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Review Article

Nasal carriage rate of methicillin resistant *Staphylococcus aureus* among Iranian healthcare workers: a systematic review and meta-analysis

***Mohammad Emaneini*[1], *Fereshteh Jabalameli*[1], *Hosseinali Rahdar*[1], *Willem B. van Leeuwen*[2], *and Reza Beigverdi*[1]**

[1]. Department of Microbiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran. [2]. Department of Innovative Molecular Diagnostics, Faculty of Science & Technology, University of Applied Sciences. Leiden. Netherlands.

Abstract

Globally, methicillin-resistant *Staphylococcus aureus* (MRSA) remains a major cause of healthcare-associated infections. Healthcare workers (HCWs), patients and the environment may act as reservoirs for the spread of MRSA to patients and other HCWs. Screening and eradication of MRSA colonization is an effective method of reducing the MRSA infection rate. There are limited data on the prevalence of MRSA among Iranian HCWs. We performed a systematic search by using different electronic databases including Medline (via PubMed), Embase, Web of Science, and Iranian Databases (from January 2000 to July 2016). Meta-analysis was performed using the Comprehensive Meta-Analysis (Biostat V2.2) software. The meta-analyses showed that the prevalence of *S. aureus* and MRSA among HCWs were 22.7% [95% confidence interval (CI): 19.3-26.6] and 32.8% (95% CI: 26.0-40.4) respectively. The high rate of nasal MRSA carriage among Iranian HCWs has been attributed to poor compliance to hand hygiene, injudicious use of antibiotics, and ineffective infection control and prevention measures. The rational use of antibiotics plus strict infection control are the main pillars for controlling multidrug resistant microorganisms such as MRSA in the hospital setting. These measurements should be applied nationally.

Keywords: MRSA. Nasal carriage. Healthcare workers. Iran. Systematic review.

INTRODUCTION

Staphylococcus aureus is a major cause of both nosocomial and community-acquired infections[1]. Over the past decades, the incidence of methicillin-resistant *S. aureus* (MRSA) in surgical site infections, bloodstream infections, and pneumonia has increased significantly[2,3]. MRSA strains are considered to be endemic in many hospitals throughout the world and are now responsible for approximately 40-60% of healthcare-associated infections[4]. Compared to methicillin-susceptible *S. aureus* (MSSA), various studies have revealed that infection due to MRSA is associated with significant morbidity, mortality, length of hospital stay, and medical costs[5-7]. For example, the rate of death due to MRSA (11.8%) was considerably higher than that due to MSSA (5.1%)[8]. The treatment of MRSA infections has become a global burden. Treatment options for MRSA infections have become more limited[9]. *S. aureus* colonizes various niches of the human body, but the primary colonization site is the anterior nares[6]. It is estimated that 20-30% of individuals are persistent carriers of *S. aureus*, around 30% are intermittent carriers, and 40-50% are noncarriers[10]. Nasal carriage among healthcare workers (HCWs) is the main source for the transmission of MRSA and most *S. aureus* among patients within and between wards[11,12]. MRSA carriers create major problems for critically ill patients [e.g., intensive care unit (ICU) patients][13]. Screening of HCWs for early and rapid identification of MRSA carriage is recommended for reducing the spread of MRSA within hospitals[6]. In 2003, MRSA strains were first isolated from the nasal passages of HCWs in Milad Hospital in Tehran, Iran[14]. Currently, MRSA is considered a major cause of healthcare-associated infections[15]. To date, the prevalence rates of MRSA among HCWs have been reported in several Iranian studies[16,17]. Most of these studies presented local data, and no systematic study has been performed. The aim of this study was to identify the prevalence of nasal carriage of MRSA among HCWs in Iranian hospitals using a systematic review and meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

METHODS

Design

This was a systematic review and meta-analysis of the prevalence of nasal carriage of MRSA among Iranian HCWs

Corresponding author: Dr. Reza Beigverdi
e-mail: r-beigverdi@tums.ac.ir
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Search Strategies

We performed a computerized search of published studies in Medline (via PubMed), Embase, Web of Science, and an Iranian Database from January 2000 to July 2016 using the following terms: *Staphylococcus aureus* or *S. aureus* and methicillin resistant *Staphylococcus aureus* or MRSA and nasal carriage and HCWs in combination with Iran. Cross-sectional or cohort studies that reported the prevalence of MRSA in the nasal passages of HCWs were considered. The titles and abstracts were screened by two independent reviewers for possible inclusion in the review. The review was restricted to studies published in the English and Persian languages and assessed the prevalence or incidence of MRSA in the nasal passages of Iranian HCWs. Eligible articles were selected based on three stages: title, abstract, and full-text publication. Studies with the following characteristics were included: a standard method had to be used to detect MRSA, studies addressing the *S. aureus* nasal carriage in HCWs, reported data on the prevalence of MRSA. According to the guidelines of the Clinical and Laboratory Standards Institute[18], the most reliable method for detecting MRSA strains is the measurement of minimum inhibitory concentration (MIC) by methods such as broth microdilution, agar dilution, and E-test as well as molecular methods [detection of the *mecA* gene, the most common gene that mediates methicillin resistance in staphylococci, by polymerase chain reaction (PCR)]. MIC and PCR tests are accurate and gold standard methods for detecting MRSA[18,19]. Studies that had one or more of the following characteristics were excluded: studies using nonstandard methods, duplicate and overlapping studies, studies published in languages other than English or Persian, studies that did not assess nasal carriage of *S. aureus* among HCWs, studies that did not report MRSA prevalence, nonhuman studies, review articles, congress abstracts, meta-analyses or systematic reviews, as well as articles available only in abstract form.

Data extraction and definitions

The following details were extracted from each study: the first author's name, year of publication, year of study, study setting, number of cases investigated, methods of the studies, isolate source, sample size, and prevalence of nasal MRSA carriage among HCWs. Two reviewers independently extracted all data from the included studies, and the results were reviewed by a third reviewer. Inconsistencies between the reviewers were resolved by a general consensus.

Quality assessment of studies

The quality of the included studies was independently assessed by two reviewers, using the Joanna Briggs Institute Checklist for Systematic Reviews and Research Syntheses[20]. The checklist consists of 10 inquiries in which the reviewers responded to questions on the selected articles on an individual basis according to the evidence. The Yes answer for each question got a point; evidently, the scores ranged from zero to ten. Eventually, studies that attained greater than 6 points were included in this study.

Statistical analyses

Meta-analysis was performed using the Comprehensive Meta-Analysis (Biostat V2.2) software. We reported the amount of residual heterogeneity by using the I^2 statistic and Q statistic to test the heterogeneity among the studies. In order to assess any possible publication bias, the Begg rank correlation and Egger weighted regression methods in combination with a funnel plot were used. $p < 0.05$ was considered indicative of statistically significant publication bias. We used the EndNote referencing software to collate the search results and remove duplicates.

RESULTS

Overall, 4,241 studies were identified. Of these, 2,527 articles remained after the duplicates were removed. By screening the titles and abstracts, 1,787 studies were excluded because they were not relevant. Of the remaining 740 articles, only 22 studies were included in this meta-analysis. The study selection process and reasons for exclusion are shown in **Figure 1**, and the main characteristics of the selected studies are described in **Table 1**. Based on the 22 selected articles, the pooled prevalence of *S. aureus* and MRSA was 22.7% [95% confidence interval (CI): 19.3-6.6] and 32.8% (95% CI: 26.0-40.4), respectively, as shown in **Table 2**. Heterogeneity between studies (I^2=91, p <0.001 for *S. aureus* and I^2=85, p <0.001 for MRSA) were found, so a random effects model was used for the meta-analysis. **Figure 2** shows forest plots for the prevalence rate of MRSA among Iranian HCWs. As shown in **Table 2**, no evidence of publication bias was detected by Begg's rank correlation test (p =0.2 for *S. aureus* and p =0.5 for MRSA) and Egger's weighted regression (p =0.3 for *S. aureus* and p =0.7 for MRSA). However, the asymmetric shape of the funnel plot (**Figure 3**) shows some evidence of publication bias among the evaluated studies.

DISCUSSION

To the best of our knowledge, the current study is the first comprehensive systematic review regarding the prevalence of *S. aureus* and MRSA among Iranian HCWs. Based on the meta-analysis results, the pooled prevalence of *S. aureus* and MRSA were 22.7% (95% CI: 19.3-26.6) and 32.8% (95% CI: 26.0-40.4), respectively[14,16,17,21-39]. In Egypt, Hefzy et al. showed that the prevalence of nasal carriage of *S. aureus* among Egyptian HCWs was 22.9% and among these 58.8% was MRSA[40]. In Ethiopia, Shibabaw et al. reported that the prevalence of *S. aureus* among Ethiopian HCWs was 28.8% and among these 44.1% was MRSA[9]. In China, Chen et al. reported that that the prevalence of *S. aureus* among Chinese HCWs was 21.6 % and among these 4.7% was MRSA[41]. In a meta-analysis study conducted by Albrich et al. the average *S. aureus* and MRSA prevalence among HCWs were 23.7 and 4.6 %, respectively[42]. However, nasal carriage of MRSA differs noticeably among countries[9,40-44] which may reflect methodological differences (sampling technique, sample size, culture techniques, the sites chosen for sampling) and differences in infection control policies, among other factors[12,43]. Several factors may explain the high incidence rate of *S. aureus* and MRSA among HCWs observed in this study. First, infection control policies are likely to be ineffective in Iran[45]. For instance, hand hygiene (effective handwashing) is widely regarded as the most important way of

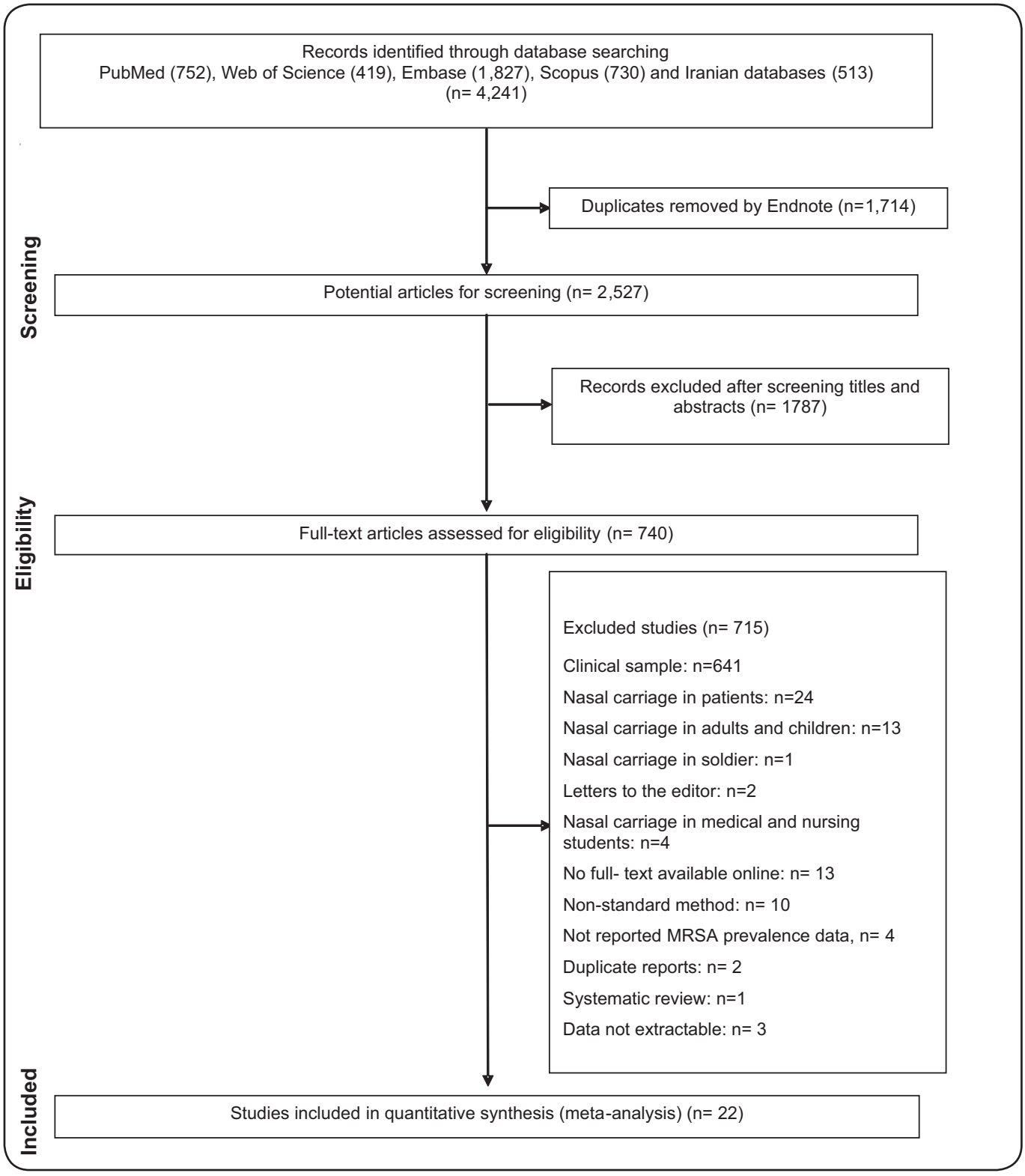

FIGURE 1 - Summary of the literature search and study selection**. MRSA:** methicillin-resistant *Staphylococcus aureus*.

TABLE 1

Characteristics of studies included in the meta-analysis.

First author of the study	Time of study	Year of Publication	Province	Nasal swab	*Staphylococcus aureus* (no)	MRSA (no)	Detection Method
Rahbar et al.[14]	2002	2003	Tehran	230	92	35	Agar dilution method
Saderi et al.[21]	2002-2003	2004	Tehran	348	87	10	Agar dilution method
Nikbakht et al.[22]	2004-2005	2007	Tabriz	220	72	22	Agar dilution method
Armin et al. [23]	2006	2007	Tehran	237	50	17	Micro-dilution method
Nafisi et al.[24]	2007	2008	Shahrekord	204	52	27	Agar dilution method, PCR
Askarian et al.[16]	2006	2009	Shiraz	600	186	32	E-test, PCR
Khalili et al.[25]	2007-2008	2009	Yazd	742	94	57	Agar dilution method
Rahimialang et al.[26]	2009	2010	Gorgan	333	69	9	Micro-dilution method
Moradi et al.[27]	2007	2011	Bandar abbas	85	24	4	Agar dilution method
Rastegarlari et al.[17]	2010	2011	Tehran	270	72	23	Agar dilution method
HosainZadegan et al.[28]	2010	2011	khorramabad	300	64	16	Agar dilution method
Afrough et al.[29]	2010-2011	2013	Tehran	157	70	29	Agar dilution method
Talaei et al.[30]	2011	2012	Tehran	70	17	6	Agar dilution method
Zeinalineia et al.[31]	2011	2011	Tehran	261	70	29	PCR
Mamishi et al.[32]	2010	2012	Tehran	190	47	7	Agar dilution method, PCR
Khalili et al.[33]	2010-2011	2012	Yazd	151	29	8	Agar dilution method
Kalhour et al.[34]	2006	2013	Shahrekord	204	52	23	Agar dilution method
Janaati et al.[35]	2010	2013	Ardabi	173	41	8	Agar dilution method, PCR
Saadat et al.[36]	2012	2013	Jahrom	397	47	9	E-test
Ahanjan et al.[37]	2012	2014	Sari	148	14	10	Micro-dilution method
Navidinia et al.[38]	2012-2013	2015	Tehran	229	27	21	PCR
Ohadian Moghadam et al.[39]	2013	2015	Tehran	270	39	17	E-test, PCR

MRSA: methicillin-resistant *Staphylococcus aureus*; **PCR**: polymerase chain reaction.

TABLE 2

Meta-analysis of prevalence of *Staphylococcus aureus* and MRSA among Iranian HCWs.

Subgroups	Studies (no)	Prevalence	n/N	Heterogeneity test, I2	Heterogeneity test, *p* value	Begg's test	Egger's test
S. aureus	22	22.7 (19.3-26.6)	1,315/5,819	91	<.001	0.2	0.3
MRSA	22	32.8 (26.0-40.4)	419/1,315	85	<.001	0.5	0.7

MRSA: methicillin-resistant *Staphylococcus aureus*; **HCWs**: healthcare workers; **n:** number of events (*S. aureus and* MRSA); **N: total number of** HCWs and *S. aureus*; ***S:*** *Staphylococcus*.

reducing the spread of MRSA and other nosocomial pathogens such as vancomycin-resistant enterococci[45,46]. Hand hygiene compliance among Iranian HCWs is generally low. Heavy workload, understaffing, limited infrastructure (lack of sinks, unavailability of hygiene products), behavioral aspects, and skin irritation by hand hygiene products are important barriers to appropriate compliance[45-47]. Lack of knowledge about the modes of transmission (direct skin-to-skin contact, indirect contact via contaminated hands, surfaces, and medical devices), lack of knowledge regarding the importance of hand hygiene in reducing the spread of MRSA and on how hands become contaminated, lack of knowledge regarding correct hand hygiene techniques, patient overcrowding, and lack of national guidelines on hand hygiene are additional barriers to hand

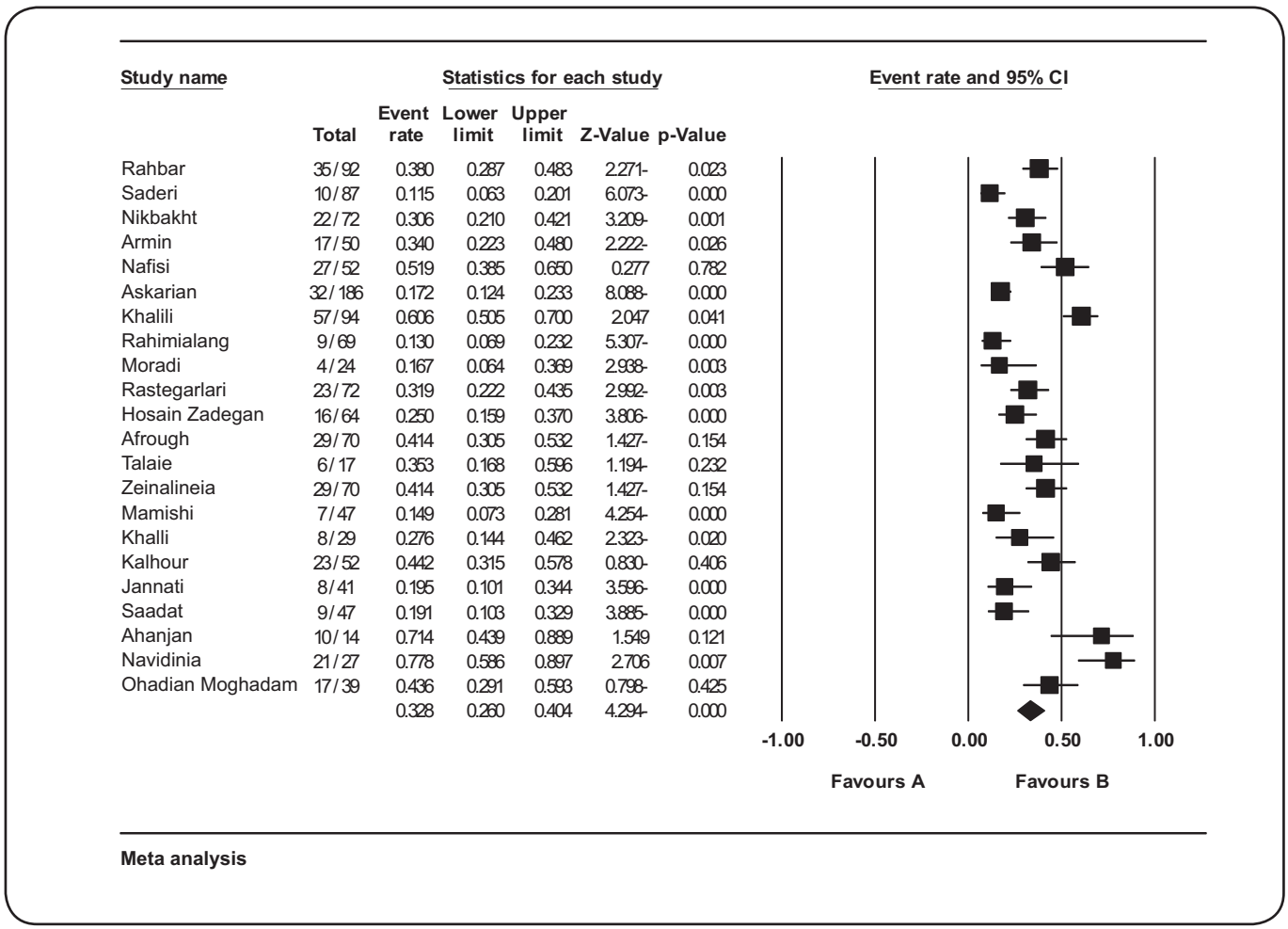

FIGURE 2 - Forest plot of prevalence of MRSA among HCWs. (The squares represent the point estimates of individual studies with their 95% confidence intervals and the size of the square represents the weight given to each study in the meta-analysis. The diamond represents the overall result and 95% confidence interval of the random effect meta-analysis. Vertical line: null value). **95% CI**: 95% confidence interval; **MRSA:** methicillin-resistant *Staphylococcus aureus*; **HCWs**: healthcare workers.

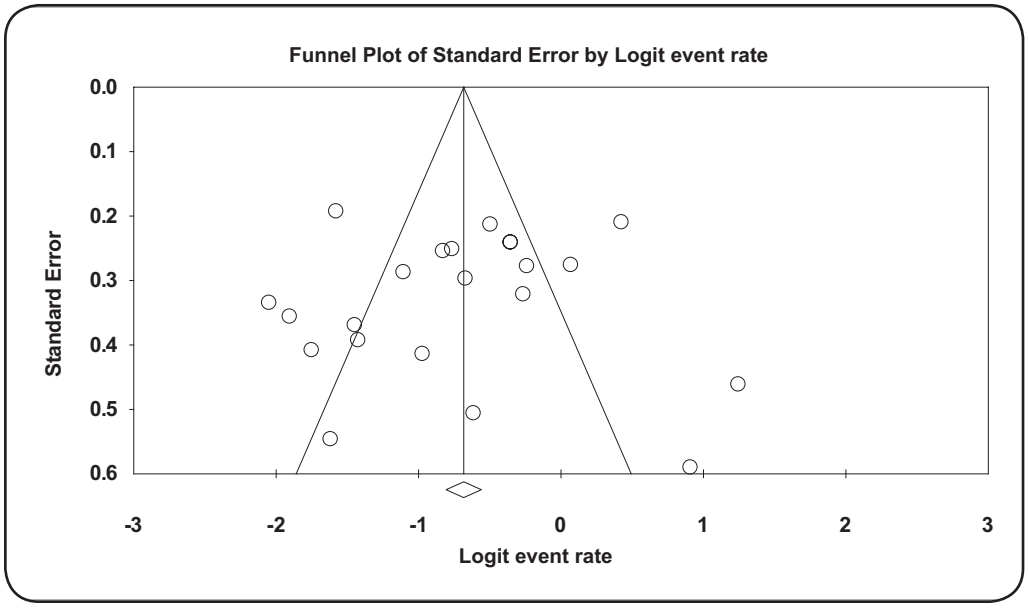

FIGURE 3 - Funnel plot of prevalence of MRSA among HCWs. (Funnel asymmetry suggests bias in the meta-analysis). **MRSA:** methicillin-resistant *Staphylococcus aureus*; **HCWs**: healthcare workers.

hygiene compliance[45,48]. On the other hand, Iranian hospitals are poorly resourced with regard to personal protective equipment (PPE) (gowns, gloves, mask)[45,49]. In contrast, in the Netherlands, all hospitals are equipped with appropriate PPEs[45,49]. Second, it has been proven that treatment with intranasal mupirocin can reduce the rates of nosocomial MRSA infection[50]. It seems that the identification and treatment of nasal carriers (patients and HCWs) with mupirocin were not performed in Iran, or if performed, the existing MRSA strains had become resistant to this agent. High-level mupirocin resistance in clinically-acquired MRSA infections has been reported in Iran[51]. Third, overprescribing or unregulated use of antibiotics in developing countries such as Iran is common[45,48,52]. For example, the use of cephalosporins and fluoroquinolones is prevalent, and their overuse may elicit the emergence of MRSA in hospitals[53]. On the other hand, clinicians face serious problems in choosing effective antimicrobial agents due to lack of good microbiological laboratory capacity; therefore, the overuse or misuse of antibiotics has led to the emergence and spread of MRSA[45,48]. Fourth, hospitals do not have a sufficient number of isolation rooms; thus, MRSA-infected patients are admitted to the general wards together with uninfected patients[45]. As a result, there is an increased risk of transmission of MRSA from patients to both patients and HCWs[45]. Fifth, decontamination of the hospital environment is likely to be ineffective in Iran[45]; thus, MRSA can be spread by contact with contaminated surfaces[45]. In recent years, the incidence of MRSA infection has increased dramatically in Iranian hospitals[15]. Finally, the hospital infection control teams are inexperienced, inadequate, not well trained, and worst of all, most of them do not include a clinical microbiologist[45]. As a result, there is failure in controlling or reducing the transmission of MRSA. The present review has several limitations. First, the study could not fully assess the prevalence of MRSA among HCWs in Iran since the magnitude of MRSA among HCWs has not been identified in different regions of the country. Second, we only considered published articles in the current meta-analysis; just like any other meta-analysis, the potential for publication bias should be considered as well.

Third, heterogeneity was observed among the included studies which may be due to differences in sample size, different methods for the detection of MRSA and geographical diversity.

In conclusion, poor hand hygiene compliance, non-judicious use of antibiotics and ineffective infection control measures may explain the relatively high nasal carriage of *S. aureus* and MRSA among Iranian HCWs. Therefore, reducing antibiotic overuse, adherence to hand hygiene, screening and decolonization of carriers, education and training in antibiotic prescribing, environmental cleaning, routine environmental cultures, contact precautions, and active surveillance are recommended strategies for the prevention and control of MRSA transmission in our healthcare setting.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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