

Original Article

Surveillance of surgical-site infections and antimicrobial resistance patterns in a tertiary hospital in Alexandria, Egypt

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Abstract

Introduction: Surveillance and antimicrobial resistance (AMR) monitoring are fundamental to Health care associated infections control. Limited data are available from developing countries for both. This study aimed to evaluate incidence and risk factors of surgical site infections (SSIs), etiological pathogens and AMR patterns identification.

Methodology: A prospective active surveillance study was implemented over a 24- month period at a 110-bed multispecialty non-teaching tertiary hospital. Follow up data were collected for 30-90 days. SSI was diagnosed according to Centers for Disease Control and Prevention and National Healthcare Safety Network (CDC/NHSN) criteria. The SSI isolates were identified by Matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF/MS). Antibiotics susceptibility test was performed according to Clinical Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST).

Results: Out of a total of 3,642 patients, 70% had complete follow-up. SSI was detected in 57 cases (2.3%), 61.4% of which were detected post discharge. Factors significantly associated with increased SSI risk included smoking, diabetes, ASA score 5/E, ICU admission, previous admission and increased hospital stay. Sixty-five isolates were obtained; 70.8% were GNB while 24.6% were GPC and 4.6% were *Candida albicans*. Regarding AMR, 58.7% of isolates were extended spectrum β lactamase (ESBL) producers while 45.7% were Carbapenem resistant. Multi drug resistant (MDR) was detected in 13% of isolates, 54.3% were extended drug resistant (XDR) and 10.9% were pan drug resistant (PDR). Eighty-six percent of *Staphylococci* isolates were methicillin-resistant.

Conclusion: Despite low SSI rates detected, the high incidence of AMR identified is alarming.

Key words: Surgical site infections; surveillance; epidemiology; MALDI-TOF; antimicrobial resistance patterns.

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Introduction

Surgical Site Infection (SSI), is defined as an infection occurring within 30 to 90 days after an invasive surgical procedure taking place in an operating room [1]. SSIs are one of the most common Healthcare associated infections (HAIs), in developed as well as low and middle-income countries [2,3]. Based on extensive epidemiologic surveys, variable percentage of SSIs from 0.6% to 9.6%, according to operation type [4]. Risk factors for acquiring SSI include a combination of intrinsic (patient) and extrinsic (procedure) related factors. Fortunately, most of these factors are modifiable [3]. Post-discharge surveillance is increasingly adapted as it is a global conduct to decrease the hospital stay [1].

Microbial pathogens isolated from HAIs are known to have high antimicrobial resistance which is rapidly increasing to unprecedented levels and physicians worldwide are running out of solutions for their

treatment [5]. Monitoring of these pathogens is becoming a high priority on both national and global levels. Using Matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) as a rapid and accurate microbial identification technique is established in developed countries but not in developing countries yet [6].

This study was carried out aiming at evaluating the incidence and risk factors of SSI in surgical patients as well as to identify etiological pathogens and their AMR.

Methodology

Study design and setting

A prospective active surveillance study of patients undergoing general, obstetric-gynecological, urologic, orthopedic and neurosurgeries was implemented over a 24- month period (from April 2016- March 2018) at a 110-bed multispecialty hospital. Before commencement of the study, awareness of the aim of

the study, Centers for Disease Control and Prevention and National Healthcare Safety Network CDC/NHSN case definition and specimen collection were thoroughly explained by the hospital infection prevention and control (IPC) team. Weekly follow up as well as monthly meetings were done. The hospital is well equipped with six capsuled operating theatres.

Data collection

A data collection sheet was designed with modification according to the CDC/NHSN program to collect and record Preoperative data, Operative data and Postoperative data [1,7].

Patients were given Ampicillin 2 g + Sulbactam 1 g (adult dose, 3 grams) or Cefazolin (2g) with or without Metronidazole (500 mg) as a surgical antibiotic prophylaxis 60 minutes before operation with redosing 2- 4hr after initiation of operation [8].

Inpatient and Post discharge Surveillance

Post discharge surveillance PDS was extended to 30-90 days after operation. PDS included: direct through follow up examination visits and Post discharge questionnaire (PDQ). At discharge patients were given a questionnaire card, a simple yes/no questions, to return at any time with any evolving symptom or at 30-90 days postoperatively whether or not they had a subsequent problem. They were informed they can reply by phone if they cannot return PDQ. If patients reported any problem, they were instructed to come for a visit where examination and microbiological examination were done as appropriate [9].

Microbiology workup

SSI classification: SSI was classified as being incisional (superficial or deep) or organ/space [1].

Specimens were obtained according to wound type: superficial incisional (within 30 days after operation) or deep incisional or organ/space (within 90 days after operation), processed and primarily identified according to standard microbiological techniques [10,11].

MALDI-TOF MS Isolate Identification

The isolated microorganisms were identified to species level by MALDI-TOF MS according to manufacturer instructions [6]. Briefly, direct transfer-formic acid method was used. 1µl of 70% formic acid was added to the bacterial spot followed by 1µl of MALDI matrix (a saturated solution of α - cyano-4-hydroxycinnamic acid (HCCA; Bruker Daltonics,

Bremen, Germany). For each run, a bacterial test standard was included. Analysis: was operated in the positive linear mode (m/z ranging from 2,000 to 20,000). Spectra were compared to fingerprint database by using the Bruker Biotyper 3.1 software and library of 5,623 entries (Bruker Daltonics, Bremen, Germany).

Antibiotics susceptibility test (AST)

AST was performed according to Clinical Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) [12,13].

Disc diffusion technique

Detection of ESBL producing strains

CLSI confirmatory method using CTX (30 µg), CAZ (30 µg) alone and in combination with clavulanic acid (CLA) was used. A ≥ 5 mm increase in the zone diameter of the cephalosporin alone and in combination with CLA was indicative of ESBL production.

Modified carbapenem inactivation method (mCIM) for Enterobacteriaceae and *Pseudomonas aeruginosa*

When the isolates were resistant to one or more carbapenem. The isolate was carbapenamase positive when zone diameter of meropenem is 6-15 mm or presence of pinpoint colonies within 16-18 mm zone.

Colistin Minimal Inhibitory Concentrate (MIC)

For the Extensively drug resistant organisms (XDR), colistin MIC was done using 1 MIU (80mg); break points: ≤ 2 and >2 µg/mL for Enterobacteriaceae, ≤ 2 and ≥ 4 µg/mL for *Acinetobacter baumannii*, ≤ 2 and ≥ 8 µg/mL for *P. aeruginosa*.

Data analysis

All completed questionnaires were revised for completeness and logical consistency. Data were fed to the computer and analyzed using IBM SPSS software package version 24.0. (Armonk, NY: IBM Corp).

Results

Distribution of departments, follow up and SSI

Out of a total of 3,642 patients, 69% had complete follow-up, 414 of which were subjected to 90 days' postoperative surveillance. Fifty-seven cases (2.3%) developed SSI of which 35 (61.4%) were detected Post-discharge. SSI Incidence rates detected in Obstetrics-Gynecology, General, Orthopedic and Urology departments were 2.8%, 2.7%, 0.55% and 0.5% respectively (Table 1).

Table 1. Distribution of surgeries according to department, follow up and SSI.

Surgeries (departments)	Total surgeries performed	Total followed up	%	No SSI	SSI	%
Obstetrics and gynecology	705	614	87.1	597	17	2.8
Urology	312	201	64.4	200	1	0.5
Surgery	2002	1405	70.2	1367	38	2.7
Neurosurgery	263	106	40.3	106	0	0
Orthopedic	360	184	51.1	183	1	0.55
Total	3642	2510	68.9	2453	57	2.3

SSI: Surgical Site Infection.

Table 2. Surgical Site Infection Patient (intrinsic) related factors.

	No SSI (n = 2453)		SSI (n = 57)		Test of Sig. χ^2	P-value	Odds ratio (OR)	95% (C.I)
	No.	%	No.	%				
Age (years)								
< 40	1322	53.9	31	54.4	0.005	0.941	1.020	0.60 – 1.73
≥ 40	1131	46.1	26	45.6				
Gender								
Male	1129	46	27	47.4	0.040	0.841	1.055	0.62 – 1.79
Female	1324	54	30	52.6				
Weight								
Min. – Max.	59.0 – 113.0		59.0 – 110.0		t = 0.0	1.000	-	-
Mean ± SD.	86.53 ± 13.31		86.53 ± 13.31					
Median	85.0		85.0					
Habits								
Nonsmoking	1428	58.2	20	35.1	12.206*	< 0.001*	0.388*	0.22 – 0.67
Smoking	1025	41.8	37	64.9				
Residence								
Urban	1,106	45.1	8	14.0	21.761*	< 0.001*	0.199*	0.09 – 0.42
Rural	1,347	54.9	49	86.0				
Diabetes								
Yes	536	21.8	34	59.6	11.013*	0.001*	5.287*	3.09 – 9.05
No	1917	78.2	23	40.4				
Cardiovascular diseases								
Yes	109	4.4	6	10.5	4.715*	FEp = 0.044*	2.530*	1.06 – 6.02
No	2344	95.6	51	89.5				
Organ Failure								
Yes	40	1.6	5	8.8	16.135*	FEp = 0.003*	5.801*	2.20 – 15.29
No	2413	98.4	52	91.2				
Previous admission								
Yes	742	30.2	28	49.1	9.331*	0.002*	2.226*	1.32 – 3.77
No	1711	69.8	29	50.9				
Associated infections								
Yes	461	18.8	39	61.7	5.897*	0.015*	9.362*	5.31 – 16.52
No	1992	81.2	18	38.3				

χ^2 , p: χ^2 and p values for Chi square test; FEp: P value for Fisher Exact for Chi square test; *: Statistically significant at $P \leq 0.05$; t, p: t and p values for Student t-test; OR: Odds ratio, CI: Confidence interval.

Table 3. Surgical Site Infection Procedure (extrinsic) related factors.

Variables	No SSI		SSI		χ^2	P-value	Odds ratio (OR)	95%(C.I)
	No. (n = 2453)	Percent (100%)	No. (n = 57)	Percent (100%)				
Showering								
Yes	1644	67.1	24	42.1	15.511*	< 0.001*	0.358*	0.21 – 0.61
No	809	32.9	33	57.9				
Hair removal								
Yes	997	40.7	20	35.1	0.714	0.398	0.789	0.46 – 1.37
No	1456	59.3	37	64.9				
ASA score								
1/E	42	1.7	1	1.8	0.001	1.000	1.025	(0.14 – 7.58)
2	1167	47.6	21	36.8	2.574	0.109	0.643	(0.37 – 1.11)
2/E	155	6.3	3	5.3	0.105	1.000	0.824	(0.25 – 2.66)
3	574	23.3	14	24.6	0.042	0.838	1.066	(0.58 – 1.96)
3/E	78	3.2	3	5.3	0.774	0.429	1.692	(0.52 – 5.53)
4	304	12.4	4	7.0	1.495	0.221	0.534	(0.19 – 1.48)
5	76	3.1	3	5.3	0.856	0.424	1.738	(0.53 – 5.68)
5/E	57	2.4	8	14.0	30.288*	< 0.001*	6.863*	(3.11– 15.16)
Wound classification								
Class I: Clean	558	22.7	2	3.5	11.896*	0.001*	0.124*	(0.03 – 0.51)
Class II: Clean-Contaminated	1038	42.3	26	45.6	0.248	0.618	1.143	(0.67 – 1.94)
Class III: Contaminated	516	21.0	16	28.1	1.650	0.199	1.465	(0.82 – 2.63)
Class IV: Dirty-infected	341	13.9	13	22.8	3.647	0.056	1.829	(0.98 – 3.43)
Elective / ER								
Elective	1431	58.3	30	52.6	0.745	0.388	0.794	0.47 – 1.34
ER	1022	41.7	27	47.4				
Drain								
Yes	1413	57.6	29	50.9	1.031	0.310	0.762	0.45 – 1.29
No	1040	42.4	28	49.1				
Operation duration (hours)								
< 2	1135	46.3	27	47.4	0.027	0.869	1.045	0.62 – 1.77
≥ 2	1318	53.7	30	52.6				
Type of anesthesia								
GA	1903	77.6	45	78.9	0.060	0.806	1.084	0.57 – 2.06
RA	550	22.4	12	21.1				
Transfusion								
No	1688	68.8	37	64.9	0.394	0.530	0.838	0.48 – 1.45
Yes	765	31.2	20	35.1				
ICU admission								
No	1719	70.1	24	42.1	3.922*	0.048*	0.311*	0.18 – 0.53
Yes	734	29.9	33	57.9				
Hospital stay duration (days)								
Preoperative								
Zero days	1080	44.26	39	68.4	13.416*	< 0.001*	2.755*	(1.57 – 4.84)
1 - 7	1248	50.8	17	29.8	9.876*	0.002*	0.410*	(0.23 – 0.73)
8 – 14	66	2.6	0	0.0	1.575	^{FE} p = 0.40	0.312	(0.02 – 5.11)
15 – 30	58	2.3	1	1.8	0.090	^{FE} p = 1.00	0.737	(0.10 – 5.42)
> 30	1	0.04	0	0.0	0.023	^{FE} p = 1.00	14.217	0.57 – 352.8
Postoperative								
Zero days	0	0.0	0	0.0	---	---	0	0
1 - 7	1467	59.8	30	52.6	1.191	0.275	0.747	(0.44 – 1.26)
8 – 14	523	21.3	8	14.0	1.773	0.183	0.603	(0.28 – 1.28)
15 – 30	450	18.3	12	21.1	0.272	0.602	1.187	(0.62 – 2.26)
> 30	13	0.5	7	12.3	97.308	< 0.001*	26.277*	(10.1 – 68.7)

χ^2 , p; χ^2 and p values for Chi square test; ^{MC}p: P value for Monte Carlo for Chi square test; *: Statistically significant at P ≤ 0.05; OR: Odds ratio; CI: Confidence interval.

The earliest and latest SSIs were detected on the 3rd and 29th day after operation respectively. The majority of SSI wounds detected were deep incisional (57.9%), followed by organ/space (26.3%) then superficial (19.3%).

Intrinsic or patient related factors

SSI development was significantly associated with smoking (OR 2.577; 95% CI: 1.49-4.47; $P < 0.001$), rural residence (OR 5.029; 95% CI: 2.37-10.66; $P < 0.001$), associated comorbidities as diabetes (OR 5.287; 95% CI: 3.09-9.05; $P = 0.001$), cardiovascular diseases (OR 2.530; 95% CI: 1.06-6.02, $P = 0.044$), organ failure (OR 5.801, 95% CI: 2.2-15.29, $P = 0.003$), remote or associated infections (OR = 9.362, CI: 5.31-16.52, $P < 0.015$) and previous hospital admission (OR 2.226; 95% CI: 1.32-3.77, $P = 0.002$) (Table 2).

Extrinsic or procedure related factors

Regarding the patients' preoperative conditions, SSI was significantly associated with preoperative non-showering (OR 2.794; 95% CI: 1.64-4.76, $P < 0.001$), ASA physical status score 5/E (OR 6.863; 95% CI: 3.11-15.16; $P < 0.001$). Class I: Clean wounds were the least to develop SSI (OR 0.124, 95% CI: 0.03-0.51, $P = 0.001$). Postoperative ICU admission (OR 3.22, 95% CI: 1.895.49; $P = 0.048$) and prolonged postoperative hospital stay (OR 26.277, 95% C.I: 10.1 – 68.7, $P < 0.001$) were found to be associated with higher incidence of SSIs (Table 3).

Isolate identification and antimicrobial susceptibility

Out of the total 57 wound samples that were cultured, 65 isolates were obtained. Of which 70.8% (46/65) were gram-negative bacilli GNB, 24.6% (16/65) were gram-positive cocci GPC and 4.6% (3/65) were *Candida albicans*. Using MALDITOF for identification to the species level, the most frequently

isolated GNB were *Escherichia coli* 21.5% (14/65) and *Klebsiella pneumonia* 20.0% (13/65). Among GPC, 7 isolates were *Staphylococcus aureus*, 7 isolates *coagulase negative staphylococci* (CoNS) spp (3 *S. haemolyticus*, 2 *S. epidermidis*, 1 *S. capitis*, 1 *S. hominis*) and 2 isolates were *Enterococcus faecalis*. Forty-three isolates were obtained from general surgery patients, *E. coli* and *K. pneumonia* were the two most commonly isolated pathogens (24/43).

Most of *E. coli* and *K. pneumonia* were ESBL producers (71% and 53% respectively). *K. pneumonia* and *Acinetobacter baumannii* were highly found to be carbapenemase producers (70%, 100% respectively) (Table 4). The only isolate from urology unit was an ESBL- producing *Proteus mirabilis* while that from orthopedic unit was a Carbapenemase producing XDR *P. aeruginosa* isolate. Thirteen percent (6/46) of the GNB were MDR (resistant to ≥ 1 agent in ≥ 3 antimicrobial categories). (Table 4). These isolates were resistant to cephalosporines, aminoglycosides and flouroquinolones but were still sensitive to b lactam/b lactamase combinations and carbapenams. More than half of GNB (25/46) were XDR (resistant to ≥ 1 agent in all but 2 or fewer antimicrobial categories) (Table 4). This group were sensitive to carbapenems and/or colistin. About 11 percent (5/46) were PDR (resistant to all agents in all antimicrobial categories) (Table 4).

Twenty isolates from the Obstetrics-Gynecology department, *Staphylococci spp* were the most commonly encountered isolates (12/20). Methicillin resistance was equally detected among *S. aureus* and CoNS isolates (86% each). None of those strains was vancomycin resistant. Both *Enterococcus faecalis* isolates were MDR but sensitive to vancomycin.

Discussion

SSI vary between developed and developing countries, according to type of operation and according

Table 4. Antibiotic resistant pattern among Gram Negative isolates.

	ESBL		MDR		XDR		PDR		Carbapenem resistance	
	No.	%	No.	%	No.	%	No.	%	No.	%
<i>Escherichia coli</i> (n = 14)	10	71.4	3	21.4	7	50.0	0	0.0	2	14.3
<i>Klebsiella pneumoniae</i> (n = 13)	7	53.8	1	7.7	9	69.2	2	15.4	9	69.2
<i>Proteus mirabilis</i> (n = 6)	4	66.7	0	0.0	3	50.0	2	33.3	2	33.3
<i>Citrobacter koseri</i> (n = 1)	0	0.0	0	0.0	0	0.0	0	0.0	0	00.0
<i>Enterobacter cloacae</i> (n = 1)	0	0.0	0	0.0	1	100.0	0	0.0	1	100.0
<i>Salmonella typhimurium</i> (n = 1)	0	0.0	0	0.0	0	0.0	0	0.0	0	00.0
<i>Pseudomonas aeruginosa</i> (n = 6)	3	50.0	2	33.3	1	16.7	1	16.7	3	50
<i>Acinetobacter baumannii</i> (n = 4)	3	75.0	0	0.0	4	100.0	0	0.0	4	100.0
Total (n = 46)	27	58.7	6	13.0	25	54.3	5	10.9	21	45.7

ESBL: extended spectrum β lactamase; MDR: Multi drug resistant (resistant to ≥ 1 agent in ≥ 3 antimicrobial categories); XDR: Extended drug resistant (resistant to ≥ 1 agent in all but 2 or fewer antimicrobial categories); PDR: Pan drug resistant (resistant to all agents in all antimicrobial categories).

to the protocol of surveillance adopted [14,15]. In this prospective study, 68.9% of surgical patients with complete follow up were enrolled with an overall SSIs rate found to be 2.27%. Overall SSI rate of 1.9% was found between 2006-2008 [14]. Low SSI Incidence rates were detected in our study, 2.8% and 2.7% in Obstetrics-Gynecology and General Surgery while 0.55% and 0.5% in Orthopedic Urology departments respectively. After abdominal hysterectomy, SSI rate was 26.9% which was the highest among all of our patients. This might be explained by the fact the most of patients in this group were elderly, diabetic and of rural residence. SSI percentages can differ even within the same country and same surgical procedure types due to difference in the duration and intensity of surveillance [16-20].

Patient risk factors as smoking, medical conditions like diabetes, previous hospitalization, having remote or associated infections and ASA score 5E were found to be significantly associated with increased SSI risk. These factors are considered controllable and modifiable and can reduce SSI by proper management and patients' compliance [8,20,21]. Regarding operative risk factors, Class I: Clean was the lowest to be associated with SSI while no statistical significance was detected in patients with operations > 2 hours vs. < 2 hours. A systematic review of 57 studies identified wound class and prolongation of surgery duration as independent predictors of SSI [22]. Long post-operative hospital stay and ICU admission were found to be risk factors for SSI. It is a global trend to shorten hospital stay to save cost, staffing and to decrease SSI. As a result, most SSI are detected postoperatively. About two thirds of SSI patient in this study were detected by PDS, most of which were detected at the outpatient clinic during their follow up visits (68.6%) followed by those detected using PDQ (22.8%). In a study with variable patient follow-up methods, most of the hospitals (73, 68%) were using PDS and showed higher SSI rates than hospitals with no PDS [23]. Telephone-based detection was found to be a useful tool for PDS in low income settings [24]. There is no scientific consensus on an ideal method of PDS and different approaches have been employed in different settings [25]. Post discharge patients typically choose a community clinic or nearby facilities to deal with their SSIs which can result in underestimation of the SSI rate.

Studies concerned with HAI surveillance monitor pathogens and their AMR pattern. MALDI-TOF MS was used in this study to rapidly identify the isolate, decrease the turnaround time of the culture result and thus improve the quality of patient care. In our study,

GNB were more prevalent accounting for 70.8%. Variations in the microbiology of SSIs may reflect the nature of operations being performed. In studies detecting SSI in orthopedics, *S. aureus* and *CoNS* are more prevalent than GNB. The reverse is true when studying SSI in general and obstetrics-gynecology surgery [16,20]. A report described HAIs in 4515 hospitals occurring in 2011–2014 found that *S. aureus* was the most prevalent SSI pathogen, but *E. coli* was more prevalent in abdominal surgery SSIs [5]. AMR is a global concern and for long no consensus for definitions of MDR, XDR and PDR making comparisons between studies impossible until international expert proposal for interim standard definitions for resistance was released [26]. Also, Carbapenemase producing enterobacteriaceae (CPE) definition was updated in NHSN in 2015 requiring resistance to one carbapenem with documented production of carbapenemase eg mCIM or molecular testing to the definition decreased false positives [27]. High rates of AMR were detected in our study. About half of GNB, mainly *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, were resistant to carbapenams. The growing threat of CPE leaves clinicians with only older highly toxic drugs eg. polymyxins to treat infected patients. Colistin resistance was also detected in 10% of our GNB isolates. Increase AMR is observed worldwide as noted in the third national summary of NHSN and a global systemic review [5,28].

Conclusion

Low SSI rates were detected in our study, but the high incidence of AMR identified is of great concern. To the best of our knowledge this is the first report from a non-teaching tertiary hospital with a dedicated IPC team, continuous surveillance with prospective data collection and data analysis giving feedback to surgeons for 2 years. It is the also the first time to use MALDI-TOF to help in rapid culture results.

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