Original Research Article

CONS in blood culture: contaminants or pathogens?

**Fatima Khan*, Samia Kirmani, Naushaba Siddiqui, Asfia Sultan,
Hiba Sami, Md. Mahtab, Meher Rizvi, Abida Khatoon, Indu Shukla and Haris M Khan**

Department of Microbiology, Jawaharlal Nehru Medical College,
Aligarh Muslim University, Aligarh, U.P., India
*Corresponding author

A B S T R A C T

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CONS isolated from blood culture are usually contaminants but are also a significant cause of bacteremia. False positive blood culture leads to additional laboratory tests, unnecessary antibiotic use and longer hospitalization of patients that increases the patients care costs. This study was done to assess the role of CONS in blood culture in relation to clinical profile and laboratory indices of patients showing blood culture positivity. This study was conducted in the Department of Microbiology, JNMCH, Aligarh over a period of 4 months. All samples submitted to Enteric lab for blood culture were screened. All isolates were identified by standard biochemical techniques and antimicrobial sensitivity was determined by Kirby Bauer disc diffusion method as per CLSI guidelines. Clinical history was taken based on preformed Proforma in all samples tested positive for CONS. A total of 1532 samples were obtained in 4 months for blood culture of which 208 (13.6%) showed growth on culture. CONS were isolated in 23 (11.1%) and *S. aureus* in 11.6%. CONS were considered true pathogens of blood stream infections in only 8 patients (34.78%). In vast majority (65.2%), they were considered mere contaminants. Oxacillin resistance was noted in 7 out of 8 positive isolates while among the 15 contaminants, 13 were oxacillin resistant. All isolates were uniformly sensitive to vancomycin. CONS are important isolates in blood culture but they can be contaminants also. Therefore differentiation of CONS into pathogenic and contaminants is important. Careful evaluation should be done before instituting therapy to avoid unnecessary use of antibiotics.

Introduction

Blood stream infections range from self-limiting infections to life threatening sepsis that requires rapid and aggressive antimicrobial treatment (Gohel *et al.,* 2014). Blood cultures are necessary to establish the diagnosis of bloodstream infections and are useful in directing appropriate antimicrobial therapy (Van der Heijden *et al.,* 2011). Contamination of blood cultures with skin flora, however, poses a substantial problem in the evaluation and management of patients. Because *Coagulase-negative*

Staphylococci (CONS) are the predominant members of the skin flora, they commonly contaminate blood cultures (Berwaldt *et al.,* 1996). CONS have long been regarded as non-pathogenic but their important role as pathogens and their increasing incidence have been recognized and studied in recent years. CONS are by far the most common cause of bacteremia related to indwelling devices (Garcia *et al.,* 2004). Most of these infections are hospital-acquired, and studies over the past several years suggest that they are often caused by strains that are transmitted among hospitalized patients (Huebner and Goldmann, 1990). Other important infections due to CONS include central nervous system shunt infections, native or prosthetic valve endocarditis, urinary tract infections, catheter associated peritonitis, cerebrospinal fluid shunt infections in neonates, especially when they are premature and endophthalmitis. They are also common opportunistic pathogens in patients who are immunocompromised (Archer and Climo, 2005). Intravenous treatment of systemic infections is usually required because CONS have become increasingly resistant to multiple antibiotics. CONS isolated from blood culture are usually contaminants but are also a significant cause of bacteremia. CONS still remain the most common contaminants in blood cultures although there is a relative increase of CONS infections including bloodstream infections in recent years (Souvenir *et al.,* 1998).

Because of their low virulence, they may not evoke sufficient inflammatory response and thus a number of patients with coagulase negative staphylococcal bloodstream infection may not have typical clinical manifestations and laboratory indices of infection. How often the coagulase negative staphylococci isolated from blood cultures are true pathogens of bloodstream infections

and how often are they mere blood culture contaminants? False positive blood culture leads to additional laboratory tests, unnecessary antibiotic use and longer hospitalization of patients that increases the patients care costs. This study was done to assess the role of *Coagulase Negative Staphylococcus* species in blood stream infections.

Material and Methods

This study was conducted in the Department of Microbiology, JNMCH, Aligarh over a period of 4 months from June 2014 to September 2014. Samples were collected using strict aseptic precautions and inoculated immediately in BHI broth and were plated on 5–10% sheep blood agar and teepol lactose agar after 24 and 48 hours of incubation. The negative result was followed-up by examining the broth daily and doing a final subculture at seventh day. All isolates were identified by standard biochemical techniques (Collee et al., 2006). Antimicrobial sensitivity was determined by Kirby Bauer disc diffusion method as per CLSI guidelines (2014) for the following antimicrobials: amikacin (30µg), oxacillin (1µg), clindamycin (2µg), azithromycin (15µg), gentamicin (10µg), ofloxacin (30 µg) and vancomycin (30µg).

Clinical data, laboratory indices, microbiological parameters and patient characteristics were analyzed on the basis of a predesigned questionnaire in 23 patients who had pure growth of *Coagulase Negative Staphylococci* in their blood cultures. Essential criteria for classification of CONS as true pathogens included (presence of ≥ three)

1. Fever > 100°C
2. TLC >12000
3. Septic appearance

4. Systolic BP <90
5. > 48 hours of hospital admission
6. Presence of any of the risk factors (long-term intravascular catheterization, immunosuppressed patients with central lines, peritoneal dialysis or hemodialysis patients, and patients with extensive postsurgical infections with CONS (Souvenir *et al.,* 1998).

Result and Discussion

Blood culture is a routine procedure for investigating the cause of fever or suspected infection in the majority of hospitalized patients. Isolation of a true pathogen from blood culture is important. For a clinical microbiologist, interpretation of the significance of isolated CONS from blood culture is complex. Gram-positive organisms predominate among contaminants and tend to be multidrug resistant, with many being susceptible only to vancomycin. In patients predisposed to nosocomial or iatrogenic infection, empiric use of vancomycin following reports of gram-positive cocci in blood cultures is common.

In the present study, blood culture positivity was seen in 208 of 1532 (13.6%) cases which is quite similar to Gohel *et al.,* (2014); China and Gupta, (2013); Garg *et al.* (2007) and Mehta *et al.* (2005). However Kamga *et al.,* (2011); Kavitha *et al.,* (2010) and Roy *et al.,* (2002) noted higher blood culture positivity in their studies. Low incidence in our study may be because ours is a tertiary care hospital. Most patients are referred from nearby villages and had already taken treatment before they come to the hospital.

The most frequent pathogen isolated from blood was *Klebsiella* species 90 (43.3%) followed by *S. aureus* 24 (11.6%). *Pseudomonas* species in 20 (9.2%),

Acinetobacter species 19 (9.1%), *Citrobacter species* 15(7.2%) (Figure 1). CONS were isolated in 23 (10.6%) cases. CONS are frequently isolated from blood cultures and are emerging as important nosocomial pathogen. Most of the patients (95.7%) in whom CONS were isolated were of paediatric age group. CONS was isolated in 4.5% of cases in study by Gohel *et al.,* (2014) and among 4% cases by van der Heijden *et al.* (2011). Reported isolation of CONS was 20.16% (Arora and Devi, 2007); 33% (Akpaka *et al.,* 2006); 42% (Karlowsky *et al.,* 2004) and 16.5% (Roy *et al.,* 2002). Colonization of body surfaces by CONS and poor venepuncture techniques may contribute to the high prevalence of CONS in blood cultures.

Out of 23 patients with CONS isolates in their blood culture, 15 (65.2%) were males and remaining 34.8 % were females. Van der Heijden *et al.* (2011) found 56% of the patients were males.

Ascertaining the clinical significance of an isolate of CONS from blood culture is difficult. CONS were considered true pathogens of blood stream infections in only 8 patients (34.78%) on the basis of criteria discussed above. In vast majority (65.2%), they were considered mere contaminants (Figure 2). Bodonaik and Moonah (2006) reported 73.3% CONS isolates in the study as blood culture contaminants.

Among the 8 patients considered to have CONS as true pathogens in their blood culture fever was present in 7 (87.5%), septic appearance in 5 (62.5%) and raised TLC in 4 (50%) (Figure 3). Seven out of 8 significant CONS isolates were hospital acquired (Figure 3).

Oxacillin resistance was noted in 7 out of 8 positive isolates while among the 15 contaminants, 13 were oxacillin resistant

(Figure 2). The majority (68.6%) of the CONS isolates were methicillin-resistant in study by Rahman et al. (2013). The high levels of resistance to methicillin and empirically applied anti-staphylococcal penicillins and cephalosporins in CONS are well documented (Ben Jemaa *et al.,* 2004; Huang *et al.,* 2003; Raad *et al.,* 1998; Cercenado *et al.,* 1996). Multidrug resistance was found among 6 (75%) out of 8 significant isolates (Table 1). None of the isolate showed resistance to vancomycin in present study (Table 1). Similar findings were found by Akpaka et al. (2006). The heavy use of antibiotics like vancomycin may select for multiple-resistant commensal organisms such as methicillin resistant *S. epidermidis* (MRSE). Sensitivity against cephalosporins is not done as per CLSI guidelines because oxacillin resistant strains are also resistant to other β lactum antibiotics including cephalosporins.

**Table.1** Sensitivity pattern of 8 significant CONS isolates

| Antibiotics CONS isolates	Amika-cin	Gentamyc-in	Oxacill-in	Vanco-mycin	Azithr-omycin	Clindam-ycin	Ofloxac-in
I	S	S	S	S	S	R	S
II	R	R	R	S	R	R	R
III	S	S	R	S	S	S	S
IV	R	R	R	S	R	S	S
V	S	S	R	S	R	R	R
VI	R	R	R	S	R	R	R
VII	S	S	R	S	R	R	R
VIII	S	S	R	S	R	R	R

Figure.1 Microorganisms (n = 208) isolated from blood culture
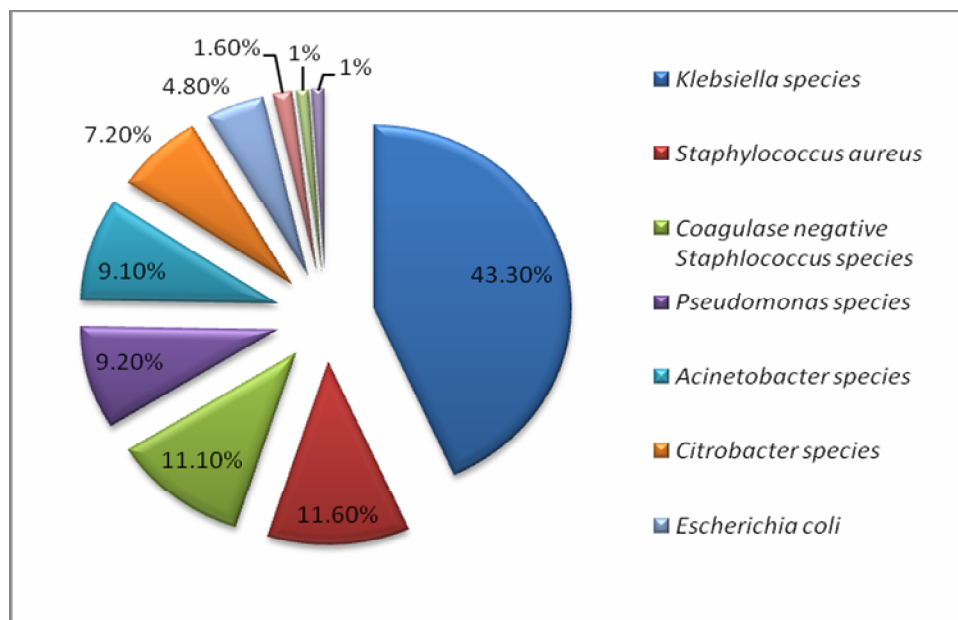
Figure.2 Clinical significance of CONS isolated from blood cultures along
with their sensitivity to oxacillin
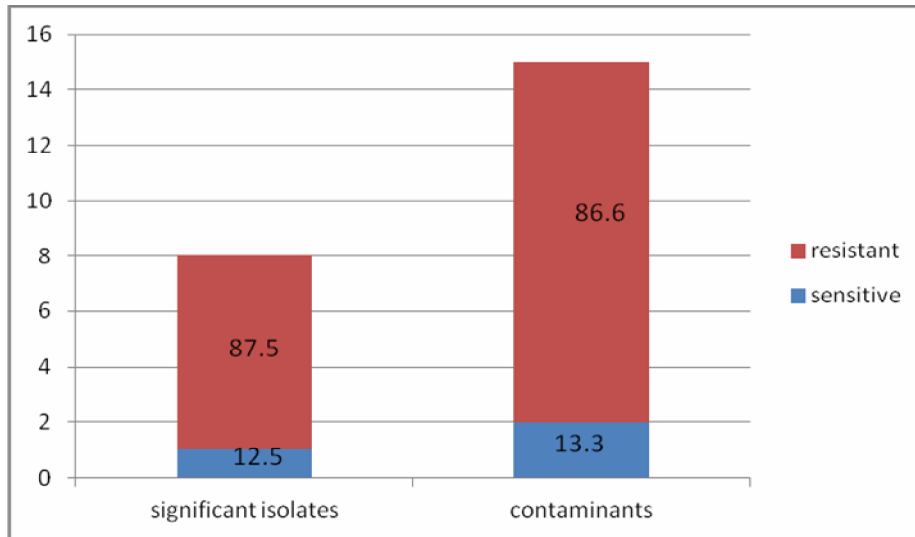
Figure.3 Essential criteria noted in significant CONS isolates (n=8)
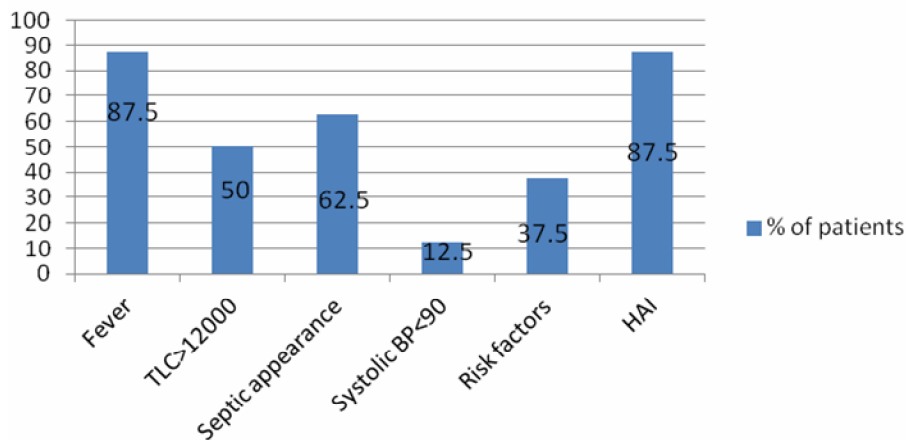
Amikacin and Gentamycin resistance was found among 3 (37.5%) significant isolates each while Clindamycin and azithromycin resistance was found among 6 (75%) significant isolates.

Blood culture contamination is problematic; it can lead to unnecessary and costly treatment. CONS are important isolates in blood culture but they can be contaminants too. Therefore differentiation of CONS into pathogenic and contaminants is important. The high prevalence of CONS is mostly attributable to skin contamination. The practice of proper venepuncture and hand-washing techniques by medical staff are recommended to circumvent the difficulty of interpreting blood cultures. Careful evaluation should be done before instituting therapy to avoid unnecessary use of antibiotics.

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