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Choice of Empirical Treatment in Patients with Wound Infection

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ABSTRACT

Objective: We aimed to determine the distribution of infectious agents in wound culture specimens, their resistance rates, and to evaluate empirical treatment choices in wound infections.

Methods: Wound culture results of adult patients between 2016-2020 were retrospectively investigated. Determination of bacteria and antibiotic sensitivity tests were done using conventional methods and automatized systems.

Results: A total of 2576 wound specimens were sent, and significant bacterial growth was detected in 1254 (48.7%). Most frequently isolated agent was *Escherichia coli (E.coli)* (24.2%), followed by *Staphylococcus aureus (S.aureus)* (16.8%). The highest rate of resistance in *Enterobacterales* species was against amoxicillin-clavulanate (AMC), except *Proteus mirabilis.* Antibiotics that *Enterobacterales* species were most sensitive were amikacin and carbapenems, while it was trimethoprim – sulfamethoxazole (TMP-SXT) for *Acinetobacter baumannii,* and amikacin for Pseudomonas aeruginosa. The highest rate of resistance in S.aureus strains was against penicillin, with a methicillin resistance rate of 22.9%, while no resistance was found against vancomycin.

Conclusion: Initial treatment in wound infections is empirical, and the range of treatment is narrowed when results of culture and sensitivity tests are obtained. Clindamycin, AMC, TMP – SXT and ciprofloxacin seem to be appropriate for outpatients, while TMP-SXT or vancomycin for gram-positive cocci, and TMP-SXT and amikacin combination for gram – negatives, and carbapenems as a last resort.

Keywords: Wound infection, empirical treatment, antibiotic resistance

1. INTRODUCTION

Wound infections (WI), which result from infection of the skin and soft tissues (SST) with pathogenic microorganisms, are frequently encountered. They may be seen in a wide spectrum, ranging from a clinically mild infection to life-threatening serious necrotizing infections. The responsible agents may differ according to the site of infection and patient risk factors, which include age, co-morbidities, immune deficiency, circulatory disorders, long – term hospitalization, trauma and contact with animals (1-4). Clinical features and risk factors of the patient are considered in the diagnosis and treatment of SST infections, culture samples are obtained from the wound for antibiotic sensitivity tests, and empirical treatment is initiated (5). Penicillins effective against gram-positive microorganisms, penicillins resistant to penicillinase, cephalosporins, macrolides, linkosamides, fluoroquinolons and trimethoprim – sulfamethoxazole (TMP-SXT) are preferred for empirical treatment. Vancomycin against methicillin-resistant *Staphylococcus aureus* (MRSA) in hospitalized patients, and carbapenems for resistant gram-negative bacteria are also used (4,6).

In our hospital, oral amoxicillin-clavulanate, ciprofloxacin or TMP-SXT are used empirically in outpatients with SST infections, while intravenous (iv) vancomycin or teicoplanin, piperacillin-tazobactam or carbapenem are used alone or in combinations in hospitalized patients. We aimed to determine the distribution of microorganisms growing in wound culture samples of outpatients and hospitalized patients in our center, to determine the antibiotic resistance rates, and provide guidence for choosing empirical antibiotics.

2. METHODS

Our study was approved by the Ethics Committee of Clinical Investigations of Balıkesir University (21.10.2020, approval Nr 2020/188). Samples for culture obtained from wounds of ambulatory or hospitalized adult patients with injector or

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swab between 2016-2020 were evaluated at the Microbiology Laboratory. Our hospital is a secondary care state hospital with 400 patient beds and 54 intensive care unit beds.

All wound samples were stained with Gram stain on slides, examined with direct microscopy, and the results were entered into the laboratory data management system (LDMS). Leukocyte density, presence of epithelium, and presence of mixed flora bacteria were evaluated by the microscopic examination. Since the localization of wound samples is not always specified when sending them to the laboratory, such a classification was not made in the study.

All samples were inoculated in blood agar (RTA, Türkiye), Eosin Methylene Blue (EMB) agar (RTA, Türkiye) and chocolate agar (RTA, Türkiye), and were incubated at 37°C for 24-48 hours. Strains that were isolated were identified by conventional methods (colony morphology, gram staining, catalase, coagulase, oxydase, urease tests) and by BD Phoenix 100 automated identification system (BD Phoenix System, Beckton Dickinson, US). Culture samples in which mixed skin flora bacteria grew were considered as skin contamination. In vitro susceptibility tests of isolates which were considered as infectious agents were determined according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) (7) criteria, using the Phoenix TM 100 automated identification and antibiotic susceptibility test system (BD Phoenix System, Beckton Dickinson, US). The first isolate was evaluated in patients with multiple samples. Possible results obtained from the automated system were reported in detection of extended spectrum beta lactamase (ESBL), without confirmation tests. Methicilline resistance in *S.aureus* strains were investigated by using the MIC value of cefoxitin at the automated system.

2.1. Statistical Analysis

All the data were recorded and statistical analysis was performed with SPSS 22.0 (SPSS INC, Chicago, IL, US) software. Categorical data were presented as percents. Chi-Square test was used in comparison of independent groups containing categorical variables. p values below .05 were considered as statistically significant.

3. RESULTS

A total of 2576 wound specimens were sent to our laboratory in five years, in 1185 of which (46.0%) microbial growth was not detected, and mixed skin flora bacteria grew in 137 (5.3%). A significant, pure growth was detected in 1254 samples (48.7%), and these were included in this study. Also 65.6% of these 1254 wound samples were taken from hospitalized patients (clinics and intensive care unit), and 34.4% were obtained from outpatients (Table 1). The clinics were general surgery, orthopedic surgery, plastic surgery and internal medicine. Among the wound cultures, 71.5% were Gram negative bacteria, 28.3% were Gram positive bacteria and 0.2% were fungi. The most frequently isolated organism among all samples was *Escherichia coli (E.coli)* (24.2%), followed by *Staphylococcus aureus* (*S.aureus)* (16.8%). When samples obtained from ambulatory and hospitalized patients were separately evaluated, *S.aureus* was the most frequently isolated microorganism in outpatients while *E.coli* was the most frequently isolated microorganism in hospitalized patients (both surgical/medical clinics and intensive care units). The other microorganisms isolated from 1254 wound samples included *Pseudomonas aeruginosa (P.aeruginosa)* (11.5%), *Klebsiella pneumonia (K.pneumoniae)* (10.3%), *Acinetobacter baumannii (A.baumannii)* (8.8%), *Proteus mirabilis (P.mirabilis)* (8.6%), *Streptococcus pyogenes (S.pyogenes)* (8.3%), other *Enterobacterales* species (7.1%), other Gram positive bacteria (3.2%), other nonfermenter Gram negative bacteria (1%) and *Candida* spp. (0.2%), respectively (Table 2).

Table 1. *Distribution of wound culture samples in which growth was detected according to clinic and years (n/%)*

Year	Outpatients		Hospitalized patients in clinics		ICU* patients		Total
	n	%	n	%	n	%	
2016	95	36.3	107	40.8	60	22.9	**262**
2017	88	34.4	102	39.8	66	25.8	**256**
2018	94	34.3	119	43.4	61	22.3	**274**
2019	90	37.3	78	32.4	73	30.3	**241**
2020	65	27.0	63	26.1	93	46.9	**241**
Total	**432**	**34.4**	**469**	**37.4**	**353**	**28.2**	**1254**

**ICU:Intensive care unit*

Table 2. *Distribution of agents isolated from wound cultures (n/%)*

Microorganism*	Outpatients		Hospitalized patients in clinics		ICU** patients		Total	
	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)
E.coli	59	13.7	158	33.7	86	24.3	303	24.2
S.aureus	127	29.4	76	16.2	7	2.0	210	16.8
P.aeruginosa	42	9.7	40	8.5	62	17.4	144	11.5
K.pneumoniae	20	4.6	51	10.9	58	16.4	129	10.3
A.baumannii	19	4.4	31	6.6	60	17.0	110	8.8
P.mirabilis	36	8.3	27	5.8	45	13.4	108	8.6
S.pyogenes	82	19.0	19	4.1	3	0.8	104	8.3
Other *Enterobacterales*	37	8.6	40	8.5	12	3.2	89	7.1
Other gram positive bacteria	7	1.6	23	4.9	10	2.7	40	3.2
Other NFGN bacteria	1	0.2	2	0.4	9	2.5	12	1.0
***Candida* spp.**	2	0.5	2	0.4	1	0.3	5	0.2
Total	432	34.4	469	37.4	353	28.2	1254	48.7

**Microorganisms; E.coli: Escherichia coli, S.aureus: Staphylococcus aureus, P.aeruginosa:Pseudomonas aeruginosa, K.pneumoniae: Klebsiella pneumoniae, A.baumannii:Acinetobacter baumannii, P.mirabilis: Proteus mirabilis, S.pyogenes: Streptococcus pyogenes, Other NFGN bacteria: Other non-fermenting Gram negative bacilli*

***ICU:Intensive care unit*

The highest rate of resistance in *Enterobacterales* species, except *P.mirabilis* was against amoxicillin-clavulanate (AMC), whereas the highest rate of resistance in *P.mirabilis* was against trimethoprim-sulfametoxazole (TMP-SXT). *Enterobacterales* species showed the highest sensitivity to amikacin and carbapenems. A statistically significant increase was observed in resistance rates of *E.coli* strains against AMC, ceftriaxon and carbapenem, while piperacillin-tazobactam (TZP) resistance showed a significant decrease (p< .001, p< .001, p= .003, p< .001). Significant changes were observed over the years in resistance rates of *K.pneumoniae* against AMC, gentamicin, ceftriaxon, ciprofloxacin, TZP and TMP-SXT (p< .001, p< .001, p= .015, p= .014, p< .001). ESBL rates were 55.1% in *E.coli* strains, 52.7% in *K.pneumoniae*, showing a statistically significant increase in years (p< .001, p< .001) (Table 3).

The highest resistance rates in *A.baumannii* and *P.aeruginosa* were against ciprofloxacin. TMP-SXT was the antibiotic that *A.baumannii* was most susceptible, while amikacin was the antibiotic that *P.aeruginosa* was most susceptible. Carbapenem resistance rates showed a significant increase for both organisms in time (p= .001, p< .001) (Table 4).

Highest resistance rate in *S.aureus* strains was against penicilline, with a methicilline resistance rate of 22.9%, and a significant increase was detected in resistance in time (p=.033) (Table 5).

Table 3. *Antibiotic resistance profiles of bacteria of Enterobacterales species growing in wound cultures according to years (%)*

		AMC	AK	GEN	CRO	CIP	CARB	TZP	TMP-SXT	ESBL
E.coli **(n=303)**	**2016**	50.0	6.3	29.7	42.2	42.2	1.6	43.8	46.9	40.6
	2017	72.9	6.8	32.2	50.8	52.5	0.0	23.7	50.8	50.8
	2018	84.5	5.2	36.2	50	48.3	3.4	17.2	53.4	63.8
	2019	65.8	8.9	40.5	54.4	53.2	7.6	19.0	48.1	53.2
	2020	69.8	2.3	25.6	74.4	53.5	0.0	11.6	51.2	74.4
	***Total**	68.0	6.3	33.7	53.1	49.8	3.0	23.8	49.8	55.1
	p	**< .001**	**= .297**	**= .201**	**< .001**	**= .395**	**= .003**	**< .001**	**= .916**	**< .001**
K.pneumoniae **(n=129)**	**2016**	73.7	10.5	52.6	73.7	68.4	21.1	52.6	68.4	20.9
	2017	89.7	13.8	48.3	72.4	65.5	17.2	58.6	72.4	58.6
	2018	100	20.6	47.1	52.9	47.1	17.6	38.2	41.2	35.3
	2019	80.0	16.0	32	68.0	60.0	20	60	60	64
	2020	54.5	9.1	27.3	63.6	54.5	9.1	50	68.2	54.4
	*Total	82.2	14.7	41.9	65.1	58.1	17.1	51.2	60.5	52.7
	p	**< .001**	**= .129**	**< .001**	**= .015**	**= .017**	**= .173**	**= .014**	**< .001**	**< .001**
P.mirabilis **(n=108)**	**2016**	12.5	0.0	37.5	6.3	37.5	6.3	0.0	50	-
	2017	28.6	4.8	42.9	4.8	61.9	0.0	0.0	71.4	-
	2018	47.1	5.9	47.1	0.0	76.5	0.0	0.0	76.5	-
	2019	29.4	29.4	64.7	29.4	76.5	5.9	11.8	76.5	-
	2020	18.9	2.7	40.5	10.8	56.8	0.0	2.7	51.4	-
	*Total	25	7.4	45.4	10.2	61.1	1.9	2.8	63.0	-
	p	**< .001**	**< .001**	**= .001**	**< .001**	**< .001**	**= .001**	**< .001**	**< .001**	**-**
Other *Enterobacterales* Species (n=83)	**2016**	16.7	3.3	3.2	13.3	16.7	3.3	10.0	6.7	**-**
	2017	60	0.0	10.0	10.0	5.0	0.0	5.0	15	**-**
	2018	73.3	0.0	0.0	0.0	13.3	0.0	0.0	13.3	**-**
	2019	80	0.0	0.0	0.0	20.0	10.0	0.0	20.0	**-**
	2020	100	38.5	53.8	92.3	53.8	23.1	15.4	46.2	**-**
	*Total	59	7.2	12	21.7	20.5	6.0	7.2	13.9	**-**
	P	**< .001**	**< .001**	**< .001**	**< .001**	**< .001**	**< .001**	**< .001**	**< .001**	**-**

**E.coli: Escherichia coli, K.pneumoniae: Klebsiella pneumonia, P.miarbilis: Proteus mirabilis*
AMC:Amoxycilline-Clavulanate, AK:Amikacin,GEN:Gentamicin, CRO:Ceftriaxon, CIP: Ciprofloxacin, CARB:Imipenem-Meropenem, TZP: Piperacillin-Tazobactam, TMP-SXT:Trimethoprim-Sulphametoxazole, ESBL: extended spectrum beta lactamase

Table 4. *Antibiotic resistance profiles of Acinetobacter baumanni and Pseudomonas aeruginosa strains growing in wound cultures according to years (%)*

Antibiotic	*A.baumannii* (n=110)							*P.aeruginosa* (n=144)						
	2016	2017	2018	2019	2020	*Total	*p*	2016	2017	2018	2019	2020	*Total	*p*
AK	70.4	50.0	64.5	90.0	86.4	**70.0**	**< .001**	13.9	9.1	0.0	0.0	16.0	**8.3**	**< .001**
GEN	96.3	75.0	90.3	100	95.5	**90.9**	**< .001**	19.4	12.1	12.0	24.0	36.0	**20.1**	**< .001**
CARB	92.6	85.0	83.9	100	86.4	**88.2**	**= .001**	19.4	6.1	8.0	12.0	28.0	**14.6**	**< .001**
CAZ	-	-	-	-	-	**-**		36.1	18.2	36.0	8.0	24.0	**25.0**	**< .001**
FEP	-	-	-	-	-	**-**		33.3	18.2	36.0	8.0	24.0	**24.3**	**< .001**
TZP	-	-	-	-	-	**-**		33.3	21.2	28.0	8.0	32.0	**25.0**	**< .001**
TMP-SXT	66.7	60.0	67.7	100	68.2	**69.1**	**< .001**	-	-	-	-	-	**-**	
CIP	100	85.0	87.1	100	90.9	**91.8**	**< .001**	36.1	24.2	12.0	32.0	52	**31.3**	**< .001**

* *AK:Amikacin,GEN:Gentamicin, CARB:Imipenem-Meropenem,CAZ:Ceftazidim, FEP:Cefepim, TZP: Piperacillin – Tazobactam, TMP-SXT:Trimethoprim-Sulphametoxazole, CIP: Ciprofloxacin,*

Table 5. *Antibiotic resistance profiles of Staphylococcus aureus strains growing in wound cultures according to years (%)*

Antibiotic	*S.aureus* (n=210)						
	2016	2017	2018	2019	2020	*Total	*P*
GEN	17.0	15.6	8.3	15.4	7.0	**12.9**	**= .105**
PEN	100	82.2	94.4	94.9	88.4	**91.9**	**< .001**
CC	4.3	15.6	11.1	17.9	11.6	**11.9**	**= .028**
E	8.5	8.9	8.3	20.5	14.0	**11.9**	**= .026**
TE	6.4	26.7	41.7	41.0	79.1	**38.1**	**< .001**
CİP	8.5	6.7	8.3	10.3	4.7	**7.6**	**= .725**
TMP-SXT	4.3	02.2	8.3	5.1	0.0	**3.8**	**= .039**
VA	0.0	0.0	0.0	0.0	0.0	**0.0**	**-**
TEI	0.0	0.0	0.0	0.0	0.0	**0.0**	**-**
DAP	0.0	2.2	2.8	0.0	0.0	**1.0**	**= .089**
LIN	0.0	0.0	0.0	0.0	0.0	**0.0**	**-**
MET	17.0	22.2	31.3	28.2	34.9	**22.9**	**= .033**

* *GEN:Gentamicin, PEN:Penicillin, CC: Clindamycin, E: Erythromycin, TE: Tetracycline, CIP: Ciprofloxacin, TMP – SXT:Trimethoprim-Sulphametoxazole, VA: Vancomycin, TEI: Teicoplanin,DAP:Daptomycin, LIN:Linezolid, MET: Methicillin*

4. DISCUSSION

Wound infections affect the skin and soft tissues, and cause morbidity and mortality. Wound culture samples are important both for supporting the diagnosis and guidence of treatment. It is important to be careful in obtaining samples for culture in order to avoid contamination with skin flora bacteria (8-10). A significant growth was detected in 48.7% of culture samples in our study, with growth of mixed skin flora bacteria in 5.3%. This reflects an acceptable level of contamination in our hospital, while it also reflects the fact that we have to pay still more attention for antisepsis in obtaining wound samples.

While SST infections may more frequently be seen in outpatients as non-complicated forms, they may be encountered as complicated forms in hospitalized patients. Gram positive bacteria such as *S.aureus* and *Streptococcus* spp. are frequently isolated in non-complicated infections, and Gram negatives such as *E.coli*, *P.aeruginosa, K.pneumoniae* and *P.mirabilis* are more frequently found in complicated infections (4,8,11,12). The most frequently isolated agent in SST infections in a study conducted in 28 countries was *S.aureus,* according to European Antimicrobial Resistance Surveillance (EARS) data. In another study, it was reported that gram-negative microorganisms were frequently associated with surgical site infection, and *E.coli* and *P.aeruginosa* were frequently isolated (13).

Avcıoğlu et al (14) have isolated 53.0% gram negative bacteria, 46.4% gram positive bacteria and 0.6% fungi from wound samples of outpatients and hospitalized patients between 2016 – 2018. When compared with our study, the rate of Gram negative bacteria was found to be higher in our study. We think that this may reflect the fact that most of the samples in the study by Avcıoğlu et al (14) was from

outpatients, while most of the samples in our study were from hospitalized patients.

In the 1-year study by Eren et al (15) evaluating neurological intensive care unit (ICU) patients, *A.baumannii* and *S.aureus* were most frequently isolated as the pathogen agent of SST infection. Sisay et al (8) have detected 36% *S.aureus*, 13% *E.coli,* 9% *P.aeruginosa*, 9% *K.pneumoniae,* and 8% *P.mirabilis* in wound samples in their analysis of 21 studies conducted in Etiopia between 2000-2018. Tanrıverdi Çaycı et al (16) have found *E.coli* (20.5%), *S.aureus* (12.7%) and *P.aeruginosa* (11.6%) as the most frequent three microorganisms in their study evaluating outpatients and hospitalized patients between 2015-2017.

We detected *E.coli*, *S.aureus* and *P.aeruginosa* as the most frequent three microorganisms among 1254 culture specimens included in our study. On the other hand, when the patients were evaluated in three separate group consisting of outpatients, hospitalized patients and ICU patients, the most frequently isolated organisms were *S.aureus* (29.4%) and *S.pyogenes* (19.0%) in outpatients; *E.coli* (33.7%) and *S.aureus* (16.2%) in hospitalized patients, and *E.coli* (24.3%) and *P.aeruginosa* (17.4%) in ICU patients. Also, *E.coli*, *P.aeruginosa, A.baumannii, K.pneumoniae and P.mirabilis* was detected in 88.5% of wound culture specimens of ICU patients. First, it is necessary to know the distribution of pathogen agents in a certain clinic, in order to determine a rational empirical treatment. In this respect, the choice of empirical treatment for ICU patients may aim on Gram negative agents, while a combination treatment aiming both Gram negative and positive agents may be more beneficial for ambulatory and hospitalized patients.

When SST infections develop, culture specimens are obtained, after which empirical treatment is initiated with an antimicrobial agent with the highest probability to be effective against this organism, and the spectrum of treatment is narrowed after culture and antibiogram results are obtained. With this approach, success rate of treatment is increased and emergence of resistant bacteria is prevented with rational use of antimicrobials (17-19).

AMC is used against gram positive bacteria in outpatients in our hospital for the empirical treatment of SST infections, and ciprofloxacin or TMP-SXT is used against gram negatives. We found *S.aureus* as the most frequently isolated agent in outpatients, and penicillin resistance was 91.9%. This resistance rate shows that penicillin is not an appropriate choice in empirical treatment, even when gram staining shows gram positive cocci. Also, resistance against clindamycin was 11.9% in *S.aureus* strains. In *Enterobacterales* species, resistance against AMC was 25-82.2%, while resistance was 10.2 – 65.1% against ceftriaxon, 10.2-65.1% against ciprofloxacin, and 13.9-63% against TMP – SXT. Considering that the antibacterial activity of AMC against gram positive microorganisms is stronger than ceftriaxone, AMC is a better choice for infections suspected to be due to gram positives in outpatients, while clindamycin is better for clinical anaerobic infection suspicion, and ciprofloxacin or TMP-SXT for suspicion of gram negative infections, as their resistance rates are similar. The oral form of these four antimicrobial agents may be preferred for empirical treatment in outpatients. Also, as treatment have to be initiated in outpatients mostly before results of microscopic examinations are obtained, the procedure used in our hospital seem to be appropriate.

Resistance rates reported in different studies evaluating wound cultures of outpatients and hospitalized patients are 81.4-100% against penicillin, 8.9-24% against ciprofloxacin, 3.5 – 11% against TMP-SXT, and 7.6-23.1% against clindamycin in *S.aureus.* Also methicillin resistance was between 16.7-36%, while resistance against vancomycin and teicoplanin was not reported. In *Enterobacterales* species, resistance against AMC was 44-72%, and TZP was 9 – 61%, ciprofloxacin was 18-72.9%, TMP-SXT was between 10-65.2%, similar to our study (14,20-22).

Vancomycin or teicoplanin (iv) and TZP (iv) are used alone or in combination in the treatment of SST infections in hospitalized patients (4), which is also used commonly in our hospital. Vancomycin and teicoplanin are medications that are used as a last resort in the treatment of MRSA, and they are not appropriate for empirical treatment (23). We did not find resistance against vancomycin or teicoplanin in our study, but we found resistance against daptomycin, which also has a place in MRSA treatment. It is obvious that resistance against these agents will develop in the future, if they are not used rationally. As *S.aureus* is a frequently encountered agent in hospitalized patients, we believe that the decision to include vancomycin in empirical treatment should be based on the results of gram staining.

Another empirical treatment option is TZP, which is a broad-spectrum antimicrobial also having anti-pseudomonal activity (17). In our study, resistance was below 24% in *Enterobacterales* species, except *K.pneumoniae,* which was 51.2%, while resistance rate was 25% in *P.aeruginosa*. For this reason, considering the distribution of Gram negative agents, it seems to be the appropriate choice for hospitalized patients.

Carbapenems are important in the treatment of resistant Gram negative infections. As the patients in ICU were frequently treated with broad-spectrum antibiotics in initiation of empirical treatment, and shifting to an agent with narrower spectrum according to culture– antimicrobial sensitivity test results seem to be more rational. Therefore, iv carbapenem is used in the empirical treatment of UTI in hospitalized patients (17,24).

Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR), one of the members of which is our country, determine infectious agents in blood and spinal fluid samples and find their resistance rates. According to their data, carbapenem resistance in *E.coli* have increased from 2% – 3% between 2015-2019, while increasing from 30% to 39% in *K.pneumoniae*, from 32% to 38% in *P.aeruginosa*, and from 89% to 90% in *A.baumannii* at the same period. Methicilline resistance in *S.aureus* was reported to increase from 25% in

2015 to 31% in 2019 (25,26). In our study, it was observed that carbapenem resistance reached 23.1% in *Enterobacterales* species, 28% in *P.aeruginosa*, and varied between 83.3-100% in *A.baumannii* over a five-year period. According to this observation, carbapenems seem to be the most probable choice in empirical treatment of patients with a history of broad-spectrum antibiotic use in the past or history of microbial growth of resistant Gram negative microorganisms, as in ICU patients. Although the evaluated specimens were not the same as ours in CAESAR data, a similar resistance problem in especially *K.pneumoniae,* similar to *P.aeruginosa* is obvious. Thus, carbapenem use requires great care. On the other hand, carbapenems are not effective against infections with *A.baumannii*. Amikacin and TMP-SXT combination also does not seem to be appropriate, in light of resistance rates that we have found. While colistin is an important antibiotic in the treatment of these infections, it was not included in the evaluation because it could not be studied with the broth microdilution method as in EUCAST recommendations in our hospital. This is a limitation of our study.

As resistance to antibiotics may change in time, the change in resistance rates according to years were also evaluated in our study, and statistical analysis were done. Methicilline resistance in *S.aureus* strains seem to increase significantly over the years. TZP resistance in *E.coli* strains seems to decrease significantly in time, resistance to ceftriaxone seems to increase, and a significant decrease for AMC was seen between 2018-2019. The rates of resistance to AMC, ceftriaxone and TMP-SXT in *K.pneumoniae* have changed significantly over the years; an increase was seen in resistance of *A.baumannii* to carbapenem, and a significant change in *P.aeruginosa* for both carbapenem and TZP resistance. Thus, it appears that detection of frequently seen infectious agents at periodical examinations, and determination of the antibiotic resistance distribution will be helpful in decision on selection of empirical treatment (27).

5. CONCLUSION

Skin and soft tissue infections are diagnosed clinically, after which empirical treatment is initiated and treatment is narrowed after results of culture-antibiograms are obtained. Gram stain slides prepared on the same days with cultures are important, as they yield results on the same day and they are helpful to the clinician in antibiotic selection. Collaboration between the microbiology laboratory and the clinicians is very important in this respect. Clindamycin, AMC, TMP-SXT and ciprofloxacin for outpatients, TMP-SXT or vancomycin for gram positive cocci, TZP, TMP-SXT and amikacin combination for the therapy of gram negative microorganisms caused infections, and carbapenems as a last resort seem to be appropriate choices in empirical treatment.

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