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Commonly Isolated Pathogens from Postoperative Wounds and Antibiotic Susceptibility Testing At a Tertiary Care Hospital in Stip, North Macedonia

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Abstract: The increasing rates of hospital infections and bacterial resistance to commonly used antibiotics have created huge problem in the management of different infections. The objective of this study was to identify isolated pathogens from swab samples of postoperative woundstaken at a tertiary care hospital in Stipandto determine microbial susceptibility to antibiotics. Therefore, a total of 139 wound swab samples from two different departments (surgery and orthopedics) at a tertiary care hospital were processed using standard microbiological techniques. The colonies grown were identified based on colony morphology, Gram stains, and biochemical tests for accurate microbial identification. Antimicrobial susceptibility testing was performed by Kirby–Bauer disc diffusion technique. Among total 139 wound swab samples processed, from a total of 2344 operated patients, 100 samples (4,3%) were culture positive. The most common isolated gram-positive bacteria were *Staphylococcus aureus* (27 samples), among which 44% contained MRSA and *Enterococcus*(9 samples) among which 50% were found to have multidrug resistance to penicillin, macrolides, cephalosporines, clindamycin, folate synthesis inhibitors and quinolones. The most common isolated gram-negative bacteria were *Escherichia coli* (17 samples) and *Pseudomonas aeruginosa* (13 samples) among which 50% were found to have multidrug resistance to beta-lactam antibiotic, chloramphenicol, folate synthesis inhibitors and quinolones. The highest percentage of isolated pathogens was found in the samples obtained from the orthopaedic department.Gram-negative infections were predominant. Increased rate of MRSA resistance and multidrug resistance was noted.
Keywords: swab; postoperative wounds; antimicrobial susceptibility; bacterial resistance, multidrug resistance

I. INTRODUCTION

The increasing rates of hospital infections, as a result of wound infection, plays an important role in the development of chronic, delayed wound healing. Bacterial resistance and multidrug resistance to commonly used antibiotics have created a great problem in the management of different infections, especially methicillin resistant strains caused by *Staphylococcus* aureus[1].The increased prevalence of the methicillin resistant strains of Staphylococcus aureus has impelled usage of clindamycin for treatment of this infections. However, there are recent reports of increasing resistance of these strains also to clindamycin, due to the irrational use of the antibiotics[2].

Wounds are an underestimated but serious complication for a diverse spectrum of diseases.Bacterial infections are serious problems to the successful treatment of the wounds sometimes causing complications that lead to fatal sepsis.Therefore, for successful treatment of wound infections it is very important to identify bacterial pathogens present in infected wounds and characterize their resistance profile to the most common antibiotics used in therapy[3].

According to the literature data, the common bacterial pathogens responsible for wound infections are *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and bacteria belonging to family *Enterobacteriaceae spp.*[4,5].The most frequent pathogens who have a significant impact on morbidity and mortality are

Methicillin-resistant *Staphylococcus aureus* (MRSA), Vancomycin-resistant *Enterococcus* (VRE), *Mycobacterium tuberculosis* and *Streptococcus* pneumoniae[6].

Bacterial and multidrug resistance is a global problem that must be resolved locally, having in mind that there are significant geographical variations in the participation of certain resistant strains, as the triggers of bacterial infections. To understand bacterial resistance, there is a huge need to interpret molecular mechanisms of antibiotic resistance, especially to Gram-negative and Gram-positive clinical pathogens[7,8].

In this study, we determined the bacteriological profile of wound infections among hospitalized people at a tertiary care hospital in Stipand their antimicrobial susceptibility patterns.

II. MATERIAL AND METHODS

In a period of 18 months (from January 2018 till June 2019) swab wounds samples from 139 patients were collected from two different departments at a tertiary care hospital in Stip,We chose departments where intrahospital infections occur most frequently: surgery department and orthopedic department.

Sample collection was performed from open wound by the resident physicians using Sterile Swab Sticks as per existing departmental guidelines. The wound and surrounding skin was cleaned carefully with saline in order to avoid surface contamination. The specimens were collected on sterile cotton swab by rotating with enough pressure. Then, the samples were transferred to microbiology laboratory within an hour of collection using airtight sterile vial. Informed consent was obtained from all the patients participated in the study.

The samples were processed with standard microbiological techniques and the colonies grown were identified based on the colony morphology, Gram stains, biochemical tests and VITEK 2 system for accurate microbial identification. Antimicrobial susceptibility testing was performed by Kirby–Bauer disc diffusion technique following clinical and laboratory standards institute (CLSI) guidelines[9].The plate was observed for zone of inhibition according to CLSI guidelines.The inhibition zones around the discs were measured and interpretation of the inhibition zone values (S-sensitive / R - resistant) was based on the EUCAST v 9.0 criteria.

The antibiotic discs used were beta lactam antibiotics from the classes of penicillins, cephalosporines and carbapenems (Ampicillin, Amoxicillin+Clavulanic acid, Penicillin, Methicillin, Cefuroxime, Cefotaxime, Ceftriaxone, Cephalexin, Cefixime,Imipenem, Ertapenem, Meropenem), Aminoglycoside antibiotics (Amikacin, Gentamicin), Macrolide antibiotics (Erythromycin, Azithromycin, Josamycin), folate synthesis inhibitors (Trimethoprim+Sulfamethoxazole), Chloramphenicol, Tetracyclines (Doxycycline, Oxytetracycline), Fluoroquinolones (Pefloxacin, Ofloxacin, Ciprofloxacin, Levofloxacin, Norfloxacin) and others (Vancomycin, Clindamycin, Piperacillin+Tazobactam, Fusidic acid, Rifampicin, Nitrofurantoin, Nalidixic acid, Pipemidic acid).

Bacterial strains showing resistance to three or more classes of antibiotics at the same time were considered as multidrug resistant[10].

III. RESULTS

Distribution within departments

In our case, wound swab samples were taken from two different department at a tertiary care hospital in Stip. From a total number of 2344 operated patients, 139 wound swab samples were processed and 100 (4.3%) samples turned out to be culture positive. In the period of examination, from the total number of 1517 patients operated on the department of surgery, 31 (2.04%) had an intrahospital wound infection. From the total number of 827 patients operated on the orthopedics department, 69 (8.3%) had an intrahospital wound infection. The highest percentage of isolated pathogens was found at the orthopedics department. There is a statistically significant difference regarding the occurrence of the intrahospital wound infections between this two departments (difference between two proportions: $p = 0.0000$).

The main characteristics of distribution are shown in Table 1.

Table 1.Distribution of culture positive samples

Department	Wound swab samples		
	Total	Positive	Percent of culture positive samples
Surgery	42	31	74
Orthopedics	97	69	71

Most common isolated pathogens

The present study showed that the most common isolated pathogen in post-operative wounds was *S. aureus* (n = 27; 27%), followed by *E. coli* (n = 17; 17%), *P. aeruginosa* (n = 13; 13%), *Proteus*(n = 9; 9%) and *Enterococcus* (n = 9; 9%). The other bacteria were isolated in a relatively low percentage. Gram-negative infections were predominant (Table 2). The distribution of the most common pathogens in surgery and orthopedic departments is shown in Table 3.

Table 2.Gram-positive vs Gram-negative pathogens isolated from culture positive samples

Department	Wound swab samples		
	Total culture positive samples	Gram-positive infections	Gram-negative infections
Surgery	31	6	25
Ortopedics	69	33	36
Total	100	39	61

Table 3.Distribution of most common pathogens

Department	*S. aureus*	*E. coli*	*P.aeruginosa*	*Proteus*	*Enterococcus*
Surgery	16%	19%	32%	/	3%
Ortopedics	32%	16%	4%	13%	12%

Note: % is the percentage of pathogen relative to the total number of culture positive samples in that department

Antibiotic susceptibility testing of common isolated bacteria

A total of 100 culture positive samples were isolated. The in vitro antibiotic susceptibility of the common isolated pathogens is shown in Table 4.

Multidrug resistance was observed for *S. aureus* to penicillin's (range 22%–74%), macrolides (33%), clindamycin (33%) and aminoglycosides (29%). MRSA constituted 48% of all S. aureus isolates and MRSA isolates showed resistance.

Remarkably high resistance was observed for *P. aeruginosa* to penicillin's (ranged between 77%–85%) and folate synthesis inhibitors (69%).

Almost the same situation is notice for *E. coli* to penicillin's (range 70%–88%) and folate synthesis inhibitors (41%).

Proteus showed higher susceptibility to almost all classes of antibiotics.

Isolated *Enterococcus sp.* showed good sensitivity to carbapenems. Multidrug resistance was observed to other β-lactam antibiotics (penicillin, cephalosporins) ranged between 11-66%, clindamycin (77%), folate synthesis inhibitors (77%) and macrolides (55%).

According to the data (Table 4), the multidrug-resistant rates were highest for *P. aeruginosa* and *E. coli*, followed by *Enterococcus sp.* and *S. aureus*.

Table 4.In vitro antibiotic susceptibility of the common isolated pathogens

Antimicrobial class/agent tested	Resistance by organism (number tested) R (%)				
	S. aureus (n=27)	*E. coli* (n=17)	*P. aeruginosa* (n=13)	*Proteus* (n=9)	*Enterococcus* (n=9)
Penicillin					
Ampicillin	6 (22 %)	15 (88 %)	11 (85 %)	9 (100 %)	3 (33 %)
Amoxicillin+ Clavulanic acid	10 (37 %)	12 (70 %)	10 (77 %)		1 (11 %)
Penicillin	20 (74 %)				6 (66 %)
Methicillin	13 (48 %)				
Cephalosporins					
Cefuroxime	3 (11 %)		6 (46 %)	1 (11 %)	5 (55 %)
Cefotaxime	9 (33 %)	12 (70 %)	6 (46 %)	1 (11 %)	4 (44 %)
Ceftriaxone	3 (11 %)		6 (46 %)		2 (22 %)
Cephalexin	6 (22 %)	12 (70 %)	8 (61 %)	1 (11 %)	4 (44 %)

Cefixime	17 (63 %)	13 (76 %)	12 (92 %)	1 (11 %)	6 (66 %)
Carbapenems					
Imipenem	1 (3.5 %)				1 (11 %)
Ertapenem	2 (7 %)	3 (17 %)	1 (7 %)	1 (11 %)	
Meropenem					1 (11 %)
Aminoglycosides					
Amikacin		4 (23 %)	1 (7 %)		3 (33 %)
Gentamicin	8 (29 %)	7 (41 %)	1 (7 %)		5 (55 %)
Tetracycline					
Doxycycline		3 (17 %)	3 (23 %)		3 (33 %)
Oxytetracycline			1 (7 %)		
Macrolides					
Erythromycin	9 (33 %)				5 (55 %)
Azithromycin	9 (33 %)				5 (55 %)
Fluoroquinolones					
Pefloxacin	1 (3.5 %)	5 (29 %)	1 (7 %)	3 (33 %)	2 (22 %)
Ofloxacin	4 (185%)	6 (35 %)	5 (38 %)	1 (11 %)	4 (44 %)
Ciprofloxacin	1 (3.5 %)	2 (12 %)	3 (23 %)		1 (11 %)
Levofloxacin				1 (11 %)	
Norfloxacin				1 (11 %)	
Others					
Clindamycin	10 (33 %)	2 (12 %)	1 (7 %)	1 (11 %)	7 (77 %)
Trimethoprim+ Sulfamethoxazole	2 (7 %)	7 (41 %)	9 (69 %)	4 (44 %)	7 (77 %)
Vancomycin	3 (11 %)				
Chloramphenicol	2 (7 %)	7 (41 %)	6 (46 %)	4 (44 %)	1 (11 %)
Piperacillin+ Tazobactam		6 (35 %)	7 (54 %)	1 (11 %)	4 (44 %)
Fusidic acid	9 (33 %)				
Rifampicin	1 (3.5 %)				
Nitrofurantoin				1 (11 %)	
Nalidixic acid				1 (11 %)	
Pipemidic acid				1 (11 %)	

IV. DISCUSSION

Intrahospital infections is a heterogeneous group of infectious diseases that are associated with increased morbidity, mortality, hospitalization, and cost of care in intensive care units.Analysis of microbiological isolate together with antibiotic susceptibility testing is necessary for optimal antibiotic use and reduction of intrahospital infections and bacteria resistance.

According to the literature, the level of resistance of bacteria isolated in hospitals is higher as compared to general practice. Hospitals are often regarded as the focal point for emergence development of resistance and multidrug resistance[11].Therefore, in our study we examined the antibiotic susceptibility of common isolated pathogens in a post-operative wound swab samples at clinical for tertiary care in Stip.

At a tertiary care clinic in Stip, most of the population from eastern North Macedonia is seeking health care. This was the reason why we decided to monitor intrahospital infections at this clinic. In our case wound swab samples were taken from two different department, where intrahospital infections occur most frequently with emphasize on orthopedic department, considering that surgical site infections are persistent and preventable health care–associated infections[12].

The total rate of isolated pathogens on both of the departments was not statistically higher (4.3%) as compared to studies conducted in different parts of the world (North America and Europe) where 5% –10% of all hospitalizations result in nosocomial hospital-acquired/associated infections[13]. The rate of 8.3% on the orthopedic department is higher compared with the rate of 2.04% on the department of surgery. This situation requires additional activities and measures to be taken to improve the clinical outcome of patients.

Gram-negative infections were predominant (61 Gram-negative vs 39 Gram-positive infections).The common isolated pathogens in post-operative wounds were *S. aureus* (27%), *E. coli* (17%), *P. aeruginosa* (13%), *Proteus* (9%) and *Enterococcus sp.* (9%). Studies performed in Serbia reported similar data[14,15].

High resistance was observed for *E. coli* for penicillin's (range 70%–88%) and folate synthesis inhibitors (41%). Many authors believe that this high percentage of resistance of *E. coli* is a consequence of irrational, prophylactic and excessive use of antibiotics in general practice[16].

Pseudomonas aeruginosa is a common cause of hospital infections. This bacteria shows 100% resistance to folate synthesis inhibitors and ceftriaxone[17]. It also shows high resistance (about 90%) to antibiotics that are usually prescribed in general practice such as amoxicillin, nitrofurantoin, and cephalexin[18]. According to the literature data, 60% of the positive isolates of P. aeruginosa were sensitive only to quinolones[19].Lower percentage of resistance was reported to carbapenems, also[15].Similar resistance of *P. aeruginosa* in our study was noted to penicillin's ranged between 77%–85% and folate synthesis inhibitors (69%). Low resistance to carbapenems was observed, also.

S. aureus is usually isolated in samples from the respiratory tract and these bacteria is in relatively small percentage (about 10%) multidrug resistant. Isolates of *S. aureus* from hospital material showed significant resistance to lincosamines and macrolides[20].Based on the results of five-year retrospective studies conducted in 300 hospitals across the United States, an increase in methicillin resistant *S. aureus* (MRSA) isolated from swabs of the throat was observed[21].MRSA transmit through direct contact, open wounds and contaminated hands. It causes sepsis or pneumonia and it is highly resistant to beta-lactams[22].In our study MRSA constituted 48% of all S. aureus isolates. Similar rates of MRSA as in our study were reported in middle income countries[23,24].Multidrug resistance for *S. aureus* in our study was observed to penicillin's (range 22%–74%), macrolides (33%), clindamycin (33%) and aminoglycosides (29%).Regarding fusidic acid in literature is reported that S. aureus is almost 30% resistant[25],which was also note in our case (Table 4). The results of recently explored therapeutic efficacy of cationic charged bilayered nano-emulsion for topical delivery of fusidic acid in eradicating MRSA bacterial wound infection encourage the exploration of the potential of cationic nanogel in treating resistant microorganisms[25].

Enterococcus spp. takes a more prominent place among the causes of hospital infections[26].Vancomycin-resistant *Enterococcus faecium* is a leading cause of hospital-acquired infections[27]. Positive *Enterococcus sp.* isolates from GIT, blood and catheter samples showed the highest percentage of multidrug resistance (around 88%) in all tested classes of antibiotics[28]. According to the results of the international SENTRY project (The SENTRY Antimicrobial Surveillance Program), which included about 70 microbial laboratories around the world, high percentage of resistance (about 50-65%) shows this bacteria to gentamicin[29].Isolated *Enterococcus* sp. in our case showed good sensitivity to carbapenems. Multidrug resistance was observed to β-lactam antibiotics (penicillin, cephalosporins) ranged between 11-66%, macrolides (55%), clindamycin (77%) and folate synthesis inhibitors (77%).

Proteus species are most commonly recognized clinically as a cause of urinary tract infections[30].*Proteus* isolates in our study show higher susceptibility to almost all classes of antibiotics.

V. CONCLUSION

Our study is the first surveillance study that examined the antimicrobial susceptibilities of common pathogens in a post-operative wound swab samples from two different department at clinical for tertiary care in Stip. According to the results, the highest percentage of isolated pathogens is at the orthopaedics department. Gram-negative infections were predominant. The rate of isolated pathogens (methicillin resistant *S. aureus*, *E. coli*, *P. aeruginosa*, *Proteus* and *Enterococcus* sp.) was found to be high and requires additional activities and measures to be taken to improve the clinical outcome of patients. The data of this study will be useful for planning additional activities and strategies to reduce intrahospital infections and bacterial resistance.

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