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Changes in Five Years among Pathogens in Wound Infection and Their Susceptibility to Antimicrobials

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Abstract **Background:** Proper knowledge about the epidemiology and changing sensitivity pattern of drug in bacterial wound infection is very important in ensuring optimum management of the wound and formulating policies in infection control. Objectives of our study was to disseminate the etiology of bacterial wound infection in two time frames (in 2016 or group A and in 2011 or group B), to provide their susceptibility pattern and to highlight the changes of susceptibility pattern in order to update information regarding antimicrobial resistance and it's implication in wound management. **Method:** Bacteria isolated from wound swab, aspirates and pus samples received in year 2016 and 2011 were included in the study. Isolates were identified by conventional tests and antibiotic sensitivity was determined by disc diffusion method according to CLSI guideline. **Results:** Gram positive cocci are still the predominating organism in wound infection. Both *Staph. aureus* as well as CoNS (coagulase negative staphylococci) lead the list as pathogens of wound infection. Among Gram negative bacteria, *Acinetobacter* spp. and *Klebsiella* spp, were more common than *Pseudomonas* spp. in our study. Notable raise in ampicillin sensitivity is observed after 5 years among *Staphylococci* species. Cotrimoxazole is regaining its importance as all the isolates from wound infection have a increasing trend towards susceptibility to it in 5 years. Doxycycline also has raised activity more than 61 % on Gram positive cocci in group A or 2016. Vancomycin, linezolid for Gram positive bacteria and amikacin, meropenem, pipercillin tazobactam, and colistin for Gram negative bacteria are still useful but showing reduced sensitivity after 5 years. Amoxyclav is not very useful as a prophylactic antibiotic as only 40% pathogens were susceptible. Resistance to quinolones, cephalosporins, aminoglycosides are increasing in both Gram positive and negative bacteria with few exceptions.

Keywords: *wound infection, microorganisms, antibiotic sensitivity, changes in five years*

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1. Introduction

A normal skin is the abode of numerous microbiota (10^3 to 10^4 organism /cm^2 of skin) from environment and obviously not sterile [1]. A bacterial infection therefore may occur in a wound, irrespective of intrinsic or extrinsic factors- it may be iatrogenic or opportunistic. Use of antibiotic to combat infection sometimes become a challenge as resistance against almost all available antibiotics is increasing and making organisms "superbugs" or "nightmare bacteria" [2].

Etiology of wound infection or surgical site infection (SSI) may not necessarily be same for all individuals or in different times because of the colonization resistance [3]. Wounds can also be acute or chronic according to the etiology [4]. Healing and recovery take longer time than expected if the infection remains undiagnosed owing to the atypical etiology [5]. Any infection may also remain a perpetual problem in a hospital, if it is due to a resistant strain like MRSA or VRE posing therapeutic challenges in the employment of regular antibiotic according to the local protocol/manual of the hospital. Constant monitoring is therefore imperative. Back in 1990s there was an emergence of vancomycin resistant MRSA and *Enterococci* in certain area of USA, and Japan excluding North eastern region [6,7]. AMR (antimicrobial resistance) trends vary on specific agents, time, population and geographical variance [8,9] creating a therapeutic crisis and increasing health care associated infections (HCAI). This leads to surgical site infection (SSI), which contributes substantially to surgical mortality and morbidity each year [10,11]. Preventing SSI is the first step of reducing HCAI which will not only reduce the cost, labor & time of surgical/microbiology team, it will also provide an enormous impact on HCAI prevention and wound management [12]. WHO has documented significant gaps in AMR surveillance, methodology, and data sharing procedure [13]. In Bangladesh, antibiotics are available over the counter since dispensing is not restricted to prescription only [14]. Evidence suggests,

resistance pattern shows remarkable changes if any antibiotic is used for a short time in the locality and withdrawn for some time [15]. For effective and optimum antibiotic prescribing, a fundamental understanding on Microbiology is required based on national and local information of their efficacy [16,17]. Besides, Antimicrobial stewardship programs (involving pharmacists, physicians and other healthcare providers) should be established as antibiotic resistance increases [15]. Hospital can utilize these information/data by evaluating and formulating a policy in infection control practices [18]. De-escalation or switching of broad spectrum antibiotic to a narrowed one in empiric treatment based on C/S report on day 3 has been advocated to prevent resistance or to retain the efficacy of useful drugs and to contain the infection [19]. Effective infection control also involves aseptic intervention procedures which includes prophylactic antibiotic use or de-escalation just prior to surgery to exclude exogenous /endogenous microbial contamination [11,18]. Antimicrobial is recommended for short duration [20]. At this point, choosing an antibiotic depends on the basis of microbiological report on susceptibility pattern of responsible pathogens [21]. To observe changes in infection rates of pathogen and their susceptibility to antimicrobials, continuous surveillance is imperative. It can be a guide for appropriate and rational use of antibiotic in prevention of HCAI [11,22].

The objectives of this study are a) to disseminate the etiology of bacterial wound infection in two time frames (in 2011 and 2016) and to provide their susceptibility patterns. B) To provide an insight to the clinician about the changing susceptibility pattern if any within these five years in order to manage wound infections. It may also provide updated information to the Microbiologists regarding selection of the antimicrobials for sensitivity testing in the laboratory and to the hospital management or policy makers in updating antibiotic usage guidelines and policy.

2. Method

A retrospective study on wound infections presenting at the Microbiology laboratory of Ad Din Women's Medical College Hospital (AWMCH) was done. All culture and sensitivity (C/S) reports of wound swab, pus and aspirates sent to the laboratory during the period of 2016 and 2011, January to December (Group A and B respectively) were studied. Samples included both outdoor and indoor patients from different departments of the hospital.

2.1. Microbiology

All samples were cultured, identified and susceptibility testing was done for reporting and proper documenting as a routine work of the laboratory.

For bacterial isolation, the media used were blood agar plate and the MacConkey agar plate which were incubated at 35-37 degree centigrade for 48 hrs in aerobic condition. The organisms isolated were identified by using standard laboratory methods according to World Health Organization [23] and were subjected to susceptibility testing [24]. In total 22 antibiotics were used: ampicillin (Amp), cotrim (Cot), cephradine (Ceph), ciprofloxacin (Cip), levofloxacin (Lev), ceftriaxone (CTR), cefotaxime (CTX), amoxiclav (AMC), cefixime(CXM), amikacin (AK), meropenem (Mero) /Imepenem(Im), gentamicin(Gen), ceftazidime (CAZ), piperacillin-tazobactam (PIT), colistin (Col) with addition of oxacillin (Ox), cloxacillin (Clox), doxycycline (Do), erythromycin (Ery), vancomycin (Van), linezolid (Lz) for Gram positive bacteria.

3. Result

A total 1768 samples (pus/wound swab/aspirates) were received from indoor and outdoor departments to exclude/diagnose infection in the year 2016 (group A) of which only 451(25.5%) were deleted growth positive (Figure 1). The predominating organisms were *Staph. aureus* (25.9%), Coagulase negative Staphylococcus (CoNS) (25.3%), *Acinetobacter* (15.0%), and *Klebsiella* (11.9%) species respectively. Proteus, Pseudomonas and *Enterobacter*, *Enterococci* species were also isolated less frequently. In this group (A), Gram positive cocci (234 or 51.4%) predominated in wound infection (Table 1).

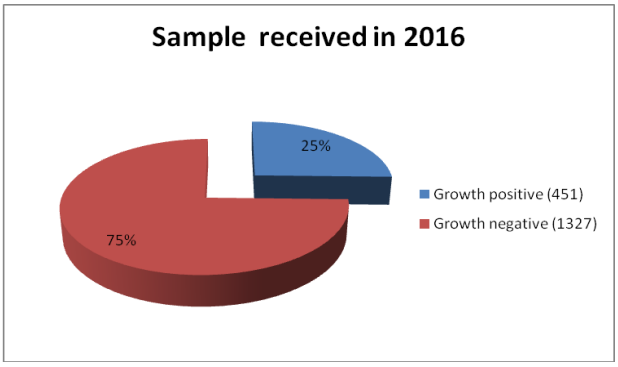

Figure 1. Distribution of total wound swab, pus and aspirates received in 2016

In the year 2011(group B), among total 882 samples 150 (17%) were growth positive only (Figure 2). Major pathogens were *Staph. aureus* (36%), *E.coli* (24%), CoNS (19.3%), respectively and similarly Gram positive cocci (86 or 56.7%) were predominating over Gram negative bacilli (Table 2).

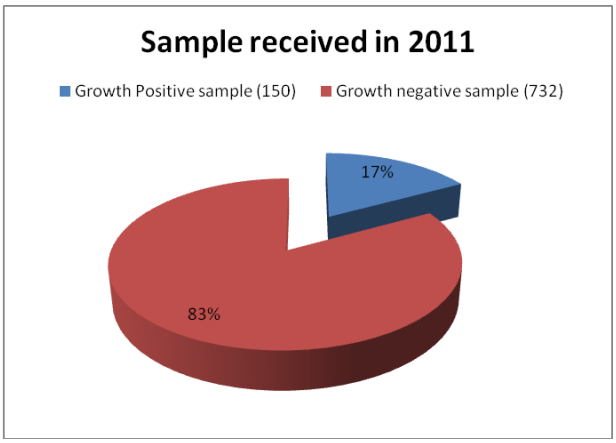

Figure 2. Distribution of total wound swab, pus and aspirates received in 2011

Comparison of Table 1 and Table 2 reveals that, occurrence rate of CoNS mediated wound infection has increased (25% in group A versus 19% in group B) in recent years. Yielding rate of *Acinetobacter* spp. and *Klebsiella* spp. became almost double in group A (15.4%, 11.7%) compared to group B (6.7%, 6%) respectively.

Table 3 and Table 4 shows the antimicrobial susceptibility pattern of Gram positive cocci and Gram negative bacilli in the year 2016 (group A). Similarly Table 5 and Table 6 shows the susceptibility pattern of Gram positive cocci and bacilli respectively in the group B.

Table 1. Distribution of isolated Gram reactive microorganisms from samples received in 2016.

Gram Reaction	Microorganisms	No	Percentages
Gram positive organism	Staph. aureus	117	26
	CoNS	114	25.3
	Enterococci	3	.1
Total Gram positive organisms		**234**	**51.4**
Gram negative organism	Acinetobacter	68	15.1
	Klebsiella	54	12
	E. coli	53	11.7
	Proteus	17	3.8
	Pseudomonas	14	3.1
	Enterobacter	11	2.4
Total Gram negative organisms		**217**	**48.6**

Table 2. Distribution of isolated Gram reactive microorganisms from samples received in 2011

Gram Reaction	Microorganisms	No	Percentages
Gram positive organism	Staph. aureus	54	36
	CoNS	29	19.3
	Enterococci	2	1.3
	S. pyogenes	1	.07
Total Gram positive organisms		86	56.7
Gram negative organism	E. coli	36	24
	Acinetobacter	10	7.7
	Klebsiella	9	6
	Proteus	4	2.7
	Pseudomonas	5	3.3
Total Gram negative organisms		64	43.3

Table 7 reveals the comparison of susceptibility pattern of different Gram positive bacteria responsible for wound infection in group A and B. It is observed that in 5 years apart between 2011 and 2016, ampicillin sensitivity of *Staph aureus* (1.9% to 13.7%) and CoNS (6.9% to 11.4%) has been remarkably increased. Regarding CoNS, higher susceptibility was also found in both doxycycline, gentamicin (increased from <30% to >60%) but negligible increase among Staph. aureus in group A rather than in B. Alarmingly reduced activity of amikacin and meropenem is seen among *Staph. aureus* and CoNS in group A (reduced from 90% to 62% and 66% respectively). Vancomycin, linezolid are both equally effective to Gram positive cocci even in 5 years apart (Table 7).

Table 3. Susceptibility pattern of Gram positive organisms isolated from wound infection in 2016

Antibiotics	CoNS (N=114)	Staph. aureus (N=117)	Enterococci (N=3)
Ampicillin (%)	13(11.4)	16(13.7)	1(33.3)
Cotrimoxazole (%)	54(47.4)	69(59)	2(66.7)
Ciprofloxacine (%)	29(25.4)	44(37.6)	1(33.3)
Levofloxacine (%)	35(30.7)	57(48.8)	2(66.7)
Ceftriaxone (%)	38(33.3)	48(41)	2(66.7)
Cefotaxime (%)	7(6.1)	38(32.5)	1(33.3)
Amoxyclav (%)	36(31.6)	47(40.2)	0 (0)
Oxacillin (%)	13(11.4)	39(33.3)	0 (0)
Cloxacillin (%)	21(18.4)	42(35.9)	0 (0)
Doxycycline (%)	76(66.7)	72(61.5)	1(33.3)
Erythromycin (%)	40(35.1)	38(32.5)	0 (0)
Amikacin (%)	32(28.1)	29(24.8)	2(66.7)
Meropenem (%)	77(66.5)	73(62.4)	2(66.7)
Gentamycin (%)	70(61.4)	67(57.3)	2(66.7)
Vancomycin (%)	108(94.7)	114(97.4)	3(100)
Linezolid (%)	112(98.2)	117(100)	3(100)

Table 4. Susceptibility pattern of Gram negative organisms isolated from wound infection in 2016

Antibiotics	E. coli (N=53)	Acinetobacter (N=68)	Klebsiella (N=54)	Enterobacter (N=11)	Proteus (N=17)	Pseudomonas (N=14)
Ampicillin (%)	2(3.8)	5(7.4)	1(1.9)	0(0)	1(5.9)	Not Used
Cephradin (%)	9(16.7)	11(16.2)	12(22.2)	2(18.2)	2(11.8)	Not Used
Cotrimoxazole (%)	2(52.8)	55(80.9)	1(35.2)	7(63.6)	8(47.1)	8(57.1)
Ciprofloxacine (%)	21(39.6)	34(50)	16(29.6)	9(81.8)	10(58.8)	6(42.9)
Levofloxacine (%)	30(56.6)	37(54.4)	21(38.9)	8(72.7)	13(76.5)	5(35.7)
Ceftriaxone (%)	29(54.7)	28(41.2)	14(25.9)	5(45.5)	4(23.5)	4(28.6)
Cefotaxime (%)	16(30.2)	17(25)	27(50)	4(36.4)	3(17.6)	2(14.3)
Amoxyclav (%)	15(28.3)	28(41.2)	15(27.8)	3(27.3)	6(35.3)	0(0)
Cefuroxime (%)	17(32.1)	19(27.9)	22(40.7)	2(18.2)	1(5.9)	1(7.1)
Amikacin (%)	42(79.2)	42(61.8)	43(79.6)	9(81.8)	12(70.6)	12(85.7)
Meropenem (%)	49(92.5)	59(86.8)	48(88.9)	10(90.9)	15(88.2)	13(92.8)
Gentamycin (%)	34(64.1)	32(47.1)	21(38.9)	2(18.2)	12(70.6)	5(35.7)
Ceftazidim (%)	16 (30.2)	13(19.1)	26(48.1)	4(36.4)	6(35.3)	4(28.6)
Piperacillin Tazobactam (%)	3(66)	52(76.5)	NU	9(81.8)	Not Used	1(78.6)
Colistin (%)	NU	63(92.6)	50(92.6)	11(100)	Not used	14(100)

Table 5. Susceptibility pattern of Gram positive organisms isolated from wound infection in 2011

Antibotics	Staph. aureus (N=54)	CoNS (N=29)	Enterococci (N=2)	S. pyogenes (N=1)
Ampicillin (%)	1(1.9)	2(6.9)	0 (0)	0
Cotrimoxazole (%)	27(50)	8(27.6)	1 (50)	0
Ciprofloxacine (%)	21(38.9)	4(13.8)	1(50)	0
Levofloxacine (%)	19(35.2)	5(17.2)	1(50)	1
Ceftriaxone (%)	18 (33.3)	9(31)	1(50)	0
Cefotaxime (%)	11(20.3)	5(17.2)	1(50)	1
Amoxyclav (%)	19(35.2)	8(27.6)	0(0)	0
Oxacillin (%)	14(25.9)	10(34.5)	0(0)	0
Cloxacillin (%)	10(18.5)	7(24.1)	0(0)	0
Doxycycline (%)	7(13)	4 (13.8)	0(0)	0
Erythromycin (%)	32(59.2)	7(24.1)	1(50)	1
Amikacin (%)	42(77.8)	21(72.4)	2(100)	0
Imipenem (%)	49(90.7)	27(93.1)	2(100)	1
Gentamycin (%)	27(50)	11(38)	1(50)	1
Vancomycin (%)	51(94.4)	27(93.1)	2(100)	1
Linezolid (%)	52(96.3)	29(100)	2(100)	1

Table 6. Susceptibility pattern of Gram negative organisms isolated from wound infection in 2011

Antibiotics	E. coli (N=36)	Acinetobacter (N=10)	Klebsiella (N=9)	Proteus (N=4)	Pseudomonas (N=5)
Ampicillin (%)	1(2.7)	1(10)	0(0)	0(0)	Not Used
Cephradin (%)	4(11.1)	1(10)	2(22.2)	0	Not Used
Cotrimoxazole (%)	1(44.4)	4(40)	3(33.3)	1(25)	0
Ciprofloxacine (%)	12(33.3)	4(40)	4(44.4)	2(50)	2(40)
Levofloxacine (%)	13(36.1)	5(50)	4(44.4)	3(75)	3(60)
Ceftriaxone (%)	16(44.4)	5(50)	5(55.6)	2(50)	2(40)
Cefotaxime (%)	9(25)	4(40)	3(33.3)	2(50)	0
Amoxyclav (%)	10(27.8)	5(50)	4(44.4)	1(25)	1(20)
Cefuroxime (%)	8(22.2)	3(30)	4(44.4)	1(25)	1(20)
Amikacin (%)	34(94.4)	8(80)	8(88.9)	4(100)	4(80)
Imipenem (%)	36(100)	9(90)	9(100)	4(100)	5(100)
Gentamycin (%)	19(52.8)	6(60)	5(55.6)	3(75)	3(60)
Ceftazidim (%)	10(27.8)	4(40)	3(33.3)	1(25)	2(40)
Piperacillin Tazobactam (%)	2(100)	8(80)	7(77.8)	NU	4(80)
Colistin (%)	NU	9(90)	Not Used	Not Used	5(100)

Table 8 represents the antimicrobial susceptibility pattern among Gram negative bacilli in two different time periods/groups (B- 2011 and A- 2016). There has been slight increase in susceptibility of cotrimoxazole, levofloxacin, ceftriaxone, gentamicin observed among E. coli spp. in group A. Cotrimoxazole showed remarkably increased sensitivity towards *Acinetobacter* spp. (40% to 80% increase in group A, but all other antibiotics have less than 55% sensitivity in *Acinetobacter* spp., except amikacin, having 61% activity (80% to 61% in 5 years). Colistin, piperacillin tazobactam, meropenem retain efficacy without much change (Table 8).

Most of the antimicrobials were resistant among *Klebsiella* species which were being susceptible only to amikacin (79%), meropenem (88%) in 2016, with remarkable reduction in amoxyclav (44% to 27%), and ceftriaxone (55% to 25% after 5 years) in 2016 (Table 8).

According to Table 8 most sensitive drugs are amikacin, meropenem, piperacillin tazobactam, colistin among all Gram negative bacilli including *Pseudomonas* spp. (80% or more), with exception of amikacin regarding *Acinetobacter* spp. mentioned earlier.

Table 7. Comparison of Susceptibility pattern of Gram positive organisms 5 year apart

Drugs	Time period	Staph. aureus (%)	CoNS (%)	Enterococci (%)	S. pyogenes (%)
Ampicillin	A	13.7	11.4	33.3	NI
	B	1.9	6.9	0	0
Oxacillin	A	33.3	11.4	0	NI
	B	25.9	34.5	0	0
Cloxacillin	A	35.9	18.4	0	NI
	B	18.5	24.1	0	0
Doxycycline	A	61.5	66.7	33.3	NI
	B	59.2	24.1	50	0
Amoxyclav	A	40.2	31.6	0	NI
	B	35.2	27.6	0	0
Cotrimoxazole	A	59	47.4	66.7	NI
	B	50	27.6	50	0
Gentamycin	A	57.3	61.4	66.7	NI
	B	50	38	50	100
Ciprofloxacine	A	37.6	25.4	33.3	NI
	B	38.9	13.8	50	0
Levofloxacine	A	48.8	30.7	66.7	NI
	B	35.2	17.2	50	100
Ceftriaxone	A	41	33.3	66.7	NI
	B	33.3	13.8	50	0
Cefotaxime	A	32.5	6.1	33.3	NI
	B	20.3	17.2	50	0
Erythromycin	A	32.5	35.1	0	NI
	B	16.7	20.7	0	0
Amikacin	A	24.8	28.1	66.7	NI
	B	77.8	72.4	100	100
Carbepenem	A	62.4	66.5	66.7	NI
	B	90.7	93.1	100	100
Vancomycin	A	97.4	94.7	100	NI
	B	94.4	93.1	100	100
Linezolid	A	100	98.2	100	NI
	B	96.3	100	100	100

NU= Not used, NI= Not Isolated

4. Discussion

Data analysis from samples revealed that Gram positive cocci is more prevalent in wound infection. *Staphylococcus aureus* is the most frequently isolated pathogen in our study. CoNS mediated infection shows upward trend (25.3% in group A compared to 19.3% in group B) (Table 1 and Table 2). CoNS are now considered to be a major nosocomial pathogen with increasing isolation rate and more resistance to glycopeptides and methicillin [25]. Among Gram negative bacteria, *Acinetobacter* and *Klebsiella* species were more common in our study which was also most frequently yielded bacteria in a surveillance done in 2012 [26]. Alarmingly, most of the *Staphylococci* strains isolated from wound infection in our study are found to be multi drug resistant (Table 3 and Table 5). Multi drug resistance among CoNS and MRSA involved in HCAI is documented previously [25,27]. Methicillin resistance is observed in this study using oxacillin disc.

Ampicillin is the first broad spectrum antibiotic and susceptibility among Gram positive cocci was unsatisfactory for many years [28]. Notable increase in ampicillin sensitivity (1% to 13% in *Staph. aureus* and 6% to 11% in CoNS) is observed in this study which is probably attributed to prolonged cessation of use.

On the other hand, oxacillin showed much decreased sensitivity among CoNS (sensitivity decreased from 34% to 11% in 2016) than *S. aureus* (sensitivity increased from 25% to 33% in 2016) (Table 7). CoNS are no more accepted as contaminant rather a potential threat for HCAI who are capable of becoming multi drug resistant [29]. Oxacillin resistance has been found to be associated with mecA gene [26] and it is possible that rapid transfer of resistance gene in the hospital environment would be detrimental for HCAI prevention activities. Infection by CoNS should be taken more seriously by the hospital authority/hospital infection control team.

The increased activity of cotrimoxazole after 5 years is revealed among all Gram negative and Gram positive bacteria in our study (Table 7 and Table 8). Rate of effectivity even raised to double against *Acinetobacter* (40 -80%), *Pseudomonas* (20-57%) and *Proteus* (25-47%) species (Table 7 and Table 8). This may be considered as reversal of activity of cotrimoxazole in our study groups. Ampicillin and cotrimoxazole were hardly being used in Bangladesh in the last decade. This increasing trend must be followed up periodically so these drugs can be included in the local list for the doctors to be used in future. Rising cotrimoxazole sensitivity on Gram positive and Gram negative bacteria have also been documented by other studies in recent years [30,31]. In this study, doxycycline sensitivity increased in 5 years from 24% to 66% among CoNS indicating reversal of the antimicrobial after prolonged withdrawal of use by the doctors. So based on available data, doxycycline should be considered among the group of first-line oral antibiotic agents for uncomplicated cutaneous infections by Gram positive organisms [32].

Table 8. Comparison of susceptibility pattern of Gram negative organisms in 5 year apart

Drugs	Time period	E.coli (%)	Acinetobacter (%)	Klebsiella (%)	Pseudomonas (%)	Proteus (%)	Enterobacter (%)
Ampicillin	A	3.8	7.4	1.9	NU	5.9	0
	B	2.7	10	0	NU	0	NI
Cephradin	A	16.7	16.2	22.2	NU	11.8	18.2
	B	11.1	10	22.2	NU	0	NI
Cotrimoxazole	A	52.8	**80.9**	35.2	**57.1**	**47.1**	63.6
	B	44.4	**40**	33.3	**20**	**25**	NI
Ciprofloxacine	A	39.6	50	29.6	42.9	58.8	81.8
	B	33.3	40	44.4	40	50	NI
Levofloxacine	A	56.6	54.4	38.9	35.7	76.5	72.7
	B	36.1	50	44.4	60	75	NI
Gentamycin	A	64. 1	47.1	38.9	35.7	70.6	18.2
	B	52.8	60	55.6	60	75	NI
Amoxyclav	A	28.3	41.2	27.8	0	35.3	27.3
	B	27.8	50	44.4	20	25	NI
Ceftriaxone	A	54.7	41.2	25.9	28.6	23.5	45.5
	B	44.4	50	55.6	40	50	NI
Ceftazidim	A	30.2	19.1	48.1	28.6	35.3	36.4
	B	27.8	40	33.3	40	25	NI
Cefotaxime	A	30.2	25	50	14.3	17.6	36.4
	B	25	40	33.3	0	50	NI
Cefuroxime	A	32.1	27.9	40.7	7.1	5.9	18.2
	B	22.2	30	44.4	20	25	NI
Amikacin	A	79.2	61.8	79.6	85.7	70.6	81.8
	B	94.4	80	88.9	80	100	NI
Carbapenem	A	92.5	86.8	88.9	92.8	88.2	90.9
	B	100	90	100	100	100	NI
Piperacillin Tazobactam	A	66	76.5	NU	78.6	NU	NU
	B	100	80	NU	80	NU	NU
Colistin	A	NU	92.6	NU	100	NU	NU
	B	NU	90	NU	100	NU	NI

NU= Not used, NI= Not Isolated

Unfortunately, amikacin sensitivity has dropped to <30% from >70% in 2016 compared to 2011 among *Staph. aureus* and CoNS strains of our study. Similar resistance pattern of aminoglycosides on *Staph. aureus* and CoNS were also observed by other study decades ago. They found that resistance to these drugs in *Staph. aureus* and CoNS develops quickly in areas where these antimicrobial agents are widely used [33,34]. In more than 50% strains out of 380 MRSA were susceptible to gentamycin in Japan in 1997 [28]. Whereas, in Poland 24.4% amikacin and gentamycin resistance observed among *S. aureus* in a study in 2008 [35]. But in Bangladesh, this rapid emergence of amikacin resistance (more than 70% in 5 years) in both *Staphylococci* species of our study indicates doubtful efficacy. Careful use of other drugs is crucial, as few alternate exist in case of multi drug resistant *Staph aureus* and CoNS. Meropenem also found to have noteworthy decreased activity among the Gram positive cocci (reduced from 90% to 60%). As a broad spectrum antibiotic meropenem has less efficacy on Gram positive bacteria than *Enterobacteriaceae*, imipenem is more suitable in coverage of both Gram reactive bacteria [36]. Our finding supports this statement as Gram positive organisms were much susceptible to carbapenems in 2011 than 2016 (imipenem was used in 2011 in this study). Susceptibility rate of both *Staphylococci* species to vancomycin and linezolid (93% to 100%) did not show much variation (Table 7).

Table 8 represents the antimicrobial susceptibility pattern among different Gram negative bacilli recovered from wound infection in 2011(period B) and 2016(A). All generation cephalosporins including 3rd generations (CTR, CTX, CAZ), amoxyclav, ciprofloxacin, gentamycin are found to be resistant considerably among Gram negative bacilli (sensitivity less than 50 %) though gentamycin showed 64% sensitivity on *E. coli* strains and 70% on *Proteus* spp. which is worth mentioning (Table 8). The other quinolone derivative (levofloxacin) has good sensitivity for *Proteus* (75%), and more than 50% for *E. coli*, *Acinetobacter* spp. (Table 8). In this era of ESBLs (extended spectrum beta lactamases), and MBLs or metallo beta lactamases [37,38,39], above mentioned findings of our study may in future attribute to the serious therapeutic problem in absence of any promising alternative regimens as well as may become a barrier in controlling HCAI. Such low sensitivity, renders the drug unusable for prophylactic use in wound infection or prior to surgery. Action of piperacillin tazobactam has been found to be similar among the isolates except *E. coli* spp. (susceptibility greatly reduced from 100% to 66% in 2016), that warrants careful use by extreme caution. Amikacin, meropenem, pipercillin tazobactam and colistin are found to have good sensitivity on *Pseudomonas* spp. and also on other bacilli with exception of *Acinetobacter* spp. where both amikacin, gentamycin activity reduced to 60% and 47% respectively in group A /2016.

Acinetobacter spp. *Klebsiella* spp., *Pseudomonas* spp., and coagulase positive / negative staphylococci spp., are not only important nosocomial pathogens, also known to be biofilm producers that can create chronic infection and therapeutic challenges as they are found to be hospital acquired and multidrug resistant [40]. Unfortunately, the incidence of isolation of those organisms in wound infection has considerably increased in last 5 years (Table 1 & Table 4). Regarding these bacteria, careful observation on their susceptibility pattern is essential in order to reduce treatment failure. In this respect, our study has a scope of elaborate discussion regarding changing pattern of antimicrobials on them in 5 years difference.

One of the major limitations of our study is that samples from outdoor/indoor could not be differentiated and so HCAI or nosocomial infections could not be separated. Species of all bacteria could not identified because of inadequate laboratory settings. Antimicrobial susceptibility testing was done by disc diffusion technique rather than MIC method.

5. Conclusion

Changes in both etiology of wound infection and in their susceptibility pattern is observed in 5 years apart. *Staphylococci* species (both coagulase positive/negative) and *Acinetobacter* species are commonest among pathogens isolated in wound infection. Cotrimoxazole and doxycycline showed higher activity among most of the strains comparing two groups of study samples after 5 years. Reduced activity of quinolones, aminoglycosides, and cephalosporins observed in the study renders them unusable as prophylaxis or de escalation of antibiotics. Vancomycin, linezolid for Gram positive bacteria and amikacin, meropenem, piperacillin tazobactam, colistin for Gram negative bacteria are still effective.

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