Journal of Global Antimicrobial Resistance 20 (2020) 238–247

Contents lists available at ScienceDirect

Journal of Global Antimicrobial Resistance

journal homepage: www.elsevier.com/locate/jgar

Review

Mupirocin resistance in *Staphylococcus aureus*: A systematic review and meta-analysis

Masoud Dadashi[a,b], Bahareh Hajikhani[c], Davood Darban-Sarokhalil[d], Alex van Belkum[e], Mehdi Goudarzi[c,*]

[a] Department of Microbiology, School of Medicine, Alborz University of Medical Sciences, Karaj, Iran
[b] Non Communicable Diseases Research Center, Alborz University of Medical Sciences, Karaj, Iran
[c] Department of Microbiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[d] Department of Microbiology, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran
[e] Data Analytics Unit, bioMérieux 3, La Balme-les-Grottes, France

ARTICLE INFO

Article history:
Received 14 January 2019
Received in revised form 29 July 2019
Accepted 31 July 2019
Available online 20 August 2019

Keywords:
Mupirocin
High-level resistance
Staphylococcus aureus
MRSA

ABSTRACT

Objectives: Staphylococcus aureus is one of the most common pathogens causing nosocomial and community-acquired infections associated with high morbidity and mortality. Mupirocin has been increasingly used for treatment of methicillin-susceptible *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) infections. The aim of this study was to determine the prevalence of mupirocin-resistant *S. aureus* (MuRSA), mupirocin-resistant MRSA (MuRMRSA), high-level MuRSA (HLMuRSA) and high-level MuRMRSA (HLMuRMRSA) worldwide.

Methods: Online databases including Medline, Embase and Web of Science were searched (2000–2018) to identify studies addressing the prevalence of MuRSA, MuRMRSA, HLMuRSA and HLMuRMRSA. STATA v. software was used to interpret the data.

Results: Of the 2243 records identified from the databases, 30 and 63 studies fulfilled the eligibility criteria for MuRSA and MuRMRSA, respectively. Finally, 27 and 60 studies were included separately for HLMuRSA and HLMuRMRSA, respectively. The analyses revealed pooled and averaged prevalences of MuRSA, MuRMRSA, HLMuRSA and HLMuRMRSA of 7.6% [95% confidence interval (CI) 6.2–9.0%], 13.8% (95% CI 12.0–15.6%), 8.5% (95% CI 6.3–10.7%) and 8.1% (95% CI 6.8–9.4%), respectively.

Conclusion: Overall, these results show a global increase in the prevalence of HLMuRSA and HLMuRMRSA among clinical *S. aureus* isolates over time. However, there was only a significant increase in the prevalence of MuRMRSA compared with the other categories, especially MuRSA. Since mupirocin remains the most effective antibiotic for MSSA and MRSA decolonisation both in patients and healthcare personnel, a reduction of its effectiveness presents a risk for invasive infection. Monitoring of mupirocin resistance development remains critical.

Contents

* Corresponding author.
E-mail address: gudarzim@yahoo.com (M. Goudarzi).

http://dx.doi.org/10.1016/j.jgar.2019.07.032

1. Introduction

Despite the application of surveillance programmes in healthcare settings, *Staphylococcus aureus*, a leading cause of nosocomial infections, remains a major health problem worldwide, causing a variety of infections [1–3]. Serious infections such as pneumonia and bacteraemia and their sequelae result in prolonged hospitalisation and a significant economic burden, especially in the case of methicillin-resistant *S. aureus* (MRSA) [4–6]. Soon after the introduction of penicillin into infectious diseases therapy in the early 1940s, resistance to β-lactams started to develop in *S. aureus*. After the first MRSA was identified in 1960, it was shown to harbour the causal *mecA* gene encoding a modified penicillin-binding protein (PBP), designated PBP2a, that has a lower affinity for β-lactam antibiotics and confers methicillin resistance to staphylococci [7–9]. The only approved antibiotic for decolonisation of MRSA and methicillin-susceptible *S. aureus* (MSSA) both in patients and healthcare personnel is mupirocin (pseudomonic acid A) [1]. This antibiotic acts by binding to the enzyme leucine-specific tRNA aminoacyl synthetase, thus inhibiting protein synthesis. Shortly after widespread use of mupirocin for prolonged periods was allowed, especially for decolonisation of healthcare personnel and for bedsores and other skin lesions, resistance emerged [1]. Two types of resistance to mupirocin have been described, with high-level and low-level mupirocin resistance being associated with the plasmid-mediated *mupA* gene and chromosomal point mutations, respectively [1,10]. The high-level mupirocin resistance phenotype can be transferred by conjugation between different staphylococcal strains or species. The main mechanisms for development of high-level mupirocin resistance are not completely clear, and even the need for previous exposure to mupirocin to induce or select emerging resistance is controversial in some studies [1,4]. The emergence of mupirocin resistance in MRSA strains has been described previously [11–13]. MRSA colonisation of the nose and other body sites of patients, nurses and other healthcare personnel defines the possible reservoirs of MRSA and plays a crucial role in the induction and spread of staphylococcal infections [3,14,15]. Topical use of mupirocin does not eliminate MRSA strains with high-level mupirocin resistance and sometimes even low-level mupirocin resistance [11]. There are currently no comprehensive data available on the prevalence of mupirocin resistance in *S. aureus* isolates around the world. Therefore, the aim of this study was to perform a systematic review and meta-analysis of the scientific literature in order to report the prevalence of mupirocin resistance among *S. aureus* and MRSA isolates worldwide.

2. Methods

2.1. Literature search

A systematic search was performed for the prevalence of mupirocin-resistant *S. aureus* (MuRSA), mupirocin-resistant MRSA (MuRMRSA), high-level MuRSA (HLMuRSA) and high-level MuRMRSA (HLMuRMRSA) based on the following keywords: (*Staphylococcus aureus*, *Staphylococcus*, mupirocin, Bactroban and pseudomonic acid) using the three main electronic databases, including Medline (via PubMed), Embase and Web of Science, from 2000 to 2018. The search was restricted to original articles published in English that indicated the prevalence or incidence of MuRSA, MuRMRSA, HLMuRSA and HLMuRMRSA. The bibliographies of identified articles were also searched for additional articles mentioned among the literature references.

2.2. Inclusion and exclusion criteria

All original papers presenting cross-sectional studies on the prevalence of MuRSA, MuRMRSA, HLMuRSA and HLMuRMRSA were evaluated. The selected studies were analysed based on title, abstract and full-text. Studies were included in the analysis based on the following criteria: (i) original articles that provided sufficient data on MuRSA, MuRMRSA, HLMuRSA and HLMuRMRSA; and (ii) used standard methods, including (A) disk diffusion method (B) agar dilution, microdilution and macrodilution methods or Etest, and (C) molecular methods to detect MuRSA, MuRMRSA, HLMuRSA and HLMuRMRSA according to Clinical and Laboratory Standards institute (CLSI) 2018 guidelines (https://clsi.org/standards/). Phenotypically, mupirocin resistance was determined based on (i) no zone of inhibition with a 200 μg mupirocin disk or (ii) minimum inhibitory concentration (MIC) breakpoints with susceptible being ≤4 mg/L, low-level mupirocin-resistant being 8–256 mg/L and high-level mupirocin-resistant being ≥512 mg/L. Exclusion criteria were: (i) articles studying non-human samples; (ii) studies considering (A) mupirocin-resistant bacteria other than *S. aureus and* (B) other types of antibiotic resistance except mupirocin; (iii) reviews; (iv) abstracts reported in conferences; and (v) duplicate publications.

2.3. Data extraction and definitions

The author's last name, date of the investigation, year of publication, country/continent, number of *S. aureus*, MRSA, MuRSA, MuRMRSA, HLMuRSA and HLMuRMRSA, the detection method and source of isolates were extracted from the included studies. The prevalence of MuRSA, MuRMRSA, HLMuRSA and HLMuRMRSA isolates was also extracted. Two independent researchers recorded the data to avoid bias.

2.4. Quality assessment

All reviewed studies were subjected to a quality assessment (designed by the Joanna Briggs Institute) and only high-quality investigations were evaluated in the final analysis.

2.5. Meta-analysis

The analysis was performed using Stata Statistical Software: Release 14 (StataCorp LP, College Station, TX, USA). Data were pooled using a fixed-effects model [16] and a random-effects

model [17]. Statistical heterogeneity was assessed using the Cochran Q and I^2 statistical methods [18].

3. Results

3.1. Characteristics of included studies

After removing duplicates, 2243 articles were identified in the database search. Based on title and abstract evaluation in a secondary screening, 1043 and 850 of the chosen articles were excluded, respectively (see Fig. 1, which also includes the reasons for exclusion). In the next step, upon full-text review 30 and 63 articles were included (out of 350) for MuRSA and MuRMRSA, respectively [4,10,11,19–84]. Finally, articles containing sufficient data regarding HLMuRSA (27 studies) and HLMuRMRSA (60 studies) were included (Fig. 1). The characteristics of the included articles are shown in Tables 1 and 2.

3.2. Prevalence of MuRSA, MuRMRSA, HLMuRSA and HLMuRMRSA

The pooled and averaged prevalences of MuRSA, MuRMRSA, HLMuRSA and HLMuRMRSA were 7.6% [95% confidence interval (CI) 6.2–9.0%] among 10 903 *S. aureus* isolates, 13.8% (95% CI 12.0–15.6%) among 15 028 MRSA isolates, 8.5% (95% CI 6.3–10.7%) among 10 524 *S. aureus* isolates and 8.1% (95% CI 6.8–9.4%) among 14 834 MRSA isolates, respectively. Moreover, the pooled prevalence of HLMuRSA among 753 MuRSA isolates and of HLMuRMRSA among 1582 isolates MuRMRSA was 60.1% (95% CI 47.1–74.4%) and 44.4% (95% CI 31.8–57.0%), respectively (Tables 3 and 4).

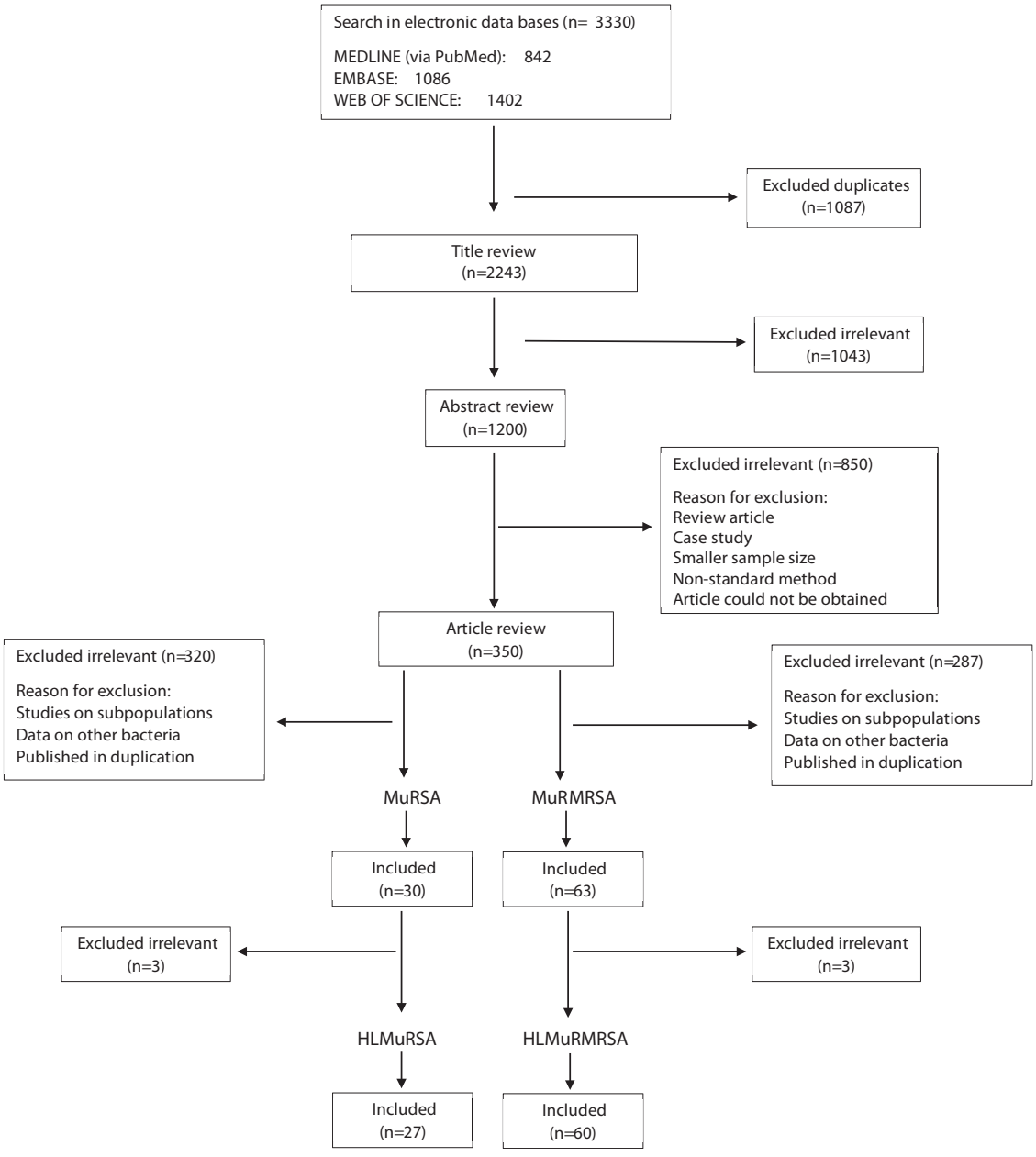

Fig. 1. Flow chart of study selection for inclusion in the systematic review. MuRSA, mupirocin-resistant *Staphylococcus aureus*; MuRMRSA, mupirocin-resistant methicillin-resistant *S. aureus*; HLMuRSA, high-level MuRSA; HLMuRMRSA, high-level MuRMRSA.

Table 1
Characteristics of included studies regarding mupirocin-resistant *Staphylococcus aureus* (MuRSA) and high-level MuRSA (HLMuRSA).

Continent/study	Study period	Study location	No. of *S. aureus*	No. of MuRSA	Detection method	Source of isolates	MuRSA frequency [*n*/*N* (%)]	No. of HLMuRSA	HLMuRSA frequency [*n*/*N* (%)] among:	
									S. aureus	MuRSA
Asia										
Kaur, 2014 [39]	2013–2014	India	38	2	DDM	Nasal swabs	2/38 (5.3)	1	1/38 (2.6)	1/2 (50.0)
Jayakumar, 2013 [35]	2011–2012	India	113	3	DDM, MIC	Wound swabs, tissues and pus	3/113 (2.7)	2	2/113 (1.8)	2/3 (66.7)
Rudresh, 2015 [69]	2014	India	98	25	DDM, MIC	SSTI	25/98 (25.5)	8	8/98 (8.2)	8/25 (32.0)
Oommen, 2010 [61]	2008	India	98	1	DDM	Pus, blood, catheters, tracheal aspirates, urine	1/98 (1.0)	1	1/98 (1.0)	1/1 (100)
Gadepalli, 2007 [31]	2004–2005	India	200	12	DDM, MIC	SSTI	12/200 (6.0)	10	10/200 (5.0)	10/12 (83.3)
Hesami, 2014 [34]	2012–2013	Iran	150	8	DDM, MIC, PCR	Blood, wounds, nares, urine, sputum, catheter	8/150 (5.3)	7	7/150 (4.7)	7/8 (87.5)
Ohadian Moghadam, 2015 [53]	2013	Iran	39	5	DDM, MIC, PCR	Nasal swabs	5/39 (12.8)	3	3/39 (7.7)	3/5 (60.0)
Abbasi-Montazeri, 2013 [4]	2007–2008	Iran	96	11	DDM, PCR	Nostrils	11/96 (11.5)	11	11/96 (11.5)	11/11 (100)
Nikfar, 2016 [58]	2015	Iran	53	2	DDM, PCR	Nasal swabs	2/53 (3.8)	NR	NR	NR
Yari, 2016 [81]	2015	Iran	150	7	DDM, PCR	Skin	7/150 (4.7)	0	0/150 (0.0)	0/7 (0.0)
Saderi, 2008 [70]	2006–2007	Iran	222	6	DDM, MIC	Blood, wound, sputum	6/222 (2.7)	1	1/222 (0.5)	1/6 (16.7)
Shahsavan, 2012 [10]	2010–2011	Iran	106	42	DDM, PCR	Burns patients	42/106 (39.6)	27	27/106 (25.5)	27/42 (64.3)
Arianpoor, 2015 [21]	2011–2012	Iran	238	22	DDM	Clinical samples	22/238 (9.2)	22	22/238 (9.2)	22/22 (100)
Yun, 2003 [82]	2000–2002	Korea	319	16	MIC	Clinical samples	16/319 (5.0)	16	16/319 (5.0)	16/16 (100)
Kwon, 2007 [42]	2006	Korea	108	9	MIC, PCR	Clinical samples	9/108 (8.3)	NR	NR	NR
Kwon, 2007 [42]	2003	Korea	218	5	MIC, PCR	Clinical samples	5/218 (2.3)	NR	NR	NR
Teo, 2011 [74]	2008–2009	Singapore	18	7	MIC, PCR	Clinical samples	7/18 (38.9)	7	7/18 (38.9)	7/7 (100)
Liu, 2009 [47]	2003–2007	China	984	1	MIC	Clinical samples	1/984 (0.1)	0	0/984 (0.0)	0/1 (0.0)
Liu, 2017 [46]	2010–2011	China	34	6	MIC	Clinical samples	6/34 (17.6)	5	5/34 (14.7)	5/6 (83.3)
Europe										
Stratchounski, 2005 [73]	2000	Russia	879	3	MIC	Wound, abscess, blood, peritoneal fluid	3/879 (0.3)	0	0/879 (0.0)	0/3 (0.0)
Kresken, 2004 [40]	2001	Germany	787	30	MIC	Clinical samples	30/787 (3.8)	7	7/787 (0.9)	7/30 (23.3)
Sareyyüpoğlu, 2008 [71]	2004–2005	Turkey	77	35	DDM, PCR	Blood, nostril, surgical wound, urine, catheter	35/77 (45.5)	35	35/77 (45.5)	35/35 (100)
Fawley, 2006 [28]	1999	UK	376	12	MIC	Nasal swabs	12/376 (3.2)	0	0/376 (0.0)	0/12 (0.0)
Americas										
Rotger, 2005 [67]	1999–2002	USA	50	4	MIC	Clinical samples	4/50 (8.0)	1	1/50 (2.0)	1/4 (25.0)
Antonov, 2015 [19]	2012–2013	USA	358	112	MIC	Skin (paediatrics)	112/358 (31.3)	96	96/358 (26.8)	96/112 (85.7)
Fritz, 2013 [29]	2007–2009	USA	2425	50	DDM, MIC, PCR	Wound	50/2425 (2.1)	50	50/2425 (2.1)	50/50 (100)
Gales, 2004 [32]	2000–2001	Latin America	1346	42	MIC	Blood, RTI, SSTI, UTI	42/1346 (3.1)	0	0/1346 (0.0)	0/42 (0.0)
Rubin, 2011 [68]	2006–2008	Canada	99	12	DDM, MIC	Clinical samples	12/99 (12.1)	12	12/99 (12.1)	12/12 (100)
Africa										
Shittu, 2006 [72]	2001–2003	South Africa	227	2	DDM, PCR	Clinical samples	2/227 (0.9)	2	2/227 (0.9)	2/2 (100)
Wasserman, 2014 [79]	2013	South Africa	997	277	DDM, PCR, VITEK®	Clinical samples	277/997 (27.8)	234	234/997 (23.5)	234/277 (84.5)

DDM, disk diffusion method; MIC, minimum inhibitory concentration; SSTI, skin and soft-tissue infection; NR, not reported; RTI, respiratory tract infection; UTI, urinary tract infection.

3.3. Prevalence of MuRSA, MuRMRSA, HLMuRSA and HLMuRMRSA in different study periods

To determine longitudinal changes in the prevalence of HLMuRSA and HLMuRMRSA in recent years, subgroups across three periods of publication (before 2006, 2006–2010 and 2011–2015) were designed (Tables 3 and 4). The incidence rate of HLMuRSA and HLMuRMRSA strains gradually decreased from 4.7% (95% CI 0.9–8.5%) of 5245 *S. aureus* isolates and 8.2% (95% CI 5.6–10.8%) of 5888 MRSA isolates before 2006 to 3.3% (95% CI 1.1–5.4%) of 2958 isolates and 5.9% (95% CI 4.3–7.5%) of 7010 isolates in 2006–2010, reaching 11.2% (95% CI 5.0–17.4%) of 2321 *S. aureus* isolates and 14.3% (95% CI 10.6–18.0%) of 1936 MRSA

Table 2
Characteristics of included studies regarding mupirocin-resistant methicillin-resistant *Staphylococcus aureus* (MuRMRSA) and high-level MuRMRSA (HLMuRMRSA).

Continent/study	Study period	Study location	No. of MRSA	No. of MuRMRSA	Detection method	Source of isolates	MuRMRSA frequency [*n*/*N* (%)]	No. of HLMuRMRSA	HLMuRMRSA frequency [*n*/*N* (%)] among:	
									MRSA	MuRMRSA
Asia										
Liu, 2009 [47]	2003–2007	China	11	1	MIC	Clinical samples	1/11 (9.1)	NR	NR	NR
Liu, 2010 [11]	2005–2007	China	803	53	DDM, MIC	Clinical samples	53/803 (6.6)	53	53/803 (6.6)	53/53 (100)
Liu, 2011 [48]	2008–2009	China	126	5	MIC	Clinical samples	5/126 (4.0)	5	5/126 (4.0)	5/5 (100)
Kaur, 2014 [39]	2013–2014	India	20	2	DDM	Nasal swabs	2/20 (10.0)	1	1/20 (5.0)	1/2 (50.0)
Kaur, 2015 [38]	2012–2014	India	36	19	DDM	Pus, blood, sputum, miscellaneous, urine	19/36 (52.8)	13	13/36 (36.1)	13/19 (68.4)
Jayakumar, 2013 [35]	2011–2012	India	46	1	DDM, MIC	Wound swabs, tissue, pus	1/46 (2.2)	1	1/46 (2.2)	1/1 (100)
Rudresh, 2015 [69]	2014	India	22	5	DDM, MIC	SSTI	5/22 (22.7)	1	1/22 (4.5)	1/5 (20.0)
Oommen, 2010 [61]	2008	India	48	1	DDM	Pus, blood, catheters, tracheal aspirates, urine	1/48 (2.1)	1	1/48 (2.1)	1/1 (100)
Krishnan, 2002 [41]	1994–1998	India	65	1	DDM, MIC, PCR	Clinical samples	1/65 (1.5)	1	1/65 (1.5)	1/1 (100)
Gadepalli, 2007 [31]	2004–2005	India	110	10	DDM, MIC	SSTI	10/110 (9.1)	9	9/110 (8.2)	9/10 (90.0)
Nicholson, 2010 [57]	2008	India	33	18	DDM	BSI, SSTI, UTI, RTI	18/33 (54.5)	8	8/33 (24.2)	8/18 (44.4)
Mahmoodzadeh Hosseini, 2017 [50]	2011–2014	Iran	188	2	DDM, PCR	Wounds, blood, pleural effusion, bile	2/188 (1.1)	2	2/188 (1.1)	2/2 (100)
Hesami, 2014 [34]	2012–2013	Iran	50	5	DDM, MIC, PCR	Blood, wounds, nares, urine, sputum, catheter	5/50 (10.0)	5	5/50 (10.0)	5/5 (100)
Abbasi-Montazeri, 2013 [4]	2007–2008	Iran	78	11	DDM, PCR	Nostrils	11/78 (14.1)	11	11/78 (14.1)	11/11 (100)
Shahsavan, 2012 [10]	2010–2011	Iran	62	42	DDM, PCR	Burns patients	42/62 (67.7)	27	27/62 (43.5)	27/42 (64.3)
Watanabe, 2001 [80]	1990–1999	Japan	404	55	MIC	Respiratory tract	55/404 (13.6)	0	0/404 (0.0)	0/55 (0.0)
Nakajima, 2011 [56]	2001–2009	Japan	178	6	MIC, PCR	Blood or CSF	6/178 (3.4)	1	1/178 (0.6)	1/6 (16.7)
Fujimura, 2003 [30]	1997–2001	Japan	261	2	MIC	Sputum, pharynx, pus, catheter	2/261 (0.8)	0	0/261 (0.0)	0/2 (0.0)
Fujimura, 2003 [30]	1998–2001	Japan	268	3	MIC	Sputum, pharynx, pus, catheter	3/268 (1.1)	0	0/268 (0.0)	0/3 (0.0)
Fujimura, 2003 [30]	1999–2001	Japan	307	2	MIC	Sputum, pharynx, pus, catheter	2/307 (0.7)	0	0/307 (0.0)	0/2 (0.0)
Fujimura, 2003 [30]	2000–2001	Japan	278	11	MIC	Sputum, pharynx, pus, catheter	11/278 (4.0)	0	0/278 (0.0)	0/11 (0.0)
Fujimura, 2003 [30]	2001	Japan	254	6	MIC	Sputum, pharynx, pus, catheter	6/254 (2.4)	0	0/254 (0.0)	0/6 (0.0)
Lee, 2013 [44]	2006–2009	Korea	456	62	MIC, PCR	Clinical samples	62/456 (13.6)	9	9/456 (2.0)	9/62 (14.5)
Yun, 2003 [82]	2000–2002	Korea	237	15	MIC	Clinical samples	15/237 (6.3)	15	15/237 (6.3)	15/15 (100)
Park, 2013 [62]	2011–2012	Korea	101	74	VITEK®2, MIC	Clinical samples	74/101 (73.3)	74	74/101 (73.3)	74/74 (100)
Park, 2012 [83]	2008–2009	Korea	193	27	MIC	Clinical samples	27/193 (14.0)	11	11/193 (5.7)	11/27 (40.7)
Udo, 2001 [75]	1999	Kuwait	267	75	DDM, MIC	Clinical samples	75/267 (28.1)	75	75/267 (28.1)	75/75 (100)
Udo, 2001 [75]	1999	Kuwait	72	55	MIC	Clinical samples	55/72 (76.4)	19	19/72 (26.4)	19/55 (34.5)
Apisarnthanarak, 2011 [20]	2010	Thailand	9	2	MIC	Nasal	2/9 (22.2)	0	0/9 (0.0)	0/2 (0.0)
Norazah, 2001 [60]	1997–1999	Malaysia	400	5	MIC	Bloodstream, RTI, UTI, abdominal cavity, tissue infection, CSF, skin lesions, catheters	5/400 (1.3)	4	4/400 (1.0)	4/5 (80.0)
Lim, 2010 [45]	2003–2007	Malaysia	188	10	DDM, MIC	Clinical samples	10/188 (5.3)	0	0/188 (0.0)	0/10 (0.0)
Joshi, 2017 [37]	2014–2015	Nepal	29	15	MIC, PCR	Nasal swabs	15/29 (51.7)	15	15/29 (51.7)	15/15 (100)
Nizamuddin, 2011 [59]	2008–2009	Pakistan	200	2	DDM	Abscess, tracheal aspirates, blood, urine	2/200 (1.0)	0	0/200 (0.0)	0/2 (0.0)
Teo, 2011 [74]	2008–2009	Singapore	11	6	MIC, PCR	Clinical samples	6/11 (54.5)	6	6/11 (54.5)	6/6 (100)
Choudhury, 2012 [25]	2009–2010	Singapore	307	24	DDM	Nasal	24/307 (7.8)	24	24/307 (7.8)	24/24 (100)
Europe										
Us, 2009 [76]	2002–2004	Turkey	595	35	DDM, MIC	Nosocomial infections	35/595 (5.9)	23	23/595 (3.9)	23/35 (65.7)
Sareyyüpoğlu, 2008 [71]	2004–2005	Turkey	57	27	PCR, MIC	Blood, nostril, surgical wound, urine, catheter	27/57 (47.4)	27	27/57 (47.4)	27/27 (100)
Potel, 2007 [66]	1997–2005	Spain	210	9	DDM, MIC, PCR	Clinical samples	9/210 (4.3)	3	3/210 (1.4)	3/9 (33.3)
Lozano, 2013 [49]	2009	Spain	204	11	DDM, PCR	Clinical samples	11/204 (5.4)	11	11/204 (5.4)	11/11 (100)

Muñoz-Gallego, 2016 [55]	2012–2014	Spain	134	50	DDM, MIC, PCR	Nasal swab, blood	50/134 (37.3)	37	37/134 (27.6)	37/50 (74.0)
González-Domínguez, 2015 [84]	2009–2010	Spain	118	30	DDM, MIC	Clinical samples	30/118 (25.4)	NR	NR	NR
González-Domínguez, 2016 [33]	2009–2010	Spain	147	40	DDM, MIC	Clinical samples	40/147 (27.2)	40	40/147 (27.2)	40/40 (100)
Fang, 2016 [27]	2014	Sweden	743	5	MIC	Clinical samples	5/743 (0.7)	3	3/743 (0.4)	3/5 (60.0)
Fawley, 2006 [28]	1999	UK	156	8	MIC	Clinical samples	8/156 (5.1)	0	0/156 (0.0)	0/8 (0.0)
Mongkolrattanothai, 2008 [54]	2007–2008	UK	156	37	DDM, MIC	Nasal swabs	37/156 (23.7)	8	8/156 (5.1)	8/37 (21.6)
Desroches, 2013 [26]	2011–2012	France	367	8	MIC	Clinical samples	8/367 (2.2)	3	3/367 (0.8)	3/8 (37.5)
Kresken, 2004 [40]	2001	Germany	163	27	MIC	Clinical samples	27/163 (16.6)	5	5/163 (3.1)	5/27(18.5)
Americas										
Champion, 2014 [24]	2008–2010	USA	277	3	VITEK® 2, MIC	Clinical samples from ICU patients	3/277 (1.1)	0	0/277 (0.0)	0/3 (0.0)
Babu, 2009 [22]	2007–2008	USA	591	20	MIC	Nasal swabs	20/591 (3.4)	3	3/591 (0.5)	3/20 (15.0)
Perkins, 2008 [65]	2006–2007	USA	409	247	MIC	Sputum, pharyngeal cultures	247/409 (60.4)	5	5/409 (1.2)	5/247 (2.0)
Warren, 2016 [78]	2005–2012	USA	504	35	DDM, PCR	Skin, wounds, trachea, sputum, nasopharyngeal, lower respiratory tract, blood, urine, synovial fluid, catheter, body fluids	35/504 (6.9)	35	35/504 (6.9)	35/35 (100)
Jones, 2007 [36]	2002–2004	USA	302	40	MIC, PCR	Anterior nares	40/302 (13.2)	26	26/302 (8.6)	26/40 (65.0)
McDanel, 2013 [51]	2008–2011	USA	829	101	MIC, PCR	Nasal swab	101/829 (12.2)	78	78/829 (9.4)	78/101 (77.2)
LaPlante, 2007 [43]	2004–2005	USA, America	98	9	MIC	Nasal samples	9/98 (9.2)	5	5/98 (5.1)	5/9 (55.6)
McDougal, 2010 [52]	2005–2008	USA	823	22	PCR	Blood, nares, tissue, sputum, urine	22/823 (2.7)	22	22/823 (2.7)	22/22 (100)
Rotger, 2005 [67]	1999–2002	USA	15	4	MIC	Clinical samples	4/15 (26.7)	1	1/15 (6.7)	1/4 (25.0)
Antonov, 2015 [19]	2012–2013	USA	65	36	MIC	Clinical samples	36/65 (55.4)	NR	NR	NR
Fritz, 2013 [29]	2007–2009	USA	755	14	DDM, MIC, PCR	Skin (paediatrics)	14/755 (1.9)	14	14/755 (1.9)	14/14 (100)
Pérez-Roth, 2006 [64]	1998–2002	USA	375	48	DDM, MIC, PCR	Wounds	48/375 (12.8)	48	48/375 (12.8)	48/48 (100)
Rubin, 2011 [68]	2006–2008	Canada	51	10	DDM, MIC	Clinical samples	10/51 (19.6)	10	10/51 (19.6)	10/10 (100)
Vasquez, 2000 [77]	1990–1995	Tennessee, USA	632	126	MIC	Nares, sputum, wound, blood, urine, percutaneous gastric catheter	126/632 (19.9)	53	53/632 (8.4)	53/126 (42.1)
Pereira, 2014 [63]	NR	Brazil	11	0	DDM, MIC		0/11 (0.0)	0	0/11 (0.0)	0/0 (0.0)
Africa										
Barakat, 2016 [23]	2013–2015	Egypt	73	13	MIC, PCR	Pus, wound swabs	13/73 (17.8)	8	8/73 (11.0)	8/13 (61.5)
Shittu, 2006 [72]	2001–2003	South Africa	61	1	DDM, PCR	Clinical samples	1/61 (1.6)	1	1/61 (1.6)	1/1 (100)

MIC, minimum inhibitory concentration; NR, not reported; DDM, disk diffusion method; SSTI, skin and soft-tissue infection; BSI, bloodstream infection; UTI, urinary tract infection; RTI, respiratory tract infection; CSF, cerebrospinal fluid; ICU, intensive care unit.

Table 3
Pooled and averaged prevalences of mupirocin-resistant *Staphylococcus aureus* (MuRSA) and high-level MuRSA (HLMuRSA) based on study periods and continents.

	Category	Subcategory	No. of studies	No. of strains	Prevalence (%) (95% CI)
MuRSA	Overall	MuRSA/*S. aureus*	30	769/10 903	7.6 (6.2–9.0)
	Study period	Before 2006	11	162/5463	3.0 (1.8–4.2)
		2006–2010	7	96/3066	5.2 (2.5–7.8)
		2011–2015	12	511/2374	15.2 (8.1–22.3)
	Continent	Asia	19	190/3282	7.3 (5.0–9.6)
		Europe	4	80/2119	6.6 (2.4–10.8)
		Americas	5	220/4278	10.5 (6.0–15.0)
		Africa	2	279/1224	*
HLMuRSA	Overall	HLMuRSA/*S. aureus*	27	558/10 524	8.5 (6.3–10.7)
	Study period	Before 2006	9	71/5245	4.7 (0.9–8.5)
		2006–2010	6	82/2958	3.3 (1.1–5.4)
		2011–2015	12	405/2321	11.2 (5.0–17.4)
	Continent	Asia	16	121/2903	6.4 (3.9–8.9)
		Europe	4	42/2119	1.0 (0.4–1.7)
		Americas	5	159/4278	10.6 (0.0–21.2)
		Africa	2	236/1224	*
	Overall	HLMuRSA/MuRSA	27	558/753	60.1 (47.1–74.4)
	Study period	Before 2006	10	71/157	42.3 (30.5–54.1)
		2006–2010	6	82/87	16.7 (13.2–46.5)
		2011–2015	11	405/509	72.0 (60.6–83.3)
	Continent	Asia	16	121/174	61.2 (43.6–78.7)
		Europe	4	42/80	23.3 (8.2–38.5)
		Americas	5	159/220	59.1 (37.9–77.6)
		Africa	2	236/279	*

CI, confidence interval.
* Cannot be analysed using meta-analysis methods.

Table 4
Pooled and averaged prevalences of mupirocin-resistant methicillin-resistant *Staphylococcus aureus* (MuRMRSA) and high-level MuRMRSA (HLMuRMRSA) based on study periods and continents.

	Category	Subcategory	No. of studies	No. of strains	Prevalence (%) (95% CI)
MuRMRSA	Overall	MuRMRSA/MRSA	63	1649/15 028	13.8 (12.0–15.6)
	Study period	Before 2006	25	590/5899	10.5 (8.0–13.0)
		2006–2010	23	781/7128	13.4 (10.1–16.6)
		2011–2015	15	278/2001	23.8 (18.5–29.0)
	Continent	Asia	35	633/6118	13.4 (10.9–15.9)
		Europe	12	287/3050	14.1 (10.3–18.0)
		Americas	14	715/5726	15.1 (10.6–19.6)
		Africa	2	14/134	*
HLMuRMRSA	Overall	HLMuRMRSA/MRSA	60	860/14 834	8.1 (6.8–9.4)
	Study period	Before 2006	24	315/5888	8.2 (5.6–10.8)
		2006–2010	22	354/7010	5.9 (4.3–7.5)
		2011–2015	14	191/1936	14.3 (10.6–18.0)
	Continent	Asia	34	391/6107	12.1 (9.2–14.9)
		Europe	11	160/2932	8.0 (5.4–10.6)
		Americas	13	300/5661	5.9 (3.8–7.9)
		Africa	2	9/134	*
	Overall	HLMuRMRSA/MuRMRSA	60	860/1582	44.4 (31.8–57.0)
	Study period	Before 2006	24	315/589	48.4 (34.7–62.1)
		2006–2010	22	354/751	30.6 (5.2–55.9)
		2011–2015	14	191/242	60.8 (49.7–71.9)
	Continent	Asia	34	391/632	47.4 (30.3–64.6)
		Europe	11	160/257	44.1 (22.9–65.4)
		Americas	13	300/679	35.6 (12.3–58.9)
		Africa	2	9/14	*

CI, confidence interval.
* Cannot be analysed using meta-analysis methods.

isolates in 2011–2015, respectively (Tables 3 and 4). The changes in MuRSA and MuRMRSA prevalence as well as the changes in HLMuRSA and HLMuRMRSA prevalence in all three periods are shown in Tables 3 and 4.

3.4. Prevalence of MuRSA, MuRMRSA, HLMuRSA and HLMuRMRSA in different regions of the world

Tables 3 and 4 also show the prevalences of MuRSA, MuRMRSA, HLMuRSA and HLMuRMRSA based on geographic area in the subgroup analysis of the included studies. The frequency of HLMuRMRSA in Asia was 1.5- and 2.1-fold higher than the frequency in Europe and the Americas, respectively. Tables 5 and 6 show the prevalence of MuRSA, MuRMRSA, HLMuRSA and HLMuRMRSA in different countries.

4. Discussion

The rate of mupirocin resistance among clinical *S. aureus* isolates varies according to geographic region and/or patient population. According to this systematic review, resistance to mupirocin accounted for 7.6% (95% CI 6.2–9.0%) of clinical *S. aureus*

Table 5
Pooled and averaged prevalences of mupirocin-resistant *Staphylococcus aureus* (MuRSA) and high-level MuRSA (HLMuRSA) based on countries.

	Category	Subcategory	No. of studies	No. of strains	Prevalence (%) (95% CI)
MuRSA	Overall	MuRSA/*S. aureus*	30	769/10 903	7.6 (6.2–9.0)
	Country	India	5	43/547	6.6 (1.8–11.5)
		Iran	8	103/1054	9.9 (5.1–14.6)
		Korea	3	30/645	4.5 (1.6–7.4)
		USA	3	166/2833	13.8 (0.1–33.7)
HLMuRSA	Overall	HLMuRSA/*S. aureus*	27	558/10 524	8.5 (6.3–10.7)
	Country	India	5	22/547	3.1 (0.9–5.3)
		Iran	7	71/1054	9.1 (3.4–14.8)
		USA	3	147/2833	10.1 (0.2–23.1)
	Overall	HLMuRSA/MuRSA	27	558/753	60.1 (47.1–74.4)
	Country	India	5	22/43	58.0 (24.3–91.7)
		Iran	7	71/103	58.4 (31.5–85.4)
		USA	3	147/166	59.1 (32.6–87.3)

CI, confidence interval.

Table 6
Pooled and averaged prevalences of mupirocin-resistant Methicillin-resistant *Staphylococcus* (MuRMRSA) and high-level MuRMRSA (HLMuRMRSA) based on countries.

	Category	Subcategory	No. of studies	No. of strains	Prevalence (%) (95% CI)
MuRMRSA	Overall	MuRMRSA/MRSA	63	1649/15 028	13.8 (12.0–15.6)
	Country	China	3	56/940	6.1 (4.6–7.6)
		India	8	57/380	15.2 (7.6–22.8)
		Iran	4	60/378	22.6 (0.9–44.3)
		Japan	7	85/1950	3.2 (1.3–5.1)
		Korea	4	178/987	26.2 (8.9–43.5)
		Spain	5	140/813	17.4 (6.1–28.6)
		USA	12	579/5043	15.1 (10.2–20)
HLMuRMRSA	Overall	HLMuRMRSA/MRSA	60	860/14 834	8.1 (6.8–9.4)
	Country	India	8	35/380	6.8 (2.4–11.3)
		Iran	4	45/378	16.2 (1.8–30.7)
		Japan	7	1/1950	0.6 (0.0–1.7)
		Korea	4	100/987	20.7 (6.9–34.6)
		Spain	4	94/813	14.7 (4.6–24.8)
		USA	12	237/5043	5.1 (3.1–7.2)
	Overall	HLMuRMRSA/MuRMRSA	60	860/1582	44.4 (31.8–57.0)
	Country	India	8	35/57	57.6 (32.8–82.6)
		Iran	4	45/60	64.3 (49.8–78.8)
		Japan	7	1/85	16.7 (0.1–46.5)
		Korea	4	100/178	26.3 (0.7–51.9)
		Spain	5	94/140	56.2 (16.7–95.8)
		USA	12	237/579	59.1 (35.7–90.7)

CI, confidence interval.

isolates, highlighting the relatively low prevalence of MuRSA strains. Worryingly, the prevalence of MuRSA strains in certain regions and institutes will be higher than the prevalence of 7.6% found here. The Americas (10.5%) showed the highest pooled prevalence of MuRSA strains, whilst in Europe and Asia this figure was found to be 6.6% and 7.3%, respectively. An increasing trend in the overall prevalence of MuRSA strains in the period 2011–2015 was also observed. One potential explanation for this is a significant increasing trend among overall *S. aureus* infections and a shift in antibiotic pressures. Although mupirocin as a cornerstone of decolonisation regimens is widely used for eradication of *S. aureus* nasal colonisation and the control of MRSA transmission in healthcare settings, the emergence of mupirocin resistance among *S. aureus* isolates will result in a decrease in the efficacy of this antibiotic [39,84,85]. Physicians should be continuously educated about the problem of unrestricted and widespread use of mupirocin in patients with *S. aureus* infections and also in individuals not carrying *S. aureus* as it may lead to cross-transferable resistance in coagulase-negative staphylococci. The current systematic review showed that the prevalence of resistance to mupirocin among MRSA strains was 13.8% (95% CI 12.0–15.6%) compared with 7.6% for MSSA. Although mupirocin effectively reduces MRSA carriage [78], colonisation and cross-transmission of MRSA in community and healthcare settings as well as the high relative prevalence of MuRMRSA strains again highlights the need for physician's awareness. Moreover, control measures as a powerful framework and strategy for reducing the prevalence of MuRMRSA strains should also be taken into consideration. The current analyses showed that the prevalence of high-level mupirocin resistance among *S. aureus* (8.5%, 95% CI 6.3–10.7%) was almost the same as for MRSA (8.1%, 95% CI 6.8–9.4%). This finding highlights that both *S. aureus* and MRSA isolates must be evaluated routinely in terms of resistance to mupirocin. According to this analysis, the rate of HLMuRMRSA in Asia (12.1%) was found to be higher than the reported rate in Europe (8.0%) and the Americas (5.9%). Therefore, it is reasonable to assume that overuse or inappropriate, less controlled use of mupirocin would similarly be higher in Asian countries, which may be linked to easy access to antibiotics without prescription, inexpensive drugs, a high rate of antibiotic misuse and the frequency of empirical treatment in these regions. Furthermore, because of differences in the number of studies and studied isolates, the rates of resistance in different countries are not reliable. Overall, the prevalence of resistance to mupirocin among *S. aureus* and MRSA isolates in the years 2011–2015 was higher than other study periods. Furthermore, it is notable that today both laboratory personnel and

clinicians need to be educated to develop diagnostic tests and in test interpretation. Regarding routine diagnosis of mupirocin resistance, it seems not to be performed everywhere [36]. The present study has limitations that should be considered when interpreting the findings. First, analysis of two African studies was not possible using meta-analysis because meta-analysis software such as STATA and comprehensive meta-analysis cannot analyse data from less than three studies. Second, only published scientific studies were considered for the present meta-analysis and potential publication bias had to be considered. Third, we could not fully represent the prevalence of MuRSA and MuRMRSA since there were insufficient data regarding this topic.

5. Conclusion

In summary, this systematic review demonstrated the highly significant prevalence of mupirocin resistance among clinical *S. aureus* and MRSA isolates. The findings support the notion that routine diagnostic testing, identification of carriers, national and organisational guidelines for infection control, surveillance and antibiotic stewardship measures, education and mupirocin prophylaxis are extremely important in the successful reduction of resistance to mupirocin, especially in MRSA isolates.

Funding

None.

Competing interests

None declared.

Ethical approval

Not required.

References

[1] Caffrey AR, Quilliam BJ, LaPlante K. Risk factors associated with mupirocin resistance in meticillin-resistant *Staphylococcus aureus*. J Hosp Infect 2010;76:206–10.
[2] Chen Y, Liu Z, Duo L, Xiong J, Gong Y, Yang J, et al. *Staphylococcus aureus* Characterization of from distinct geographic locations in China: an increasing prevalence of spa-t030 and SCC*mec* type III. PLoS One 2014;9:e96255.
[3] Dadashi M, Nasiri MJ, Fallah F, Owlia P, Hajikhani B, Emaneini M, et al. Methicillin-resistant *Staphylococcus aureus* (MRSA) in Iran: a systematic review and meta-analysis. J Glob Antimicrob Resist 2018;12:96–103.
[4] Abbasi-Montazeri E, Khosravi AD, Feizabadi MM, Goodarzi H, Khoramrooz SS, Mirzaii M, et al. The prevalence of methicillin resistant *Staphylococcus aureus* (MRSA) isolates with high-level mupirocin resistance from patients and personnel in a burn center. Burns 2013;39:650–4.
[5] Goudarzi M, Fazeli M, Goudarzi H, Azad M, Seyedjavadi SS. *Staphylococcus aureus*spa typing of strains isolated from clinical specimens of patients with nosocomial infections in Tehran, Iran. Jundishapur J Microbiol 2016;9:e35685.
[6] Armin S, Fareghi F, Fallah F, Dadashi M, Nikmanesh B, Ghalavand Z. *hlg*Prevalence of and *pvl* genes in methicillin resistant *Staphylococcus aureus* (MRSA) isolated from health care staff in Mofid Children Hospital, Tehran, Iran. J Pure Appl Microbiol 2015;9:1001–5.
[7] Hanssen AM, Ericson Sollid JU. SCC*mec* in staphylococci: genes on the move. Pathog Dis 2006;46:8–20.
[8] Lim KT, Yeo CC, Suhaili Z, Thong KL. *Staphylococcus aureus*Comparison of methicillin-resistant and methicillin-sensitive strains isolated from a tertiary hospital in Terengganu, Malaysia. Jpn J Infect Dis 2012;65:502–9.
[9] Neela V, Moghaddam HG, van Belkum A, Horst-Kreft D, Mariana NS, Rad EG. *Staphylococcus aureus*First report on methicillin-resistant of spa type t037, sequence type 239, SCC*mec* type III/IIIA in Malaysia. Eur J Clin Microbiol Infect Dis 2010;29:115–7.
[10] Shahsavan S, Emaneini M, Khoshgnab BN, Khoramian B, Asadollahi P, Aligholi M, et al. A high prevalence of mupirocin and macrolide resistance determinant among *Staphylococcus aureus* strains isolated from burnt patients. Burns 2012;38:378–82.
[11] Liu Q-Z, Wu Q, Zhang Y-B, Liu M-N, Hu F-P, Xu X-G, et al. Prevalence of clinical meticillin-resistant *Staphylococcus aureus* (MRSA) with high-level mupirocin resistance in Shanghai and Wenzhou, China. Int J Antimicrob Agents 2010;35:114–8.
[12] Orrett FA. The emergence of mupirocin resistance among clinical isolates of methicillin-resistant *Staphylococcus aureus* in Trinidad: a first report. Jpn J Infect Dis 2008;61:107–10.
[13] Seah C, Alexander DC, Louie L, Simor A, Low DE, Longtin J, et al. MupB, a new high-level mupirocin resistance mechanism in *Staphylococcus aureus*. Antimicrob Agents Chemother 2012;56:1916–20.
[14] Asadolahi P, Farahani N, Mirzaii M, Khorramroozi S, Van Belkum A, Asadollahi K, et al. Distribution of the most prevalent spa types among clinical isolates of methicillin-resistant and -susceptible *Staphylococcus aureus* around the world: a review. Front Microbiol 2018;9:163.
[15] Ben-David D, Mermel LA, Parenteau S. *Staphylococcus aureus*Methicillin-resistant transmission: the possible importance of unrecognized health care worker carriage. Am J Infect Control 2008;36:93–7.
[16] Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. J Natl Cancer Inst 1959;22:719–48.
[17] DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177–88.
[18] Higgins J, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002;21:1539–58.
[19] Antonov NK, Garzon MC, Morel KD, Whittier S, Planet PJ, Lauren CT. High prevalence of mupirocin resistance in *Staphylococcus aureus* isolates from a pediatric population. Antimicrob Agents Chemother 2015;59:3350–6.
[20] Apisarnthanarak A, Warren DK, Fraser VJ. Prevalence of nasal carriage of mupirocin-resistant *Staphylococcus aureus* among hospitalized patients in Thailand. Infect Control Hosp Epidemiol 2011;32:522–3.
[21] Arianpoor A, Estaji F, Naderinasab M, Askari E. Antimicrobial susceptibility pattern of *Staphylococcus aureus* isolates against newly marketed antibiotics: a report from Imam Reza Hospital of Mashhad, Iran. Razavi Int J Med 2015;3:.
[22] Babu T, Rekasius V, Parada JP, Schreckenberger P, Challapalli M. Mupirocin resistance among methicillin-resistant *Staphylococcus aureus*-colonized patients at admission to a tertiary care medical center. J Clin Microbiol 2009;47:2279–80.
[23] Barakat GI, Nabil YM. *Staphylococcus aureus*Correlation of mupirocin resistance with biofilm production in methicillin-resistant from surgical site infections in a tertiary centre, Egypt. J Glob Antimicrob Resist 2016;4:16–20.
[24] Champion E, Miller M, Popowitch E, Hobbs M, Saiman L, Muhlebach M, et al. Antimicrobial susceptibility and molecular typing of MRSA in cystic fibrosis. Pediatr Pulmonol 2014;49:230–7.
[25] Choudhury S, Krishnan P, Ang B. *Staphylococcus aureus*Prevalence of high-level mupirocin resistance among meticillin-resistant isolates in a tertiary care hospital in Singapore. J Hosp Infect 2012;82:56–7.
[26] Desroches M, Potier J, Laurent F, Bourrel A-S, Doucet-Populaire F, Decousser J-W, et al. Prevalence of mupirocin resistance among invasive coagulase-negative staphylococci and methicillin-resistant *Staphylococcus aureus* (MRSA) in France: emergence of a mupirocin-resistant MRSA clone harbouring *mupA*. J Antimicrob Chemother 2013;68:1714–7.
[27] Fang H, Fröding I, Gian B, Hæggman S, Tollström U-B, Ullberg M, et al. Methicillin-resistant *Staphylococcus aureus* in Stockholm, Sweden: molecular epidemiology and antimicrobial susceptibilities to ceftaroline, linezolid, mupirocin and vancomycin in 2014. J Glob Antimicrob Resist 2016;5:31–5.
[28] Fawley W, Parnell P, Hall J, Wilcox M. Surveillance for mupirocin resistance following introduction of routine peri-operative prophylaxis with nasal mupirocin. J Hosp Infect 2006;62:327–32.
[29] Fritz SA, Hogan PG, Camins BC, Ainsworth AJ, Patrick C, Martin MS, et al. Mupirocin and chlorhexidine resistance in *Staphylococcus aureus* in patients with community-onset skin and soft tissue infections. Antimicrob Agents Chemother 2013;57:559–68.
[30] Fujimura S, Watanabe A. *Staphylococcus aureus*Survey of high-and low-level mupirocin-resistant strains of methicillin-resistant in 15 Japanese hospitals. Chemotherapy 2003;49:36–8.
[31] Gadepalli R, Dhawan B, Mohanty S, Kapil A, Das BK, Chaudhry R, et al. Mupirocin resistance in *Staphylococcus aureus* in an Indian hospital. Diagn Microbiol Infect Dis 2007;58:125–7.
[32] Gales AC, Andrade S, Sader HS, Jones R. Activity of mupirocin and 14 additional antibiotics against staphylococci isolated from Latin American hospitals: report from the SENTRY antimicrobial surveillance program. J Chemother 2004;16:323–8.
[33] González-Domínguez M, Seral C, Potel C, Sáenz Y, Álvarez M, Torres C, et al. *Staphylococcus aureus*Genotypic and phenotypic characterization of methicillin-resistant (MRSA) clones with high-level mupirocin resistance. Diagn Microbiol Infect Dis 2016;85:213–7.
[34] Hesami S, Hosseini SD, Amouzandeh-Nobaveh A, Eskandari S, Ghaznavi-Rad E. Phenotypic and genotypic determination of mupirocin resistance among methicillin susceptibility and resistance in staphylococci isolated from nosocomial infections. J Mazandaran Univ Med Sci 2014;23:30–9.
[35] Jayakumar S, Meerabai M, Shameem Banu A, Renu Mathew KM, Binesh Lal Y. Prevalence of high and low level mupirocin resistance among staphylococcal isolates from skin infection in a tertiary care hospital. J Clin Diagn Res 2013;7:238–42.
[36] Jones JC, Rogers TJ, Brookmeyer P, Dunne Jr WM, Storch GA, Coopersmith CM, et al. *Staphylococcus aureus*Mupirocin resistance in patients colonized with methicillin-resistant in a surgical intensive care unit. Clin Infect Dis 2007;45:541–7.
[37] Joshi PR, Acharya M, Aryal R, Thapa K, Kakshapati T, Seng R, et al. Emergence of staphylococcal cassette chromosome *mec* type I with high-level mupirocin

resistance among methicillin-resistant *Staphylococcus aureus*. Asian Pac J Trop Biomed 2017;7:193–7.
[38] Kaur DC, Chate SS. *Staphylococcus aureus*Study of antibiotic resistance pattern in methicillin resistant with special reference to newer antibiotic. J Glob Infect Dis 2015;7:78–84.
[39] Kaur DC, Narayan PA. *Staphylococcus aureus*Mupirocin resistance in nasal carriage of among healthcare workers of a tertiary care rural hospital. Indian J Crit Care Med 2014;18:716–21.
[40] Kresken M, Hafner D, Schmitz F-J, Wichelhaus TA. Prevalence of mupirocin resistance in clinical isolates of *Staphylococcus aureus* and *Staphylococcus epidermidis*: results of the Antimicrobial Resistance Surveillance Study of the Paul-Ehrlich-Society for Chemotherapy, 2001. Int J Antimicrob Agents 2004;23:577–81.
[41] Krishnan P, Miles K, Shetty N. Detection of methicillin and mupirocin resistance in *Staphylococcus aureus* isolates using conventional and molecular methods: a descriptive study from a burns unit with high prevalence of MRSA. J Clin Pathol 2002;55:745–8.
[42] Kwon A-R, Yoon E-J, Yoon J-M, Kim H, Shim M-J, Choi E-C. Activities of clindamycin, Synercid, telithromycin, linezolid, and mupirocin against Gram-positive coccal strains resistant to erythromycin in Korea. Arch Pharm Res 2007;30:840–3.
[43] LaPlante KL. *Staphylococcus aureus*In vitro activity of lysostaphin, mupirocin, and tea tree oil against clinical methicillin-resistant. Diagn Microbiol Infect Dis 2007;57:413–8.
[44] Lee H, Lim H, Bae IK, Yong D, Jeong SH, Lee K, et al. Coexistence of mupirocin and antiseptic resistance in methicillin-resistant *Staphylococcus aureus* isolates from Korea. Diagn Microbiol Infect Dis 2013;75:308–12.
[45] Lim KT, Hanifah YA, Yusof MYM, Thong KL. *Staphylococcus aureus*Prevalence of mupirocin resistance in methicillin-resistant strains isolated from a Malaysian hospital. Jpn J Infect Dis 2010;63:286–9.
[46] Liu X, Deng S, Huang J, Huang Y, Zhang Y, Yan Q, et al. Dissemination of macrolides, fusidic acid and mupirocin resistance among *Staphylococcus aureus* clinical isolates. Oncotarget 2017;8:58086–97.
[47] Liu Y, Kong F, Zhang X, Brown M, Ma L, Yang Y. *Staphylococcus aureus*Antimicrobial susceptibility of isolated from children with impetigo in China from 2003 to 2007 shows community-associated methicillin-resistant *Staphylococcus aureus* to be uncommon and heterogeneous. Br J Dermatol 2009;161:1347–50.
[48] Liu Y, Li X, Yang Y, Wang M, Shen X. *Staphylococcus aureus*Diverse clonal, multidrug-resistant community-acquired, methicillin-resistant isolated from Chinese children. Int J Infect Dis 2011;15:S17–8.
[49] Lozano C, Porres-Osante N, Benito D, Zarazaga M, Torres C, Rojo-Bezares B, et al. Changes in genetic lineages, resistance, and virulence in clinical methicillin-resistant *Staphylococcus aureus* in a Spanish hospital. J Infect Chemother 2013;19:233–42.
[50] Mahmoodzadeh Hosseini H, Kiyani N, Amin M, Hedayati Ch M, Imani Fooladi AA. Distribution of high-level mupirocin resistance among clinical MRSA. J Chemother 2017;29:215–9.
[51] McDanel JS, Murphy CR, Diekema DJ, Quan V, Kim DS, Peterson EM, et al. Chlorhexidine and mupirocin susceptibilities of methicillin-resistant *Staphylococcus aureus* from colonized nursing home residents. Antimicrob Agents Chemother 2013;57:552–8.
[52] McDougal LK, Fosheim GE, Nicholson A, Bulens SN, Limbago BM, Shearer JE, et al. Emergence of resistance among USA300 methicillin-resistant *Staphylococcus aureus* isolates causing invasive disease in the United States. Antimicrob Agents Chemother 2010;54:3804–11.
[53] Ohadian Moghadam S, Pourmand MR, Davoodabadi A. *Staphylococcus aureus* The detection of mupirocin resistance and nasal carriage of methicillin resistant among healthcare workers at university hospitals of Tehran, Iran. Iran J Public Health 2015;44:361–8.
[54] Mongkolrattanothai K, Mankin P, Raju V, Gray B. Surveillance for mupirocin resistance among methicillin-resistant *Staphylococcus aureus* clinical isolates. Infect Control Hosp Epidemiol 2008;29:993–4.
[55] Muñoz-Gallego I, Infiesta L, Viedma E, Perez-Montarelo D, Chaves F. *Staphylococcus aureus*Chlorhexidine and mupirocin susceptibilities in methicillin-resistant isolates from bacteraemia and nasal colonisation. J Glob Antimicrob Resist 2016;4:65–9.
[56] Nakajima J, Hitomi S, Kurihara Y. Detection of methicillin-resistant *Staphylococcus aureus* with high-level resistance to mupirocin. J Infect Chemother 2011;17:868–71.
[57] Nicholson A, Thoms C, Wint H, Didier M, Willis R, McMorris N, et al. The detection of mupirocin resistance and the distribution of methicillin-resistant *Staphylococcus aureus* at the University Hospital of the West Indies, Jamaica. West Indian Med J 2010;59:509–13.
[58] Nikfar G, Jamali H, Ahmadzadagan J. Simultaneous detection of methicillin- and mupirocin-resistant genes in *Staphylococcus aureus* isolated with multiplex PCR from patients in the city of Darab, Fars Province, Iran. Int J Med Res Health Sci 2016;5:125–31.
[59] Nizamuddin S, Irfan S, Zafar A. *Staphylococcus aureus*Evaluation of prevalence of low and high level mupirocin resistance in methicillin resistant isolates at a tertiary care hospital. J Pak Med Assoc 2011;61:519–21.
[60] Norazah A, Koh YT, Kamel AG, Alias R, Lim VK. Mupirocin resistance among Malaysian isolates of methicillin-resistant *Staphylococcus aureus*. Int J Antimicrob Agents 2001;17:411–4.
[61] Oommen S, Appalaraju B, Jinsha K. Mupirocin resistance in clinical isolates of staphylococci in a tertiary care centre in South India. Indian J Med Microbiol 2010;28:372–5.
[62] Park S-H, Kim S-Y, Lee J-H, Park C, Lee D-G. *Staphylococcus aureus*Community-genotype strains of methicillin-resistant with high-level mupirocin resistance in a neonatal intensive care unit. Early Hum Dev 2013;89:661–5.
[63] Pereira MFB, Berezin EN, Carvalho RL, Scheffer DK, Mimica MJ. *Staphylococcus aureus*Mupirocin susceptibility in nasal and oropharyngeal isolates from Brazilian children. J Chemother 2014;26:373–4.
[64] Pérez-Roth E, López-Aguilar C, Alcoba-Florez J, Méndez-Álvarez S. High-level mupirocin resistance within methicillin-resistant *Staphylococcus aureus* pandemic lineages. Antimicrob Agents Chemother 2006;50:3207–11.
[65] Perkins D, Hogue JS, Fairchok M, Braun L, Viscount HB. Mupirocin resistance screening of methicillin-resistant *Staphylococcus aureus* isolates at Madigan Army Medical Center. Mil Med 2008;173:604–8.
[66] Potel C, Alvarez M, Alvarez P, Otero I, Fluiters E. Evolution, antimicrobial susceptibility and assignment to international clones of methicillin-resistant *Staphylococcus aureus* isolated over a 9-year period in two Spanish hospitals. Clin Microbiol Infect 2007;13:728–30.
[67] Rotger M, Trampuz A, Piper KE, Steckelberg JM, Patel R. Phenotypic and genotypic mupirocin resistance among staphylococci causing prosthetic joint infection. J Clin Microbiol 2005;43:4266–8.
[68] Rubin J, Chirino-Trejo M. Antimicrobial susceptibility of canine and human *Staphylococcus aureus* collected in Saskatoon, Canada. Zoonoses Public Health 2011;58:454–62.
[69] Rudresh MS, Ravi GS, Motagi A, Alex AM, Sandhya P, Navaneeth BV. Prevalence of mupirocin resistance among staphylococci, its clinical significance and relationship to clinical use. J Lab Physicians 2015;7:103–7.
[70] Saderi H, Owlia P, Habibi M. Mupirocin resistance among Iranian isolates of *Staphylococcus aureus*. Med Sci Monit 2008;14:BR210–3.
[71] Sareyyüpoğlu B, Özyurt M, Haznedaroğlu T, Ardic N. Detection of methicillin and mupirocin resistance in staphylococcal hospital isolates with a touchdown multiplex polymerase chain reaction. Folia Microbiol (Praha) 2008;53:363–7.
[72] Shittu AO, Lin J. *Staphylococcus aureus*Antimicrobial susceptibility patterns and characterization of clinical isolates of in KwaZulu-Natal Province, South Africa. BMC Infect Dis 2006;6:125.
[73] Stratchounski L, Dekhnich A, Kretchikov V, Edelstain I, Narezkina A, Afinogenov G, et al. Antimicrobial resistance of nosocomial strains of *Staphylococcus aureus* in Russia: results of a prospective study. J Chemother 2005;17:54–60.
[74] Teo BW, Low SJ-X, Ding Y, Koh TH, Hsu L-Y. High prevalence of mupirocin-resistant staphylococci in a dialysis unit where mupirocin and chlorhexidine are routinely used for prevention of catheter-related infections. J Med Microbiol 2011;60:865–7.
[75] Udo E, Jacob L, Mathew B. The spread of a mupirocin-resistant/methicillin-resistant *Staphylococcus aureus* clone in Kuwait hospitals. Acta Trop 2001;80:155–61.
[76] Us T, Kural M, Yayla B, Kiremitçi A, Cetin E, Akgün Y. *Staphylococcus aureus* Investigation of mupirocin resistance in nosocomial methicillin-resistant isolates by phenotypic and genotypic methods [in Turkish]. Mikrobiyol Bul 2009;43:353–64.
[77] Vasquez JE, Walker ES, Franzus BW, Overbay BK, Reagan DR, Sarubbi FA. *Staphylococcus aureus*The epidemiology of mupirocin resistance among methicillin-resistant at a Veterans' Affairs hospital. Infect Control Hosp Epidemiol 2000;21:459–64.
[78] Warren DK, Prager M, Munigala S, Wallace MA, Kennedy CR, Bommarito KM, et al. *qacA*Prevalence of *B* genes and mupirocin resistance among methicillin-resistant *Staphylococcus aureus* (MRSA) isolates in the setting of chlorhexidine bathing without mupirocin. Infect Control Hosp Epidemiol 2016;37:590–7.
[79] Wasserman E, Orth H, Senekal M, Harvey K. *Staphylococcus aureus*High prevalence of mupirocin resistance associated with resistance to other antimicrobial agents in isolated from patients in private health care, Western Cape. S Afr J Infect Dis 2014;29:126–32.
[80] Watanabe H, Masaki H, Asoh N, Watanabe K, Oishi K, Furumoto A, et al. Emergence and spread of low-level mupirocin resistance in methicillin-resistant *Staphylococcus aureus* isolated from a community hospital in Japan. J Hosp Infect 2001;47:294–300.
[81] Yari R, Khamehchi M, Mehrabi M. *Staphylococcus aureus*Evaluation of mupirocin chromosomal resistance in strains and mapping of *Alu*I enzymatic digestion. J Babol Univ Med Sci 2016;18:.
[82] Yun H-J, Lee SW, Yoon GM, Kim SY, Choi S, Lee YS, et al. Prevalence and mechanisms of low- and high-level mupirocin resistance in staphylococci isolated from a Korean hospital. J Antimicrob Chemother 2003;51:619–23.
[83] Park SY, Kim SM, Park SD. *Staphylococcus aureus*The prevalence, genotype and antimicrobial susceptibility of high- and low-level mupirocin resistant methicillin-resistant. Ann Dermatol 2012;24:32–8.
[84] González-Domínguez M, Seral C, Potel C, Constenla L, Algarate S, Gude MJ, et al. Antimicrobial resistance, virulence factors and genetic lineages of hospital-onset methicillin-resistant *Staphylococcus aureus* isolates detected in a hospital in Zaragoza. Enferm Infecc Microbiol Clin 2015;33:590–6.
[85] George S, Leasure AR, Horstmanshof D. Effectiveness of decolonization with chlorhexidine and mupirocin in reducing surgical site infections: a systematic review. Dimens Crit Care Nurs 2016;35:204–22.