Increased incidence of methicillin-resistant Staphylococcus aureus (MRSA) outside the hospital: an emerging clinical problem

A. Camporese, G. Tizianel
Clinical Microbiology and Antibiotic Therapy Unit
Clinical Pathology Department
"S.Maria degli Angeli" Hospital

Abstract. Methicillin resistant *Staphylococcus aureus* (MRSA) is a major nosocomial pathogen, with worldwide outbreaks in the hospitals.
From a problem almost exclusively encountered in hospital patients, MRSA infection has become also outside the hospital a cause of urinary tract, skin, soft tissue and even systemic infections, but the true incidence of MRSA in the community is not yet known .
Even though the origin of the emerging MRSA strains is not known, the prevalence of these strains in the community seems likely to increase substantially.
Our study was conducted between January 1998 and June 2001 to estimate the evolution of MRSA in our community. The aim of this study was to evaluate the incidence of MRSA in outpatients with acute and chronic infections.
During the study, a total of 423 *Staphylococcus aureus* strains were isolated from outpatients: 93 in 1998, 117 in 1999, 149 in 2000 and 64 in the first six months of 2001, obtained from various clinical specimens, i.e. wounds and soft tissue exudates, pus, urine samples, and others.
A retrospective review shows that the rate of MRSA in our region increased during the years and such an increase seems to be extended to acute and chronic outpatients with several community infections.
Previous hospital admission and cross transmissions between community and non-hospital nursing homes and/or residential home care centers seem to be, as other studies showed, an important risk factor for the acquisition of MRSA in our community.
The growing rate of MRSA and the incidence of MRSA community infections will require efficacious and rapid infection control measures.

Introduction

Methicillin resistant *Staphylococcus aureus* (MRSA) is a major nosocomial pathogen, with hospital-based outbreaks occurring worldwide (1,2).
Up to now one of the most serious aspects of the treatment of *Staphylococcus aureus* infections is its resistance to methicillin, which in clinical terms means resistance to all beta-lactam antibiotics.
Now, from a major problem almost exclusively encountered in hospital patients, MRSA infection has become a cause of urinary tract, skin, soft tissue and systemic infections even outside the hospital, but the true extent of MRSA in the community is not yet known (3-6). In fact, interpretation of community MRSA epidemiological trends is a problem, since the term is ill-defined and the related data are hardly included into a context (7-9).
Recent reports indicate that community-acquired MRSA infections are anyway increasing and may now involve also persons without predisposing risk factors (2,10,11,12).
This changing epidemiology of MRSA bears striking similarity to the emergence of the penicillinase-mediated resistance of *Staphylococcus aureus* observed decades ago.
Even though the origin of the emerging MRSA strains is not known, the prevalence of these strains in the community seems likely to increase substantially (9,13).
The changing epidemiology of MRSA is today important for many reasons, but principally because of the increasing number of patients discharged into the community, carrying or infected with MRSA, that increase the possibilities of spreading the resistance among several institutions: for the future, the general practicioners should thus consider the real possibility of nosocomially acquired MRSA and indeed of other antimicrobial-resistant microorganisms, such as extended spectrum beta-lactamase (ESBL) enterobacteria, when initiating empirical treatment of infections in patients who had been previously admitted to hospital (14).
Furthermore, distinguishing a genuine community MRSA infection which arises *de nov*o can be very difficult today (7,15,16,17) and MRSA isolates should truly be considered as community-acquired if the patient had no hospital admissions within the

Corrispondenza a: Clinical Microbiology and Antibiotic Therapy Unit - Clinical Pathology Department S. Maria degli Angeli Hospital - Via Montereale 24 - 33170 Pordenone - Fax 0039 0434 399685 - e-mail: alessandro.camporese@aopn.fvg.it

preceding six months at least and if the organism had been obtained from an outpatient culture or was isolated within 24 hours of hospital admission (10).
That being said, the aim of our retrospective study was to estimate the incidence of MRSA not in colonized subjects, but in acute and chronic outpatients with *Staphylococcus aureus* infections, who yielded the microbiological samples collected between January 1998 and June 2001.

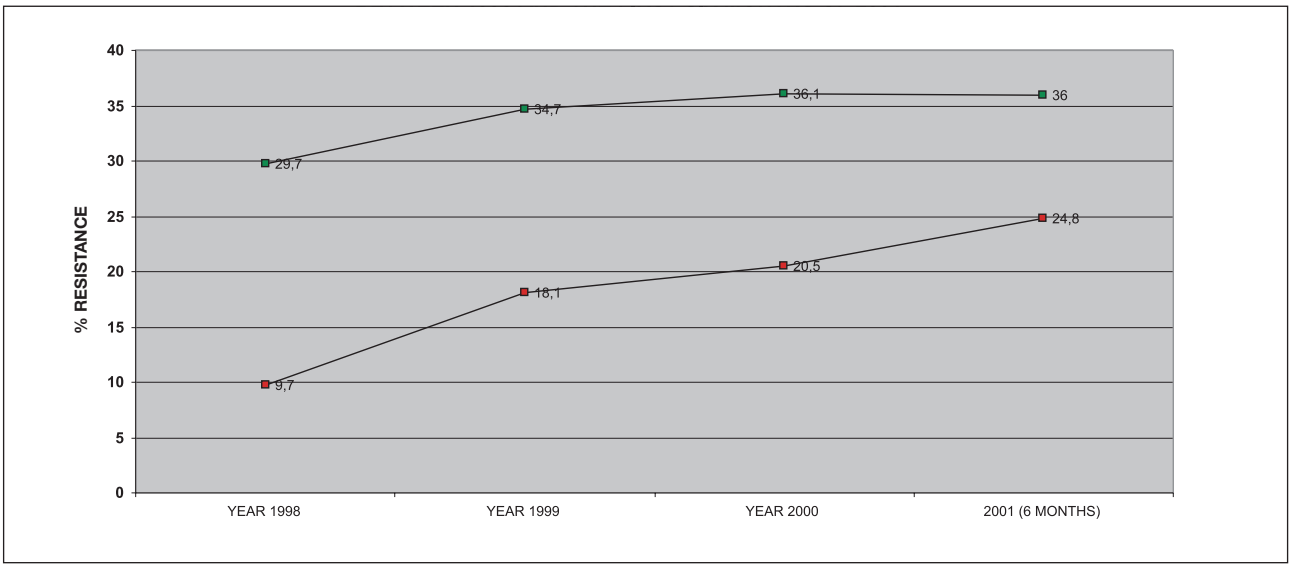
Materials and methods

The retrospective study was conducted between January 1998 and June 2001 to estimate the evolution of MRSA in our community, according to the microbiological samples collected in that period.
During the period, a total of 423 *Staphylococcus aureus* strains were isolated from outpatients: 93 in 1998, 117 in 1999, 149 in 2000 and 64 in the first six months of 2001.
Of all outpatients, 371 (about 87.7%) came from community or from nursing homes and 52 (about 12.3%) came from residential home care centers.
All the isolates were obtained from various clinical specimens, like swabs from non-healing wounds with clinical signs of infection, skin ulcers and soft tissue exudates (about 50%), pus (10%), urine samples (18%) and other such as sputum, intravenous catheter, ear, urethral and conjunctival swabs, obtained from patients with acute and chronic infections.
Some sites known to harbor resistant organisms like MRSA (as nostrils or perianal area) are not routinely cultured (16).
The study did not attempt to alter the routine screening laboratory practices and the samples were collected with routine techniques.
Mannitol-salt plates incubated for 24-48 hours at 35°C were used to screen for *Staphylococcus aureus* infection.
The identification of *Staphylococcus aureus* strains from mannitol-fermenting coagulase positive colonies was performed with a routine technique.
A susceptibility testing was carried out with the Kirby-Bauer disk diffusion method, using as a weekly quality control testing *Staphylococcus aureus* ATCC 25923, according to NCCLS recommendations (18).
Methicillin resistant *Staphylococcus aureus* strains were confirmed by the oxacillin agar screen test, using as control quality testing *Staphylococcus aureus* ATCC 29213 (susceptible) and *Staphylococcus aureus* ATCC 43300 (resistant), according to NCCLS recommendations (18).
All confirmed *Staphylococcus aureus* isolates were also tested for susceptibility to other antibiotics, such as erythromycin, ciprofloxacin, gentamycine, clindamycin and trimethoprim-sulfamethoxazole using the same Kirby-Bauer disk diffusion method.

Results

During the study, a total of 423 *Staphylococcus aureus* strains were isolated from the tested outpatients: 93 in 1998, 117 in 1999, 149 in 2000 and 64 in the first six months of 2001.
Of these patients, 371 (about 87.7%) were diagnosed in community or from nursing homes and 52 (about 12.3%) came from residential home care centers.
The most common samples obtained from sites of *Staphylococcus aureus* infection were swabs taken from skin ulcers, wound and soft tissue exudates (about 50%), followed by urine samples (about 18%), pus (about 10%) and other site-specific cultures, like sputum, intravenous catheter, ear, urethral and conjunctival swabs.
As we see in Figure 1, in all the 423 *Staphylococcus aureus* strains isolated from these patients, methicillin resistance rate increased during the years from

Figure 1: MRSA isolation rate in outpatients and inpatients betwen 1998 and the first six months of 2001.



9.7% to 24.8%, being only 9.7% in 1998, but respectively 18.1% in 1999, 20.5% in 2000 and 24.8% in the first six months of 2001.
On the contrary, during the same period, methicillin resistance rate for *Staphylococcus aureus* strains isolated from the hospital patients reached a steady-state level in the last two years: the rate was in fact 29.7% in 1998, 34.7% in 1999, 36.1% in 2000 and 36% in the first six months of 2001(Figure 1).
The highest rate of MRSA infection occurred in subjects over the age of 62, with rates in females being slightly higher than those in males.
Most of *Staphylococcus aureus* isolated in our region, either MRSA or MSSA (methicillin susceptible *Staphylococcus aureus*) demonstrated resistance also to other antibiotics (Figure 2), such as erythromycin (18.3% in 1998, 29.1% in 1999, 30.2% in 2000, 33.1% in 2001), ciprofloxacin (12% in 1998, 21.4% in 1999, 22.8% in 2000, 21.1% in 2001) gentamycine (18.3% in 1998, 29.1% in 1999, 34.2% in 2000, and 23% in 2001).

Discussion

From an infection almost exclusively encountered in hospital patients, MRSA seems likely to increase substantially in the community and has become a cause of urinary tract, skin, wound, soft tissue and even systemic infections outside the hospital.
Our study provides additional information concerning the rate of MRSA in our region and suggest that MRSA represents today an important emerging community pathogen.
Our data in fact show that the incidence rate of MRSA in our region increased during the years and the increase seems to be extended over all acute and chronic outpatients with several community infections.
We can say in agreement with other studies (8,10), that MRSA seems to prefer the elderly and/or debilitated subjects : in fact, the highest rate of MRSA infection occurred in chronic subjects over the age of 62, often debilitated, with rates in females being slightly higher than those in males.
Previous hospital admission and cross transmission among community, nursing homes and/or non-hospital residential home care centers seem to be, as other studies showed (10,19), an important risk factor for the acquisition of MRSA and for the related infections in our community.
The increasing number of patients discharged into the community from the hospital, carrying or infected with MRSA is probably one of the reasons for the changing epidemiology of MRSA and can explain the increasing possibilities for MRSA transfer to the community and to other community-related institutions.
This kind of patients, when readmitted to the hospital can also have a high probability of reintroducing there these microorganisms: for that reason we think that screening for MRSA in previously hospital admitted chronic patients at the time of re-admission might reduce the nosocomial spread and indirectly the incidence of MRSA in the community, albeit only a real implementation of infection control precautions will limit the nosocomial spread and therefore the incidence of MRSA in the community.
Many hospitals today attempt some degree of control of transmissible multi-resistant bacterial pathogens (20), and one of the specific pathogens in this category that warrants infection control measures is MRSA: the steady-state level of methicillin resistance of the *Staphylococcus aureus* strains isolated during the last three year from our hospital patients (Figure 1) is really related with a satisfying nosocomial infection control.
On the contrary, the growing rate of MRSA community infections outside the hospital, the several reservoirs of *Staphylococcus aureus* resistant strains and their facility to cause outbreaks will require efficacious and rapid infections control measures in the community, nursing homes and residential homes (21-25) and these infection control issues will need to be truly implemented to reduce transmission and prevent outbreaks.
Nevertheless, if MRSA dissemination is facilitated by person to person transmission due to poor infection control practice, and the causes of the rapid emergence and dissemination of antibiotic-resistant bacteria are multi-factorial, another core issue is widely accepted: MRSA emergence is highly correlated with the selective pressure (8) resulting from heavy and often less than judicious use of antibiotics (e. g.fluoroquinolones).
In the future we need to better explore the relationships of the various factors contributing to the emergence and spread of the community MRSA, i.e. antibiotics consumption data, control measures used to limit or optimize antibiotic use, antibiotic policies and infection control policies. There is a wealth of data which might be used to convince doctors that changing their prescription and infection control habits is worthwhile and not detrimental to their patients.
However the changing epidemiology of MRSA is also important because it will consequently change the general practicioners education: doctors, in fact, will consider the possibility of nosocomially acquired MRSA and/or other resistant microorganisms like ESBL enterobacteria when initiating the empirical treatment of infections in their patients who have been in hospital previously (26). An immediate microbial culture should hence be performed rather than waiting for a failed treatment (7,14) but, on the other hand, hospital doctors will need to consider their screening strategy regarding patients admitted from community, nursing homes and residential homes.
Both hospital and non-hospital physicians will need relevant surveillance data to direct their empirical

treatment and advice on prevention of infections in their patients.

The growing rate of MRSA and the incidence of MRSA community infections will also require efficacious and rapid infections control measures in the community.

Regarding this matter, we think that it will be an important priority to establish who will handle the information on these community problems and how the situation can be improved in our region.

References

1. Hryniewicz W. Epidemiology of MRSA. Infection 1999; suppl.2:S13-16.
2. Bukharie HA, Abdelhadi MS, Saeed IA, Rubaish AM, Larbi EB. Emergence of methicillin resistant *Staphylococcus aureus* as a community pathogen. Diagn Microbiol Infect Dis 2001;40:1-4.
3. Shopsin B, Mathema B, Martinez J, Ha E, Campo ML, Fierman A, et al. Prevalence of methicillin resistant and methicillin-susceptible *Staphylococcus aureus* in the community. J Infect Dis 2000;182:359-62.
4. Mylotte JM, Goodnough S, Tayara A. Antibiotic-resistant organisms among long-term care facility residents on admission to an inpatient geriatrics unit: restrospective and prospective surveillance. Am J Infect Control 2001;29:139-44.
5. Boyce JM. Are the epidemiology and microbiology of methicillin resistant *Staphylococcus aureus* changing? JAMA 1998;279:623-4.
6. Bjork DT, Pelletier L, Tight RR. Urinary tract infections with antibiotic resistant organisms in catheterized nursing home residents. Infect Control 1984;5:173-6.
7. Cookson BD. Methicillin-Resistant *Staphylococcus aureus* in the community: new battlefronts, or are the battles lost? Inf Contr and Hosp Epidemiol 2000; 21:398-403.
8. Bergoge-Berezin E. Resistance and new antibiotic strategies. The problem with staphylococcus. Presse Med 2000;29:2018-21.
9. Chambers HF. The changing epidemiology of *Staphylococcus aureus*? Emerg Infect Dis 2001;7:178-82.
10. Warshawsky B, Hussain Z, Gregson DB, Alder R, Austin M, Bruckshwaiger D et al. Hospital and community based surveillance of methicillin resistant *Staphylococcus aureus*: previous hospitalization is the major risk factor. Inf Contr and Hosp Epidemiol 2000;21:724-7.
11. Collignon P. Increased incidence of methicillin-resistant strains of *Staphylococcus aureus* in the community. J Infect Dis 1999;179:1592.
12. Moreno F, Crisp C, Jorgensen JH, Patterson JE. Methicillin resistant *Staphylococcus aureus* as a community organism. Clin Infect Dis 1995;21:1308-12.
13. Kallen AJ, Driscoll TJ, Thornton S, Olson PE, Wallace MR. Increase in community-acquired methicillin resistant *Staphylococcus aureus* at naval medical Center. Infect Control Hosp Epidemiol 2000;21:223-6.
14. Camporese A, Santini G. Surveillance of antibiotic-resistant microorganisms for the rational use of antimicrobial drugs. Le Infezioni in Medicina 1999;3:172-6.
15. Smith DW. Decreased antimicrobial resistance after changes in antibiotic use. Pharmacotherapy 1999;19:129S-137S.
16. Scudeller L, Leoncini O, Boni S, Navarra A, Rezzani A, Verdirosi S, Maserati R. MRSA carriage: the relationship between community and healthcare setting. A study in a Italian hospital. J Hosp Infect 2000; 46:222-9.
17. Abudu L, Blair I, Fraise A, Cheng KK. Methicillin-Resistant *Staphylococcus aureus*: a community-based prevalence survey. Epidemiol Infect 2001;126:351-6.
18. National Committee for Clinical Laboratory Standards. Performance standards for antimicrobial susceptibility testing: eleventh informational supplement. NCCLS 2001; document M100-S11.
19. Goetz A, Posey K, Fleming J, Jacobs S, Boody L, Wagener MM, Muder RR. Methicillin resistant *Staphylococcus aureus* in the community: a hospital-based study. Infect Control Hosp Epidemiol 1999;20:689-91.
20. British Society for Antimicrobial Chemotherapy, Hospital Infection Society and the Infection Control Nurses Association. Revised guidelines for the control of methicillin resistant *Staphylococcus aureus* infections in hospitals. J Hosp Infect 1998;39:253-90.
21. Matsumoto K, Hohashi N, Sugishita C. A study on the trasmission of MRSA among the family members including clients of visiting nurse and related infection control. Nippon Koshu Eisei Zasshi 2001;48:190-199.
22. Bradley SF. Issues in the management of resistant bacteria in long-term care facilities. Infect Control Hosp Epidemiol 1999;20:362-6.
23. Hollis RJ, Barr JL, Duebbeling BN, Pfaller MA, Wenzel RP. Familial carriage of methicillin resistant *Staphylococcus aureus* and subsequent infection in a premature neonate. Clin Infect Dis 1995;21: 328-332.
24. Masterton RG, Coia JE, Nofman AW, Kempton-Smith L, Cookson BD. Refractory methicillin resistant *Staphylococcus aureus* carriage associated with contamination of the home environment. J Hosp Infect 1995;29:318-9.
25. Ayliffe GAJ, Blemkinsop R, Cooke EM, Casewell MWC, Cookson BD, Cox RA, et al. Guidelines for the control of epidemic methicillin resistant *Staphylococcus aureus* in elderly care and nursing homes. Report of a combined working party of the Hospital Infection Society and the British Society of Antimicrobial Chemotherapy. J Hosp Infect 1995;31:1-12.
26. O'Brien FG, Pearman JW, Gracey M, Riley TV, Grubb WB. Community strain of methicillin resistant *Staphylococcus aureus* involved in a hospital outbreak. J Clin Microbiol 1999;37:2858-62.