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SHORT REPORT
Epidemiology and associated factors for nosocomial methicillin-resistant *Staphylococcus aureus* infection in a tertiary-care hospital

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SUMMARY

We analysed nosocomial MRSA cases between January 2004 and December 2006 in a retrospective case-control study in a 250-bed tertiary-care teaching hospital. During the study period, 265 nosocomial *Staphylococcus aureus* infections were identified in 231 patients. There was a significant increase in methicillin resistance in isolates (MRSA) from these infections with frequencies for 2004 of 39/88 (44·3%), 2005 (62/80, 77·5%), and 2006 (75/97, 77·3%) ($P<0·001$). Multivariate analysis showed that associated factors for nosocomial MRSA infection were prolonged hospitalization (OR 3·982, 95% CI 2·235–7·094, $P<0·001$), mechanical ventilation (OR 3·052, 95% CI 1·666–5·590, $P<0·001$), surgical operation (OR 2·032, 95% CI 1·102–3·748, $P=0·023$), and male sex (OR 2·000, 95% CI 1·081–3·699, $P=0·027$). The determination of associated factors for methicillin resistance in nosocomial *S. aureus* infections in hospitals will play an important role in efforts to reduce MRSA infection rates.

Key words: Associated factors, MRSA, nosocomial.

Methicillin-resistant *Staphylococcus aureus* (MRSA) infections are now among the most frequently seen antibiotic-resistant infections in many areas in the world [1–3]. Moreover, MRSA rates continue to increase worldwide according to current data supplied by ongoing surveillance monitoring such as the National Nosocomial Infections Surveillance System (NNIS) and the European Antimicrobial Resistance Surveillance System (EARSS). Indeed, the incidence of MRSA in intensive-care units (ICUs) in the USA reached 60% in 2003 showing an 11% increase compared with the previous time interval 1998–2002 [2]. On the other hand, the prevalence of MRSA infection shows considerable variation between countries, even in different areas of the same country and in different hospitals in the same area [4–6]. According to EARSS data, the prevalence of MRSA in hospitals in some Northern European countries such as The Netherlands is low (<4%) but exceeds 25% in Southern Europe, the UK and Ireland [6].

The prevalence of MRSA in Turkey has been reported to be between 45% and 70% depending on the study population [5, 7, 8]. Turkey joined EARSS in 2005, but has been participating in the Antibiotic Resistance Surveillance and Control in the Mediterranean region (ARMed) project and data for

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2003 to 2005 were added to the EARSS database. MRSA infections showed a significant decrease from 43% in 2003 to 36% in 2006 despite the fact that the data were limited to only the 14 participant hospitals in Turkey [6].

In the present study, the rates of nosocomial MRSA infections were determined over a 3-year period in a tertiary-care teaching hospital in Turkey. Further, the influence of institution-specific and patient-associated factors on the rates of infection was investigated.

The tertiary-care teaching hospital has 250 beds and three ICUs: anaesthesiology & recovery (six beds), neurosurgical (five beds) and cardiovascular (four beds) ICUs. Each patient's room has a sink with unmedicated soap for hand washing. Dispensers of hand antiseptic solutions are placed only in high-risk areas, not in all patients' rooms, and colour posters emphasizing the importance of hand washing are displayed in these areas. Moreover, an educational programme for health-care personnel is carried out by the infection control team.

Medical records of patients hospitalized between January 2004 and December 2006 were analysed retrospectively. Nosocomial *S. aureus*-infected cases were defined as those individuals who grew *S. aureus* from culture of specimens collected at least 48 h after admission. MRSA-infected cases (case patients) were those who had nosocomial *S. aureus* that showed methicillin resistance, while those with methicillin-sensitive *S. aureus* were classified as nosocomial MSSA cases (controls). Infections were defined using the Centers for Diseases Control and Prevention (CDC) criteria.

Clinical and epidemiological data were collected by a specialist in infectious diseases and the Infection Control Committee Nurse. Information about associated factors for development of nosocomial MRSA infections was collected from patients' files and included prolonged hospitalization (>21 days), hospital ward, surgery, diabetes mellitus, malignancy, renal insufficiency, obesity, trauma, surgery, mechanical ventilatory assistance, previous antibiotics, and insertion of vascular catheter, urinary catheter, or nasogastric tube.

S. aureus was identified by Gram stain, catalase reaction, tube coagulation test, and Api-Staph test (bioMérieux, France). Methicillin resistance was determined by Kirby–Bauer disk diffusion method according to National Committee for Clinical Laboratory Standards (NCCLS) criteria [9].

Continuous variables were compared using the independent-samples t test and categorical variables were compared using the χ^2 test or Fisher's exact test for association. Differences were considered statistically significant when $P<0{\cdot}05$. Statistical calculations were performed using SPSS for Windows 11.0 (SPSS, USA). Forward stepwise multiple logistic regression was performed to identify the independent predictors of outcome, determine factors associated with the presence of methicillin resistance in nosocomial *S. aureus* infections as the dependent variable and all factors significant on univariate analyses as covariates. Variables with significant collinearity were omitted from the analysis.

A total of 13 511, 13 775, and 17 757 patients were hospitalized in 2004, 2005, and 2006, respectively. Rates of ventilator use in the anaesthesiology & recovery ICU were 0·79 (2004), 0·67 (2005) and 0·71 (2006), rates in the neurosurgical ICU were 0·43 (2004), 0·45 (2005), and 0·41 (2006), and rates in the cardiovascular ICU were 0·50, 0·71, and 0·51, respectively for each of the three years.

During the study period 265 nosocomial *S. aureus* infections were identified in 231 patients, and 66·4% were due to MRSA. One hundred and thirty-eight patients (60%) were male and ranged in age from newborn to 93 years with a mean of 51·3 years (S.D. = 22·2). The incidence rate of nosocomial *S. aureus* decreased from 5·6 cases/1000 admissions in 2004 to 5·0 cases/1000 admissions in 2006 ($P=0{\cdot}52$). Correspondingly the incidence of MRSA infection increased linearly with years from 2·4 cases/1000 admissions in 2004, to 3·77 cases/1000 admissions in 2006 (χ^2 for linear trend 3·850, $P=0{\cdot}05$). The number of MRSA infections rose from 39/88 patients (44·3%) in 2004 to 62/80 (77·5%) in 2005, and this was maintained in 2006 (75/97, 77·3%) (χ^2 for linear trend 21·797, $P<0{\cdot}001$). MRSA prevalence was highest in the anaesthesiology & recovery ICU and general surgery unit and lower in the paediatrics unit ($P=$ 0·001) (Table 1). The most common clinical presentation was pneumonia which was present in almost half (49·4%) of patients (Table 2).

Table 3 shows the univariate analysis for the main potential associated factors for MRSA infections and identified the statistically significant variables as prolonged hospitalization, type of hospital ward, surgical operation, urinary catheterization, mechanical ventilation, male sex, presence of nasogastric tube and previous antibiotics usage. Results from the multivariate analysis showed that, when considered

Table 1. *Comparison of the prevalence of methicillin resistance in ICUs and non-ICUs*

Unit	MRSA ($n=150$) n (%)	MSSA ($n=81$) n (%)	P value
Intensive care	97 (64·7)	35 (43·2)	0·002
Non-intensive care	53 (35·3)	46 (56·8)	
Intensive care			
Anaesthesiology & recovery	57 (58·8)	15 (42·9)	
Neurosurgical	31 (32)	15 (42·9)	
Cardiovascular	9 (9·3)	5 (14·3)	0·262*
Non-intensive care			
Surgical wards	34 (64·2)	15 (32·6)	
General surgical	12 (22·6)	3 (6·5)	
Orthopaedics	9 (17)	5 (10·9)	
Plastic surgery	5 (9·4)	1 (2·2)	
Others	8 (15·1)	6 (13)	0·002†
Medical wards	19 (35·8)	31 (67·4)	
Internal medical	8 (15·1)	11 (23·9)	
Paediatrics	4 (7·5)	12 (26·1)	
Others	7 (13·2)	8 (17·4)	

ICU, Intensive-care unit.
* Comparison between ICUs.
† Surgical *vs*. medical wards.

Table 2. *Nosocomial MSSA and MRSA infections in hospitalized patients by site of infection, 2004–2006*

Infection	MRSA n (%)	MSSA n (%)
Pneumonia	87 (49·4)	23 (25·8)
Bacteraemia	34 (19·3)	11 (12·4)
Surgical site	26 (14·8)	20 (22·5)
Skin and soft tissue	14 (8·0)	10 (11·2)
Others*	15 (8·5)	25 (28·1)
Total†	176† (66·4)	89† (33·6)

* Omphalitis, central nervous system, urinary tract, indwelling catheter, osteomyelitis and septic arthritis.
† Number of nosocomial MRSA and MSSA infections.

together, prolonged hospitalization (OR 3·982, 95% CI 2·235–7·094, $P<0·001$), mechanical ventilation (OR 3·052, 95% CI 1·666–5·590, $P<0·001$), surgical operation (OR 2·032, 95% CI 1·102–3·748, $P=0·023$), and male sex (OR 2·000, 95% CI 1·081–3·699, $P=0·027$) were significantly and independently associated with MRSA infection.

Our study revealed the overall mean proportion of MRSA in nosocomial *S. aureus* infections in a Turkish tertiary-care hospital was 66·4%. Although MRSA rates reported by EARRS for 14 participating hospitals in Turkey were often at the higher end in European countries, our rate proved to be even higher. However, similarly high rates have been reported from another hospital in Turkey (66%) and Brazil (60·2%) [8, 10]. Since MRSA was first recognized in 1960, rates of MRSA have increased worldwide in the ensuing decades with some fluctuations [4, 6, 10]. An interesting finding from the present study was that in spite of stable rates of overall *S. aureus* nosocomial infections, there was a statistically significant increasing trend in the proportion of MRSA infections, We believe that one of the important contributing factors to this issue is the limited financial resources available for implementation of infection control practices in our hospital such as the provision of hand-washing solutions in each patient's room and contact isolation of MRSA-infected patients. Although there was a significant increase in the number of hospitalized patients in our institution, a similar trend was not evident in the rate of ventilator use in ICUs. There was a concomitant increase in the incidence rate of nosocomial MRSA infection from 2·4 cases/1000 admissions in 2004 to 3·77 cases/1000 admissions in 2006. However, the retrospective design of the study is not ideal to establish the incidence rate. Shitrit *et al*. [11] found that with implementation of active surveillance and contact isolations, the incidence of nosocomial MRSA bacteraemia decreased

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Table 3. *Univariate analysis of associated factors for methicillin resistance in nosocomial* S. aureus *infections*

Associated factors	Patients with MRSA infection, *n* (%)	Patients with MSSA infection, *n* (%)	*P* value
Age, yr, mean (S.D.)	52·4 (19·3)	48·6 (27·1)	0·267
Male sex	98 (65·3)	40 (49·4)	0·018
Hospitalization (>21 days)	54 (64)	56 (39·4)	<0·001
Type of unit			
Intensive care	97 (64·7)	35 (43·2)	0·002
Non-intensive care	53 (35·3)	46 (56·8)	
Underlying diseases			
Diabetes mellitus	23 (15·3)	8 (9·9)	0·246
Malignancy	9 (6)	2 (2·5)	0·337
Renal insufficiency	13 (8·7)	5 (6·2)	0·5
Obesity	11 (7·3)	7 (8·6)	0·723
Trauma	15 (10)	3 (3·7)	0·122
Surgical operation	94 (62·7)	34 (42)	0·003
In-dwelling device			
Vascular catheter	122 (81·3)	60 (74·1)	0·198
Urinary catheter	118 (78·7)	41 (50·6)	<0·001
Mechanical ventilation	87 (58)	23 (28·4)	<0·001
Nasogastric tube	65 (43·3)	14 (17·3)	<0·001
⩾2 or more devices	129 (86)	52 (64·2)	0·005
Previous antibiotics	143 (95·3)	67 (82·7)	0·001

from 0·74 to 0·37 cases/1000 admissions. Similarly, a recent study reported that the implementation of surveillance programmes resulted in a decrease in MRSA infection rates from 6·1 to 4·1 infections/1000 census days [3].

In a recent study [4], the prevalence of MRSA was highest in patients admitted to ICUs and, this is confirmed by our finding of significantly higher rates in the anaesthesiology & recovery ICU and general surgery unit and lower in the pediatrics unit. MRSA prevalence was found to be lowest for bacteraemia as a primary site of infection and highest for respiratory tract infections in that study. Here, in all sites of infection MSSA was similar to or more frequently isolated than MRSA with the exception of nosocomial *S. aureus* pneumonia which was caused predominantly by MRSA. This may have been due to more frequent use of mechanical ventilation in the ICUs as the multivariate analysis showed that this was the second most significant factor associated with acquisition of MRSA infection. This is a very important finding that could help us to guide the initial antimicrobial therapy in patients with nosocomial pneumonia.

Of the associated factors revealed by the univariate analysis, prolonged hospitalization, mechanical ventilation, surgical operation, and male gender proved to be independent risk factors for hospital-acquired MRSA infection as has been reported in other studies [1, 7, 10, 12]. Our data indicate that MRSA infection increased almost fourfold where patients were hospitalized >3 weeks. The reason for prolonged hospitalization may be the severity of the primary illness and not always related to MRSA infection. Surgical operation increased MRSA infections by twofold, in keeping with other published studies [1, 13]. The influence of gender on MRSA rates is controversial. Like us, Selvey *et al*. [12] found males predominated in MRSA cases but another study disagreed with this finding [14]; therefore this is an area clearly requiring further investigation.

Patients with MSSA were used as a control group but a limitation of the study was the lack of a group of patients without *S. aureus* infection. Selection of the MSSA group as controls may have magnified the risk of individual factors and falsely identified risk factors [15]. Nevertheless, several factors proved to be independently associated with MRSA in this Turkish population and this has significant implications for the selection of empirical treatment or restriction of antibiotics and strategy for control measures.

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DECLARATION OF INTEREST

None.

REFERENCES

1. **Graffunder EM, Venezia RA.** Risk factors associated with nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) infection including previous use of antimicrobials. *Journal of Antimicrobial Chemotherapy* 2002; **49**: 999–1005.
2. **National Nosocomial Infections Surveillance System.** National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. *American Journal of Infection Control* 2004; **32**: 470–485.
3. **Clancy M, *et al.*** Active screening in high-risk units is an effective and cost-avoidant method to reduce the rate of methicillin-resistant *Staphylococcus aureus* infection in the hospital. *Infection Control and Hospital Epidemiology* 2006; **27**: 1009–1017.
4. **Asensio A, *et al.*** Nosocomial and community-acquired meticillin-resistant *Staphylococcus aureus* infections in hospitalized patients (Spain, 1993–2003). *Journal of Hospital Infection* 2006; **63**: 465–471.
5. **Alp E, *et al.*** MRSA genotypes in Turkey: persistence over 10 years of a single clone of ST239. *Journal of Infection*. 2009; **58**: 433–438.
6. **European Antimicrobial Resistance Surveillance System** (EARSS). Annual Report 2006 (http://www.rivm.nl/earss/result/Monitoring_reports/). Accessed October 2007.
7. **Topeli A, Unal S, Akalin HE.** Risk factors influencing clinical outcome in *Staphylococcus aureus* bacteraemia in a Turkish University Hospital. *International Journal of Antimicrobial Agents* 2000; **14**: 57–63.
8. **Esel D, *et al.*** Prospective evaluation of blood cultures in a Turkish university hospital: epidemiology, microbiology and patient outcome. *Clinical Microbiology and Infection* 2003; **9**: 1038–1044.
9. **National Committee for Clinical Laboratory Standards.** *Performance Standards for Antimicrobial Disk Susceptibility Tests, Approved standard*, M2-A8, 8th edn. Wayne, PA: NCCLS, 2003.
10. **Guilarde AO, *et al.*** *Staphylococcus aureus* bacteraemia: incidence, risk factors and predictors for death in a Brazilian teaching hospital. *Journal of Hospital Infection* 2006; **63**: 330–336.
11. **Shitrit P, *et al.*** Active surveillance for methicillin-resistant *Staphylococcus aureus* (MRSA) decreases the incidence of MRSA bacteremia. *Infection Control and Hospital Epidemiolology* 2006; **27**: 1004–1008.
12. **Selvey LA, Whitby M, Johnson B.** Nosocomial methicillin-resistant *Staphylococcus aureus* bacteremia: is it any worse than nosocomial methicillin-sensitive *Staphylococcus aureus* bacteremia? *Infection Control and Hospital Epidemiology* 2000; **21**: 645–648.
13. **Coello R, *et al.*** Risk factors for developing clinical infection with methicillin-resistant *Staphylococcus aureus* (MRSA) amongst hospital patients initially only colonized with MRSA. *Journal of Hospital Infection* 1997; **37**: 39–46.
14. **Manzur A, *et al.*** Predictive factors of methicillin resistance among patients with *Staphylococcus aureus* bloodstream infections at hospital admission. *Journal of Hospital Infection* 2007; **66**: 135–141.
15. **Harris AD, *et al.*** Control-group selection importance in studies of antimicrobial resistance: examples applied to *Pseudomonas aeruginosa*, Enterococci, and *Escherichia coli*. *Clinical Infectious Diseases* 2002; **34**: 1558–1563.