The obesity in hospitalized people has been proven to be an increased risk to develop types of infectious complications as sepsis, pneumonia, bacteraemia, wound infection and catheter infections on obese hospitalized people, but the cause of these immunological changes is not clarified, yet\textsuperscript{6}. The initial injuries of skin and soft tissue staphylococcal infections (SSTI) are caused by irritation and sweating in skin’s folds in obese patients, followed by the loss of skin’s integrity barrier function. Impairing peripheral microcirculation and of lymphatic circulation, the structural and functional alteration of collagen are favouring factors for microbial invasion\textsuperscript{5}. Methicillin Resistant Staphylococcus Aureus (MRSA) was originally related to nosocomial infections (HO-MRSA) (Hospital Associated - Methicillin Resistant Staphylococcus Aureus).
However, the significant increase of these strains in the community has been ascertained, either as typical community infections (CA-MRSA) (Community Associated - Methicillin Resistant Staphylococcus Aureus), or as community health-care associated infections (HA-MRSA)(6).

Case definitions developed by the Centers for Diseases Control and Prevention (CDC) for these types of infections are based on epidemiological criteria, but differentiate CA-MRSA strains and HA-MRSA can be proven by microbiological and genetic features(7).

The MRSA strains have acquired resistance to beta-lactam antibiotics but also to macrolides, aminoglycosides, fluoroquinolones, tetracycline and lincosamides. Until a few years ago, vancomycin was considered safe effective in MRSA infections, but overuse of this antibiotic has favored the emergence of resistance(8).

The current challenges on the epidemiology of staphylococcal infections globally are limiting transmission by strict hygiene measures, improving performance on the laboratory diagnosis of MRSA and judicious use of antibiotics to prevent the development and spread of antimicrobial resistance.

**Aims**

The aims of the study were to evaluate the antibiotic susceptibility of SA isolated in the SSTI, to identify the factors that influence the antibiotic resistance of SA and to argue the local recommendations for first-line treatment of these infections.

**Materials and methods**

The study retrospectively analyzed the epidemiological aspects of SSTI in the patients admitted to the Infectious Diseases Hospital Galati, from 01.01.2011 to 31.12.2013. The cases were identified by the computer software.

The reports of Diagnosis - Related Group (DRG) are sorted by codes B95.6-95.8 and L01-08 or I83. The exclusion criteria were age under 18 and nosocomial infection source, according to the CDC case definition (2011)(9).

Demographic data and co-morbidities in patients with SSTI were extracted from hospital medical records. The diagnosis of obesity has been considered if the body mass index (BMI) was greater than 30 kg/m2. Microbiological data were collected from the workbooks of the laboratory from Infectious Diseases Hospital Galati.

The duplicate results obtained by repeating the same patient were excluded. To calculate the rate of methicillin-resistance, each patient was enrolled only once. Thus, if a patient had recurrent infections, the strain isolated from the first presentation during the study was statistical analyzed.

Cultures from the secretions of pus, wounds, varicose ulcers or other representative skin lesions were made in the first 24 hours of hospitalization, according the internal protocols, included in the manual for sampling laboratory. Isolation culture media was followed by identification by conventional biochemical tests. Antibiotic susceptibility testing was performed by classic Kirby-Bauer method, containing the diffusion of antibiotic disc in subculture and the standardized manual measurement. Methicillin-resistant strains were isolated using the test disc Oxacillin, compared to a control strain ATCC 25923. In cases of patients with recurrent SSTI with SA strains isolated in at least two hospitalizations during the study, we compared the sensitivity to antibiotics and we calculated the incidence of resistance, if changes have occurred: sensitive (S) $\rightarrow$ resistant (R).

The incidence of resistance= (No. patients with MSSA change$\rightarrow$MRSA)/(No. patients with recurrent SSTI).

Statistical analysis was performed using software “Statistical Analysis XL-STAT Toolpack”.

Univariate analysis was based on Chi-square test or Fisher Exact Test. Logistic regression analysis allowed calculating the odds ratio (OR) and confidence intervals (CI95%). The level of correlation considered the Pearson coefficient with statistical significance $p< 0.05$.

The study was approved by the Ethics Council of “Dunarea de Jos” University from Galati.

**Results**

From 1.01.2011 to 31.12.2013, they were hospitalized 266 patients with SSTI and bacteriological evidence of SA positive culture, collected within 24 hours of admission. The median age was 70 years, varying between 22 and 92 years. Most of patients were males (M/F: 155/111) from rural living areas (R/U: 142/124). Frequency of the patients with infections classified as health care associated (HA) was 30.5%, while 69.5% cases corresponded to the present definition of community infections (CA).

The frequency of patients experiencing recurrent infections was 22.1% (59/266), with variations
between 2 and 7 episodes. Obesity with BMI over 30 kg/m² was associated to 20.3% (54/212) of patients.

Other significant co-morbidities listed in the discharge diagnostic were cardiovascular diseases 45.86% (122/264), diabetes 9.39% (25/241), HIV/AIDS 2.25% (6/260) and cancer diseases 1.5% (4/262). The antibiotic sensitivity analysis of staphylococci isolated from lesions of SSTI has found 41.72% (111/155) methicillin-resistant strains, concomitant with high rates of resistance to other antibiotics: 97.73% (259/265) Penicillin, 71.96% (190/264) Erythromycin, 63.39% (168/265) Clindamycin, 59.68% (114/191) Doxycycline, 40.8% (98/262) Ciprofloxacin, 39.21% (100/255) Gentamicin, 30.76% (52/16) TMP-SMX, 27.12% (67/247) Rifampicin. Vancomycin and Teicoplanin are proved to be active antibiotics, with susceptibility level of 99.6% (246/247) and 97.45% (253/257), respectively (Figure 1).

Table 1: Factors related to Methicillin Resistance in SSTI.

<table>
<thead>
<tr>
<th></th>
<th>MRSA</th>
<th>MSSA</th>
<th>OR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>35/76</td>
<td>19/136</td>
<td>3.29</td>
<td>1.79, 6.04</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Type-1 diabetes</td>
<td>7/104</td>
<td>2/153</td>
<td>5.1</td>
<td>1.20, 21.61</td>
<td>0.03</td>
</tr>
<tr>
<td>Cardio-vascular diseases</td>
<td>55/60</td>
<td>67.88</td>
<td>1.28</td>
<td>0.79, 2.10</td>
<td>0.307</td>
</tr>
<tr>
<td>Exposure to Health-Care (HA) before the current hospitalization</td>
<td>42/69</td>
<td>39/116</td>
<td>1.81</td>
<td>1.07, 3.06</td>
<td>0.038</td>
</tr>
<tr>
<td>Recurrence</td>
<td>32/79</td>
<td>27/128</td>
<td>1.92</td>
<td>1.07, 3.42</td>
<td>0.02</td>
</tr>
<tr>
<td>Rural living area</td>
<td>68/43</td>
<td>74/81</td>
<td>1.73</td>
<td>1.05, 2.83</td>
<td>0.029</td>
</tr>
<tr>
<td>Male</td>
<td>69/42</td>
<td>86/69</td>
<td>1.31</td>
<td>0.80, 2.16</td>
<td>0.276</td>
</tr>
<tr>
<td>Age &gt; 65</td>
<td>72/39</td>
<td>97/58</td>
<td>1.10</td>
<td>0.66, 1.83</td>
<td>0.401</td>
</tr>
</tbody>
</table>

The prevalence of MRSA strains was 41.7%, in which 38% (42/111) were HA-MRSA and 62% (69/111) CA-MRSA. Compared with ECDC (European Centers for Diseases Control and Prevention) report on antibiotic resistance, these data correspond to the general situation in Romania, estimated at 25-50% MRSA⁹

Most types of infection were complications of varicose ulcers (85%), that were related to health care infections (p=0.005, OR=3.44), but not to MRSA isolated strains (p=0.404). Age over 65 years was observed in 62.4% of patients and was not significant for the association of MRSA etiology (p=0.600). Methicillin-resistance was correlated with rural residence, although we expected that greater access to health services inside urban settings have contributed to developing more antibiotic resistance.

Immunosuppression caused by HIV infection and cancers have been identified in a small number of patients, and no significant differences between strains of methicillin - sensitive and resistant. There has been no case of undergoing dialysis.

The diagnosis rate of diabetes was 9.39% that is similar to the prevalence rate of diabetes in Romania¹⁰. Diabetes mellitus type 1 was associated with methicillin- resistance (p=0.030). Although the immunosuppression associated with diabetes is a known risk factor for staphylococcal infections, the influence of diabetes in the development of methicillin resistance it is not clarified¹¹,¹².

The frequency of obesity was 20.3%, similar to the average prevalence in the European states¹³. Obesity was associated with methicillin-resistance, and resistance to aminoglycosides (p=0.001), lincosamides (p=0.003), rifampicin (p=0.031), previous exposure to health care (p=0.038) and recurrent skin and soft tissue infections (p=0.020) (Table 1).

Discussion

Patients evaluated in this study were cared in a hospital exclusive for infectious disease that does not have emergency services and intensive care unit. The competence of medical management is limited to the common forms of infectious diseases.

Patients with infectious surgical complications and decompensate co-morbidities are deferred to the regional multidisciplinary hospital. Most patients come from home, therefore SSTI are representative for community acquired infections.

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trimethoprim-sulfamethoxazole (p=0.002). Among patients with recurrent infections with MRSA, 11/27 were obese, with statistically significant difference compared to methicillin sensitive SA group (p=0.250). These results differ from the findings of the prospective study conducted by Parr AM, when the obese patients had a 2-fold higher risk of presenting recurrent infections skin and soft tissue infections caused by MRSA, compared with patients who were not obese. The difference could be explained by the different design of his study and more severe cases.

The high prevalence of MRSA is limiting the first line therapeutic options for SSTI. The IDSA Guidelines for the management of staphylococcal infections recommends clindamycin, trimethoprim-sulfamethoxazole, tetracycline, or linezolid as alternative therapy for MRSA. Other antistaphylococcal drugs as vancomycin, daptomycin, telavancin or cefazolin should be reserved for hospitalized patients with severe infections.

In this study, only five strains were tested for linezolid, because the specific antibiotic discs were rarely available and the accessibility for therapy was limited by the high cost. Daptomycin, telavancin and cefazolin were not available for use in Romania, during the study. Rifampicin resistance was found in 27% of the strains isolated. Due to the risk of rapid development of resistance, rifampicin is not recommended for the treatment of SSTI, although it has bactericidal activity, penetrates the biofilm and performs high intracellular concentrations.

The choice of antibiotics to treat MRSA is difficult for high density extended to several classes of antibiotics, as results from this analysis. Resistance rate for Clindamycin was 59.3% and is limiting the empirical use of this antibiotic.

The local protocol for management of soft tissue infections should recommend the assessment of the risk of MRSA, taking into account the exposure to health care, obesity, and association of type-1 diabetes. For eligible cases systemic antibiotic therapy, TMP-SMX (Trimetoprim-Sulphametoxazole) or doxycycline may be the first line options.

However, we consider that the newer antistaphylococcal antibiotics as linezolid or ceftaroline would be preferable in the first line therapy of SSTI from our hospital in the health care associated context. Subsequently adjustment of antimicrobial therapy should be considered, based on antibiotic resistance evidence.

**Limits of the study**

The number of patients in the study is relatively small for statistical evaluation of epidemiological MRSA prevalence.

Study duration was short. The dynamic monitoring for developing the methicillin-resistance was only available in 17.5% (27/155) cases and the evaluation was limited to patients who were readmitted in our hospital. Data may be underestimated, given the possibility of recurrent infections admitted in other medical units.

Evaluation of antibiotic susceptibility was based on classical methods, but genetic testing had not been available, in order to clarify specific epidemiological aspects of staphylococcal infections.

**Conclusion**

Frequency of skin and soft tissue infections with methicillin-resistant staphylococcus is 41.7%.

Development of staphylococcal antibiotic resistance, including methicillin-resistance is favored by exposure to health care, obesity and type-1 diabetes. The current profile of staphylococcal antibiotic resistance requires the use of new antistaphylococcal drugs.

**References**


