ORIGINAL ARTICLE

Device Associated Infections in Intensive Care Units in a Tertiary Care Hospital

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ABSTRACT

Objective: To isolate the bacteria in Device associated infections (DAI) and assess their sensitivity patterns in Intensive Care Units of Services Hospital, Lahore from January to December 2010.

Materials & **methods**: This cross-sectional study was carried out on bacterial isolates from samples of devices from various Intensive Care Units of Services Hospital Lahore in the Microbiology section, Department of Pathology, Services Institute of Medical Sciences Lahore. All samples isolates were tested for anti-biotic sensitivity pattern.

Results: In 2010, eight hundred and eighty-six samples were submitted to Microbiology Section for culture from different ICUs. Three hundred and fifty samples (39.5%) were devices or samples from devices. Trachea derived samples were 212(60.6%), Central Venous tips(CV tips) 96(27.4%) and Folley's catheter 43(12.28%).Maximum positive cultures were obtained from tracheal samples (50.7%) followed by CV tips (14%) and least from Folley's catheter (6.7%). Thirty-two CV tips (10%) 32(9%) trachea derived samples and 13(3.7%) did not yield any growth on culture. Bacterial yield was obtained from 67.7% device associated samples and fungal from 8.6% samples. Gram negative isolates comprised 216 (91%) of the total 237 isolates and Gram positive 21(8.8%) of which maximum number again were of tracheal origin followed by CV tips. Almost one fourth (24.4%) *Acenatobacters* exhibited resistance to all drugs used with (52.3%) sensitive to one drug only, mainly Imepenem (26.7%). Two drug sensitivity was exhibited by (21%) whereas sensitivity to three or more drugs was exhibited only in 3 cases. The converse was true for the rest of 130(60%) Gram' negative isolates as *Pseudomonas* and Enterobacteriaceae. Resistance to all the drugs tested was exhibited by 30(13.9%) Gram's negative isolates. Grams positive isolates as ORSA, OSSA and coagulase negative staphylococci comprised 21 bacteria. ORSA were sensitive to Vancomycin, Fucidic acid and Linezolid but OSSA and coagulase negative staphylococcal were sensitive to one drug.

Conclusion: Use of devices and device associated infections are on the rise and so are the samples sent for culture especially from Intensive Care Units. Inappropriate use of antibiotics leads to multiresistant and pan-resistant strains. This alarming increase of drug resistant infections in ICUs has been presented in this study. Bacterial and fungal cultures should be requested with their drug sensitivity patterns.

Key words: ICU, DAI, *Acinetobacter*, *Pseudomonas*, *Klebsiella*, *Candida*, drug resistance

INTRODUCTION

Intensive care unit (ICU) acquired infection itself is an independent risk factor for hospital mortality[1]. Risk factors include increased length of stay (>48 hours), mechanical ventilation, trauma, central venous, pulmonary artery and urinary catheters[2]. ICUs in countries with limited resources have highbrates of device associated health-care associated infection (HAIs) including central line associated blood stream infection (CLAB), ventilator associated infection (VAP), and catheter associated urinary tract infection (CAUTI) three to five times higher than North America, Western Europe and Australian ICUs[3]. The pathophysiology of nosocomial infections include colonization of host by potentially dangerous pathogens from exogenous and endogenous sources e.g., methicillin resistant *Staphylococcus aureus* (MRSA), Vancomycin resistant *enterococcus* (VRE), azlo resistant candida spp. and extended spectrum beta lactamases (ESBLs)[4]. To survive within hostile environments as in host tissue (antibodies, phagocytes) or on inert surfaces exposed to inhospitable conditions (UV light, desiccation, heat, cold), they have adapted by existing as adherent populations of sessile bacteria. In such adverse environments, bacteria grow as colonies surrounded in an extracellular matrix of carbohydrate or exopolysaccharide[5,6,7,8]. A large collection of these groups of bacterial cells adhering to a surface is called a bacterial biofilm[5,6,7]. Sessile bacteria growing on surfaces have nutrient limitations, have restricted mobility and hence grow more slowly[8] but they are able to resist or evade such destructive forces by forming aggregates, altering their physiology, and taking advantage of deficiencies in the host clearance mechanisms. Such infections involving biofilms are chronic and difficult to treat[5,6,7,8]. They may also

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exhibit biofilm-specific biocide-resistant phenotype to antibiotics and hence therapeutic failures[7].

Natural substances are now being used to overcome such problems such as to reduce the production of rhamnolipid, a compound that shields the biofilm bacteria from the white blood cells[9].

MATERIAL & METHODS

This cross-sectional, observational study was carried out at the Microbiology Section, Department of Pathology, SIMS from the period January to December 2010 on intensive care units of Services Hospital Lahore. Clinical specimens from devices were obtained from Medical and Surgical ICUs. These included tracheal aspirates & tubes, urine catheter tips, central venous tips and drainage tubes.

Samples were cultured onto appropriate culture media as Blood agar, MacConkey's agar, Chocolate agar, CLED. Culture plates were incubated aerobically for 24-48 hours at 37^0C. Isolates were identified by colony morphology, Gram's staining, catalase, coagulase, oxidase and relevant biochemical tests[10].

Antimicrobial sensitivity testing was performed on Mueller Hinton agar using Kirby- Bauer Disc Diffusion Method[11]. Antibiotic discs used for Gram negative bacteria were Ampicillin, Augmentin, sulfamethoxazole/ trimethoprim, Ceftrioxone, Cefoperazone, Doxycycline, Azectam,, Ofloxacin, Imipenem, Amikin, Tazobactam. Antibiotic discs used for Gram positive isolates were Ampicillin, Augmentin, Vancomycin, Oxacillin, Ciproxin, Erythrocin, Doxycycline, Gentacin. Septran, Linezolid and Fucidic acid. All the antibiotic discs used in the present study were manufactured by Oxoid UK. Tigecycline and polymyxins were not used in all cases hence not included in results

In the present study, organisms resistant to all the above groups of antibiotics were labelled as Resistant (R) organisms. This excludes tigecycline. The results were analyzed statistically by determination of frequency of different parameters.

RESULTS

In the year 2010, a total of 886 samples from ICUs of Services Hospital, Lahore were submitted to the Microbiology section of Pathology Department, Services Institute of Medical Sciences, Lahore. Device or device- associated samples comprised 350(39.5%) of these submissions. Cultures were put up for all the received samples, 267 (76.2%) samples yielded a growth, whereas 83 samples (23.7%) did not yield any growth on culture. Trachea derived samples were 212(60.6%), Central Venous (CV) tips 96 (27.4%) and Folley's catheter 43 (12.28%). Maximum positive cultures were obtained from tracheal samples (52.8%) followed by CV tips (20.5%) and least from Folley's catheter (9.7%). Thirty-four CV tips (10%) did not yield any growth. Positive bacterial cultures were obtained from 67.7% device associated samples and fungal from 8.6% samples of total 350 samples. Gram's negative isolates comprised 216(91%) and Gram positive bacteria 21(8.8%) of the total 237 bacterial isolates. A single bacterial pathogen was isolated from 187 samples, double from 26 and tripple from 3 samples. Samples with a mixed growth i.e., both bacteria and *Candida* were 5 in number. & Totally 180 microorganisms (74.26%) were isolated from 212 tracheal samples with *Acinetobacters(40%)*, *Pseudomonas (2*1.7%) , *E coli* (18.5%) and *Klebsiella* (16.6%). Of the total 35 resistant strains 26 were isolated from trachea (Tables 1 & 4).

Of the total 267 microorganisms, 216(81%) Gram's negative bacteria were isolated with 133 non fermenters (61.5%) and 83fermenters (38.4%). *Acinetobacter* was the commonest isolate comprising 40% of all Gram negatives followed by *Pseudomonas* (21.7%), *E coli* (18.5%) and *Klebsiella* (16.6%). Almost one fourth (24.4%) *Acinetobacter* spp. exhibiting resistance to all drugs used, one drug sensitivity was exhibited by half of them(52.3%) mainly to Imepenem (26.7%), 2 drug sensitivity by (21%) and 3 drug sensitivity by 3(0.85%) bacteria. In total thirty-nine isolates (40.2%) *Acinetobacter* were sensitive to Imepenem ; 26 (9.5%) bacteria showed single drug sensitivity to Imepenem whereas the rest in were sensitive to other drugs as well. Fourteen *Acenatobacter* were sensitive to amikin, 11(4%) were sensitive to doxycycline, tazobactem or septran as well. Three and more than three drug sensitivity were obtained by three strains only. With 21(24.2) resistant strains and 45 sensitive to one drug only, 18 to 2 drugs, a total of 63(73.2%)strains were potentially resistant (Table 3).

The converse was true for the rest of 130(60%) Gram' negative isolates i.e., *Pseudomonas* and *Enterobacteriaceae*. *Pseudomonas* showed a total 94.4% sensitivity to Imepenem alone or with other drugs. Response to 2 drugs was 22.2% and to 3 or more groups of drugs was 55.5%. Only 8(3.3%) were resistant to all drugs used whereas 78 isolates were 3 or more drug sensitive mainly to Imepenem, Amikin and tazobactem. Resistance to all the drugs tested was exhibited by 30(13.9%) Gram's negative isolates. Gram's positive isolates as ORSA, OSSA and coagulase negative staphylococci comprised 21 bacteria (8.9% of 237 bacterial isolates). ORSA were sensitive to Vancomycin, Fucidic acid and Linezolid but OSSA and coagulase negative staphylococcal were sensitive to one drug i.e., Vancomycin or 2 drugs Vancomycin and Fucidic acid or Linezolid. *Candida* infections (11.2%) alone (25 samples) or as mixed infection with bacteria as single pathogen (5 samples) or two bacteria (3 samples).

Table 1: Break up of device associated infections (n=350) in ICU's in the year 2010

Bacteria isolated	No. of bacteria	Tracheal samples	Central venous TIPS	Folley's catheter
Gram's Negative	216(80.8%)	166(47.4%)	50(14%)	24(6.7%)
Acinetobacter	86	76	9	1
Pseudomonas	47	38	7	2
Klebsiella	36	23	6	7
E coli	40	20	13	7
Proteus	8	4	3	1
Gram positive	21(7.9%)	10(2.86%)	7(2%)	4(1.5%)
ORSA	5	5	-	-
OSSA	7	4	1	2
Staphylococcus spp	6	2	4	1
Streptococci	1	1	-	-
Fungus c*andida*	30(11.2%)	9(2.57%)	15(4.28%)	6(1.7%)
Total	267	180(51.4%)	62(17.6%)	30(8.5%)

ORSA: Oxacillin resistant *Staphylococcus aureus* OSSA: Oxacillin Sensitive *Staphylococcus aureus*

Table 2: Break up of the devices with no growth on culture from patients with device in ICU's in the year 2010 (n=350)

Name of device	=n	%age
Trachea	32	9
Cv Tip	34	9.6
Folley's Cathetar	13	3.6
Hepatic Drain	2	0.6
Chest Tube	2	0.6
Total: No Growths	83	23.7%

Table 3: Drug sensitivity patterns of device -associated gram negative bacteria

Isolates	No	1 Drug Sensitive						2 Drug sensitive				3 drug S
Bacteria		No	Imp	Taz	Ak	Sxt	Do	No	ImpTaz	ImpAk	ImpTgc	Taz/ Im/ak No
Acenatobacter	86	45	23	2	9	5	3	18	6	2	1	3
Pseudomonas	47	10	9	-	1	-	-	4	1	1	-	32
Klebsiella	36	7	5	1	1	-	-	7	5	2	-	27
E coli	40	7	6	-	1	-	-	13	2	6	5	15
Proteus	7	1	1	-	-	-	-	1	-	1	-	4
Total	216	70	44	3	12	5	3	43		12	6	81

Table 4: Bacteria with device-associated anti biotic resistance

Resistant Bacteria	No	Trachea	CV Tip	Folley's Catheter
Acenatobacter	21	16	2	3
Pseudomonas	1	-		1
Klebsiella	4	2R; 2 ESBL		2
E coli	3	3 ; 1R;2ESBL		
Proteus	1			1
ORSA	5	5		
Total 237	**35**(14.7%)	**26** (10.9%)	**2(0.84%)**	**7(2.9%)**

Table 5: Break-up of Bimicrobial dai in ICU in 2010:

Devices	Total Samples26	*Acena*+ *Pseud* 8		*Acenato*+ *Kleb* 7		*Acenato*/ *Ecoli* 3		*Pseud*+ *Kleb* 5		Gram's positive 3; 2 *Pseud* 1 *E coli*
Trachea	23	8	8	5	5	3	3	4	4	3
CV tip	2	-		2	2					-
Folley's catheter	1			0				1 R	1	-
1drug S; 12		2Imp/ Tgc	2 Imp	2 Imp DO	1 Imp	1 Imp	1 Imp		1 imp	2:*Pseudo* Imp Ak
2 drug S 10		3	2	1Imp, DO		1Imp, Taz	I Imp Ak	1Imp, Taz		1SS
3>drug S 18		0	4	0	5			3 TIA	3 TIA	1 ORSA, 1 OSSA+ *Ecoli*
Resistant 8		3	0	3	-	1		1		
ESBL 3					1		1		1	

Total *Acinetobacters* 17; *Pseudomonas* 15; *Klebsiella* 12; *E coli* 4; *Proteus* 4; Gram's positive isolates 3

Table 6: Device asociated infection with candida:

	Device	*Candida* only	*Candida* & *Acinetobacter*	Drug S	*Candida* & *Ecoli*	Drug S	*Candida* & *Kleb*	Drug S
Tracheal	9	7	1	1 Imp	1	TIA		
CV Tip	15	13			1	TIA		
Folley's cathetar	6	4	1	R			1	1 Ak
Total	30	25	2		2		1	

*TIA: Tazobacem, Imepenem, Amikin

Table 7: Comparative studies of acinetobacter and pseudomonas isolates with their drug sensitivity/resistance.

Study	Total Isolates	*Acinetobacter*					*Pseudomonas*				
	ICU/Wards	Total	PDR%	MDR%	ImpS%	Ak S%	Total	PDR%	MDR%	ImpS%	AkS%
2011 Karachi[16]	196DR	158		158			38		38		
2011Rawalpindi[17]	434	17			70	30	33			86	58
2011 Jordan[18]	78	8			50	25	34			64	41
2010 Karachi[19]	632		55		0	0					
2009Rawalpindi[20]		126	44.1	68.2	30						
Present study	263	97		26.8	40	17	54		3.7	94	57

DISCUSSION

Intensive care units are a close space environment with critically ill, immunocompromised and dependant segment of patients. These spaces harbour an emergent resistant bacterial population as a result of intense antibiotic/s pressure. The indwelling devices used in these patients are a cause of nosocomial infections. The pathogenesis of DAI is a multifaceted interaction between bacteria, device and host[12]. Urinary catheters are a source of 95% urinary tract infections, intravenous catheters cause 87% bloodstream infections, respirators, tracheal intubation cause 86% of pneumonias[13].Ventricular assist devices (14) also are a cause of morbidity and mortality. In the present study tracheal samples constituted 60.6%, CV tips (27.4%), Folley's catheter (12.28%) and drains 2(0.57%). The Device - associated infection rate comprised 4.36% medical ICU in a study from India (15). In our study 30% samples submitted, yielded a growth.

In the study from India, non-fermenters were common pathogens (73.68%) and fermenters (enterobacteriaceae) caused 21.05% infections. *Acinetobacter* (26.31%) was the commonest bacterium followed by *Pseudomonas* and *Klebsiella* (10.52%) each[13]. In the present study non fermenters comprised (61.6%) with *Acinetobacter* (40%) of Gram negatives organisms, taking the lead as the single most common pathogen followed by *Pseudomonas* (21.7%), *E coli*, (18.5%), *Klebsiella (*16.6%) Proteus (3.2%). Comparison with other studies is given in Table 7.

The double pathogens were associated with 12 resistant strains in total (Table5). Drug sensitivity to single drug was exhibited by five *Acinetobacters* and four *Klebsiellas*. Ten bacteria were sensitive to two drugs and 3 drug sensitivities by18 bacteria mainly *Pseudomonas* and *Klebsiella*. In mixed infections with Gram's positive and Gram's negative organisms, *Acinetobacter's* associated infections were more resistant. Mixed Gram positive/ negative pathogens also would demand therapeutic drugs against both or all types of bacteria. Even candida-associated infections, alone or mixed (Table 6) would be more resistant due to lack of anti fungal therapy and failures could be accounted for giving anti bacterial drugs alone.

Pseudomonas aeruginosa has been recognized in human medicine to form antibiotic resistant biofilms on implanted devices and within tissues[3]. The *Pseudomonas* isolates in biofilm cells exhibit more resistance to other drugs but with enrofloxacin reasonable clinical activity was demonstrated in a study. Fluorinated quinolones have been shown to be effective in treatment of most *Pseudomonas* infections[1,3]. This mandates sending and following culture and sensitivity results for therapeutic success.

Ongoing researches on biofilm by *Pseudomonas* hold promise for cystic fibrosis patients as a Garlic-derived substance ajoene inhibits 11 genes involved controlled by quorum sensing which is important for communities of bacteria. Ajoene helps to reduce the production of rhamnolipid, a compound that shields the biofilm bacteria from the white blood cells that otherwise would destroy bacteria, and that by combining ajoene with the antibiotic tobramycin, it was possible to kill over 90% of bacteria living in a biofilm"[9].

DAI is a problem which is on the rise especially in ICUs with increase use of devices. Unnecessary use of such devices and antibiotics should be limited to prevent drug resistance, a dread in the hospital setting. In the present study, samples were sent for

culture without informing the laboratory of the type and duration of antibiotic therapy instituted. Special cultures as fungal or anaerobic were never requested for by the clinicians, so they were not put up. Careful assessment of the type of pathogen could help in the selection of a suitable antimicrobial drug and prevent device associated nosocomial infection.

CONCLUSION

Inappropriate use of antibiotics leads to multiresistant and pan-resistant strains especially in ICU patients with devices. Bacterial and fungal cultures should be requested with their drug sensitivity patterns. Use of devices should be minimized to prevent resistant strains and therapy failure.

Recommendations: Control measures should be implemented by isolation of patient, adopting personal protective measures and hand hygiene. Decontamination procedures should be followed for equipment and environment. Antibiotics should be used only when necessary and according to the culture sensitivity report. A Policy on the management of therapeutic devices is essential to prevent Device associated nosocomial infections (DANI) and cross infections.

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