conflict [23-27].

**Yunus and colleagues** demonstrated that sensitivity and specificity of PCT for septic shock

were 63 and 65%. Procalcitonin values proved a statistically significant and directly proportionate association to severity of sepsis as determined by septic shock requiring vasopressors. Mean PCT was 32.7 ± 52.2 ng/ml in patients with septic shock necessitating vasopressors and 9.6 ± 22.7ng/ml in patients with sepsis only [23]. **Ahmed and colleagues** reported that PCT levels with a median value of 2.14 µg/l in the culture positive group were significantly higher compared to culture negative group. Furthermore, median CRP levels and median WBC levels were also higher in the culture positive groups [24].

**Kim and Tambo** and their colleagues in their studies reported that PCT level was highest in the septic shock group. While, **Alju-Beita and colleagues** results conflicted with the current study as they reported that baseline PCT levels did not differ between patients with sepsis and those with septic shock [25-27].

**Alju-Beita** and colleagues explained their results by the fact that they analyzed the patients along two separate periods of time. Beside lack of microbiological confirmation of sepsis which was identified only depending on clinical criteria. That explains the difference to the current study in which results were analyzed in a single period of time beside microbiological confirmation of each case in the study [27].

## Conclusion

Documented infection control training program confirmed by assessment for ICU base line and process observation plays a vital role in decreasing the blood stream infection rates. Also, PCT can be used as rapid and accurate marker for diagnosing BSI and associated sepsis.

## Recommendations

Necessity of periodic infection control training to the nursing staff and all the health care workers, that training should be followed by work observation and on job training if needed. Procalcitonin can be used as rapid marker for early diagnosis of blood stream infection and sepsis.

## Limitations of the study

- Infection control training program was not introduced, the study just assessed and compared between the ICUs on the basis of the already existed program.
- Limited number of study population. A larger sample would have better validity and reliability.

- The study didn't evaluated role of PCT in other infections as fungal and viral infections.
- Association between PCT and systemic illness not associated with infection was not assessed.

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