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Abstract

Background: Mupirocin has been recommended for decolonization in methicillin-resistant *Staphylococcus aureus* (MRSA) carriers for recurrent skin and soft tissue infections and treatment for impetigo. However, the indiscriminate use of mupirocin causes mupirocin resistance, associated with decolonization failure. The aim of the study was to investigate the epidemiology of mupirocin resistance and to identify clinical characteristics among children in a single center. **Method:** From January 2011 to October 2020, we retrospectively analyzed the epidemiology of antibiotic resistance and clinical characteristics of pediatric patients under 19 years old in whom *S. aureus* was firstly isolated at any body site. **Result:** Of the 3,414 *S. aureus* isolates, 46% (1569/3414) were methicillin-resistant, and 20.3% (692/3414) were mupirocin resistant. Among MRSA, Mupirocin-resistant (MupR) was 22.6% (354/1569), and among methicillin-sensitive *S. aureus* (MSSA), MupR was 18.3% (338/1845) ($P<0.001$). The median age of MupR MRSA patients was 0.14 years (interquartile range 0.04-0.79), and the median age of MupR MSSA patients was 5.0 years (interquartile range 2.0-8.1) ($P=0.000$). Of 692 MupR *S. aureus*, 94.2% (652/692) were mainly detected in the skin. MupR MRSA was most frequently isolated in the neonatal intensive care unit (40.1%, 142/354), but MupR MSSA was most frequently isolated in the outpatient setting (81.4%, 275/338) ($P<0.001$). Of these, 43% (119/275) patients were diagnosed with atopic dermatitis. By age, mupR MRSA was the more commonly isolated in infants younger than one year (77.4%, 274/354), and MupR MSSA was more commonly isolated in children older than three years old (65.4%, 221/338) ($P<0.001$). The frequency of MupR MRSA and MSSA showed an increase in trend over time ($P<0.001$). Among other topical agents, 6.5% (102/1569) of MRSA was resistant to fusidic acid. **Conclusion:** As mupirocin resistance gradually increases, a test for mupirocin susceptibility should be performed before applying the skin lesions or decolonization for MRSA. In addition, clinicians should carefully prescribe mupirocin to prevent the development of MupR *S. aureus*.

Backgrounds

- Mupirocin has been recommended for decolonization in methicillin-resistant *Staphylococcus aureus* (MRSA) carriers for recurrent skin and soft tissue infections and treatment for impetigo.
- The indiscriminate use of mupirocin causes mupirocin resistance, associated with decolonization failure.
- The aim of the study was to investigate the epidemiology of mupirocin resistance and to identify clinical characteristics among children in a single center.

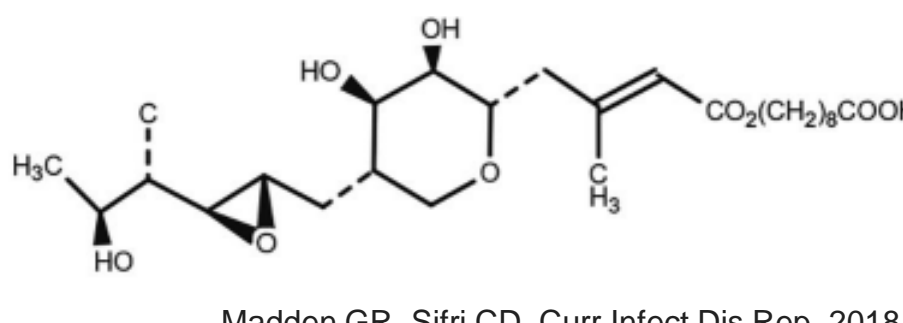


Figure 1. Chemical structure of mupirocin

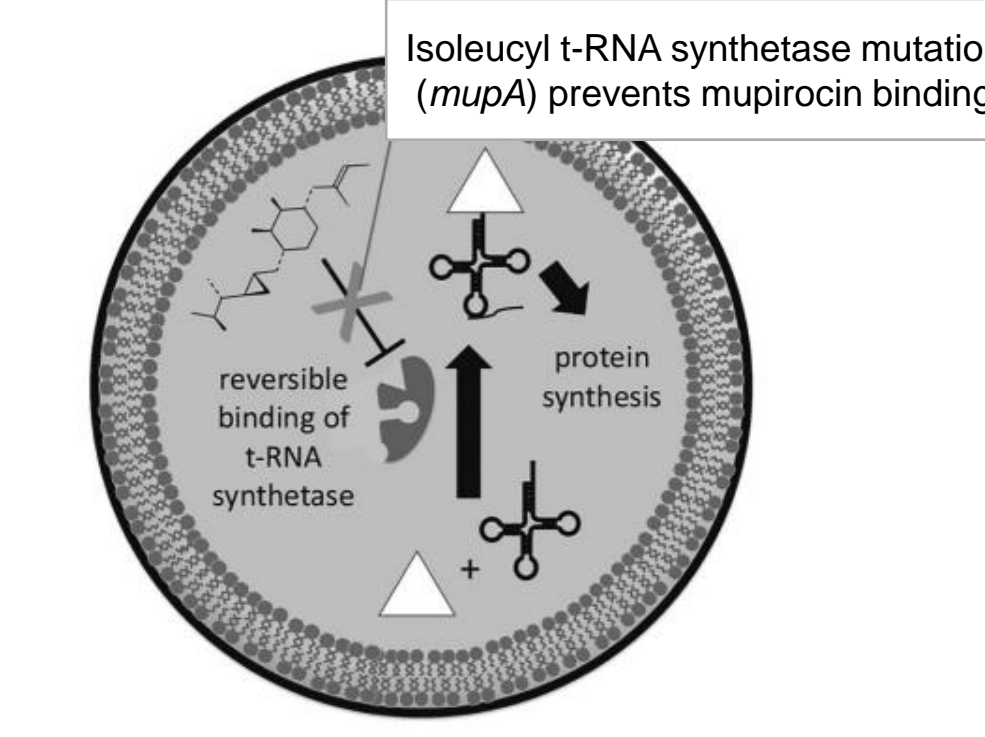


Figure 2. Mechanisms of bactericidal activity and resistance to mupirocin

Methods

- Study periods:** January 2011 ~ October 2020
- Study patients:** pediatric patients under 19 years old with *Staphylococcus aureus* in whom firstly isolated from any body site
- Study design:** Retrospectively electronic chart review for the epidemiology of mupirocin resistance and clinical characteristics for *S. aureus*
- Statistical analysis:** Chi-square test or Fisher's exact test for comparing between mupirocin resistance and sensitive group by using the using the SPSS software version 27 (IBM Corp., Armonk, NY, USA)

Abbreviation: t-RNA, transfer ribonucleic acid; *mupA*, mupirocin resistance gene; MupR, mupirocin resistant; MupS, mupirocin sensitive; MRSA, methicillin resistant *S. aureus*; MSSA, methicillin sensitive *S. aureus*; NICU, neonatal intensive care unit; PICU, pediatric intensive care unit; CA, cardiology unit; OPD, outpatient clinic

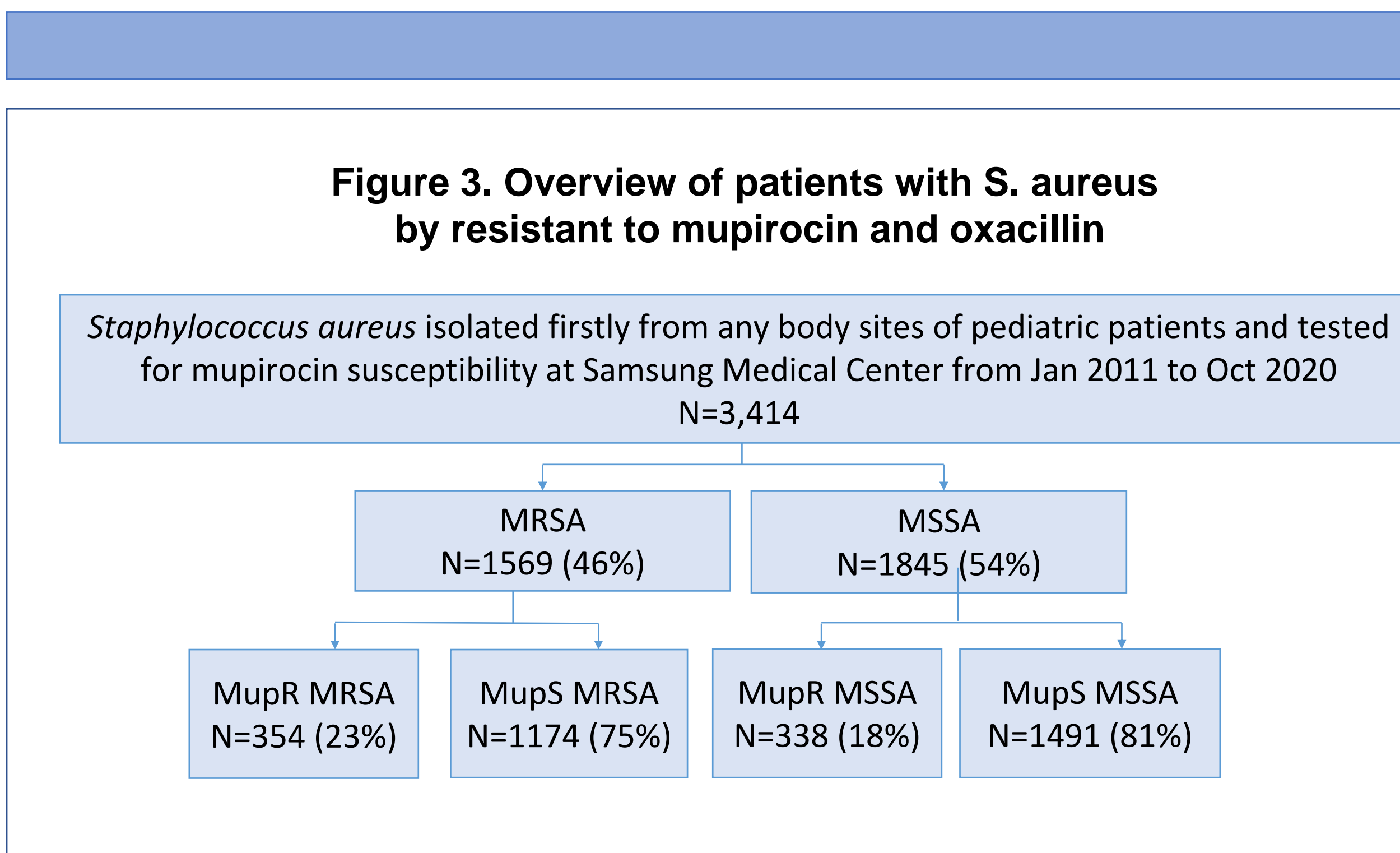


Table 1. Baseline demographics

	MupR <i>S. aureus</i> (N = 692)	MupS <i>S. aureus</i> (N = 2,665)	P-value
Sex, male (%)	405 (58.5%)	1509 (56.6%)	0.368
Median age (IQR)	1.1 (0.1-5.6)	0.5 (0.1-5.3)	0.004
MRSA	0.1 (0.03-0.8)	0.4 (0.07-3.4)	
MSSA	5.0 (2.0-8.1)	0.7 (0.1-7.5)	
Outpatients	378 (55%)	1026 (38%)	<0.001
Inpatients			
NICU	173 (25%)	844 (32%)	
CA	74 (11%)	253 (9.5%)	
PICU	27 (3.9%)	196 (7.4%)	
Others	40 (5.8%)	346 (13%)	
Body site			<0.001
Skin	657 (95%)	2226 (84%)	
Respiratory	11 (2%)	167 (6%)	
Blood	2 (0.2%)	103 (4%)	
Sterile site	3 (0.4%)	40 (1.5%)	
GI tract	2 (0.2%)	37 (1.4%)	

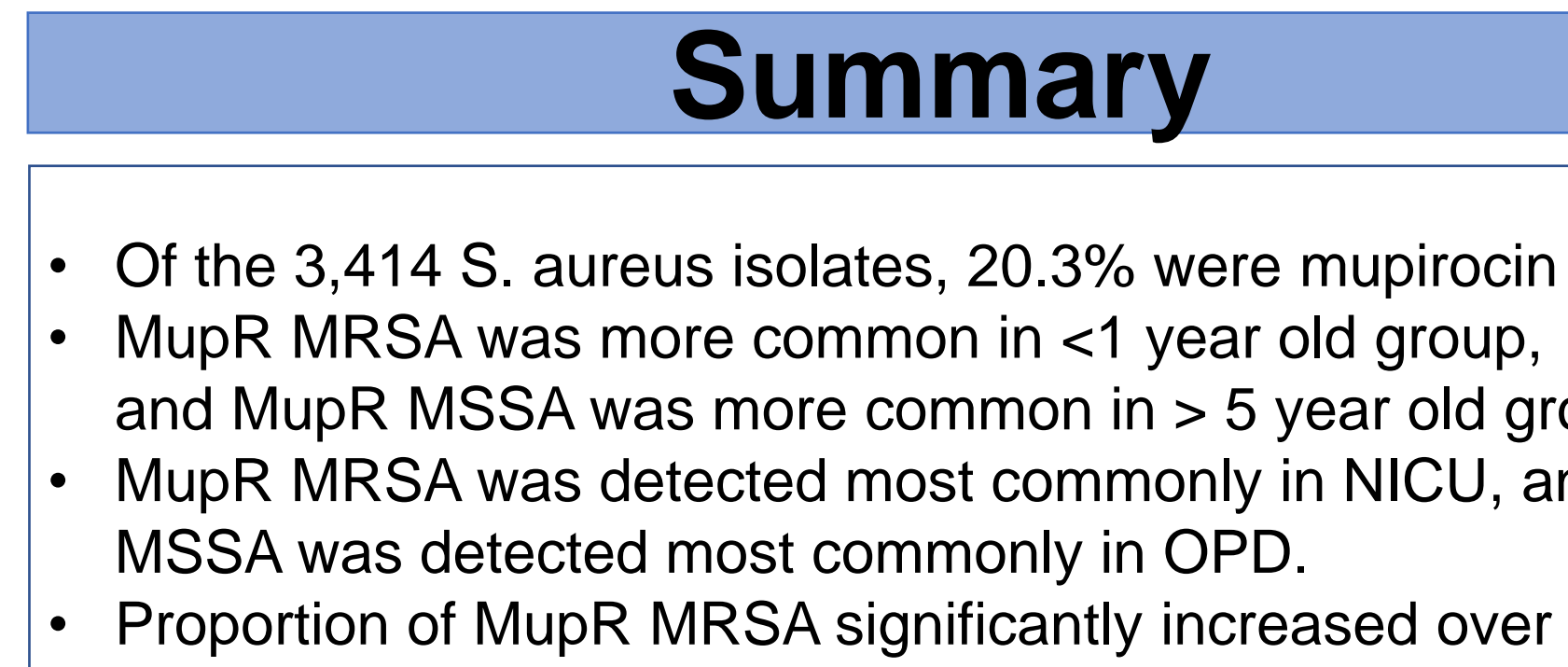
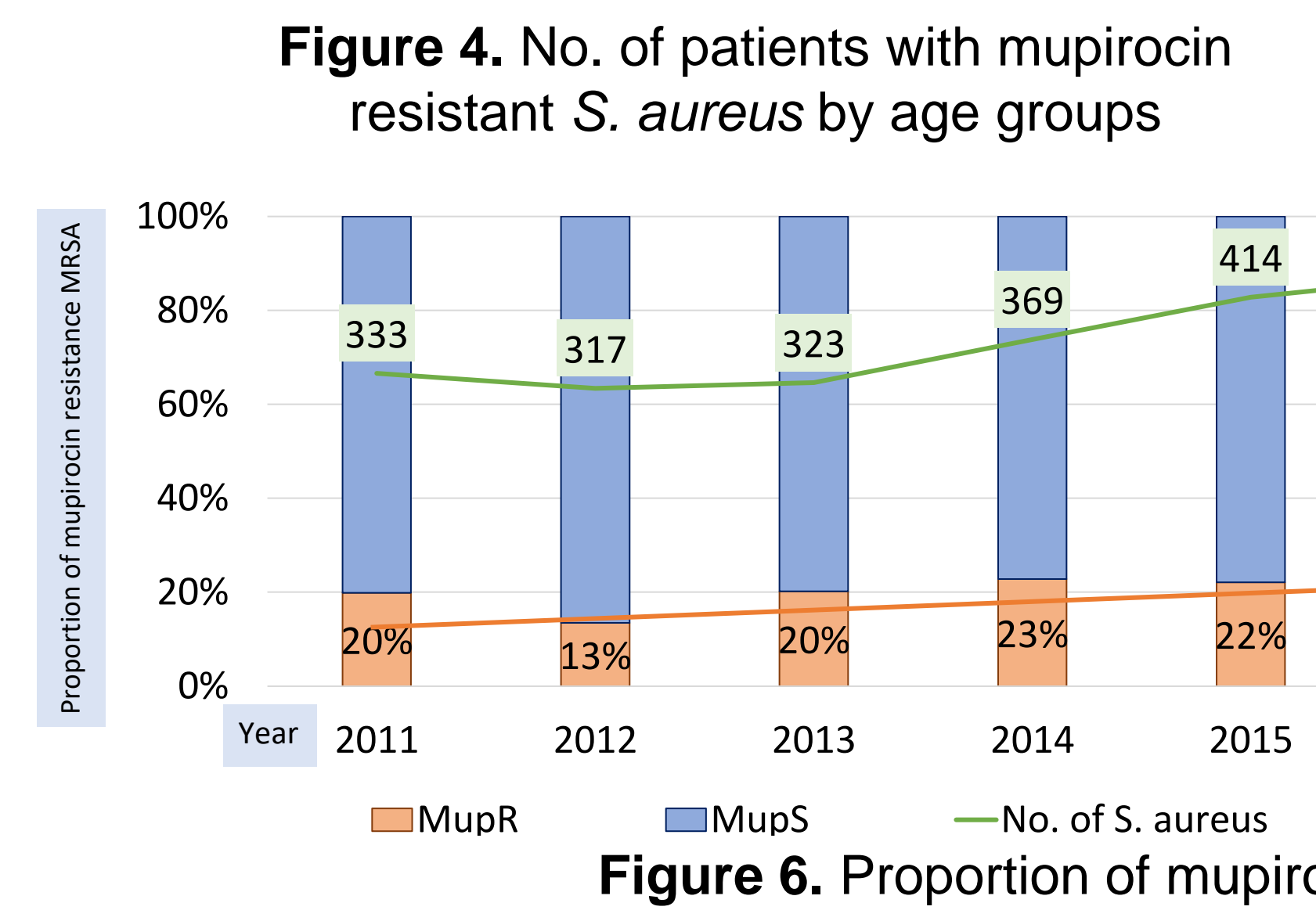
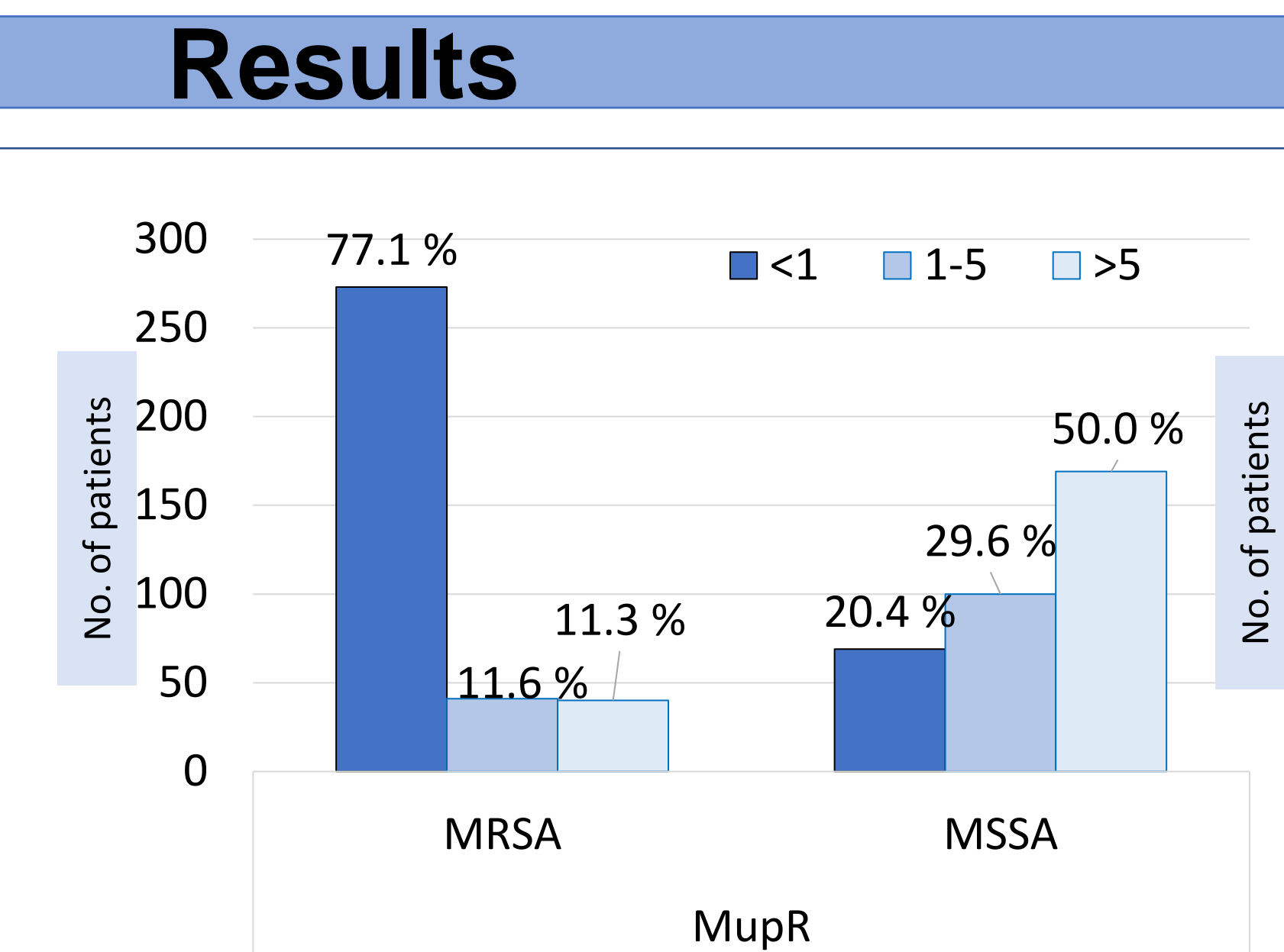


Figure 6. Proportion of mupirocin resistance MRSA by year

Results

Figure 3. Overview of patients with *S. aureus* by resistant to mupirocin and oxacillin

Figure 4. No. of patients with mupirocin resistant *S. aureus* by age groups

Figure 5. No. of patients with mupirocin resistant *S. aureus* by locations

Figure 6. Proportion of mupirocin resistance MRSA by year

Summary

- Of the 3,414 *S. aureus* isolates, 20.3% were mupirocin resistant.
- MupR MRSA was more common in <1 year old group, and MupR MSSA was more common in > 5 year old group.
- MupR MRSA was detected most commonly in NICU, and MupR MSSA was detected most commonly in OPD.
- Proportion of MupR MRSA significantly increased over time ($P<0.001$).

Conclusions

- As mupirocin resistance gradually increases, a test for mupirocin susceptibility should be performed before applying the skin lesions or decolonization for MRSA.
- Furthermore, clinicians should carefully prescribe mupirocin to prevent the development of MupR *S. aureus*.