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Prevalence of multidrug resistance pathogens in dermatology: A retrospective study in Romania, 2018-2022

Alina-Viorica Iancu [1,2,3†] (iD), Nicoleta-Maricica Maftei [1,4,5*] (iD), Caterina Dumitru [1,2,5**] (iD), Liliana Baroiu [1,2] (iD), Gabriela Gurau [1,3,4] (iD), Alina Mihaela Elisei [1,5] (iD), Claudia Simona Stefan [1,5†] (iD), Alin Laurentiu Tatu [1,2,6†] (iD), Alexandru-Florin Iancu [1] (iD), Manuela Arbune [1,2,3] (iD)

[1] Faculty of Medicine and Pharmacy, "Dunărea de Jos" University, Galați, ROMANIA
[2] Clinical Hospital of Infectious Diseases "Sf. Cuvioasa Parascheva", Galați, ROMANIA
[3] Research Laboratory of Microbiology, Imunology and Clinical Application of Infections Diseases, "Dunărea de Jos" University, Galați, ROMANIA
[4] Clinical Hospital of Children Hospital "Sf. Ioan", Galați, ROMANIA
[5] Research Center in Medical-Pharmaceutical Field, "Dunărea de Jos" University, Galați, ROMANIA
[6] Multidisciplinary Integrated Center of Dermatological Interface Research Center, "Dunărea de Jos" University, Galați, ROMANIA
*Corresponding Author: naron@ugal.ro
**Corresponding Author: caterina.dumitru@ugal.ro
[†] These authors contributed equally to this work.

ARTICLE INFO	ABSTRACT
	Antimicrobial resistance (AMR) is now a major challenge to clinicians in treating patients. The purpose of our study was to determine the incidence of multidrug resistant (MDR) strains and antibiotic resistance profile in department of dermatology-venereology from a Romanian infectious disease's hospital. We analyzed 1,152 bacterial strains, we obtained 34.5% MDR strains, identifying the following species: *staphylococcus aureus* 43.6%, *enterococcus* spp 16.7%, *escherichia coli* 31.0%, *proteus* spp 27.1%, *klebsiella* spp. 22.4%, *pseudomonas* spp. 34.8%. Overall, the rate of methicillin-resistant *staphylococcus aureus* was 76.1%; extended spectrum beta-lactamase production was 46.1% for *escherichia coli* and 66.0% for *klebsiella pneumoniae*; carbapenems-resistance was 51.0% for *pseudomonas aeruginosa*. All strains of *E. coli* and *klebsiella* were sensitive to meropenem. Our results confirm the high level of AMR, and continuous monitoring is essential for updating the local diagnostic and treatment protocols for dermatological infections. **Keywords:** multidrug resistant, microorganisms, dermatology

INTRODUCTION

Antimicrobial resistance (AMR) is an increasing health concern that has attracted the attention of scientists and clinicians over the past years [1]. The COVID-19 pandemic accelerated AMR crisis through exposure to antibiotics and hospitalizations [2-6]. Excessive use of antibiotics, along with agricultural usage, animal healthcare and the food system have a significant impact on accelerating multidrug resistance (MDR), as well as the evolution of bacterial strains and natural selection [1, 7, 8]. Unfortunately, the rate at which pathogens develop resistance to currently available antibiotics has exceeded the rate at which new antibiotics are developed. This fact is due to its increasing impact care costs on morbidity and mortality [9]. Centers for disease control and prevention (CDC) estimate that AMR infections already cause one death every 15 minutes in the United States [10]. Worldwide, AMR has become a public health worry [2, 11, 12] and is now accountable for more deaths than malaria or HIV/AIDS; bacterial infections with MDR microorganisms were associated with a near 4.95 million deaths worldwide, including 1.27 million deaths that were

straight attributable to antibiotic resistance, in 2019 [12]. *S. aureus*, *K. pneumoniae*, and *P. aeruginosa* resistance are among those that CDC and World Health Organization (WHO) consider prioritized threats [10, 11]. CDC estimates that 50.0% of outpatient antibiotics are incorrectly prescribed based on agent selection, duration, or dosing, and at least 30.0% of outpatient antibiotics are given needlessly [13, 14]. Outpatient prescribing patterns are a critical target for stewardship efforts, because over 80.0% of all human antibiotic use arises in the outpatient setting [15].

Similar studies have highlighted that MDR is expanding globally, being a challenge in the treatment of bacterial infections. Thus, making the use of backup antibiotics is essential and cost-effective and with a low safety profile [9, 16]. *E. faecium, S. aureus, K. pneumoniae, A. baumannii, P. aeruginosa, E. coli,* and *Proteus* spp. are MDR microorganisms that can evade the activity biocide of antibiotics [16-21]. These microorganisms are distinguished by pathogenic, transmission and resistance characters, which are characterized by target change and mechanical protection by biofilm synthesis, cell permeability alteration, by porin loss, increasing the expression of efflux pumps, and enzyme inactivation [9, 16].

Also, the antibacterial activity of antibiotics may sometimes determine the appearance of disorders in the skin microbiome, including the associated to endosymbionts. However, dermatology is a domain, which utilizes topical glucocorticoids (as in psoriasis), thusly this leading to secondary effects, which have the disadvantage of predisposing the skin to severe infections, some of the infections being infections with MDR microorganisms [22, 23]. In dermatology, antibiotics are often used for prolonged treatments of soft tissue and skin infections and common inflammatory skin conditions, which increases the risk of the alteration of the microbiome and the appearance of secondary effects connected to antibiotics, leading to a selective pression on the pathogenic and nonpathogenic bacteria [2]. In conclusion, it is essential that all physicians in all specialties can identify, manage, and prevent cases of AMR. Even the discovery of new antibiotics is very far from keeping pace with the pace of progress of MDR strains. However, the actions of rational use of antibiotics are measures assumed as a primary objective in antibiotic administration programs. Thus, by making these actions mandatory, we can increase the hospital's quality standards, which are in accordance with WHO and European antimicrobial resistance surveillance network [24, 25].

This article examines dermatologic conditions in which the development of MDR strains is a risk and discusses mechanisms basic the development of resistance.

MATERIALS & METHODS

Bacterial Strains

We conducted a retrospective study, conducted from the annual database of microbiology laboratory, from 2018-2022, in accordance with the Helsinki Declaration. This retrospective study included MDR bacterial strains isolated from biological products taken for diagnostic purposes from hospitalized patients. Bacterial strains from various biological samples (purulent secretions from wounds or ulcers of the foot, urine, and blood) of hospitalized patients were isolated from department of dermatology-venereology from Clinical Hospital of Infectious Diseases "Sf. Cuvioasa Parascheva", in Galați, Romania.

Identification of Bacteria

Microorganisms were identified using the conventional methodology [26] for microbial culture, using agar-based solid media, and area inoculation and depletion technique. Biochemical identification of bacterial isolates was carried out by multi-testing and automatic method vitek 2 compact and further investigated for antibiotic resistance [27-31]. Duplicate samples were excluded.

Antimicrobial Resistance Testing

AMR was tested by using the Kirby-Bauer disk diffusion-method on the Mueller-Hinton standardized medium and the minimal inhibiting concentration method (MIC)–vitek 2 compact, using an identification card (ID-GP; ID-GN) and susceptibility card (AST-592; AST-204; AST-222). Antibiotic susceptibility testing was determined using Clinical and Laboratory Standards Institute (CLSI). Phenotypic confirmation for extended spectrum beta-lactamase (ESBL) production at enterobacterales was identified by using double-disc synergy test (DDST) (cefotaxime-amoxicillin/clavulanic acid) and the vitek 2 compact software [27-31]. Cefoxitin disk diffusion was used to determine methicillin-resistant staphylococcus aureus (MRSA), test was less than 22 mm.

The multidrug resistance profile was determined according to the international guidelines. MDR was defined by being non-susceptible to at least one agent in three or more antimicrobial categories [32]. Only the acquired antibiotic resistance was accounted for, not the intrinsic one. The following antimicrobial classes were used: β-lactams (penicillin-10 U, amoxicillin/clavulanic acid-20/10 μg, piperacillin/tazobactam-00/10 μg, cefotaxime-30 μg, cefuroxim-30 μg, cefoxitin-30 μg, ceftazidim-30 μg, cefepime-30 μg), carbapeneme (meropenem-10 μg), fluoroquinolones (ciprofloxacin-5 μg, norfloxacin-10 μg), macrolides (erythromycin-15 μg), nitrofurans (nitrofurantoin-300 μg), aminoglycosides (gentamicin-10/120 μg, amikacin-30 μg), glycopeptides (vancomycin- 30 μg), and oxazolidinones (linezolid-30 μg).

The multidrug resistance analysis was focused on the microorganisms, which are frequently isolated in the department of dermatology-venereology: *S. aureus, enterococcus* spp., *E. coli, klebsiella* spp., *proteus* spp., *acinetobacter* spp., *Pseudomonas* spp.

Quality Control

They were used reference strains for quality control in the identification and antibiotic resistance testing: ATCC 29213, 25923-*S. aureus*; (quality control for disk diffusions and MIC); ATCC 25922-*E. coli* și ATCC 27853-*P. aeruginosa* (quality control for GN) and ATCC 700327-*E. casseliflavus* (quality control for identification GP). Microbiology laboratory is accredited SR EN ISO 15189.

Statistical Analysis

The results were collected from the database for monitoring antibiotic resistance in the microbiology laboratory and subjected to statistical analysis using Microsoft XL software. We used descriptive statistics, depending on the frequency distribution.

RESULTS

### Evolution of Hospital Indicators

During 2018 and 2022, 4717 patients were hospitalized from which 1152 bacterial strains were isolated in department of dermatology-venereology from Clinical Hospital of Infectious Diseases "Sf. Cuvioasa Parascheva", in Galați, Romania. Presented in dynamic, the number of isolated strains progressively decreased from 2018 to 2022, having an even more abrupt decrease in the pandemic years 2020-2022, when 80.0-90.0% of the hospitalized patients had COVID-19 infection. In comparison to 2018, the number of admissions reduced by 74.0% in 2020, while the number of bacterial strains isolated decreased by 65.0%, in the context of a low number of biological samples, but also of isolated bacterial strains due to the context of the long period of dedication of hospital care to COVID-19.

Prevalence of Multidrug Resistant Strains Isolated from Department of Dermatology-Venereology

During the study period, were processed in microbiology laboratory a total of 2,965 bacterial cultures, with 1,152 (38.85%) isolated bacterial strains. MDR strains made up
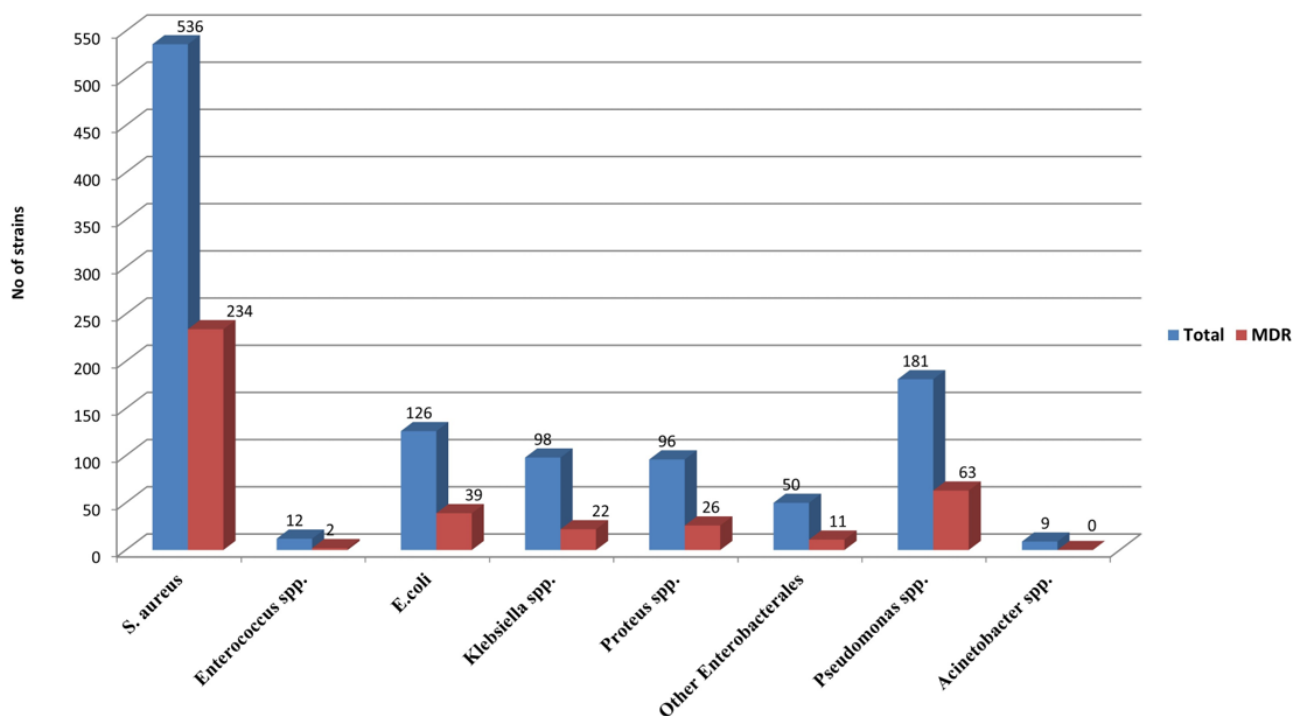
Figure 1. Incidence of MDR strains of species main isolated (Source: Authors' own elaboration)
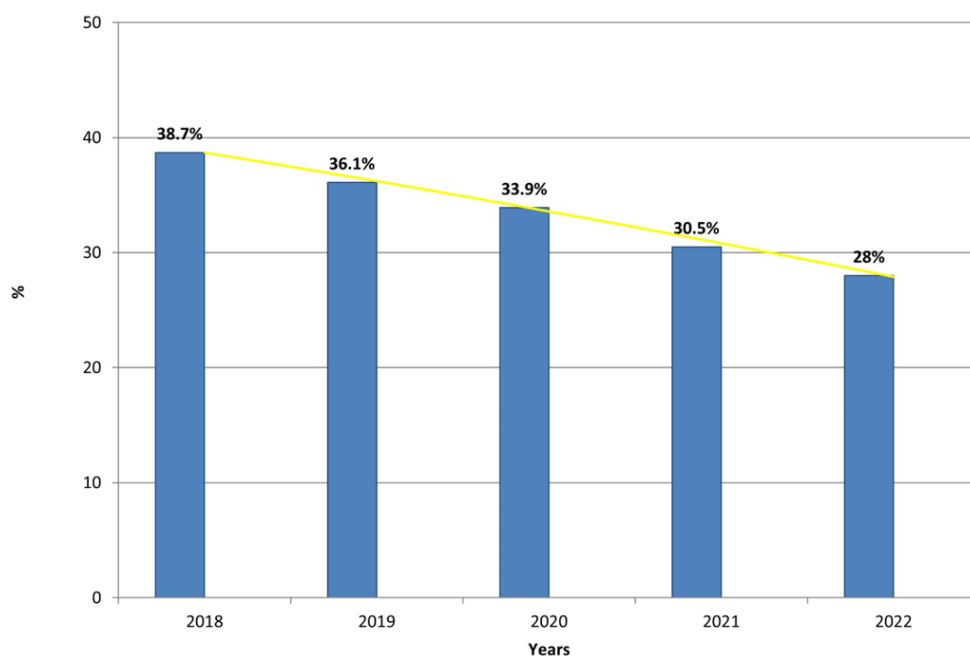
Figure 2. MDR microorganisms rate progression (2018-2022) (Source: Authors' own elaboration)

34.50% (397/1,152) from the bacterial strains isolated from 2018 to 2022; 40.55% (161/397) being Gram-negative bacilli and 59.44% (236/397) Gram-positive cocci.

No extensive drug resistant (XDR) and pan drug resistant (PDR) strains were detected. From Gram-positive cocci, the leading strain was *S. aureus* (234/536), *enterococcus* spp (2/12), followed by Gram-negative bacilli group, the first place was held by enterobacterales: *E. coli* (39/126), *proteus* spp. (26/96), *klebsiella* spp. (22/98), and other enterobacterales (11/50). Non-fermentative Gram-negative bacilli were represented by *pseudomonas* spp. (63/181). In the department of dermatology-venereology we did not isolate MDR strains of acinetobacter spp. (0/9) (**Figure 1**).

The rate of MDR strains had a decreasing tendency from 2018 to 2022 (**Figure 2**). Most isolated bacterial strains were obtained from purulent secretions from ulcers of the foot (73.29%), from cutaneous secretions/collections (19.90%) and uroculture (5.50%), and rarely from other biological products, such as hemoculture, pharyngeal or nasal secretions (**Table 1**).

Evaluation of Antimicrobial Resistance of Multidrug Resistant Microorganisms

Staphylococcus aureus

*S. aureus* was the most frequent germ isolated in the department of dermatology-venereology, 71.4% of cases being

Table 1. Distribution of MDR microorganisms according to type of biological sample in Galaţi, Romania

Isolated MDR microorganisms	Isolation source					Total
	Purulent secretions from ulcers of foot	Wound or abscess	Uroculture	Hemoculture	Others	
	n/%	n/%	n/%	n/%	n/%	n
Gram-positive bacteria						236
S. aureus	167 /71.4	62/26.5	0/0.0	1/0.4	4/1.7	234
E. faecalis	1/100	0/0.0	0/0.0	0/0.0	0/0.0	1
Enterococcus faecium	0/0.0	0/0.0	1/100	0/0.0	0/0.0	1
Gram-negative bacteria						161
E. coli	18/46.1	6/15.4	15/38.5	0/0.0	0/0.0	39
K. pneumoniae	14/77.8	1/5.5	3/ 16.7	0/0.0	0/0.0	18
K. oxytoca	2/50.0	0/0.0	2/50.0	0/0.0	0/0.0	4
P. mirabilis	15/75.0	4/20.0	1/5.0	0/0.0	0/0.0	20
P. vulgaris	6/ 100	0/0.0	0/0.0	0/0.0	0/0.0	6
Other enterobacterales	10/91.0	1/9.0	0/0.0	0/0.0	0/0.0	11
Pseudomonas spp.	24/92.3	2/7.7	0/0.0	0/0.0	0/0.0	26
P. aeruginosa	33/92.0	3/8.0	0/0.0	0/0.0	0/0.0	36
P. putida	1/100	0/0.0	0/0.0	0/0.0	0/0.0	1
Total	**291(73.3%)**	**79(19.9%)**	**22(5.5%)**	**1(0.25%)**	**4(1%)**	**397**

Table 2. Antibiotic-resistant of Gram-positive cocci from MDR strains

	OXA	P	ERY	DA	GM*	CIP	NOR	SXT	TE	LNZ
S. aureus	76.1	98.7	89.3	81.7	37.1	43.1	NT	9.8	82.5	0.5
MRSA	100.0	100.0	88.1	76.2	35.0	53.1	NT	7.9	16.3	0.0

Note. *Except for high level; OXA: Oxacillin; P: Penicillin; ERY: Erythromycin; DA: Clindamycin; GM: Gentamicin; CIP: Ciprofloxacin; NOR: Norfloxacin; SXT: Sulfamethoxazole-trimethoprim; TE: Tetracycline; LNZ: Linezolid; MDR: Multidrug resistance; MRSA: Methicillin resistant staphylococcus aureus; & NT: Not tested
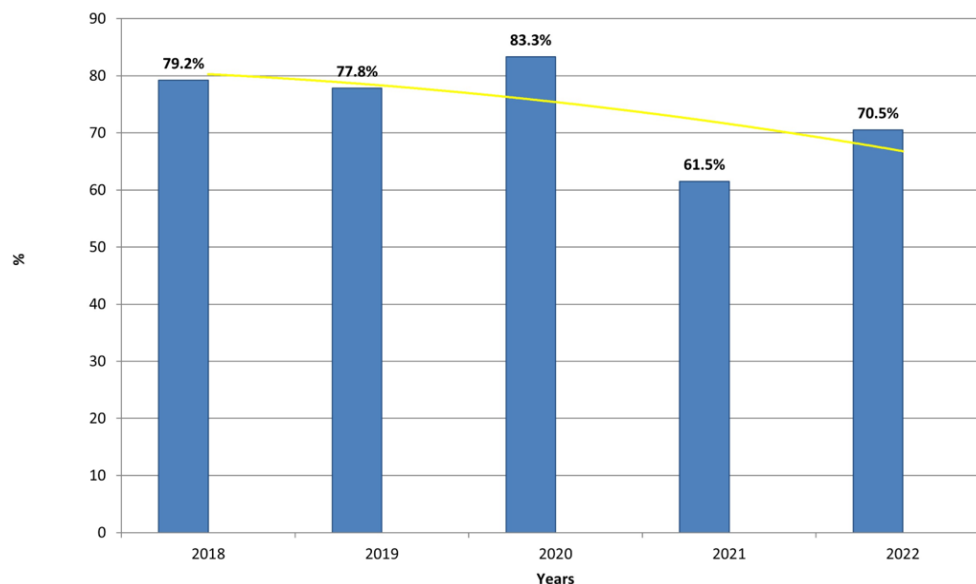
Figure 3. MRSA rate progression (2018-2022) (Source: Authors' own elaboration)

obtained from purulent secretions from ulcers of the foot and 26.5% from other cutaneous secretions. Out of total 536 *S. aureus* isolated, 234 (43.6%) were MDR (**Figure 1**).

The analyzed MDR strains of *S. aureus* showed high rates of resistance to the tested antibiotics (**Table 2**); 98.7% were resistant to penicillin; 89.3% of strains were resistant to erythromycin; 81.7% showed resistance to clindamycin and only 0.5% were resistant to linezolid. Methicillin resistance (76.1%) was correlated with a significantly increased rate of resistance as compared to other antibiotics, including MDR.

The rate of MRSA had a decreasing tendency from 2018 to 2019, followed by an increase from 2021 to 2022, and it reached its peak level of 83.3% in 2020 (**Figure 3**).

Enterococcus spp.

In our study were isolated two MDR bacterial strains: *E. faecalis* from purulent secretions and *E. faecium* from uroculture. *E. faecium* strain revealed AMR for ampicillin, penicillin, and fluoroquinolone (ciprofloxacin and norfloxacin). *E. faecalis* was resistant to high levels of aminoglycosides resistance (HLAR) and tetracycline. Both bacterial strains were resistant to macrolides and sensitivity to vancomycin.

Enterobacterales

The commonest MDR strains from enterobacterales, were detected at *E. coli* 39/126 (31.0%), 46.1% of cases being found from purulent secretions from ulcers of the foot and 26.5% in urocultures (**Table 1**). ESBL producing strains were isolated in

Table 3. Antibiotic-resistant of Gram-negative rods from MDR strains

	AMC	TZP	CXM	CTX	CAZ	FEP	MEM	GM	AK	SXT	CIP	NOR	NF
E. coli	87.1	0.0	58.9	46.1	NT	0.0	0.0	35.9	5.0	69.2	53.8	55.5	6.6
K. pneumoniae	77.7	11.1	72.2	66.6	NT	0.0	0.0	38.8	5.5	72.2	27.7	71.4	0.0
K. oxytoca	100.0	0.0	75.0	25.0	NT	0.0	0.0	25.0	0.0	100	25.0	NT	NT
P. mirabilis	60.0	0.0	35.0	25.0	NT	0.0	0.0	75.0	5.0	90.0	50.0	NT	NT
P. vulgaris	100.0	0.0	100.0	100.0	NT	0.0	0.0	50.0	16.6	83.3	33.3	NT	IR
P. aeruginosa	IR	69.4	IR	IR	66.6	60.0	51.0	97.2	69.4	IR	100	NT	NT
Pseudomonas spp.	IR	57.6	IR	IR	42.3	39.0	35.0	92.3	34.6	IR	96.1	NT	NT

Note. IR: Intrinsic resistance; NT: Not tested; AMC: Amoxicillin-clavulanate; TZP: Piperacillin-tazobactam; CXM: Cefuroxime; CTX: Cefotaxime; CAZ: Ceftazidime; FEP: Cefepime; MEM: Meropenem; GM: Gentamicin; AK: Amikacin; SXT: Sulfamethoxazole-trimethoprim; CIP: Ciprofloxacin; NOR: Norfloxacin; NF: Nitrofurantoin; CO: Colistin; & MDR; Multidrug resistance

46.1%, decreasing in the pandemic years of 2020-2021, possible by reducing the number of isolates analyzed; 69.2% were resistant to trimethoprim/sulfamethoxazole; 53.8% vs 55.5% of strains were resistant to ciprofloxacin/norfloxacin; 35.9% showed resistance to gentamicin.

The majority (77.8%) of *K. pneumoniae* strains were isolated from purulent secretions from ulcers of the foot. The tested MDR strains of *K. pneumoniae* showed high rates of resistance for amoxicillin-clavulanate (77.7%), sulfamethoxazole-trimethoprim (72.2%), norfloxacin (71.4%), while 66.6% bacterial strains produced ESBL. All strains of *klebsiella* spp. were sensitive to cefepime and meropenem (**Table 3**). From 2018 to 2022, MDR prevalence for *proteus* spp. was 27.1%. ESBL frequency varied between 25.0% for *P. mirabilis* and 100% for *P. vulgaris* (**Table 3**).

Pseudomonas aeruginosa

36 MDR strains of *P. aeruginosa* were identified, most of them from skin infections. All bacterial strains were resistant to ciprofloxacin and with significant resistance to gentamicin (97.2%), piperacillin-tazobactam (69.4%), ceftazidime (66.6%) and carbapenems-resistance (CR) of 51.0% (**Table 3**).

DISCUSSION

Currently, MDR is strongly studied because of the need for improved strategies for the treatment of infection produced by these opportunistic pathogens. MDR strains for patients and healthcare providers represent a clinical and financial stress and are real challenges and the cost of care for this type of patient can be more than double compared to the patient without MDR infection. ECDC declared that the COVID-19 pandemic pointed out the weaknesses of national health systems and weak interconnection between countries and continents [33]. The years 2020-2022 (pandemic years), in the infectious diseases hospital, has a particular profile of bacterial strains reporting and antibiotic resistance because of reducing the number of isolates analyzed. Each year, microbiology laboratory reports isolated microorganisms in the hospital and in each department.

Our research focused on the phenotypic profile of AMR for selected strains belonging to MDR microorganisms. Between 2018 and 2022, in the department dermatology-venereology were isolated 34.5% MDR strains from the clinical samples. The majority group of pathogens were thus distributed: *S. aureus* 43.6%, *enterococcus* spp 16.7%, *E. coli* 31.0%, *proteus* spp 27.1%, *klebsiella* spp. 22.4%, *pseudomonas* spp. 34.8%. In other studies, hospital-acquired soft tissue infection is commonly caused by MDR pathogens, with *staphylococcus, pseudomonas*,

and *enterococcus* species posing the biggest threat [1]. It was declared that the most prevalent MDR in their research was E. coli (31.6%), followed by klebsiella pneumoniae (30.0%) [34]. Although were observed decreasing tendencies for MRSA, ESBL, and MDR, the resistance profile for MDR germs did not register significant statistical annual variations during the analyzed time frame within the infectious diseases hospital (dermatology department). More common were infections isolated from purulent secretions from ulcers of the foot (73.29%) and cutaneous secretions/collections (19.90%), in accordance with other studies [35]. MRSA and ESBL prevalence are high levels, but the low number of strains analyzed annually, particularly during the pandemic years do not support an adequate statistical analysis. The data reported by Romania, within ECDC network (European center for disease prevention and control), regarding the evolution of AMR are limited to the reporting of bacterial strains from invasive infections, being collected from a few university hospitals, but are not representative at the regional level.

S. aureus causes nosocomial infections, being the most common MDR Gram-positive pathogen and a major cause of morbidity and mortality globally. Soft tissue infection begins with bacterial strain invasion into areas of microtrauma to the skin and bacterial surface proteins bind to extracellular matrix proteins. This thing allows bacteria to multiply on the damaged tissue [36]. Individuals with skin barrier dysfunction are susceptible to secondary skin colonization with *S. aureus*, including MRSA. *S. aureus* produces several virulence factors thought to be important for skin and soft tissue infection: cytolytic proteins, superantigenic factors, molecules used for immune evasion, and cell wall-anchored proteins [37]. Similar studies have shown that MRSA is a common cause of both hospital-acquired infections and community-acquired also, for the patients with risk factors and healthy people [36, 38, 39]. Risk factors include several comorbidities such as diabetes mellitus, cardiovascular disease, peripheral vascular disease, renal disease, chronic wounds, immunosuppression, drug use and the presence of an abscess [40]. S. aureus can cause a wide range of infections. These infections can be soft tissue infections but also infections that can endanger life including pneumonia, osteomyelitis, meningitis, bacteremia, and sepsis. WHO lists MRSA as one of the serious threats because it's one the high-priority pathogens regarding the need to develop new antibiotics [41]. In a study effectuated in a communal dermatological setting, a growth of 17.0% was reported of the proportions of isolation of MRSA during a period of three years. This is due to the frequent use of beta-lactams in medical practice, staphylococci have developed resistance mechanisms by producing beta-lactamase (inactivation of penicillin) and change of target structure PBP (methicillin resistance) [42] or reduced drug uptake, frequently mediated

through mutations in the tet(k) gene [1]. In the recent time, have been approved by food and drug administration, only a small number of novel antibiotics effective against MRSA and vancomycin resistant enterococci (VRE); for example: dalbavancin, oritavancin, telavancin; ceftaroline, ceftobiprole; tedizolid, besifloxacin, ozenoxacin, delafloxacin and omadacycline [40]. The data provided by ECDC for Romania show an increased rate of resistance of bacterial strains from invasive infections of 45.7% MRSA, with the decreasing trend of meticillin-resistant [35, 42], compared to the average EU/EEA 15.5%. In our study we obtained a high level of MRSA 76.1%, for MDR strains tested.

Enterococcus spp. is commensal under normal conditions, but if the commensal relationship is disturbed, enterococci can cause localized and invasive infections. Infections usually occur in immunocompromised patients and may be due to an intestinal translocation in the digestive tract or may cause nosocomial infections. According to other studies, more common are infections located in the urinary tract (46.6%) followed by soft tissue infections (19.4%) [43], like our study. VRE is a major concern in enterococcal infections, which occurs due to abnormal bacterial synthesis of peptidoglycan, leading to a decrease in vancomycin affinity for the target peptide [44]. *Enterococcus* spp. is difficult to treat because these microorganisms are resistant to several classes of antibiotics. Treatment options for VRE infections include linezolid, daptomycin, quinupristine/dalfopristine, and tigecycline [45]. All strains of *enterococcus* spp. were sensitive to vancomycin, in the present study.

E. coli is the agent colonizer of the lower digestive tract, it can cause systemic and localized infections: urinary tract infections, biliary infections, intra-abdominal infections, or postoperative, soft tissue infections. According to the European surveillance data, Romania showed resistance to third-generation cephalosporin 20.3%, fluoroquinolones 30.2%, CR 0.6%, and MDR was 6.6% for invasive infections [33, 35, 42]. Studies have reported frequent MDR concerning *E. coli* in Iran. *E. coli* MDR strains, which are resistant to cephalosporins, co-trimoxazole and ampicillin, were found with high frequency (96.9%) [46]. In our study, MDR strains showed high resistance levels: 46.1% cefotaxime; 53.8% ciprofloxacin; 69.2% sulfamethoxazole-trimethoprim; AMR evaluated in this study is higher than resistances reported nationally from invasive infections.

K. pneumoniae frequently colonizes the human intestine, but in hospitalized patients can also be isolated from the skin, oropharynx, or respiratory system. The severity of infections is variable; in cases of systemic infection, especially if they are produced of MDR strains, lethality is high. This germ represents a major public health problem, as it is "a laboratory" for new production carbapenemases, which can then be transmitted to other Enterobacterales. A major problem is carbapenem-resistant strains, therapeutic alternatives are limited, the options being colistin, tigecycline, ceftazidim-avibactam, ceftolozan-tazobactam and sulfamethoxazole-trimethoprim [42]. According to the available data, Romania ranks third among EU/EEA countries, after Greece and Bulgaria to resistance to third-generation cephalosporin 65.2%; fluoroquinolones 64.5%, CR 35.4% and MDR was 48.4% for invasive infections [33, 34, 41]. In the department of Dermatology, we obtained a resistance to cefotaxime 66.6% and fluoroquinolones 27.7%. All strains of *E. coli* and *klebsiella* were sensitive to meropenem.

P. aeruginosa is a common cause of soft tissue infection (from folliculitis to diabetic foot infection) [45]. Nearly 13.0% of nosocomial infections caused by *P. aeruginosa* are resistant to at least one antibiotic (some strains are resistant to nearly all antibiotics) [47, 48]. A major adaptability of P. aeruginosa to antibiotics is owned partially to its large genome of five-seven Mbps, as such leading to the increase of the probability of genomic rearrangements [49]. Resistance is conferred by beta-lactamase production, target site modification and efflux-mediated and porin-related resistance [48]. *P. aeruginosa*'s extensive, intrinsic resistance mechanisms (due to the membrane external difficult to cross) make antipseudomonal drug development challenging. Due to the limited treatment options and life-threatening nature of invasive infections the multidrug-resistant pseudomonal infections are an urgent threat. The infections, life-threatening, disproportionately affect those with extensive skin breakdown and the immunocompromised [49]. Invasive infections require prompt and careful antimicrobia selection due to their high mortality rates, whilst localized skin infections have good prognoses [49, 50]. Typically, the treatment of a pseudomonas soft tissue infections typically relies on an antipseudomonal ß-lactam or a fluoroquinolone in combination with surgical intervention [51]. Our study showed high resistance levels: ceftazidime 66.6% and CR of 51.0% for MDR strains, Romania reporting from invasive infections a resistance to ceftazidime of 49.5%, 59.5% CR, by more than 3.0% compared to the average EU [33, 42]. Combined resistance to ≥3 antimicrobial groups was 49.1%, the highest level in European countries.

As demonstrated by the COVID-19 pandemic response, antimicrobial strategies must contend with the ability of microorganisms to adapt and resist. The development of conventional antimicrobial drug has tried to keep pace with AMRs development. Resistance reduction strategies are simple yet effective and include the avoidance of antibiotic monotherapy and the limitation of the duration of oral antibiotic use [52]. The surveillance of MDR bacterial strains must be developed by implementing EUCAST standards, increasing clinical vigilance for infectious diagnosis and using rapid identification methods with increased accuracy, as well as applying the principles of antibiotic administration in medical practice.

Limits of Study

The small number of bacterial strains included in this study was linked to the context of the pandemic in which hospitals were crowded with COVID-19 patients, and recommendations for microbiological investigations were limited. This adds to the reluctance of patients with other medical problems in terms of hospitalization. The small sample affects the reliability of statistical analysis. Another limit would be the need to implement the Eucast guidelines to reduce the variability of clinical interpretation between different countries and regions.

CONCLUSIONS

Over the past two decades, the dermatology treatment guidelines issued by expert panels consistently emphasize the need for judicious antibiotic use. During the period between the years of 2008 and 2016 a drop of 36.6% was noticed referring to the general prescription of antibiotics by dermatologists. However, the utilization of oral antibiotics

associated with surgical treatment increased with 69.6% for the same period, this suggesting that there may still be improvement areas [53].

Dermatologists should adhere to evidence-based infectious diseases guidelines in the treatment of purulent secretions from the skin to use the appropriate antibiotic selection and be know of local resistance patterns for key pathogens. To prevent AMR continued support for research into innovative strategies for the treatment of skin disease and the off-target effects of antimicrobials on the cutaneous microbiome are necessary. ESKAPE (*E. faecium, S. aureus, K. pneumoniae, A. baumannii, P. aeruginosa,* and *enterobacter* spp.) pathogens are mostly microorganisms, which are identified in dermatology department, the main problems being ESBL, MRSA and CR. The development of local antibiotic stewardship programs needs to consider the risk of transferring microorganisms from one hospital to another or to the community and AMR surveillance. The development of bacterial identification method is necessary to improve the etiologic diagnosis of the hospitalized infection. For earlier microbiological diagnosis and appropriate therapeutic decisions the identification of the resistance genes and the use of molecular techniques are necessary.

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