

Incidence of Nosocomial Blood Stream Infection (BSI) in Intensive Care Units (ICUs) in Cairo and Beni-Suef University Hospitals

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Abstract: Background: Nosocomial infections (NCIs) are more frequently encountered in ICUs than in other hospital areas and represent a major socioeconomic burden. **Aim of the Work:** The current study aimed to evaluate the rate of nosocomial blood stream infections (BSIs) in both the adult and neonatal ICUs, the causative microorganisms, antimicrobial resistance, outcome of infection, risk factors, and to identify the most common isolates with molecular detection of the resistance gene. **Methods:** One thousand and ninety one patients (adults & neonates) admitted to the ICUs during the one year study period (March 2011 till February 2012) were monitored daily and those who were suspected to develop nosocomial BSIs, according to the criteria stated by the CDC, were selected for enrollment in the present study. Blood cultures were done and positive blood culture samples were subjected to colony identification to detect the causative organisms and antibiotic susceptibility testing for isolates. Detection of extended spectrum beta – lactamase producers (ESBLs) was conducted among Gram negative isolates by a screening test and confirmed by double-disc synergy test (DDST). *Coagulase negative staphylococci (CoNS)* isolates were tested by PCR for detection of *mecA* gene as they were the most common isolates in all ICUs. Two hundred and fifty intravenous catheters (IVCs) were collected and cultured by the standard quantitative catheter segment method to detect primary BSIs. **Results:** Out of the 1091 patients 117 had nosocomial BSIs. The rate of nosocomial BSI was 10.7% with the highest percentage in the NICU (29.9%), followed by the adult ICU of Beni-Suef University Hospital (10.6%) and the lowest rate was recorded in the adult ICU of Cairo University Hospital (5.8%). Out of those positive cases, 46 patients died representing a crude mortality rate of 39% (highest mortality rates were observed with *CoNS* infections). Analysis of the isolated organisms showed that Gram positive organisms were reported in 84 isolates (62.2%); *CoNS* was the most prevalent (37%) followed by *S. aureus* (12.6%). Gram negative bacilli were reported in 46 isolates (34.1%), where *K. pneumoniae* was the most common (12.6%) followed by *Acinetobacter baumannii* (11.1%). *Candida albicans* was reported in only 5 isolates (3.7%). Concerning antibiotic susceptibility, Gram positive isolates were mostly sensitive to vancomycin (95%), while Gram negative isolates were mostly sensitive to levofloxacin (63%). *CoNS*, the most common strain in different ICUs (n=50), were tested for production of *mecA* gene by antibiotic susceptibility and PCR. PCR results indicated that 66 % (33/50) were *mecA* gene producers while 96% (48/50) were cefoxitin resistant and resistant to other B-lactam antibiotics by susceptibility testing. Regarding the 250 IVCs cultured, 20 (8%) were culture positive and coincided with results of blood cultures. The highest number of isolates was reported from the NICU and *CoNS* was the most common isolate (80%). These cases represent BSI with a primary site at the vascular access catheter insertion point. **Conclusion:** Nosocomial BSIs represent a major problem in ICUs. BSI with multi-drug resistant pathogens (especially *CoNS*) is difficult to treat and associated with increased mortality. Of all available antimicrobial agents, vancomycin is the most active and reliable treatment option, however over-use may lead to emergence of resistance. Therefore, restricting the use of vancomycin, along with implementation of infection control programs are the most effective means for controlling and decreasing BSIs and spread of *CoNS*.

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1. Introduction:

Hospital Acquired Infections (HAIs) are defined as infections occurring 48 hours after hospital admission as a result of complications due to the presence of pathogens not present or incubating at the

time of admission. These infections cause significant morbidity and mortality and have a considerable impact on healthcare costs (*Zingg et al., 2008*). Among all types of HAIs, nosocomial blood stream infection (BSI) creates a serious health problem in hospitals all

over the world. In addition, patients admitted to intensive care units (ICUs) carry an even higher risk of nosocomial BSI than those admitted to other hospital units (*Leibovitch et al., 2005 and Piette&Verschraegen, 2009*).

Data obtained from the National Surveillance Study of Nosocomial Infection in adult ICUs in Barcelona/Spain, shows that BSIs represents 25-30% of nosocomial infections in the ICU, of which 70 % are catheter related BSI (CRBSI) (*Álvarez-Lerma et al., 2007*). Nosocomial BSI is the tenth leading cause of death in the U.S.A, and approximately 250,000 cases of BSI occur in the U.S.A annually (*Wisplinghoff et al., 2004*). In an Egyptian study conducted in member hospitals of the International Nosocomial Infection Control Consortium (INICC) that included adult ICUs and pediatric ICUs, the overall recorded rate was 32.8% and 24.5% respectively concluding that CRBSI in ICUs pose greater threats to patient safety than in industrialized countries (*Rasslanet al., 2012*).

The incidence of neonatal BSI ranges from 1 to 10 cases for every 1,000 infants, with much higher values found in preterm, low birth weight infants admitted to neonatal intensive care units (NICU) (*Bizzaro et al., 2005*).

BSI is considered the seventh leading cause of infant mortality in USA (*Sherry et al., 2012*).

The source of nosocomial BSI varies according to microorganism. *CoNS* and *S. aureus* are commonly associated with CRBSI, whereas Gram negative bacilli are the main cause of BSI following respiratory tract, intra abdominal and urinary tract infections. Most BSIs of unknown origin are caused by Gram-positive microorganisms, mainly *CoNS*, and they may also originate from catheter and not diagnosed at the time of the development of the BSI (*Garrouste-Orgeas et al., 2006 and Valles&Ferrer, 2009*).

Moreover, the increased importance of catheter as a source of BSI has paralleled the increased use of long-term central and peripheral lines for chemotherapy access and for parenteral nutrition (PN). Concomitantly, “sticky” organisms of low virulence, such as *CoNS*, which are capable of adhering to the surfaces of catheter materials, have become more prominent as etiologic agents of BSI (*Michalopoulos et al., 2011*).

The present study aimed at evaluating the rate of nosocomial BSI, causative microorganisms, antimicrobial resistance, outcome of infection, risk factors, and identifying the most common isolates with molecular detection of the resistance gene.

2. Subjects and methods:

1- Study design and patients:

The study was conducted over a period of 12 months (March 2011 to February 2012) at different ICUs (adult ICU of Cairo University Hospital, and both adult and NICU of Beni-Suef University Hospital). All patients (adults & neonates) admitted were monitored daily by the attending physician and those who were suspected to develop nosocomial BSIs according to the criteria stated by *CDC, 2011* which must meet at least one of the following criteria were included in the study. **Criterion 1:** Patient has a recognized pathogen cultured from one or more blood cultures and the organism cultured from blood is not related to an infection at another site. **Criterion 2:** Patient has at least one of the following signs or symptoms: fever (> 38°C), chills, or hypotension and a common skin contaminant (e.g., diphtheroids, *Bacillus* spp., *CoNS*, or micrococci) is cultured from two or more blood cultures drawn on separate occasions.

2- Collection and processing of samples:

a- Blood: 5 to 10 ml of venous blood were collected from adult patients using sterile syringes and inoculated immediately under complete aseptic conditions into bottles containing 50 ml of brain heart infusion broth. In neonates, only 1.5ml of blood was collected into bottles containing 10 ml of brain heart infusion broth (*Koneman et al., 1997*).

b- Intravascular catheter: CVC and PVC were removed when local signs of infection appeared or blood culture was positive and no infection could be detected elsewhere

Processing: Blood samples: Blood culture bottles were incubated aerobically and anaerobically at 37°C for 7 days. The bottles were examined daily for evidence of bacterial growth. Subcultures, using sterile syringes, were done on blood agar, chocolate agar, MacConkey's agar, Sabouraud dextrose agar and Bile Esculin Azide agar daily for 7 days before reporting blood cultures as negative (*Cheesbrough, 2006*).

Catheters samples: About 5 cm of catheter segment was placed in one ml broth then vortexed for a minute. Then, 0.1ml of the suspension was streaked into blood agar plate (*Brun-Buisson et al., 1987*). The plates were incubated aerobically for 72 hours at 35°C; the number of recovered colonies was counted (*Garcia de Viedma et al., 2000*). Microorganisms recovered from plates were fully identified by standard microbiological methods (*D'Amato et al., 1985*). A count of more than 100 CFU per catheter segment is deemed positive (*Mermel et al., 2001*).

3- Microbiological and Molecular examination:

The microbiological and molecular part of this work was done in Medical Microbiology and Immunology Department of Beni-Suef Medical School.

a- Identification of blood culture isolates and catheters cultures were based on colony morphology, Gram staining, biochemical tests such as catalase, coagulase, oxidase, urease. Other tests (optochin and bacitracin) were used for final identification. Germ tube test was used for differentiation of *Candida albicans* from other *Candida* species.

CoNS or other commensal skin flora were considered pathogenic if they were isolated from the two blood cultures. BSI was considered to be catheter-related if both blood and catheter tip cultures showed the same organism.

b- Identification of *ESBLs* was done by screening test of isolates exhibiting reduced susceptibility to one or more of the following third generation cephalosporins: ceftazidime, cefpodoxime, cefotaxime, ceftriaxone or aztreonam. Confirmatory test by Double Disc Synergy test (DDST) followed that step by placing ceftazidime (30µg), cefotaxime (30µg) ceftriaxone (30µg) discs around an amoxicillin/clavulanic acid disc (10µg) at a distance of 30mm center to center. Following an overnight aerobic incubation at 35-37, clearly visible extension of the edge of inhibition zone of any disc towards amoxicillin/clavulanic acid disc was interpreted as phenotypic evidence of *ESBL* production (*CLSI., 2008*).

c- Antimicrobial Susceptibility testing by modified Kirby-Bauer disc diffusion method; (*Koneman et al., 1997*): The following antibiotics were used: for Gram positive bacteria: (Amoxicillin/clavulanic acid, Ceftriaxone, and Cefoxitin, Erythromycin, Amikacin, Gentamicin, Doxycyclines, Levofloxacin, Rifampicin, Vancomycin, Trimethoprim/sulfamethoxazole) and for Gram negative bacteria: (Amoxicillin/clavulanic acid, Ceftriaxone, Ceftazidime, Cefoxitin,

Cefotaxime, Cefoxitin, Imipenem, Amikacin, Gentamicin, Tobramycin, Levofloxacin, Chloramphenicol, Trimethoprim/sulfamethoxazole).

d- Detection of *mec A* gene in *CoNS* isolates by PCR: *CoNS* strains were the commonest between study isolates (n=50). The susceptibility of the isolates to cefoxitin was done as a preliminary screening test for the existence of *mecA* gene, using disc diffusion method (*Cheesbrough, 2006*). Then tested for *mecA* gene by PCR method.

4- Statistical analysis

Data entry and statistical analysis was done using the SPSS version 15. Data were statistically described in terms of mean \pm standard deviation (\pm SD), median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student *t* test for independent samples. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5. *p* values less than 0.05 was considered statistically significant.

3. Results:

Analysis of nosocomial BSIs results:

The current study included 1091 patients who were admitted to different ICUs. 10.7% of those patients developed nosocomial BSIs. The rate of BSIs among different ICUs is illustrated in **table 1**, showing that the highest percentages were in NICU (29.9%) followed by adult ICU of Beni-Suef University Hospital (10.6%) then, adult ICU of Cairo University Hospital (5.8%).

Table (1): BSI rate among different ICUs

ICU	Number of admitted patients	No of positive blood cultures	Rate
ICU-Beni	246	26	10.6%
ICU-Cairo	671	39	5.8%
NICU-Beni	174	52	29.9%
Total	1091	117	10.7%

Out of 117 bloodstream infections, 135 microorganisms were isolated and all were aerobic. Monomicrobial infections were 84.6 % (99/117), while 15.4% (18/117) were polymicrobial (two microorganisms) with a total of 135 isolated organisms. **Table 2** shows types and distribution of isolated microorganisms from different ICUs.

Analysis of these isolates showed that Gram positive organisms were reported in 62.2% (n = 84); *CoNS* was the most prevalent (50/135, 37%), followed by *S. aureus* (17/135, 12.6%). Gram negative bacilli were reported in 34.1% (n = 46). *Klebsiella pneumoniae* was the most common (17/135, 12.6%) followed by *Acinetobacter baumannii* (15/135, 11.1%). *Candida albicans* was reported only in 3.7% (n=5) of isolates. Distribution of microorganisms within different ICUs was variable. *CoNS* recorded the highest number in all ICUs followed by *S.aureus* (24.4%) in Cairo University Hospital ICU, *Acinetobacter baumannii* (26.7%) in Beni-Seuf University Hospital ICU and *K. pneumoniae* (20.3%) in NICU (**Table 2 & Figure 1**).

CoNS strains showed variable existence in different ICUs with the highest percentage in NICU 54% (27/50), followed by ICUs of Cairo University Hospital(ICU-1) 30% (15/50), then ICUs of Beni-Suef University Hospital (ICU-2) 16% (8/50) (**Table 3**).

Crude Mortality: 46/117 patients with nosocomial BSI died, representing a crude in-hospital mortality rate of 39% with a notable variation in the underlying organisms (**Figure 2**). The predisposing risk factors for BSI are summarized in **tables 4&5** which were statistically non significant.

Table (2): Isolated microorganisms and their distribution among different ICUs

	Organism	NO %	ICU			Total NO and % of the organism in all ICUs(n=135)
			ICU-C N=41	ICU-B N=30	NICU N=64	
Monomicrobial	<i>CoNS</i>	No	15	8	27	50
		%	36.6%	26.7%	42.2%	37%
	<i>S.aureus</i>	No	10	3	4	17
		%	24.4%	10%	6.3%	12.6%
	<i>MRSA</i>	No	-	1	5	6
		%	0%	3.3%	7.8%	4.4%
	<i>Viridans Streptococci</i>	No	-	1	3	4
		%	0%	3.3%	4.7%	3%
	<i>Enterococcus spp</i>	No	1	5	1	7
		%	2.4%	16.7%	1.6%	5.2%
	<i>K.pneumoniae.</i>	No	3	1	13	17
		%	7.3%	3.3%	20.3%	12.6%
	<i>Acinetobacterbaumannii</i>	No	3	8	4	15
		%	7.3%	26.7%	6.3%	11.1%
<i>Pseudomonusaeruginosa</i>	No	3	1	3	7	
	%	7.3%	3.3%	4.7%	5.2%	
<i>Pr.mirabilis</i>	No	2	-	-	2	
	%	4.9%	0%	0%	1.5%	
<i>E.coli</i>	No	3	-	2	5	
	%	7.3%	0%	3.1%	3.7%	
<i>Candida albicans</i>	No	1	2	2	5	
	%	2.4%	6.7%	3.1%	3.7%	
Polymicrobial	<i>Acinetobacterbaumannii&CoNS</i>	No	1	1	-	1
		%	2.4%	3.3%	0%	0.7%
	<i>Pseudomonusaeruginosa&CoNS</i>	No	1	1	-	2
		%	2.4%	3.3%	0%	1.5%
	<i>MRSA&CoNS</i>	No	-	1	2	3
		%	0%	3.3%	3.1%	2.2%
	<i>K.pneumoniae.&CoNS</i>	No	-	-	5	5
		%	0%	0%	7.8%	3.7%
	<i>S.aureus&CoNS</i>	No	-	-	1	1
		%	0%	0%	1.6%	0.7%
	<i>K.pneumoniae.&S.aureus</i>	No	-	1	-	1
		%	0%	3.3%	0%	0.7%
	<i>K.pneumoniae.&MRSA</i>	No	-	-	1	1
		%	0%	0%	1.6%	0.7%
<i>K.pneumoniae.&E.coli</i>	No	-	-	1	1	
	%	0%	0%	1.6%	0.7%	
<i>Acinetobacterbaumannii& Candida albicans</i>	No	-	1	-	1	
	%	0%	3.3%	0%	0.7%	
<i>S.aureus&Viridans Streptococci</i>	No	-	-	1	1	
	%	0%	0%	1.6%	0.7%	
<i>Pseudomonusaeruginosa&S.aureus</i>	No	-	-	1	1	
	%	0%	0%	1.6%	0.7%	

NO= total number of isolates in the ICU.

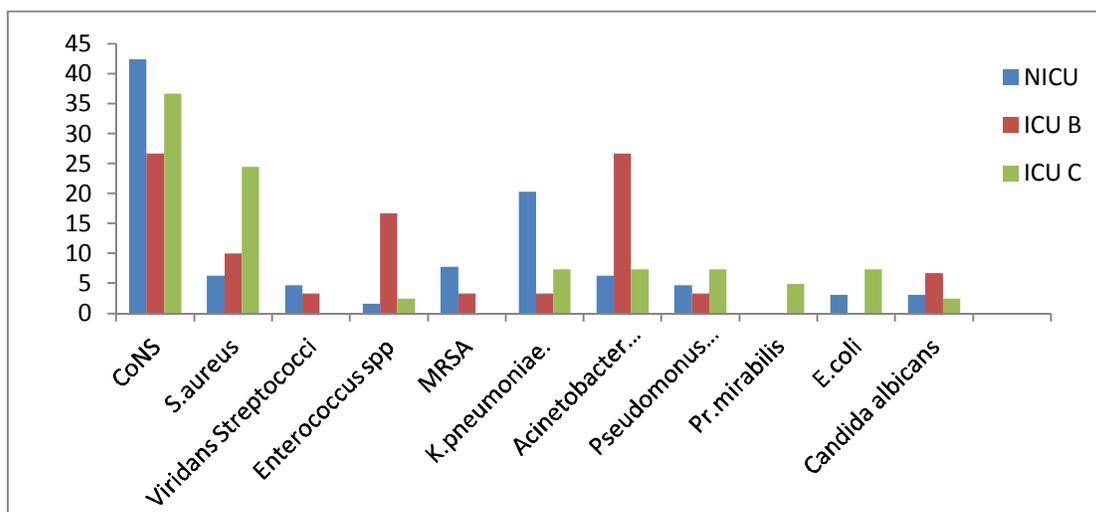


Figure (1): Microorganisms isolated from patients with positive blood cultures in different ICUs

Table (3): Distribution of CoNS in different ICUs

Microorganisms ICU	CoNS	
	NO	%
NICU	27	54
ICU-1	15	30
ICU-2	8	16
Total	50	100

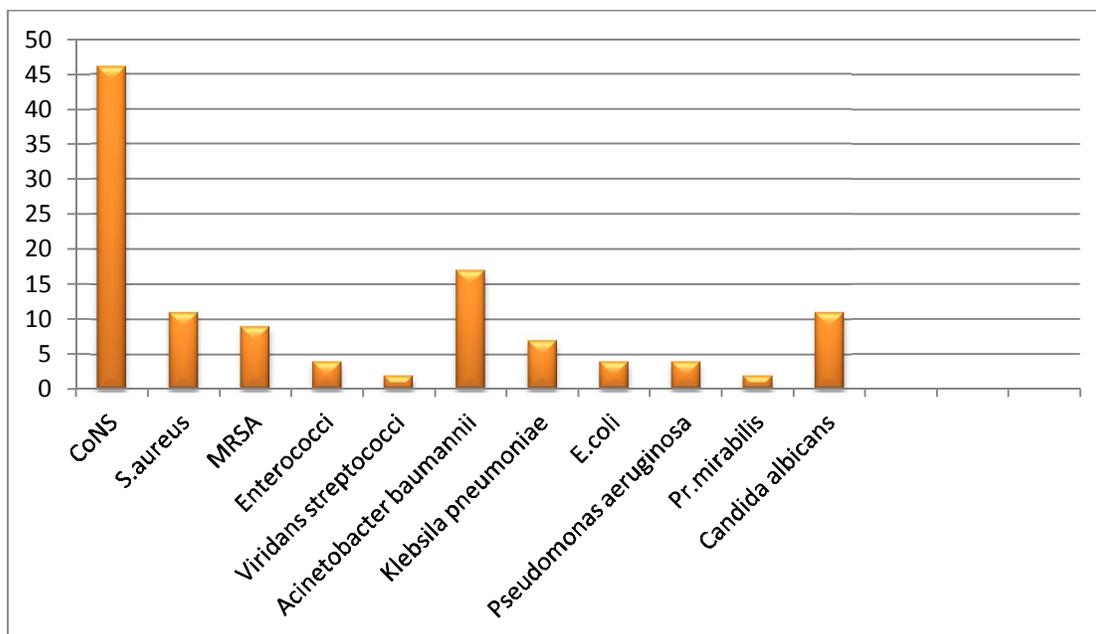


Figure (2): Variation in mortality rate by the organisms causing BSI

Table (4): Results of analysis of potential risk factors for acquisition of nosocomial BSI in adult ICUs

Predisposing factors		BSI in ICU-C		BSI in ICU-B		Total adult ICU BSI		p value
		Frequency n=39	Percent %	Frequency n=26	Percent %	Frequency n=65	Percent %	
Sex	Male	17	44	11	42	28	43	0.202
	Female	22	56	15	58	37	56	
Diabetes	Yes	15	38	8	31	23	35	0.525
	No	24	62	18	69	42	65	
Cardiac	Yes	20	51	9	35	29	45	0.185
	No	19	49	17	65	36	55	
Cancer	Yes	5	13	4	15	9	14	0.769
	No	34	87	22	85	56	86	
Leucocytopenia	Yes	8	21	3	12	11	17	0.539
	No	31	79	23	88	54	83	
Surgery	Yes	5	13	7	27	12	18	0.151
	No	34	87	19	73	53	82	
Renal dialysis	Yes	3	8	4	15	7	11	0.327
	No	36	92	22	85	58	89	
CVC	Yes	35	90	23	88	58	89	0.870
	No	4	10	3	12	7	11	
PVC	Yes	39	100	26	100	65	100	0.217
	No	-	-	-	-	-	-	
Urinary catheter	Yes	30	77	26	100	65	88	0.008
	No	9	23	-	-	9	14	
Mechanical ventilation	Yes	19	49	17	65	36	55	0.185
	No	20	5	9	35	29	45	
Other devices	Yes	6	15	4	15	10	15	1.000
	No	33	85	22	85	55	85	

Table (5): Results of analysis of potential risk factors for acquisition of nosocomial BSI in NICU.

Predisposing factors		BSI in NICU		p value
		Frequency n=52	Percent%	
Sex	Male	37	71	0.765
	Female	15	29	
Cardiac	Yes	2	4	0.285
	No	50	96	
Leucocytopenia	Yes	6	12	0.448
	No	46	88	
CVC	Yes	0	0	1.000
	No	52	100	
PVC	Yes	52	100	0.837
	No	0	0	
Mechanical ventilation	Yes	11	21	0.285
	No	41	79	
Prematurity	Yes	20	40	0.546
	No	30	60	
LBW	Yes	42	81	0.923
	No	10	19	

Antimicrobial Susceptibility testing: Gram positive isolates were mostly sensitive to vancomycin (95%), rifampicin (64%) and doxycycline (40%). However, Gram negative organisms were mostly sensitive to levofloxacin (63%), amikacin (52%) and Amoxicillin/clavulanic acid (48%).

Thirty eight out of 46 (83%) Gram negative isolates were screened for reduced susceptibility to one or more of the following third generation cephalosporins: ceftazidime, cefotaxime and ceftriaxone. They were considered as potential producers of *ESBL* according to the obtained results. On the other hand, 22/46 (52%) of these isolates confirmed to be *ESBL* producers by the DDST (**Table 6**).

Analysis of vascular catheter cultures:

Only twenty out of two hundred and fifty collected catheter samples were culture positive (8%). The distribution of culture positive samples: 3/120 CVC in ICU-1 of Cairo University Hospitals, 5/80 CVC in ICUs of

Beni-Suef University Hospital and 12/50 PVC in NICU of Beni-Suef University Hospital (**Figure 3**). Moreover, 20/117 positive blood culture cases were having a coincident vascular catheter site infection, caused by the same organism isolated from their blood cultures. *CoNS* was the most frequently isolated organism from culture positive catheter samples (16/20 isolates, 80%) and was highest in NICU (45%) as shown in the **table (7)**.

Analysis of *mecA* gene in *CoNS* strains:

50/135 (37%) isolated organisms causing BSIs were *CoNS* that were further investigated by PCR testing for assessment of *mecA* gene production. 33/50 (66%) isolates proved to be *mecA* gene producers. Moreover, 48/50 *CoNS* isolates (96%) proved to be cefoxitin resistant by antimicrobial susceptibility testing (AST). Correlation between the presence of the *mecA* gene and resistance to cefoxitin in *CoNS* strains was not statistically significant (**Table 8 & Figure 4**).

Table (6): Screening and confirmatory tests for ESBL

Organism tested	Screening	DDST
<i>E.coli</i> (5)	5(100%)	4(80%)
<i>K.pneumoniae</i> (17)	15 (88%)	9 (53%)
<i>A.baumannii</i> (15)	12 (80%)	8(53%)
<i>P.aeruginosa</i> (7)	6 (86%)	3 (43%)
<i>Pr. Mirabilis</i> (2)	-(0%)	-(0%)
Total (46)	38(83%)	24(52%)

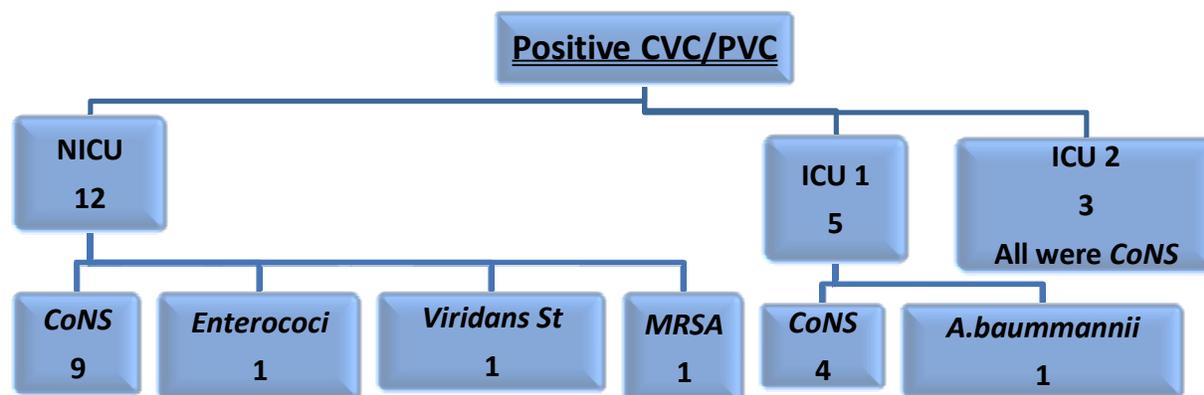


Figure (3): Distribution of organisms from positive catheters culture among different ICUs.

Table (7): Relation between blood and catheter culture' s results regarding the type of organisms

Organism	Positive blood cultures		Positive catheter cultures	
	NO	%	NO	%
<i>CoNS</i>	50	37%	16	80%
<i>S.aureus</i>	17	12.6%	-	0%
<i>MRSA</i>	6	4.4%	1	5%
<i>Enterococc</i>	7	5.2%	1	5%
<i>St. viridans</i>	4	3%	1	5%
<i>K.pneumoniae.</i>	17	12.6%	-	0%
<i>Acinetobacterbaumannii</i>	15	11.1%	1	5%
<i>Pseudomonusaeruginosa</i>	7	5.2%	-	0%
<i>Pr.mirabilis</i>	2	1.5%	-	0%
<i>E.coli</i>	5	3.7%	-	0%
<i>Candida albicans</i>	5	3.7%	-	0%
Total	135	100%	20	100%

Table (8): Comparison of phenotypic expression of methicillin resistance and production of *mecA* gene

MR CoNS N=48	<i>mecA</i> gene		<i>p</i> value
	Positive	Negative	0.876
	33	15	

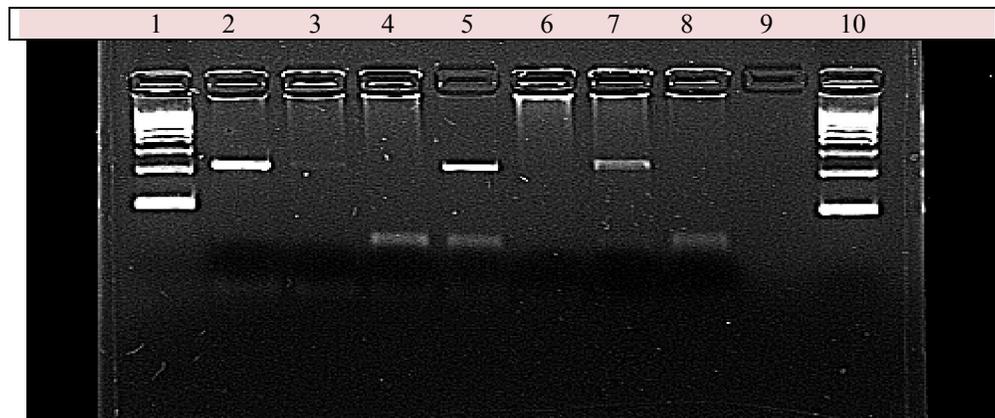


Figure (4): PCR detection of *mecA* gene. Isolates in lanes 5 and 7 were positive, showing bands at 214 kbp, while 3, 4, 6 and 8 were negative. Lanes 1 and 10 show the DNA markers. Lanes 2 & 9 stand for the positive and negative controls respectively.

4. Discussion

Nosocomial BSIs are an important public health concern and have a significant direct socioeconomic impact. Despite advances in antimicrobial treatment, BSI prolongs hospital stay, increases direct patient care costs and directly causes mortality (Klevens *et al.*, 2007).

In the current study, the reported rate of nosocomial BSI was 10.7% with the highest incidence in NICU (29.9 %) showing that neonates are possibly more vulnerable to BSI than adult especially those of LBW and premature. Our finding paralleled that of (Abo-Shadi *et al.*, 2012), who reported that the highest number of cases with nosocomial BSI among different ICUs was shown in NICU (62.6%).

In the present study, there was no significant statistical correlation between the underlying risk factors and BSI in the studied cases. Our finding came in accordance with that of (Zakariya *et al.*, 2012). They stated that the associated risk factors in their study (LBW, mechanical ventilation and prematurity) were not statistically significant in relation to BSI. The results obtained by (Prakash *et al.*, 2011) were supportive. They denoted that cardiac diseases, respiratory diseases and diabetes were not directly responsible for BSI.

A contradictory result was obtained by Biedenbach *et al.*, 2004, Šuljagic *et al.*, 2005 and Gurskis *et al.*, 2009. In their studies, they recorded the presence of a positive correlation between the risk factors and acquisition of BSI in ICUs including

previous administration of antibiotics, mechanical ventilation, the use of nasogastric tube and surgery.

Concerning the type of BSI, most of the cases in this work were monomicrobial (84.6%) while 15.4% were polymicrobial and all isolates were aerobic. Our results came in agreement with the finding of Abo-Shadi *et al.*, 2012 who reported monomicrobial BSI in 98.9% and polymicrobial in 5.2% with no detection of anaerobic isolates.

In the current study, both Gram-positive and Gram-negative bacteria have been isolated from BSI with predominance of Gram positive organisms (62.2%), while Gram negative isolates accounted for only 34.1%. Similar results were obtained by (Ballot *et al.*, 2012).

In contrast, (Kaistha *et al.*, 2009) reported that Gram-negative bacterial strains were more prevalent (69%). This contradiction could be due to change in the demography of BSI in developing countries, the difference in antibiotic policy among different ICUs (Alam *et al.*, 2011).

In the present study, the leading pathogen causing clinically significant nosocomial BSI was *CoNS* (37%), followed by, *S. aureus* (12.6%), *Klebsiellapneumoniae* (12.6%) and *Acinetobacterbaumannii* (11.1%). (Ballot *et al.*, 2012) similarly reported that the percentage of *CoNS* was 19.1% followed by, *Klebsiellapneumoniae* (12.1%) and *Acinetobacterbaumannii* (10.9%). In addition, data published by SCOPE (Surveillance and Control of Pathogens of Epidemiologic Importance) project revealed that the most common pathogens causing

nosocomial BSI in 49 participating USA hospitals from 1995-1998 were *CoNS* (32%) followed by *S. aureus* (16%) (Edmond et al., 1999).

Other studies conducted by Wisplinghoff et al., 2004 and Patel and Saiman, 2010 also confirmed the emergence of Gram-positive pathogens, especially *CoNS*, *S. aureus* and *enterococci* as the dominant organisms in nosocomial BSI.

Within the isolated Gram-positive bacteria, *CoNS* were 60% (50/84), *S. aureus* 20% (17/84) and *Enterococci* 8% (7/84) and others forming the remaining (12%). Our results were in agreement with the finding of Alam et al., 2011. The order of Gram positive isolates was: *CoNS* 63.5% (33/52), *S. aureus* 23.1% (12/52) and *Enterococci* 5.8% (3/52) as causative agents of BSI Bourneton et al., 2010 and Hira et al., 2010 all reached the same conclusion that *CoNS* was the most prevalent organisms. However, Ahmed et al., 2009 found that *MRSA* was the commonest isolate followed by *CoNS* and *Enterococci*. Mehta and coworkers (2005) reported that *S. aureus* was the most common pathogen among Gram-positive organisms implicated in BSI.

Concerning the distribution of *CoNS* (50) isolates, it was found that 54% (27/50) were isolated from NICU, a result that was congruent with that obtained by Abo-Shadi et al., 2012 (*CoNS* in NICU, 53.5%). This increase in the frequency of *CoNS* has occurred concurrently with the advanced use of invasive IVC and the poor compliance to infection control policies and procedures particularly hand hygiene which could lead to further exposure of those vulnerable patients to colonization with resistant organisms. This may reflect a change of *CoNS* from being regarded as skin flora to being viewed as clinically significant organism.

In this study, Gram negative pathogens constituted 34.1% of the total isolates (46/135). *K. pneumoniae* formed 37%, followed by *A. baumannii* (33%) and *P. aeruginosa* (15%). Similar results were obtained by Ahmed et al., 2009 and Viswanathan et al., 2011. Predominance of one type over others varies from one place to another and even in the same place over time (Kaistha et al., 2009).

Candida albicans BSI is the most common invasive fungal infection among hospitalized patients. In the USA, it is currently the fourth leading cause of nosocomial BSI among hospitalized patients and third among ICU patients (Orsini et al., 2012). *Candida albicans* was implicated in 3.7% of all BSI episodes representing the sixth most common etiologic agent in this study. Whereas Abo-Shadi et al., 2012 found that, *Candida* spp. represent the fifth most common etiologic agent causing BSI (4.6%). In contrast, Babay

et al., 2005 found that, *Candida* spp. constituted only 1.3% of the total isolates.

Among *CoNS* isolates, resistance was maximally observed to cefoxitin (96%) (indication to methicillin resistance) and erythromycin (85%). Whereas resistance was minimum to vancomycin (4%) and rifampin (32%). This is due to the frequent use of the β -lactam antibiotics in the ICUs included in the study. Our results came in agreement with that of Ghadiri et al., 2012. They stated that the highest resistance rate of the *CoNS* was against β -lactam antibiotics while the lowest resistance rate to vancomycin.

It was observed that *CoNS* were the most common isolates in general (37%) and in the present study environments' (42.2% in NICU of Beni-Suef University Hospital, 36.6% in adult ICUs of Cairo University Hospital and 26.7% in adult ICUs of Beni-Suef University Hospital). The majority of *CoNS* strains were methicillin resistant so detection of *mecA* gene was found to be essential to determine its correlation with antibiotic susceptibility to methicillin

The current study has shown that 96% (48/50) of *CoNS* strains were methicillin resistance while the rest was sensitive (4%, 2/50). *MecA* gene was present in 69% (33/48) of MR *CoNS* and absent in 31% (15/48), while it was absent in all MScoNS. Moreover, there was no statistically significant correlation ($p = 0.876$) between *mecA* gene expression and methicillin-resistance. Our results came in agreement with that of Kitao et al., 2010. They concluded that, *mecA* gene was detected in 70% of MRCoNS isolates, while Mendoza-Olazarán et al., 2013 found that *mecA* gene was carried in 81% of MRCoNS.

In the present study, Gram positive isolates showed high resistance to β -lactam antibiotics that paralleled the finding of Chen et al., 2012, and Jacqz-Aigrain et al., 2013. On the other hand, Gram negative rods showed resistance rates to the majority of antibiotics especially in adult ICU and NICU of Beni-Suef University Hospital. This could be explained by the late introduction of infection control program into the hospital policy and the unrationalized use of antibiotics, an evident barrier that limits the therapeutic choices in infections caused by such resistant strains. This finding was supported by the results of Ahmed et al. (2009) study in Egypt.

It was observed in this work that the percentage of *ESBL* producing Gram negative bacilli among patients with BSI was 52%. These findings came in agreement with that of Ahmed et al., 2009 (64.7%). The prevalence and relative distribution of *ESBL* producing pathogens vary depending on the facility and the level of care taken to control HAIs. It also

varies with geographic location and time (*Oberoi et al., 2013*).

Concerning the mortality rate associated with nosocomial BSI, a rate of 39% was recorded in the current study. *Orsi et al., 2012* reported a closely related results (34.8%). Higher rates were observed with *CoNS* (46%), *Acinetobacterbaumannii* (17%), and *Candida spp.* (11%) infections. These results came in agreement with that of *Abo-Shadi et al., 2012*. They noted that *CoNS*, *Klebsiella spp.* and *Candida spp.* were the commonly isolated organisms and associated with higher mortality rates.

IVCs are inserted in approximately half of all patients in ICUs. CRBSIs are associated with an attributable mortality of 0- 11.5% and an additional stay length of 9-12 days (*Siempos et al., 2009 & Timsit et al., 2011*).

In the present study, 250 IVCs tip segments were cultured of which 20 were culture positive and coincident with blood culture results. The highest number of isolates was reported from NICU (60%). Moreover, *CoNS* was the most frequently isolated organism from positive cultures (16/20, 80%). *Resende et al., 2011* found that *CoNS* was the most common organism causing CRBSI representing about 50% of total isolates. In their study, *Mendoza-Olazarán et al., 2013* explained a similar finding as result of biofilm formation, high prevalence of methicillin resistance and resistance to other antibiotics as *mecA* gene carried on a mobile genetic element (SCC*mec*) that help in transmission of resistance between strains. In addition, the

CVCs used in the current study were not impregnated with antibiotic lock solution that might decrease the risk of development of CRBSI.

The development of new technologies capable of further decrease in the CRBSI rate is a major challenge. New materials that decrease the risk of skin-to-vein bacterial migration, such as new antiseptic dressings and antithrombotic prophylaxis have been developed in addition to antimicrobial lock therapy (ALT) (*Walz et al., 2010; Maki et al., 2011, and Timsit et al., 2011*).

Conclusion

Nosocomial BSIs represents a current problem in ICUs. Problems associated with BSI include infection with MDR pathogens (especially *CoNS*) which are difficult to treat and are associated with increased mortality. Vancomycin is the most active and reliable treatment options. However, over use of vancomycin may lead to more resistance of these strains and other Gram positive organisms. Therefore, the rational use of vancomycin, along with implementation of infection control programs are the

most effective means of controlling, decreasing BSI and the spread of *CoNS* as well.

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