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RESEARCH ARTICLE

BACTERIOLOGICAL PROFILE AND ANTIBIOGRAM OF SURGICAL SITE INFECTION AT A TERTIARY CARE HOSPITAL, AURANGABAD, MAHARASHTRA

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Abstract

Introduction: Surgical site infections (SSIs) are defined as infections that develop at the surgical site within 30 days of surgery (or within 90 days for some surgeries such as breast, cardiac and joint surgeries including implants). Surgical site infections (SSI) is one of the major healthcare-associated or nosocomial infection with a reported incidence rates of 4-17.8 % reported by various studies done in India and abroad.

Materials and Methods: A prospective observational study was undertaken from October 2017 to September 2019 and samples from 116 cases of SSI, as per CDC criteria identified during study period were included. The bacteriological profile and antibiogram of isolates were analyzed along with associated risk factors for development of SSI.

Results: Out of 108 bacterial isolates, 68.5% were Gram negative and 31.5% were Gram positive bacteria. The most commonly isolated organism was E. coli (30.5%), followed by Coagulase negative staphylococcus (13%), Staphylococcus aureus (12%), Klebsiella pneumoniae (10.2%), Acinetobacter species (10.2%) and Pseudomonas aeruginosa (10.2%) as major isolates. Most of the isolated Gram-negative bacteria were sensitive to Amikacin and Imipenem. Most of the isolated Gram-positive bacteria were sensitive to Linezolid. While analyzing risk factors associated with SSI cases, it was found that 28.4% of these cases were anemic, 19.8% were obese, 17.2% had a history of nicotine use and diabetes was associated with 8.6% of the cases.

Conclusion: The incidence of SSI is rising due to the emergence of multi-drug resistant bacteria. Rapid diagnosis of these pathogens will reduce the morbidity and mortality rate of SSI. A well defined antibiogram will help in reducing the morbidity and mortality associated with the SSI cases.

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Introduction:-

A surgical site infection is an infection that occurs after surgery in the part of the body where the surgery took place. Surgical site infections can sometimes be superficial infections involving the skin only, but other types of other surgical site infections are more serious and can involve tissues under the skin, organs or implanted material.^[1]

Surgical site infections (SSI) is one of the major healthcare-associated or nosocomial infection with a reported incidence rates of 4-17.8 % reported by various studies done in India and abroad.^[2,3,4,5,6,7,53,58] As per Centers for disease control and prevention (CDC), SSI is the costliest healthcare associated infection, increasing the healthcare and economic cost for patient care significantly.^[8] Despite various advances in SSI control practices it remains a significant cause of prolonged hospital stay, morbidity and mortality.^[8] It has been estimated that mortality rate associated with SSI is 3% and 75% of the SSI associated deaths are directly attributable to SSI.^[9] Though every surgical procedure does not cause SSI, but those procedures which are associated with one or more of the risk factors may lead to SSI. The risk factors leading to development of SSI can be patient related, procedure related, environment related or organism related.^[10] Among various risk factors associated with SSI, significant risk factors are anaemia, obesity, hypoproteinemia, prolonged hospital stay, diabetes mellitus, severity of disease, presence of drains, razor shaving as method of skin preparation, history of previous hospitalization, wound classification and surgical duration.^[5,11,12,13,32] Though surgical site infection can be caused by a large group of microorganisms; Staphylococcus aureus, members of Enterobacteriaceae family, Pseudomonas aeruginosa and Acinetobacter spp. are the predominant organisms which are associated with the SSI.^[2,5,6,7] The widespread and uncontrolled use of antibiotics has led to the major problem of emergence of resistant organism which contribute towards high morbidity and mortality.

In view of rising number of multidrug resistant bacterial pathogens associated with SSI and paucity of data from our region regarding the same, this study was undertaken with the aim to understand the local bacteriological profile and antibiogram of SSI associated pathogens along with the percentage distribution of various comorbidities associated with SSI in patients.

Material and Methods:-

A prospective observational study was undertaken from October 2017 to September 2019 after approval of the Institutional Ethical committee. A total of 116 cases of SSI were included into it. All cases of SSI, as per **CDC criteria** identified during study period were included.

Inclusion criteria:

All cases of superficial incisional and deep incisional SSI from which sample were received in Microbiology Department for culture sensitivity were included in the study.

Exclusion criteria:

Samples received from patients of SSI with Organ space infection and suture abscesses were excluded from the study. Duplicate samples from the same patient were also excluded.

Standard bacteriological techniques including like gram staining, colony morphology, motility testing and biochemical properties^[65,66] Antimicrobial susceptibility testing was done on Muller Hinton Agar by Kirby Bauer disc diffusion method as per CLSI guidelines.^[67,68] All the media, reagents and antimicrobial sensitivity testing discs used in the present study were obtained from Hi-Media Laboratory, Mumbai. Readymade plates of 5% sheep blood agar were used and other culture media were prepared in house from dehydrated culture media powder according to manufacturer's instruction

Results:-

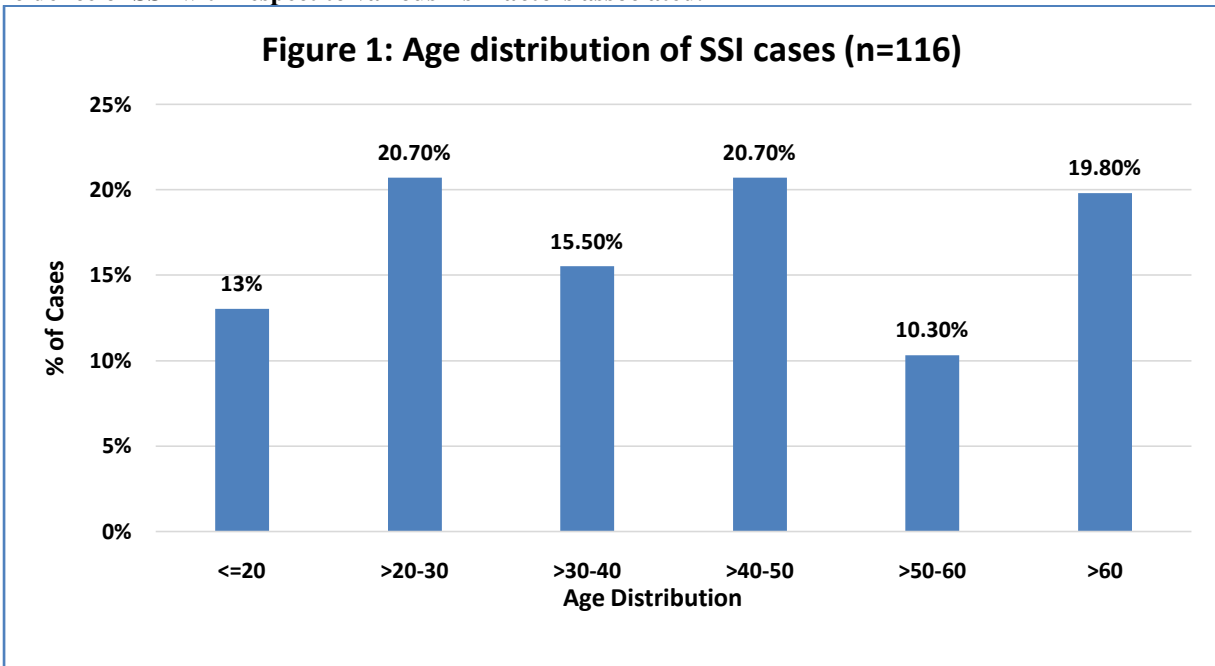
The present study was conducted in Department of Microbiology at a tertiary care hospital during period from October 2017 to September 2019 and a total of 116 samples from 116 cases of SSI cases were processed.

Out of the 116 SSI cases, 73.30% were Females and 26.70% were Males.

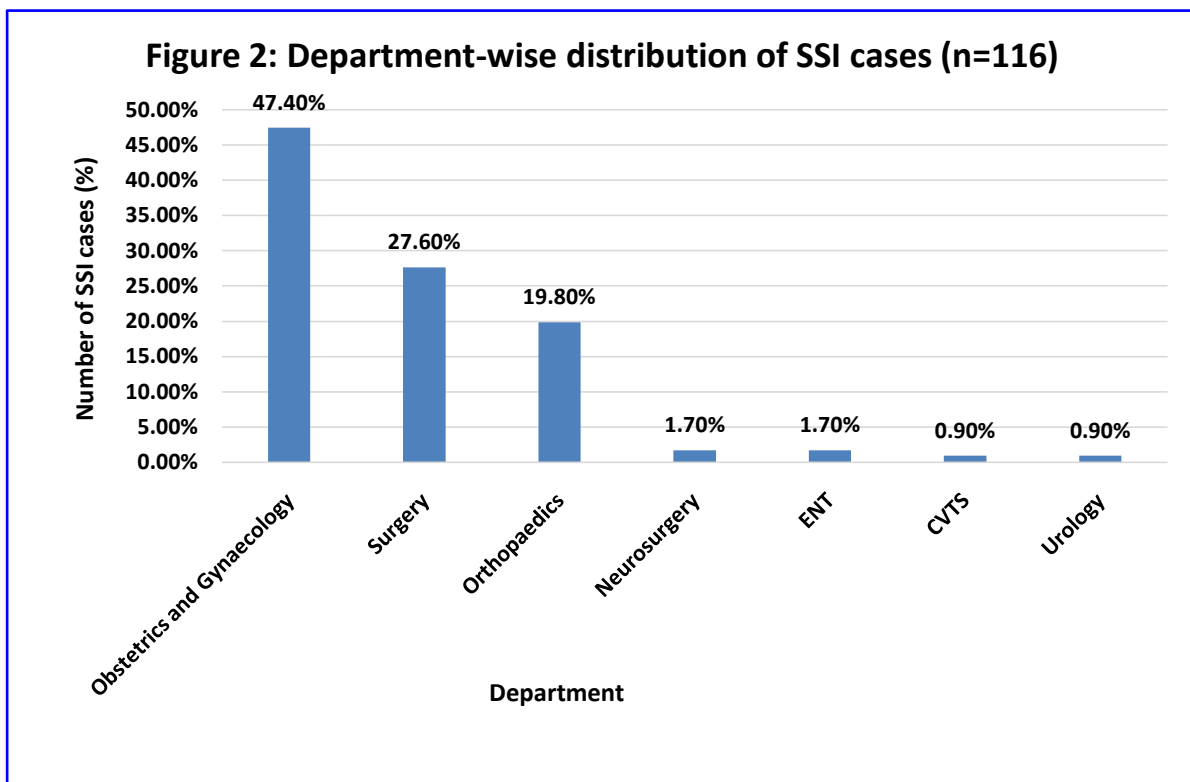
Culture positivity was found to be 77% and in 23% of cases no organism could be isolated.

Out of the 89 culture positive cases 82% cases were Monomicrobial and 18% cases were Polymicrobial.

Incidence of SSI with respect to various risk factors associated.

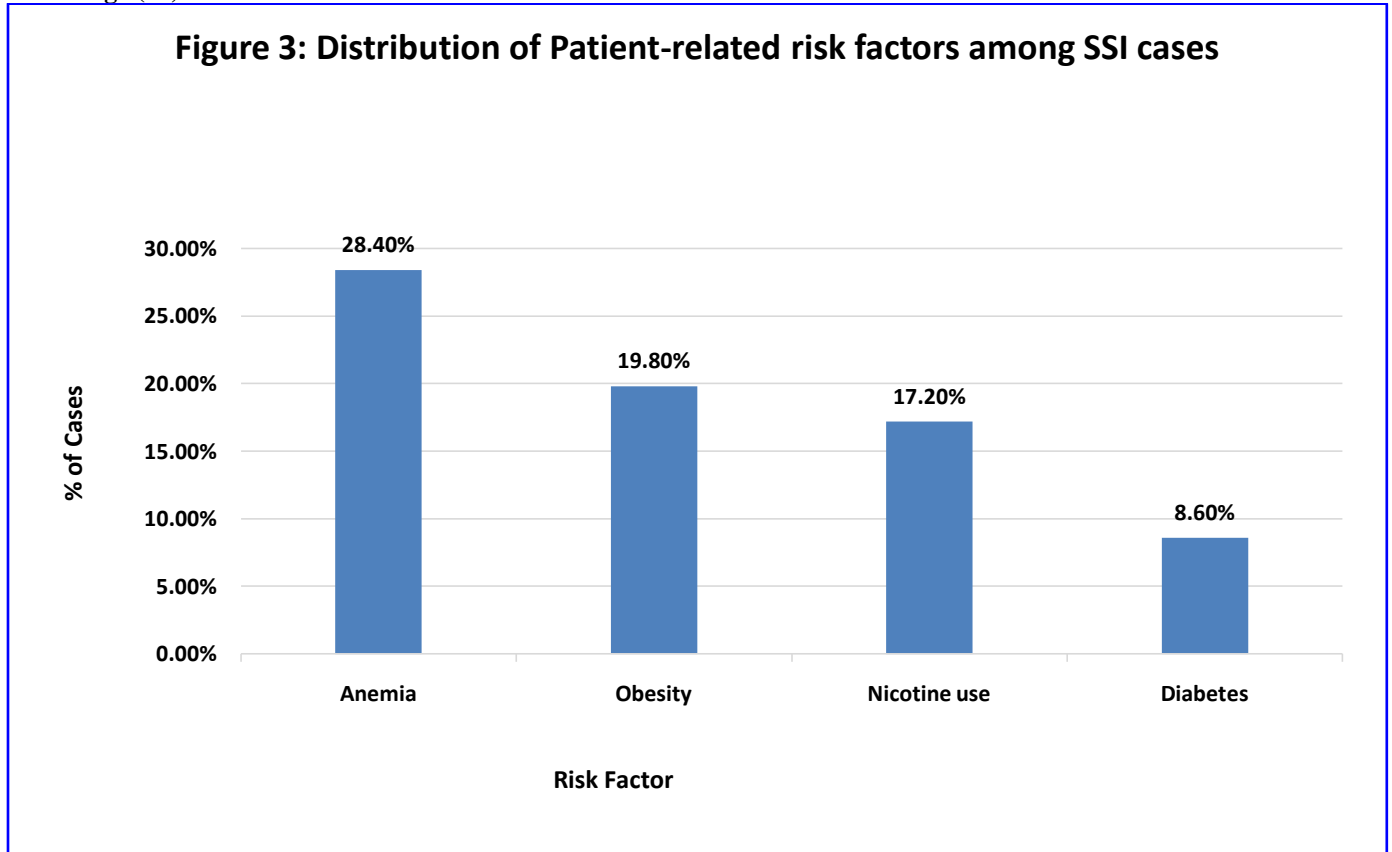


Majority of the SSI cases were from >20-30 and >40-50 age group.



Majority of the cases were from Obstetrics and Gynaecology (47.4%) followed by Surgery (27.6%) and Orthopaedics (19.8%).

Percentage (%) Distribution of various risk factors associated with SSI.



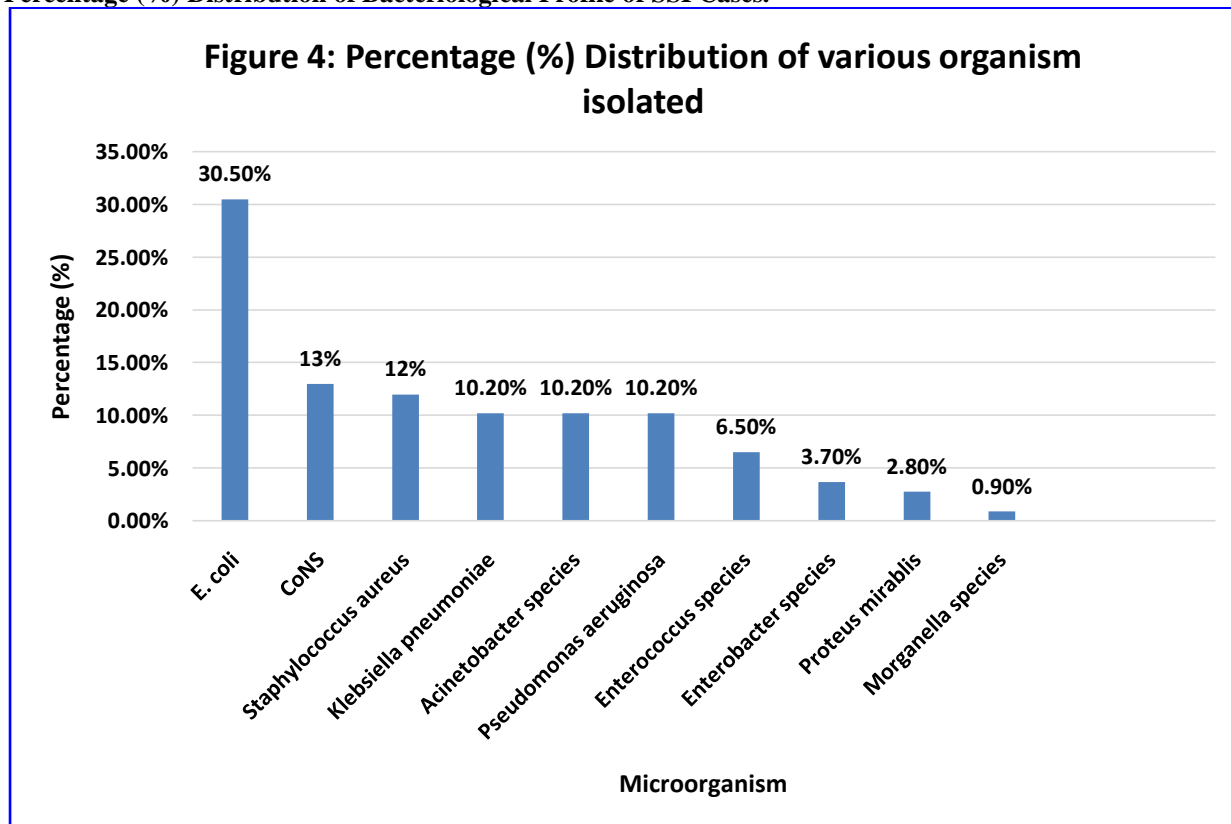
Anaemia was the major patient related risk factor associated with 28.4% of SSI cases.

Table 1:- Percentage (%) Distribution of various Procedure-related risk factors among SSI cases (n=116).

Risk Factor		Number of Cases (%)
Surgery	Elective	66.4%
	Emergency	33.6%
Preoperative Bath	Yes	58.6%
	No	41.4%
Preoperative Shaving	Yes	98.3%
	No	1.7%

Preoperative shaving was the most common procedure-related risk factor associated with majority (98.3%) of the SSI cases.

Percentage (%) Distribution of Bacteriological Profile of SSI Cases.



Out of 108 isolates, the most commonly isolated organism was E. coli (30.5%), followed by Coagulase negative Staphylococcus (13%) and Staphylococcus aureus (12%).

Table 2:- Percentage Distribution of Methicillin resistance among Gram positive isolates (n=27).

Organism	Number of isolates (n=27)		(n=)(%)
CoNS	14	MRCoNS	14 (100%)
		MSCoNS	0 (0%)
Staphylococcus aureus	13	MRSA	11 (85%)
		MSSA	2 (15%)

1. Among isolates of Staphylococcus species, Methicillin resistance was calculated using Cefoxitin (30 µg) antimicrobial disc.
2. Among 14 isolates of CoNS, 14 (100%) were methicillin resistant.
3. Among 13 isolates of S. aureus, 11 (85%) were methicillin resistant.

Antimicrobial sensitivity pattern (% Susceptibility) of Organisms Isolated from SSI cases.

Table 3:- Antimicrobial sensitivity pattern (% Susceptibility) of Gram negative isolates.

Organism Isolated (n=)	Antimicrobial												
		AK	AMP	AMC	CXM	CPM	CTR	CAZ	CIP	GEN	IMP	PIT	COT
E. coli	S	28	0	10	0	12	0	NT	3	22	23	15	8

(n=33)		(85%)	(0%)	(30%)	(0%)	(36%)	(0%)		(9%)	(67%)	(70%)	(45%)	(24%)
Klebsiella pneumoniae (n=11)	S	4 (36%)	0 (0%)	1 (9%)	0 (0%)	2 (18%)	1 (9%)	NT	1 (9%)	5 (45%)	3 (27%)	1 (9%)	5 (45%)
Acinetobacter species (n=11)	S	2 (18%)	NT	NT	NT	NT	NT	0 (0%)	0 (0%)	0 (0%)	1 (9%)	1 (9%)	NT
Pseudomonas aeruginosa (n=11)	S	6 (55%)	NT	NT	NT	NT	NT	5 (45%)	6 (55%)	5 (45%)	8 (73%)	6 (55%)	NT
Enterobacter species (n=4)	S	1 (25%)	0 (0%)	0 (0%)	0 (0%)	1 (25%)	0 (0%)	NT	3 (75%)	2 (50%)	2 (50%)	0 (0%)	2 (50%)
Proteus mirabilis (n=3)	S	2 (67%)	NT	NT	NT	NT	NT	2 (67%)	2 (67%)	2 (67%)	0 (0%)	2 (67%)	NT
Morganella species (n=1)	S	1 (100%)	NT	NT	NT	NT	NT	1 (100%)	1 (100%)	1 (100%)	0 (0%)	1 (100%)	NT

Among Gram negative isolates, E. coli was the most predominant isolate (n=33), E. coli was most susceptible to Amikacin (85%), followed by Imipenem (70%), Gentamicin (67%), Piperacillin-tazobactam (45%), Cefepime (36%), Amoxicillin-clavulanic acid (30%), Cotrimoxazole (24%), Ciprofloxacin (9%), none of the isolates were susceptible to Ampicillin (0%), Cefuroxime (0%) and Ceftriaxone (0%).

Table 4: Antimicrobial sensitivity pattern (% susceptibility) of Gram positive isolates

Organism Isolated (n=)		Antimicrobial					
			CD	E	LZ	P	COT
Staphylococcus species (CoNS) (n=14)	MRCoNS (n=14)	S	5 (36%)	2 (14%)	14 (100%)	0 (0%)	5 (36%)
Staphylococcus aureus (n=13)	MRSA (n=11)	S	5 (45%)	5 (45%)	11 (100%)	0 (0%)	2 (18%)
	MSSA (n=2)	S	2 (100%)	2 (100%)	2 (100%)	1 (50%)	0 (0%)
Enterococcus species (n=7)		S	5 (71%)	1 (14%)	6 (86%)	3 (43%)	5 (71%)

All 14 isolates of CoNS were Cefoxitin resistant (MRCoNS). They showed maximum susceptibility to Linezolid (100%), followed by Clindamycin (36%), Cotrimoxazole (36%) and Erythromycin (14%), none of the isolates were susceptible to Penicillin (0%).

Among 13 isolates of Staphylococcus aureus, 11 (85%) were resistant to Cefoxitin (MRSA) and 2 (15%) were sensitive (MSSA).

Among MRSA maximum susceptibility was seen to Linezolid (100%), followed by Clindamycin (45%), Erythromycin (45%) and Cotrimoxazole (18%), none of the isolate was sensitive to Penicillin (0%).

Among MSSA maximum susceptibility was seen to Linezolid (100%), Clindamycin (100%) and Erythromycin (100%), followed by Penicillin (50%), none of the isolate was sensitive to Cotrimoxazole (0%).

Discussion:-

Despite various advances in SSI control practices such as improved operating room ventilation, better sterilization methods, use of barriers, advancement in surgical techniques and availability of better antimicrobial prophylaxis,

SSIs remain a significant cause of prolonged hospital stay, morbidity and mortality. ^[8] The rapidly rising resistance among microorganisms to the available antimicrobials is further complicating the situation.

Usually under normal conditions, most of the patients do not develop surgical site infection as there are variety of host defense factors playing their part to eliminate the invading microbial pathogen and thus preventing any microbial build up at the surgical site. But when these host defense mechanisms fail to respond or under respond, which may be because of the various patient related risk factors like old age, diabetes, obesity, anemia, nicotine use or immunosuppression, ^[5,12,13,23,24,32] there is failure of elimination of the invading microbial pathogen and when this is associated along with greater microbial load and/or higher virulence, development of SSI proceeds.

Majority of the SSI cases in our study were from >20-30 (20.7%) and >40-50 (20.7%) age groups, which is not in accordance with findings of most of the studies, ^[2,4,7,64] as they have reported higher rate of SSI in age group > 50 years; the higher rate of SSI in our study, in these two age groups may be because of higher number of female patients undergoing Caesarean section and Hysterectomies in our study, who usually belong to these age groups. Another reason may be that pregnancy is associated with immunosuppression and immunosuppression is a known risk factor for causing SSI. ^[10,42]

In our study among 116 SSI cases, 28.4% were anaemic, 19.8% were obese, 17.2% had a history of Nicotine use and diabetes was associated with 8.6% of the cases, all these finding may be significant, as anaemia, obesity, diabetes and nicotine use are known risk factor for causing SSI, as has been reported by various studies. ^[3,16,17,18,21,22,23,24,25,26,27,28,32,52,62]

In our study 33.6% of the SSI cases had undergone emergency surgeries and 66.4% were elective surgeries, the higher association of SSI cases with elective surgeries in our study may be because of the fact that in 90% of the elective surgeries, duration was more than 1 hour. The longer duration of surgery is a known risk factor associated with SSI and has been reported by various authors. ^[34,35,36,37,38,39,52,53]

In our study, 98% of the patients had pre-operative hair removal with razor shaving, which is a known risk factor for causing SSI, as documented by various authors. ^[10,11,42] With these findings it is advised that pre-operative shaving be avoided completely, instead use of clippers or no pre-operative shaving is advised.

In our study, 100% of the patients had maintenance of normothermia. Hypothermia has been well documented as a risk factor associated with SSI. ^[10,43,44,45]

In our study, 59.5% cases had a preoperative stay longer than 2 days. Prolonged preoperative stay is a known risk factor for causing SSI. ^[5,29,30]

In the present study the, 73.3% of the SSI cases were females and 26.7% of the cases were males. This is in contrast to other studies as most of the studies done have shown higher SSI rate among male population ^[2,6,7,51,57,61], though two studies reported incidence of SSI to be more among female patients ^[53,64]. Most of the studies have reported higher incidence of SSI among male patients as compared to female patients which is in disagreement with our study, this may be because of higher number of surgeries done in OBGY department in our hospital as compared to other departments and may be also because of better awareness among staff of OBGY regarding SSI.

In our study, majority of the surgical (operative) wound type associated with SSI cases were Clean Contaminated (50.9%), followed by contaminated (23.3%), Clean (17.2%) and Dirty wounds(8.6%), this finding is not in agreement with other studies, ^[6,7,56] as most of the studies report highest number of SSI cases to be associated with dirty wounds, followed by contaminated, clean-contaminated and clean wounds. The reason for this may be due to that fact that 47.4% of the SSI cases in our study were from obstetrics & gynaecology department, and majority of those cases were clean-contaminated.

In the current study a total of 116 cases of SSI were studied and culture positivity was seen in 89 cases (77%) and a total of 108 organism were isolated. Among 89 cases, 73 cases (82%) were monomicrobial and 16 (18%) of the cases were polymicrobial. Our findings regarding culture positivity were consistent with studies done by some authors, ^[6,60,61] but some studies ^[2,56] have reported higher rate of culture positivity and Palange P et al (2019) ^[64] reported lower rate of culture positivity, this may be because of the difference in timing of sending sample

to microbiology lab for culture, after starting antibiotics and also because anaerobic culture is not routinely done in all microbiology laboratories.

Our findings regarding number of monomicrobial and polymicrobial infections in SSI cases, is consistent with most of the studies except for few studies {Mundhada A.S. et al (2015)^[52] and Akhi M.T. et al (2015)^[51]}.

The most commonly isolated organism in the present study was E.coli (30.5%), followed by Coagulase negative staphylococcus (13%), Staphylococcus aureus (12%), Klebsiella species (10.2%), Acinetobacter species (10.2%), Pseudomonas aeruginosa (10.2%), Enterococcus species (6.5%), Enterobacter species (3.7%), Proteus mirabilis (2.8%) and Morganella species (0.9%). Our findings regarding profile of bacteria causing SSI is in agreement with studies done by Shreeram G. et al (2016)^[55] and Palange P et al (2019)^[64], most of the other studies done have reported Staphylococcus aureus as the most common pathogen isolated in their study, which is in contrast to our study, but the overall bacteriological profile of majority of the studies was in accordance with our study. As per CDC, S. aureus, E. coli and CoNS are the most prevalent organisms associated with surgical wound infection, which is also in accordance with our study.^[73]

In the present study, E. coli were most susceptible to Amikacin (85%), followed by Imipenem (70%), Gentamicin (67%), Piperacillin-tazobactam (45%), Cefepime (36%), Amoxicillin-clavulanic acid (30%), Cotrimoxazole (24%), Ciprofloxacin (9%), none of the isolates were susceptible to Ampicillin (0%), Cefuroxime (0%) and Ceftriaxone (0%). In our study E. coli showed maximum susceptibility to Imipenem, Amikacin and Piperacillin-tazobactam; whereas high level of resistance was seen to Ampicillin, Ceftriaxone, Cefuroxime and Amoxicillin-clavulanic acid, moderate level of susceptibility was seen to Ciprofloxacin, Gentamicin, Cefepime and Cotrimoxazole. Our findings are in agreement with other studies as most of the studies have reported high level of resistance among E. coli to Cephalosporins and moderate to high level of sensitivity to Amikacin, Imipenem, Gentamicin and Piperacillin-tazobactam.

In the present study, Klebsiella pneumoniae were most susceptible to Gentamicin (45%), followed by Cotrimoxazole (45%), Amikacin (36%), Imipenem (27%), Cefepime (18%), Amoxicillin-clavulanic acid (9%), Ceftriaxone (9%), Ciprofloxacin (9%) and Piperacillin-tazobactam (9%), none of the isolates were susceptible to ampicillin (0%) and cefuroxime (0%). By reviewing the other studies^[2,6,51,52,55,56,64], it is clear that the most susceptible antibiotic for Klebsiella pneumoniae is Imipenem, Amikacin and Piperacillin-tazobactam, but in our study a high level of resistance was seen to these antimicrobial agents. In the present study highest susceptibility was observed to Gentamicin, this difference in susceptibility pattern may be because of indiscriminate use of these antibiotics. In our and most of the other studies^[2,6,51,52,55,56,64] Klebsiella pneumoniae was least susceptible to Ampicillin.

In the present study, Acinetobacter species showed maximum susceptibility to Amikacin (18%), followed by Imipenem (9%) and Piperacillin-tazobactam (9%). None of the isolates were susceptible to Ceftazidime (0%), Ciprofloxacin (0%) and Gentamicin (0%). In our study, Acinetobacter species showed a high level of resistance to various antibiotics tested, which is not in accordance with other studies^[2,51,55,56,64], in which high to moderate level of susceptibility was seen to Imipenem, Amikacin, Ciprofloxacin, Gentamicin and Piperacillin-tazobactam. This disparity may be because of presence of highly resistant strains in our hospital.

In the present study, Pseudomonas aeruginosa showed maximum sensitivity to Imipenem (73%), followed by Amikacin (55%), Ciprofloxacin (55%), Piperacillin-tazobactam (55%), Ceftazidime (45%) and Gentamicin (45%). In our study, Pseudomonas aeruginosa showed moderate level of susceptibility to various antimicrobials tested. None of the isolate was 100% susceptible to any of the antimicrobials tested, which is not in accordance with some of the other studies^[6,52,64], where almost 100% susceptibility was observed to Imipenem, Piperacillin-tazobactam and Amikacin. Few other studies have also reported moderate to high level of resistance to various antimicrobials.

In the present study, all isolates of CoNS were sensitive to Linezolid (100%). The susceptibility to Clindamycin, Cotrimoxazole and Erythromycin was 36%, 36% and 14% respectively. None of the isolates were susceptible to Cefoxitin (0%) and Penicillin (0%). In the present study CoNS was 100% susceptible to Linezolid, which is in accordance with other studies^[6,51,61,64]. Though other studies have reported moderate level of susceptibility to

Clindamycin, Erythromycin and Cotrimoxazole, in our study the susceptibility was slightly lower, which may be because ours is a tertiary care hospital and also may be because of indiscriminate use of these antibiotics.

In the present study, all isolates of *Staphylococcus aureus* were sensitive to Linezolid (100%), followed by Clindamycin (54%), Erythromycin (54%), Cotrimoxazole (15%), Cefoxitin (15%) and Penicillin (8%). In our and many of the other studies^[2,6,51,61,64], *Staphylococcus aureus* showed 100% susceptibility to Linezolid. Moderate level of susceptibility was seen to Clindamycin and Erythromycin in our study, which is in accordance with many of the other studies^[6,52,56,59,61]. While other studies reported moderate level of susceptibility to Cotrimoxazole, in our study high level of resistance was seen.

In our study, among isolates of *Staphylococcus aureus*, 85% were MRSA, which is in agreement with other studies^[51,61]. Syed A et al^[60] reported 100% MRSA isolates and Mundhada A.S. et al^[52] reported none of the *S. aureus* isolates to be MRSA. This difference may be because of the varying number of *S. aureus* isolated in various studies and also may be because of different levels of anti-microbial resistance among *S. aureus* in different regions.

In our study, isolates of *Enterococcus* species, *Enterobacter* species, *Proteus mirabilis* and *Morganella morganii* were fewer in number, so it very difficult to compare their susceptibility percentage to various antimicrobials, with other studies.

With the above reported results, it is clear that for SSI infections due to gram negative bacilli, Imipenem and Amikacin can be used empirically, also as most of the gram negative isolates showed a high level of resistance to Cephalosporins, use of Cephalosporins should be restricted. For SSI infections due to gram positive isolates Clindamycin and Cotrimoxazole can be used empirically and Linezolid can be reserved for serious infection due to methicillin resistant *Staphylococcal* isolates.

The high level of Cephalosporin resistance among gram negative isolates can mean that they may be ESBL producers.

Summary and Conclusion:-

Surgical site infection (SSI) is one of the major nosocomial infection. Despite of advancements in surgical techniques and availability of better antimicrobial prophylaxis, SSIs remain a significant cause of prolonged hospital stay, morbidity and mortality. The widespread and uncontrolled use of antibiotics, has led to the major problem of emergence of resistant organism, which contribute towards high morbidity and mortality associated with SSI. The present study was therefore conducted to obtain a better understanding of local bacteriological profile and antibiogram of SSI, so as to decrease the incidence of SSI, which is an indicator of health care system in a given set up.

In the present study 116 cases of SSI were studied. Majority of the patients were from >20-30 (20.7%) and >40-50 (20.7%) age group.

28.4% of these cases were anemic, 19.8% were obese, 17.2% had a history of nicotine use and diabetes was associated with 8.6% of the cases. 33.6% of the SSI cases had undergone emergency surgeries and 66.4% underwent elective surgeries. 73.30% of these SSI cases were Females and 26.70% were Males.

Among these 116 cases culture positivity was seen in 89 cases (77%). Out of these 89 cases, 73 cases (82%) were monomicrobial and 16 (18%) were polymicrobial and a total of 108 organism were isolated.

Out of 108 bacterial isolates, 74 (68.5%) were Gram negative and 34 (31.5%) were Gram positive bacteria. The most commonly isolated organism was *E. coli* (30.5%), followed by Coagulase negative staphylococcus (13%), *Staphylococcus aureus* (12%), *Klebsiella pneumoniae* (10.2%), *Acinetobacter* species (10.2%) and *Pseudomonas aeruginosa* (10.2%) as major isolates.

Isolated *E. coli* strains showed maximum susceptibility to Amikacin (85%), Imipenem (70%) and Gentamicin (67%).

Klebsiella pneumoniae showed 45% susceptibility to Gentamicin and Cotrimoxazole. Isolated strains of *Pseudomonas aeruginosa* showed 73% susceptibility to Imipenem and 55% each to Amikacin, Ciprofloxacin and Piperacillin-tazobactam.

Isolated *Acinetobacter* species showed a high level of resistance to various antibiotics tested, maximum sensitivity of 18% was seen towards Amikacin.

Isolated *Staphylococcus aureus* strains were 100% sensitive to Linezolid, 54% sensitive to Clindamycin and 54% sensitive to Erythromycin.

It was seen that 85% strains of *Staphylococcus aureus* were Methicillin resistant (MRSA). All isolates (100%) of CoNS were Methicillin resistant (MRCoNS). Isolated CoNS strains were 100% sensitive to Linezolid. The sensitivity to Clindamycin and Cotrimoxazole both was 36%. Most of the isolated Gram-positive bacteria were sensitive to Linezolid.

Most of the isolated Gram-negative bacteria were sensitive to Amikacin and Imipenem. There was no single antibiotic to which all isolated Gram positive and Gram-negative bacteria were 100% sensitive.

It can be concluded, though Surgical site infections cannot be completely eliminated, but a better understanding of the bacteriological profile and antibiogram in SSI cases can help in strengthening the antibiotic policy for better empirical and definitive treatment.

The results also show the presence of varying degree of antimicrobial resistance among both gram-positive and gram-negative organisms in our area. An effective strategy to control this problem, would be possible by proper implementation of hospital anti-microbial policy and adherence to basic infection control policies. This in turn will help to preserve the effectiveness of the drugs presently available and limit the spread of resistance.

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