

Species distribution and clinical profiles of coagulase-negative staphylococci (CoNS) isolated from blood cultures among paediatric patients in Hospital Kuala Lumpur

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ABSTRACT

Introduction: Coagulase-negative staphylococci (CoNS) is often considered as a culture contaminants but it can potentially be pathogenic to patients with risk factors. A combination of species identification and clinical criteria has been suggested in determining true CoNS bacteraemia. **Objectives:** To identify the species distribution, antibiotic susceptibility patterns and clinical profiles of CoNS isolated from blood cultures among paediatric patients in Hospital Kuala Lumpur (HKL).

Methods: This study involved CoNS isolation from blood cultures of paediatric in-patients of the Paediatric Institute HKL. Isolates were identified to species level using Analytical Profile Index Staph identification strips and antimicrobial susceptibility pattern following Kirby-Bauer Disc Diffusion method. The clinical profiles of patients were obtained from their medical records.

Results: Eleven CoNS species were identified from 148 isolates. *Staphylococcus epidermidis* was the most frequent species isolated (67.6%). The majority of the isolates showed resistance to penicillin (85.8%); while 70.3% were methicillin-resistant (MR) CoNS, which demonstrated a significant association with true infection ($p=0.021$). Predictors for significant CoNS infection included thrombocytopaenia, presence of predisposing factors, nosocomial infection, blood collected from peripheral vein, and CoNS isolated from two consecutive blood cultures. The most common predisposing factors for the isolation of CoNS were the presence of peripheral (54.1%) and central venous catheters (35.1%).

Conclusion: CoNS can cause significant bloodstream infections. The isolation of CoNS from blood cultures should be carefully interpreted by considering the predictive factors. Local data regarding predictive factors of patients with culture-positive CoNS, species distribution and antimicrobial susceptibility pattern are useful to determine the significance of blood culture results and care management of patients.

KEY WORDS:

Coagulase-negative staphylococci; CoNS; Methicillin-resistant coagulase-negative staphylococci; MRCoNS; paediatric patients

INTRODUCTION

Staphylococcus is a Gram-positive cocci species of Staphylococcaceae family. Based on its ability to produce free coagulase for the coagulation of plasma, this bacterium can be divided into two groups: coagulase-positive staphylococci and coagulase-negative staphylococci (CoNS).¹ The main interest of this study is CoNS, which are non-motile, non-spore-forming and catalase-positive facultative anaerobes.²

Coagulase-negative staphylococci cause a broad range of infection types in humans, which include bacteraemia, surgical site infections and foreign body infections.^{3,4} Bacteraemia or bloodstream infection of CoNS is the most common type of infection encountered in humans.⁵ Infection of CoNS is more likely to occur among population of high-risk groups, such as patients having immunosuppression, patients who are dependent on medical devices or indwelling catheters, and patients with foreign body placements; all of which include transplant patients, neutropenic patients, burn patients and neonates.⁶ *Staphylococcus epidermidis* is the most common species isolated from humans because this bacterium species is a permanent, ubiquitous coloniser of the human skin.⁷

Although it is well known that most CoNS infections are hospital-acquired and associated with the use of medical devices, diagnosis for true infection of CoNS remains a challenge. This is because CoNS are most commonly found as blood cultures contaminant,⁸ since they are normally harmless commensal flora of the human skin, interfering in accurate interpretation of blood culture. In addition, clinical manifestations of CoNS sepsis can be subtle and are often non-specific. These factors contribute to difficulties in differentiating CoNS as true infection from colonisation or contamination.⁹

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Coagulase-negative staphylococci are normally treated with the use of antibiotic. However, CoNS have unique characteristics that can build resistance towards multiple antimicrobial agents, in which they are used to treat *Staphylococci* infection,¹⁰ thus leading to the emergence of methicillin-resistant coagulase-negative staphylococci (MRCoNS). Currently, there are limited treatment options for CoNS infections, as the majority of CoNS isolates are MRCoNS. Methicillin-resistant coagulase-negative staphylococci infections require treatment with the glycopeptide group, such as vancomycin.

Among the general population (adults and paediatric) in Malaysia the incidence of CoNS bacteraemia is up to 33%, with higher incidence rate among the paediatric population, reportedly up to 42.9%.¹¹ Additionally, most neonatal septicemia in Malaysia is contributed by CoNS, with a prevalence rate of 43.5%.¹² A systematic review and data analysis from developing countries (including Malaysia) showed that CoNS (17%) was the third most common group of causative agents isolated from patients with nosocomial bacteraemia, including paediatric patients as well as neonates.¹³ Coagulase-negative staphylococci, especially *S. epidermidis*, was the most common pathogen isolated from blood cultures in neonates, with nosocomial infection rates in Hospital Kuala Terengganu and Hospital Universiti Sains Malaysia of 43.3% and 27.7%, respectively.¹⁴

To date, there are more than 40 species of Staphylococci that make up CoNS; however, only about half of these species have been isolated from humans.⁷ Identification of CoNS species is important, as it can assist in determining the significance of the isolates. This is because misclassification of CoNS as being significant will lead to the misuse of vancomycin and contribute to the emergence of vancomycin-resistant organisms. On the other hand, misclassification of CoNS as contaminants may downgrade the patient's care management and lead to other nosocomial infections.

The aim of this study is to determine the species distribution of CoNS, their antibiotic susceptibility patterns and the clinical profile of the paediatric patients when the CoNS were isolated from their blood cultures. Data regarding species distribution, antimicrobial profile of CoNS and underlying risk factors of patients are useful and can influence clinical decision regarding the significance of CoNS isolates.

MATERIALS AND METHODS

A descriptive cross-sectional study was conducted for this research over a 1-year period, from 1st of January 2015 to 31st of December 2015. A prospective study approach was used via a non-randomised sampling method, wherein a total of 148 suitable isolates were selected for this study. All samples used in this study were CoNS isolates recovered from the blood culture bottles in the Microbiology Laboratory of HKL. Only CoNS isolates from positive blood culture bottles were selected, in which the blood was withdrawn from either percutaneous veins or catheters of patients aged between day

1 of life and 15 years old. CoNS isolates with untraceable clinical records, duplicate CoNS sample from the same patient, and isolates inoculated from blood originated from other sterile sites, such as cerebrospinal fluid and peritoneal dialysis fluid blood, were excluded from this study. All positive blood culture bottles belonged to the paediatric inpatients of Paediatric Institute HKL. Isolates that were recovered from blood samples sent from other referral hospitals were excluded.

Phenotypic identification of an isolate was confirmed based on the coagulase reaction and a series of biochemical reactions from the API Staph system (bioMérieux, France).

Antimicrobial susceptibility testing was performed on all isolates by the Kirby-Bauer Disc Diffusion method towards 12 antibiotics, as shown in Table II, which included: penicillin, cefoxitin, vancomycin, teicoplanin, gentamicin, erythromycin, clindamycin, trimethoprim-sulfamethoxazole, chloramphenicol, rifampin, linezolid, and fusidic acid. Following an overnight incubation, the diameter of the inhibition zone was measured and interpreted as susceptible, intermediate or resistant by referring to the current Clinical and Laboratory Standards Institute (CLSI) Guidelines 2015 and European Committee on Antimicrobial Susceptibility Testing (EUCAST) Guidelines 2015 (for fusidic acid). In this study, the zone of inhibition for vancomycin disc was interpreted according to the 2008 CLSI Guidelines.

The clinical characteristics were broadly divided into three major categories in the *pro forma*: sociodemographic, clinical and laboratory parameters. The clinical and laboratory parameters, such as blood pressure, temperature, white cell count and platelet count, were interpreted based on the different cut-off point values following the age group of the patients. The identified risk factors for the isolation of CoNS from blood cultures included blood vessel catheterisation, prematurity (born at less than 37 weeks of gestational age), low birth weight (less than 2,500 gram),¹⁵ underlying immunosuppression (e.g., steroid therapy, underlying malignancy, retroviral disease, or primary immunodeficiency disease) or administration of total parenteral nutrition.^{16,17} Nosocomial-acquired was defined as isolates that were positive from blood cultures taken 48 hours or more after hospital admission, while community-acquired was defined as isolates that were positive from blood cultures taken less than 48 hours after hospital admission.⁸ The source of a blood sample was defined based on the site from which the blood was withdrawn, whether percutaneously (also termed peripheral) or from the lumen catheter.

The species identification, antimicrobial susceptibility testing results, as well as data collected from the *pro forma* were entered into the Statistical Program for Social Sciences (SPSS) version 22 for analysis. The Chi-square test or Fisher's exact test were used to evaluate the association between two categorical variables, where a p-value of less than 0.05 was considered significant.

Table I: Species distribution of CoNS isolated from the blood cultures of paediatric patients in the Paediatric Institute of Hospital Kuala Lumpur

CoNS species isolated	N	(%)
Staphylococcus epidermidis	100	67.6
Staphylococcus hemolyticus	15	10.1
Staphylococcus warneri	9	6.1
Staphylococcus xylosus	6	4.1
Staphylococcus chromogenes	4	2.7
Staphylococcus capitis	4	2.7
Staphylococcus hominis	3	2.0
Staphylococcus cohnii	3	2.0
Staphylococcus saprophyticus	2	1.4
Staphylococcus lugdunensis	1	0.7
Staphylococcus sciuri	1	0.7
Total	148	100%

Table II: Antibiotic susceptibility patterns of 148 CoNS to 12 antibiotics

Antibiotics	Antibiotic amount (ug)	Sensitive N (%)	Resistant N (%)	Intermediate N (%)
Linezolid	30	148 (100)	0 (0)	0 (0)
Teicoplanin	30	148 (100)	0 (0)	0 (0)
Vancomycin	30	148 (100)	0 (0)	0 (0)
Chloramphenicol	30	126 (85.1)	22 (14.9)	0 (0)
Rifampin	5	109 (73.6)	38 (25.7)	1 (0.7)
Trimethoprim-Sulfamethoxazole	1.25/23.75	89 (60.1)	53 (35.8)	6 (4.1)
Clindamycin	2	84 (56.8)	62 (41.9)	2 (1.4)
Gentamycin	10	78 (52.7)	69 (46.6)	1 (0.7)
Fusidic acid	10	61 (41.2)	87 (58.8)	0 (0)
Erythromycin	15	48 (32.4)	95 (64.2)	5 (3.4)
Oxacillin	1	44 (29.7)	104 (70.3)	0 (0)
Penicillin G	10	21 (14.2)	127 (85.8)	0 (0)

Table III: Association between MRCoNS and significant infection

CoNS isolates	N = 148	Significant infection		p-value
		Yes	No	
MRCoNS	104	27 (26.0)	77 (74.0)	0.021*
MSCoNS	44	4 (9.1)	40 (90.9)	

*Significant at $p < 0.05$

Note: MSCoNS: Methicillin-susceptible staphylococci

RESULTS

Species distribution, clinical significance and antibiotic susceptibility patterns of CoNS

During the study period, 148 CoNS were isolated from the blood cultures. Table I shows the species distribution of CoNS, with *S.epidermidis* being the most frequent species identified, accounting for 67.6% (n=100). Furthermore, it was found that only 31 of 148 patients with CoNS (20.9%) were treated with anti-staphylococcal antibiotic; while 79.1% were interpreted as doubtful significance isolates by the treating physician.

Table II shows the antibiotic susceptibility pattern of CoNS, with the majority resistant to penicillin and oxacillin by 85.8% and 70.3%, respectively. All isolates were sensitive to vancomycin and teicoplanin.

Of the 31 clinically significant isolates, 27 were methicillin-resistant CoNS (MRCoNS). Statistical analysis showed a significant association between the significant bloodstream infection and MRCoNS ($p=0.021$), as shown in Table III. These 31 patients were clinically diagnosed with sepsis (58.1%), catheter-related bloodstream infection (25.8%) and nosocomial pneumonia (16.1%).

Clinical profiles of patients with culture-positive CoNS

The majority of the CoNS were isolated from the neonatal, medical and oncology wards. With regard to age group, neonates (<1 month old) showed 26.4% of positive isolates. As shown in Table IV, 54.1% of patients had an abnormal temperature (38°C or 36°C), while 11.5% of them were hypotensive. As for the white blood cell count, 43.2% had an abnormal white cell count (leucocytosis or leucopenia), whereas only 31.1% of patients had thrombocytopenia. All these parameter results may indicate true infection and be able to assist in interpreting the significance of blood culture positivity rate. Approximately, 79% of the isolates were collected from the peripheral vein, while the remaining 21% from a venous catheter. Only 19.6% had isolated CoNS from two consecutive blood culture sets in keeping with the rate of clinically significant cultures in this study (20.9%).

It was also found that the majority of patients (81.1%) with culture-positive CoNS had underlying risk factors that predisposed them to infection. Catheterisation was identified as the main risk of acquiring the CoNS infection, with more than 50% coming from intravenous catheter. Of the 148 patients, 29 had CoNS isolated from two consecutive blood

Table IV: Clinical profiles of 148 patients with positive blood culture for CoNS

Clinical profile	All patients, N = 148	(%)
Age		
Neonates	39	26.4
General paediatric	109	73.6
Wards distribution		
Medical	43	29.1
Surgical	13	8.8
PICU and HDW	16	10.8
Oncology	29	19.6
DCU	3	2.0
Neonatal	44	29.7
Abnormal temperature		
Yes	80	54.1
No	68	45.9
Abnormal blood pressure		
Yes (hypotensive)	17	11.5
No	131	88.5
Abnormal white blood cell count		
Yes	64	43.2
No	84	56.8
Thrombocytopenia		
Yes	46	31.1
No	102	68.9
Presence of underlying predisposing factors		
Yes	120	81.1
No	28	18.9
Type of infection		
Nosocomial	96	64.9
Community	52	35.1
Site of blood collection		
Peripheral vein	117	79.1
Arterial or venous catheter	31	20.9
CoNS isolated from two consecutive blood cultures		
Yes	29	19.6
No	119	80.4

Note: PICU: Paediatric Intensive Care Unit; HDW: High Dependency Ward; DCU: Day Care Unit.

Table V: Types of risk factors among 120 patients with predisposition for CoNS

Risk factors	All patients, N = 148	(%)
Peripheral venous catheter	80	54.1
Arterial catheter	19	12.8
Central venous catheter	52	35.1
Received total parenteral nutrition	28	18.9
Underlying immunosuppressive condition	21	14.2
Low birth weight	28	18.9
Premature birth	27	18.2

Note: The percentage above is based on 148 total patients. The other 28 patients have no risk factor.

cultures, and it was recorded that 20 patients (68.97%) in this group had received antibiotic treatment. The distribution and percentage for other risk factors identified in this study are shown in Table V.

Association between determinant factors and CoNS infection

Statistical analysis showed a significant association between clinical profiles and CoNS infection ($p < 0.05$) for few factors such as predisposing factors, thrombocytopenia, nosocomial infection, site of blood collection and number of blood culture positivity (Table VI).

DISCUSSION

Species distribution of CoNS from blood culture

Staphylococcus epidermidis is reported to be the most common CoNS species isolated from clinical samples, with isolation rates ranging between 35% and 74%, irrespective of their significance status.¹⁸⁻²¹ In this study, the frequency of *S. epidermidis* among CoNS species isolated from blood cultures was 67.6%, which is within the range of other studies. This finding is also in accordance with the report from one local study, where *S. epidermidis* contributed to approximately 68% of all CoNS isolates.²²

Table VI: Association between determinant factors and CoNS infection

Factors	Significant CoNS			p-value
	N = 148 N (%)	Yes N (%)	No	
Presence of underlying predisposing factors				
Yes	120	30 (25)	90 (75)	0.012*
No	28	1 (3.6)	27 (96.4)	
Abnormal temperature				
Yes	80	18 (22.5)	62 (77.5)	0.614
No	68	13 (19.1)	55 (80.9)	
Abnormal blood pressure				
Yes	17	7 (41.2)	10 (58.8)	0.051
No	131	24 (18.3)	107 (81.7)	
Thrombocytopaenia				
Yes	46	15 (32.6)	31 (67.4)	0.019*
No	10	16 (15.7)	86 (84.3)	
Abnormal white blood cell count				
Yes	64	17 (26.6)	47 (73.4)	0.143
No	84	14 (16.7)	70 (83.3)	
Nosocomial infection				
Yes	96	25 (27.8)	65 (72.2)	0.011*
No	52	6 (10.3)	52 (89.7)	
Site of blood collection				
Peripheral vein	11	20 (17.1)	97 (82.9)	0.025*
Arterial or venous catheter	31	11 (35.5)	20 (64.5)	
CoNS from two consecutive blood cultures				
Yes	29	16 (55.2)	13 (44.8)	0.000*
No	119	15 (12.6)	104 (87.4)	

In the past decades, *S.epidermidis* and other CoNS species have been established as the predominant commensals inhabiting the human skin and mucosal membranes albeit the low pathogenic potential among immune-competent humans. *S.epidermidis* has also been associated with being the most common CoNS species causing persistent bacteraemia among neonates^{23,24} and the predominant organism colonising the gastrointestinal tracts in children.²⁵ The identification of individual CoNS species is important, as certain CoNS species are associated with different types of infections. The identification of *S.epidermidis* is one of the important keys in determining the significance of CoNS isolated from human samples.²⁶

The reason for *S.epidermidis* having the highest frequency of isolation from human samples compared to other CoNS species is probably because this bacterium possesses several virulence factors, such as its ability to form biofilms, adherence to medical devices via surface adhesion proteins (also known as biofilm-associated protein, or Bap), and secretion of toxins, such as delta toxin and cytolysin. Its ability to form biofilm prevents this organism from being destroyed by the host defence mechanisms or antimicrobial agents.²⁷ As such, *S.epidermidis* has become ubiquitous in nature and is able to colonise or infect humans.

Blood culture is well established as the gold standard to diagnosing bacteraemia. However, false positivity may occur if the blood sample is contaminated by bacteria such as *Micrococcus*, *Corynebacterium* and *Propionibacterium* species.^{28,29,30} Many studies have reported that these normal flora can be potentially pathogenic.²⁹ The isolation of CoNS from blood sample represents a continuous dilemma for both the clinical microbiologist and clinician in the interpretation

of their significance status. Although many studies have reported an increasing number of significant CoNS infections, this organism is still regarded as the most common blood culture contaminant³⁰ based on the clinical evaluation of clinicians. In the present study, 79.1% of CoNS were regarded as contaminants based on the clinical evaluation of the physician. Other studies have reported that the contamination rates by CoNS were approximately between 60% and 65%.^{26,31} The lack of a universally accepted, gold standard definition to distinguish the clinical significance of CoNS from contaminants may have contributed to the variation in percentage of blood culture contaminants, as different studies utilised different criteria. A systematic review has documented several factors that might influence the high contamination rate of blood cultures. These included blood cultures collected from an intravascular catheter, the use of non-sterile gloves, no exchange of needles between venepuncture and inoculation of blood culture bottles, and staff incompetency.^{28,32}

Antibiotic susceptibility pattern of CoNS

This work showed that 85.8% of the isolates were resistant to penicillin G. This result is slightly lower than that in a study conducted in Universiti Kebangsaan Malaysia Medical Centre (UKMMC), where 98.7% of the CoNS isolates were resistant to penicillin G.²² This might be due to the large number and various types of samples included in their study compared to the ones utilised in this research. A study performed in one of the tertiary care centres in India showed that 100% of CoNS isolated from various clinical samples were resistant to penicillin G.⁷ This high rate of penicillin resistance is not surprising, as CoNS have been known to be inherently-resistant to penicillin.²²

Approximately 70% of the CoNS in this study were resistant to methicillin (MRCoNS); this percentage is higher compared to the national data of only 52%.³³ Another local data from UKMMC also reported a different percentage, where approximately 58% of their CoNS species were MRCoNS.²² The percentage in this study was more similar to the local data from Hospital Universiti Sains Malaysia, where 68.6% of MRCoNS prevalence was reported.³⁴ MRCoNS exhibit similar resistance mechanisms with methicillin-resistant *Staphylococcus aureus* (MRSA) via the expression of an additional penicillin-binding protein designated as PBP2a, which is encoded by the *mecA* gene located on the staphylococcal cassette chromosome (SCC). This mobile genetic element is easily transferred among other bacterial species, especially in bacteria that colonise the hospital environment. This has contributed to the increased frequency of MRCoNS. The findings of this study also revealed that most CoNS were nosocomial in origin (64.9%); this supports previous reports that MRCoNS are more common among isolates of hospital-associated infections.⁵

All CoNS isolates in this study showed 100% susceptibility towards vancomycin and teicoplanin; this finding is in accordance with studies reported in India,⁷ United States²¹ and Israel.³⁵ Local data from UKMMC also reported that none of their CoNS was resistant to vancomycin.²²

Statistical analysis of data in this study confirmed the association between the presence of MRCoNS and significant infection (p -value = 0.021). The findings of this research are consistent with a study conducted in Italy, in which they found that the isolation of methicillin-resistant strains (p -value = 0.008) was more common among patients with significant CoNS isolates.³⁶

Clinical profiles of patients with positive blood culture for CoNS

In the present study, 26.4% of CoNS were isolated from neonates. The results also showed that CoNS were mainly isolated from the following three wards: neonatal, general medical and oncology. Neonates are known as the most predominant population implicated by CoNS infections. A local study from University Malaya Medical Centre (UMMC) showed that 50% of blood culture isolates from neonatal wards belonged to CoNS.¹¹ The importance of CoNS among neonates was also evident in a study done in United Kingdom, which reported that 80.5% of blood culture isolates from their NICU consisted of CoNS.³⁷ Statistical analysis from a study in the United States found that neonates (p = 0.002) and patients on immunosuppressive agents (p < 0.001) have significant potential risk factors for CoNS bloodstream infection (p -value=0.002).¹⁶ In susceptible patients, CoNS may serve as contaminants and, therefore, represent significant clinical isolates. A blood culture may be contaminated by the normal flora of the human skin during venepuncture. Neonates and oncology patients are vulnerable to infections due to their immature and defective immunity. In addition, oncology patients are likely to have chemoports or other intravenous catheters attached to them. Out of 148 patients with positive-culture CoNS, 120 were identified to have underlying predisposing factors for CoNS infections, with majority of them that had undergone blood vessel

catheterisation. Catheters play a significant role in CoNS colonisation, which may subsequently lead to bloodstream infections. All these factors can contribute to the high percentage of CoNS isolation from their blood culture samples.

Several patient groups (e.g., haematology-oncology patients, neonates and the elderly) and factors are associated with higher risks for CoNS infections. In the present study, 120 patients were identified to have underlying predisposing factors for CoNS infections. The most common risk factor identified in this study population was the presence of a peripheral intravenous line (54.1% of patients). The majority of patients with clinically significant CoNS (30 patients) had an underlying predisposing factor for CoNS infection. From the literature, the underlying predisposing factors for CoNS included extremely premature infants born at less than 31 weeks of gestational age, and infants with birth weight less than 1,500 gram.¹⁷ Another study showed that parenteral nutrition is also one of the significant risk factors associated with CoNS bloodstream infection.¹⁶

Association between determinant factors and CoNS infection

Statistical analysis in the present study showed that the presence of underlying predisposing factors (p =0.012), thrombocytopenia (p =0.019), nosocomial infection (p =0.011), site of blood collection (p =0.025), and CoNS isolated from two consecutive blood cultures (p <0.0001) were significantly associated with CoNS infection (p -value < 0.005). These findings are consistent with several previous studies.^{23,26,34}

Khashu et al. (2006) found that thrombocytopenia is more likely to occur among neonates with persistent CoNS bacteraemia.²³ In agreement with this, this study showed that thrombocytopenia is significantly associated with CoNS infection (p =0.019). Coagulase-negative staphylococcus is an important organism implicated in nosocomial infections. Nosocomial infections can be another predictor to assist in the determination of significant CoNS infection. This was demonstrated by a study in Spain, where a statistical analysis confirmed that nosocomial infections were a significant predictor for true CoNS bacteraemia (p <0.05).²⁶

Another determining factor is the number of positive cultures. The greater the number of bottles that are positive for CoNS, the more likely it represents significant isolates. A study conducted in a teaching tertiary care centre in India from 2013 through 2014 found that 46% of repeated CoNS isolates were significant.³⁸ A local study from the northern region of teaching hospital highlighted that the occurrence of more than one positive blood culture with similar species and antibiogram pattern serve as a screening tool for true bacteraemia, while positive culture from more than two different blood culture sets will further increase the probability of true bacteraemia.³⁴ Therefore, it is recommended to repeat blood cultures among high-risk patients in determining the significance status of CoNS isolates in order to prevent the misuse of antibiotics that will lead to the emergence of multi-drug resistance bacteria.

CONCLUSION

This study revealed that *S.epidermidis* is the most predominant CoNS species isolated from blood cultures. The majority of the isolates were MRCoNS (70.3%) and none was resistant to vancomycin. Only 21% of CoNS were treated as significant isolates following a clinical evaluation by the physician, and this was supported by poor evidence of infection exhibited by the patients, wherein only 10% to 50% had abnormal laboratory parameters and clinical features suggestive of infection.

The isolation of CoNS from blood cultures needs to be interpreted with caution, as it affects the illness(es) of the patients and management. For example, if all CoNS isolates were to be considered as contaminants, certain significant CoNS infections will be left untreated, and this may lead to devastating complications. On the other hand, a misinterpretation of CoNS being significant may result in the unnecessary use of antibiotics, especially vancomycin, thus contributing to vancomycin-resistant *Staphylococci*. *S.epidermidis* is one of the predictors for significant CoNS bacteraemia. Other predictors for significant CoNS isolates include the presence of thrombocytopenia, positive culture from peripheral venous sample, isolation from two consecutive blood cultures, MRCoNS, and nosocomial infection. Finally, a gold standard guideline should be established to distinguish contaminants and significant isolates.

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