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The Problem of Antibiotic Resistance in Cutaneous Superinfections among Burn Patients at Mohamed IV University Hospital in Marrakech

El Ouarradi[1], H. Bennani[1], A. Lamrani Hanchi[1*], N. Soraa[1]

[1]Faculty of Medicine and Pharmacy of Marrakech, Cadi Ayyad University, Mohamed VI University Hospital, Marrakech, Morocco

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***Corresponding author:** A. Lamrani Hanchi
Faculty of Medicine and Pharmacy of Marrakech, Cadi Ayyad University, Mohamed VI University Hospital, Marrakech, Morocco

Abstract **Original Research Article**

Introduction and Objective: Cutaneous superinfection is a major complication that makes the management of burn patients difficult. Our objective is to identify the profile of multidrug-resistant organisms involved in cutaneous superinfections among burn patients at Mohamed VI University Hospital in Marrakech and to ensure epidemiological surveillance in order to adapt probabilistic antibiotherapy and the prevention policy for nosocomial infections in burn patients. ***Method:*** This study, conducted over 3 years between 2018 and 2020, included all cutaneous specimens from burn patients collected in the hospital departments of the university hospital. Cytobacteriological examination was performed according to conventional methods (direct examination - culture). Bacterial identification was performed according to automated morphological, cultural, and biochemical characteristics. Antibiotic susceptibility testing was performed according to CASFM-EUCAST recommendations. Data analysis and entry were performed using EXCEL. ***Results:*** Out of 408 specimens from 236 patients, a positivity rate of 79% was noted. Enterobacteriaceae represented the most frequently found organisms. Those resistant to third-generation cephalosporins (C3G) represented 45% of all Enterobacteriaceae. Imipenem resistance among these organisms represented 25% with resistance to sulfamethoxazole-trimethoprim in 88% of cases. For *Pseudomonas aeruginosa* species, 31% showed resistance to ceftazidime and piperacillin-tazobactam. 98% of *Acinetobacter baumannii* isolates showed resistance to ceftazidime, piperacillin-tazobactam, gentamicin, and ciprofloxacin. Among the 24 *Staphylococcus aureus* isolates, 15 showed methicillin resistance, representing 62.5%.
Conclusion: This study highlights the high frequency of cutaneous superinfection in burn patients as well as the frequency of multidrug-resistant bacteria complicating the management of these fragile patients.

Keywords: Burn, bacteria, multidrug resistance, antibiotherapy.

INTRODUCTION

A burn is defined as partial or total destruction of the cutaneous covering under the action of a thermal, electrical, chemical, or radioactive agent. Its severity depends on the causative agent, circumstances of occurrence, as well as the extent, depth, and location of the burn. Skin destruction favors bacterial colonization and the occurrence of infection, which represents a major complication affecting both local and vital prognosis of the burn patient. Burn infection also generates additional costs with prolonged hospital stay.

In this context, a microbiological study was conducted at Mohamed VI University Hospital in Marrakech between 2016 and 2018 [1] to establish the local epidemiology of nosocomial organisms and the means to implement to prevent their spread.

The objective of this work is to identify the profile of multidrug-resistant organisms involved in cutaneous superinfections among burn patients managed at Mohamed VI University Hospital in Marrakech and to ensure epidemiological surveillance to allow adaptation of probabilistic antibiotherapy and prevention policy for nosocomial infections in burn patients.

MATERIALS AND METHODS

This is a retrospective descriptive study including all cutaneous specimens from burn patients collected in different hospital departments and processed in the microbiology laboratory of ARRAZI hospital during the period from January 1, 2018, to December 31, 2020.

Cutaneous specimens from burn patients were collected during dressing changes in the presence of

signs of local infection. Cytobacteriological examination was performed according to conventional methods with direct examination and culture on enriched and selective media.

Bacterial identification was performed according to automated morphological, cultural, and biochemical characteristics (MALDI-TOF). Antibiotic susceptibility testing was performed according to recommendations of the French Society of Microbiology CASFM-EUCAST.

An exploitation form allowed recording for each patient: age, sex, department, isolated organism, and antibiogram. Data analysis and entry were performed using EXCEL.

The following were considered as multidrug-resistant bacteria: *Enterobacteriaceae* resistant to third-generation cephalosporins by ESBL (Extended-Spectrum Beta-Lactamase) production, *Enterobacteriaceae* producing carbapenemases, methicillin-resistant *Staphylococcus aureus*, and *Pseudomonas aeruginosa* and *Acinetobacter baumannii* multidrug-resistant to antibiotics with resistance to ceftazidime and/or imipenem.

RESULTS

During the study period, 408 specimens from burn patients were sent to the microbiology laboratory for cytobacteriological examination. These were specimens from 236 patients, of whom 60% were hospitalized in the plastic and reconstructive surgery department, and 30% were hospitalized in the pediatric intensive care unit. Children under 15 years represented 41% of patients. The male/female sex ratio of this series was 1.36. The distribution of specimens according to months showed the presence of two frequency peaks in July and December.

The positivity rate was 79% (n=323). Isolated organisms were dominated by gram-negative bacilli, which represented 68% with a predominance of Enterobacteriaceae (48%). Among Enterobacteriaceae, *Enterobacter cloacae* dominated the profile (15%) followed by *Klebsiella pneumoniae* (10%). Non-fermenting gram-negative bacilli represented 25% of all isolated organisms, particularly *Pseudomonas aeruginosa* (13%) and *Acinetobacter baumannii* (12%). For gram-positive organisms, we noted the predominance of coagulase-negative *Staphylococci* (14%). (Table I)

Enterobacteriaceae resistant to C3G represented 45% of all Enterobacteriaceae isolated from cutaneous superinfections, mainly represented by *Enterobacter cloacae* and *Klebsiella pneumoniae* (Table II). Imipenem resistance among these organisms represented 25% with resistance to sulfamethoxazole-trimethoprim association in 88% of cases. (Figure 1)

For isolated *Pseudomonas aeruginosa* species, 31% showed resistance to ceftazidime and piperacillin-tazobactam and 37% showed resistance to ciprofloxacin. (Figure 2)

98% of *Acinetobacter baumannii* isolates in this series showed resistance to ceftazidime, piperacillin-tazobactam, gentamicin, and ciprofloxacin. (Figure 3) Among the 24 *Staphylococcus aureus* isolates, 15 showed methicillin resistance, representing 62.5%.

Table I: Distribution of organisms isolated from cutaneous superinfections in burn patients between 2018 and 2020 (n=463)

Organism	**Number**	**Percentage**
Gram-positive cocci	141	30%
Staphylococcus aureus	24	5%
Coagulase-negative Staphylococcus	67	14%
Streptococcus	24	5%
Enterococcus	26	6%
Gram-negative bacilli	313	68%
Pseudomonas aeruginosa	62	13%
Acinetobacter baumannii	56	12%
Aeromonas spp	1	0%
Enterobacteriaceae	193	42%
Klebsiella pneumoniae	45	10%
Escherichia coli	31	7%
Enterobacter cloacae	69	15%
Proteus spp	23	5%
Providencia stuartii	15	3%
Morganella morganii	4	1%
Others	6	1%
Gram-positive bacilli	6	1%
Candida spp	3	1%
Total	**463**	**100%**

Table II: Profile of C3G resistance by ESBL production among Enterobacteriaceae isolated from cutaneous superinfections in burn patients between 2018 and 2020 (n=193)

ESBL-producing Enterobacteriaceae	Number	Percentage of multidrug resistance within species
ESBL Enterobacteriaceae	88	45%
ESBL *Klebsiella pneumoniae*	29	64% of all K. pneumoniae
ESBL *Escherichia coli*	8	26% of all E. coli
ESBL *Enterobacter cloacae*	32	46% of all Enterobacter spp.

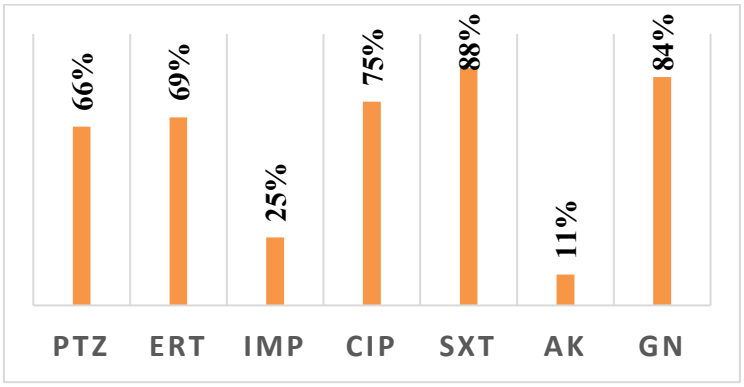

Figure 1: Antibiotic resistance profile of ESBL-producing *Enterobacteriaceae* isolated from cutaneous superinfections in burn patients between 2018 and 2020 (n=88)

PTZ: Piperacillin-Tazobactam; ERT: Ertapenem; IMP: Imipenem; CIP: Ciprofloxacin; SXT: Sulfamethoxazole-Trimethoprim; AK: Amikacin; GN: Gentamicin

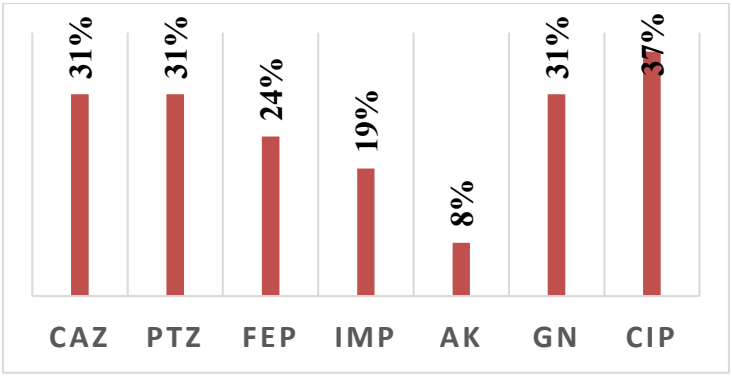

Figure 2: Percentage of antibiotic resistance in *Pseudomonas aeruginosa* isolates from cutaneous superinfections in burn patients between 2018 and 2020 at Marrakech University Hospital (n=62)

CAZ: Ceftazidime; PTZ: Piperacillin-Tazobactam; FEP: Cefepime; IMP: Imipenem; AK: Amikacin; GN: Gentamicin; CIP: Ciprofloxacin

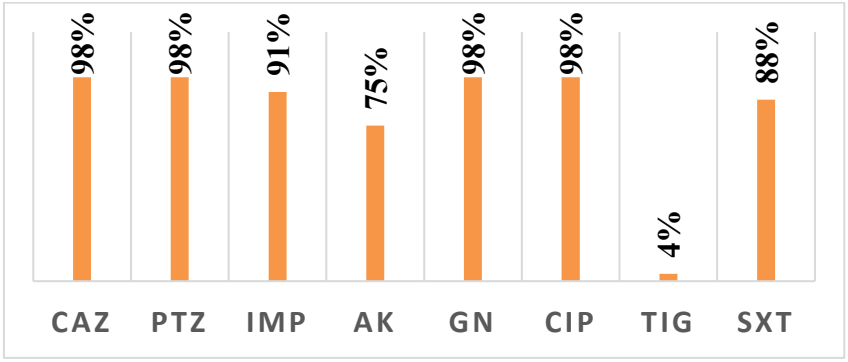

Figure 3: Percentage of antibiotic resistance in *Acinetobacter baumannii* isolates from cutaneous superinfections in burn patients between 2018 and 2020 at Marrakech University Hospital (n=56)

CAZ: Ceftazidime; PTZ: Piperacillin-Tazobactam; IMP: Imipenem; AK: Amikacin; GN: Gentamicin; CIP: Ciprofloxacin; TIG: Tigecycline; SXT: Sulfamethoxazole-Trimethoprim

Table III: Imipenem resistance of the main gram-negative bacilli isolated from cutaneous superinfections in burn patients between 2018 and 2020

Multidrug-resistant organism	Number	Percentage
Enterobacteriaceae	22	25%
Acinetobacter baumannii	51	91%
Pseudomonas aeruginosa	12	19%

DISCUSSION

The skin is a barrier between the external and internal environments of the human body. It plays several important roles, including mechanical and immune protection of the organism.

A burn is defined as destruction of the cutaneous covering or even underlying tissues following the action of thermal, electrical, chemical, and radioactive agents.

Bacterial nosocomial infection in burn patients is one of the main causes of morbidity and mortality in this fragile and immunocompromised population.

The objective of this study is to identify the profile of multidrug-resistant organisms involved in cutaneous superinfections among burn patients managed at Mohamed VI University Hospital in Marrakech and to ensure epidemiological surveillance.

In this series, we had 236 patients with a male/female sex ratio of 1.36. This male predominance is consistent with literature data [2-4]. This can be explained by the exposure of male subjects to high-risk activities and occupational accidents. However, an Indian series reports female predominance, which was explained by the nature of daily life of Indian women [5].

The mean age of patients was 27.64 years. This value is close to literature data, which fluctuates between 17.8 and 48.2.

In this series, burns occurred mainly in summer and winter, which is consistent with the results of Ahroui's 2019 study and that of Darfaoui's 2015 study [1,6]. This is explained by the need for hot water and the use of several heat sources in winter-autumn and high temperatures in summer. Burns represent an excellent bacterial culture medium. Burn infection is therefore an obligatory and inevitable phenomenon. It is beneficial because it promotes the elimination of burned tissues, but when it is extensive and severe, it must be feared because of its local and general consequences [7].

During the study period, 408 samples were analyzed. 323 cultures were positive, including 132 polymicrobial cultures, and 85 cultures were sterile.

The most frequently found gram-negative bacillus was *Enterobacter* spp (17%) followed by non-fermenting gram-negative bacilli, respectively *Pseudomonas aeruginosa* and *Acinetobacter baumannii*.

The Ahroui series showed the predominance of positive cultures for *Acinetobacter baumannii*, followed by *Pseudomonas aeruginosa* [1]. The same result was reported in other studies [8,9]. Other series showed the predominance of *Pseudomonas aeruginosa* [10-12].

For gram-positive cocci, the genus *Staphylococcus* (*Staphylococcus aureus* and coagulase-negative *Staphylococcus*) was the most frequent in the results; this is consistent with certain studies [13,14].

For yeasts, the species *Candida* was found in 3 specimens. According to a literature review on fungal infections in burn patients, it was reported that the most represented genera are *Aspergillus* and *Candida* with variable predominance according to studies [15].

In this series, 15 of the 24 isolated *Staphylococcus aureus* (62%) were methicillin-resistant (MRSA). However, all isolated MRSA strains were sensitive to glycopeptides. This result is consistent with that from China (66%) [16]. The percentage is higher than that found in the literature with 44% in the USA and different values in Europe [17].

MRSA is nowadays considered the major cause of nosocomial infections in Europe, and its prevalence continues to increase in burn centers [18,19].

For *Acinetobacter baumannii*, 98% of isolated strains were multidrug-resistant with imipenem resistance in 91% of cases. This result is higher than that observed in Ahroui's study, which remains nonetheless important (72.5%) [1]. This resistance poses an enormous problem in management; it is mainly linked to uncontrolled prescription of this molecule, thus selecting resistant strains.

Resistance to aminoglycosides and fluoroquinolones was also high and affected 98% of isolated strains. This is close to literature results [2,20,21].

It should be mentioned that colistin remained the most effective antibiotic against *Acinetobacter baumannii* with 100% sensitivity. This is close to the results of the study on antibiotic resistance in burn patients in Tunisia [12].

Regarding *Pseudomonas aeruginosa*, only 31% of isolated strains were resistant to ceftazidime with

ciprofloxacin resistance in 37% of cases. This is comparable with literature results [1,18]. This organism has been studied in several studies, according to which ceftazidime is the most effective antibiotic [22]; for another, the piperacillin-tazobactam combination was the antibiotic of choice [23].

19% of isolated *Pseudomonas aeruginosa* strains were imipenem-resistant. This is significantly lower compared to the Tunisian study [12]. However, it matches the result found in other studies [24].

Colistin maintained its sensitivity on isolated strains. According to the literature, the use of colistin in burn patients for the treatment of multidrug-resistant gram-negative bacilli by repeated systemic route for a long duration is safe, hence the interest of integrating it into the management protocol for these patients [25].

For *Enterobacteriaceae*, among the 194 isolated strains, 45% were multidrug-resistant bacteria. Some studies have reported higher values, notably Ahroui's series with a percentage of 72% [1,26]. Others have shown lower values [27]. This is due to increased prescription and often abusive use of broad-spectrum antibiotics.

For decreased carbapenem sensitivity, it was found in 25% of ESBL-producing *Enterobacteriaceae* strains isolated. This is significantly higher than the result of Ahroui's series and that of a Tunisian study with respective percentages of 14.4% and 14.43% [1,28].

Colistin has become the main agent in the treatment of carbapenem-resistant *Enterobacteriaceae*, generally associated with other antibiotics [29]. But its use should be limited to documented infections with gram-negative bacilli sensitive to this molecule in the absence of other solutions [30].

According to a study conducted in Athens, the use of colistin in monotherapy was associated with a high risk of therapeutic failure; its association with tigecycline or an aminoglycoside decreased this risk [31].

Given the emergence of these resistances, antibiotic prescription must be regulated, and technical and geographical isolation of patients carrying these strains must be implemented to prevent their transmission within burn units. It is important to highlight the role of healthcare personnel education in limiting the dissemination of these multidrug-resistant organisms within hospital structures managing burn patients.

CONCLUSION

This study highlights the high frequency of cutaneous superinfection in burn patients in our context, both in adults and children. The microbial ecology was dominated by gram-negative bacteria with the involvement of Enterobacteriaceae mainly represented by *Enterobacter cloacae* and *Klebsiella pneumoniae*. This ecology was also marked by the involvement of *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. Among gram-positive bacteria, coagulase-negative *Staphylococcus* was the most found in cutaneous superinfections in burn patients in our context.

This review of the last 3 years also highlighted the high frequency of resistance to third-generation cephalosporins by extended-spectrum beta-lactamase production among Enterobacteriaceae, as well as the frequency of strains with decreased carbapenem sensitivity, complicating the management of these patients in cases of bacteremia of cutaneous origin and also exposing them to the risk of dissemination of these plasmid resistances within a population of fragile patients.

The increased and irrational use of broad-spectrum antibiotics has favored the emergence of multidrug-resistant strains. It is also imperative to highlight the involvement of all personnel in contact with burn patients in the prevention and management of infections in these fragile patients. The cornerstone of burn patient management must be the prevention of cutaneous infection, which remains nonetheless a major cause of mortality and morbidity in these patients; hence the interest of implementing a clear and adapted protocol applied within all hospitalization departments for burn patients.

Regular epidemiological surveillance of the bacterial ecology of burn units is essential to find a management strategy for this problem within Marrakech University Hospital.

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