Methicillin Resistant *Staphylococcus Aureus* Carrier Status among Indian Healthcare Workers: A Systematic Review and Meta-Analysis

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Abstract

Infection with Methicillin Resistant *Staphylococcus aureus* (MRSA) is a threat to quality care in the hospital. Asymptomatic colonization of MRSA escalates the burden of infection. The rate of MRSA colonization among healthcare workers (HCW) is not homogenous across the globe. Even though there are individual study reports on MRSA colonization, no pooled data is available in India. Therefore, it is important to evaluate the problem of MRSA colonization to develop a policy on preventive measures. We performed a systematic review and meta-analysis of MRSA carrier status among Indian HCWs using five databases (Scopus, PubMed-Medline, IndMed, CINAHL and Google-Scholar) from the articles published from 2008 to 2017 (10 years). STATA 13.0 with metaprop package in STATA was used to find the rate of colonization. Among 2,349 HCWs, the pooled prevalence of MRSA colonization in throat, nose, axilla, palm, fingertips and web-spaces was nine percent (CI 6% - 13%; p=0.001, I^2 91.68%). Further, the forest plot of MRSA colonization in nasal cavity alone was performed, and the prevalence of nasal colonization of MRSA among 1,251 Indian HCWs was found to be 11% (CI 5-17%, p=0.001, I^2 93.3%). The colonization rate is not very high nor negligible. Therefore, the hospital administrator along with the hospital infection control committee needs to formulate a policy on periodic screening and decolonization of HCWs in high-risk areas.

***Keywords**: MRSA, colonization, nasal carriage, healthcare workers, systematic review*

Introduction

Methicillin resistant *Staphylococcus aureus* (MRSA) is a strain of antibiotic resistant *Staphylococcus aureus*. It is a Gram-positive bacteria, resistant to β-lactam antibiotics (Penicillin derivatives such as Methicillin, Oxacillin, etc.) and difficult to treat[1]. MRSA has become a threat to healthcare facilities in many countries, including India. The proportion of MRSA ranges from 20% to 80% around the globe, and this high proportion requires second-line antibiotics in prophylaxis[2]. Infection with MRSA attributes to increased risk of mortality, readmissions, excessive utilization of healthcare resources and thereby added healthcare costs[2]. MRSA can be community acquired or hospital acquired. Though community acquired MRSA exhibits susceptibility to many antibiotics, hospital associated MRSA has amplified resistant pattern to a good number of generally used non-beta lactum antibiotics[2].

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MRSA contributes to 40-60% of total hospital associated infections (HAI)[3]. However, the prevalence of MRSA infection is not homogenous in India[4]. MRSA is seen in healthy individuals as a carrier. The common locations of harboring MRSA as carrier are nose, armpit, groin, throat, palm and finger tips[5-6]. The primary colonized site in man is anterior nares[7]. Asymptomatic carrier status of MRSA endangers public health as the diagnosis of MRSA is challenging. The impact of carrier status or mere infection with MRSA is difficult to treat and increases the duration of treatment[2]. The healthcare workers serve as a reservoir, vector or victim of MRSA transmission[8].

A meta-analysis published in 2008 with 127 studies, which involved screening of 33,318 healthcare workers for MRSA carrier status around the world showed a prevalence of 4.6%[8]. There are no meta-analyses or systematic reviews published in the recent years on screening of MRSA colonization among healthcare workers. However, there are many studies reporting varied rates of MRSA carrier status ranging from 0 to 74%[9-10]. Yet, there is no systematic review available in India to estimate the burden of MRSA carrier status. Therefore, this systematic review and meta-analysis is performed with the aim to identify the prevalence of nasal carriage of MRSA among Indian healthcare workers.

Method

Inclusion criteria

We included studies conducted among healthcare workers in Indian hospitals. Healthcare workers comprised of doctors, nurses, technician and various therapists or students of any health disciplines who are involved in direct patient care activities. The articles involving both the gender and all age group of healthcare workers working in public or private hospitals were reviewed. We have included the articles published in English language only. Observational studies such as cross-sectional, descriptive, cohort, case-control or prevalence surveys were included. Case reports, case series, reviews and conference reports were excluded. The study period was for last 10 years (articles published from January 2008 to December 2017). The studies in which the sample was obtained from nose, and Methicillin resistance confirmed with Cefoxitin susceptibility testing according to guidelines of Clinical and Laboratory Standards Institute (CLSI) were included[11].

Search strategy

The major electronic data bases were systematically searched. They are Scopus, PubMed-Medline, IndMed, CINAHL and Google Scholar. The keywords used were: methicillin resistant *Staphylococcus aureus*, healthcare worker, nasal colonization, observational study and geographical area such as India. Appropriate search strategies were built as per the requirement of each database.

Quality assessment

The quality of studies was assessed by using the Joanna Briggs Institute Checklist for Systematic Reviews and Research Syntheses. The checklist consists of three sections: 1) the study details (authors details, publication related items and aim and objectives); 2) the study methods (study design, study duration, sample characteristics, dependent variable, outcome measured, ethical considerations, method of diagnostic test, method of data analysis); 3) the study results (prevalence or incidence, authors comments or limitation of the study). Two reviewers independently responded to each of the items mentioned in the checklist with a 'yes' or 'no'. Each 'yes' carried a score of one and 'no' carried a score of zero, with the total possible maximum score of 10. Section 2 and 3 were considered for quality assessment. The studies with the score of six or more than six were considered for review and meta-analysis.

Data extraction

The data were extracted using checklist prepared on the basis of the 'Meta-analysis of Observational Studies in Epidemiology (MOOSE)' guidelines[12] and 'Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)' guidelines[13]. The data extracted from each study were: the last name of the first author, name of the journal, year of publication of the study, aims and objectives, setting of the study, number of healthcare workers recruited in the study, types of healthcare worker, methodology of the study, source of sample obtained, method of testing the presence of MRSA and prevalence of MRSA carrier status. Two

reviewers have independently extracted the data. The third reviewer helped in resolving the inconstancies between the reviewers.

Statistical Analysis

The meta-analysis was performed by using STATA 13.0 version. Forest plots were built with the help of metaprop package in STATA. This review has included cross-sectional studies only. As cross-sectional studies are observational, a considerable amount of heterogeneity is expected. Hence, a random effects model was adopted instead of fixed effect model. The pooled prevalence of MRSA carrier status with 95% confidence interval along with I^2 statistic that helps in quantifying the heterogeneity of the studies was reported.

Results

From the five data bases, 333 articles were identified using appropriate search terms (Figure 1). Microsoft excel was used to remove the duplicates. After the title and abstract screen, 18 articles were considered for full text review and 315 were excluded. This review also included the article which has used CLSI with Cefoxitin (30 µg) disc diffusion for testing MRSA. Among 18 studies, seven studies were excluded. We were unable to get the percentage of MRSA colonization in one study[14] and another study reported different sample size at different time[15]. Five studies were excluded as Oxacillin disc diffusion method was employed for identifying MRSA[16-20]. Finally, 11 studies were included to find the prevalence of MRSA colonization among HCWs of Indian hospitals (Table 1).

Table 1: Characteristics of studies included in the systematic review and meta-analysis

Author (year) setting	Study title	Sample size	Screening location	MRSA Carrier status (%)
Shinde (2016) Belagavi (Karnataka)21	Screening for Methicillin Resistant Staphylococcus aureus (MRSA) colonization in healthcare workers working in critical care areas at a tertiary care hospital, Karnataka, India	63	Nasal, palm	6.4
Nambirajan, (2016) Tamilnadu22	Alarming carrier status of Methicillin Resistant Staphylococcus aureus (MRSA) among adolescent learners- prevalence and antibiotic susceptibility of the organism	619	Nasal, palm, Index finger and Dorsum	8.9
Malini (2012) Bengaluru23	Methicillin Resistant Staphylococcus aureus carriage among the healthcare workers in a tertiary care hospital	150	Nasal, throat, palms and web spaces	10
Agarwal, (2015) Uttar Pradesh24	Nasal carriage of Methicillin- and Mupirocin-resistant S. aureus among healthcare workers in a tertiary care hospital	200	Nasal	14
Satpathi, (2015) West Bengal25	Nasal carriage of Staphylococcus aureus and the quantum of their Methicillin Resistance amongst the healthcare workers in a peripheral tertiary care centre of Eastern India	183	Nasal	6.6
Radhakrishna, (2016) Karnataka26	Nasal carriage of staphylococcus aureus with special emphasis on Methicillin Resistant Staphylococcus aureus among students of a South Indian medical college - prevalence and antibiogram pattern	148	Nasal	6.1

Cont... **Table 1: Characteristics of studies included in the systematic review and meta-analysis**

Author (year) setting	Study title	Sample size	Screening location	MRSA Carrier status (%)
Radhakrishna, (2013) Mangalore, Karnataka27	Prevalence of Methicillin Resistant Staphylococcus aureus carriage amongst healthcare workers of critical care units in Kasturba Medical College Hospital, Mangalore, India	200	Nasal	2.5
Verma, (2017) Bhopal28	Utility of chromogenic medium for early detection of nasal carriage of Methicillin Resistant Staphylococcus aureus (MRSA) in healthcare professionals	120	Nasal	21.7
Visalachy, (2016) Chennai, Tamilnadu29	Carriage of multidrug resistant bacteria on frequently contacted surfaces and hands of healthcare workers	157	Hands	1.3
Hema, (2017) Bengaluru, Karnataka10	Prevalence of nasal carriers of Methicillin Resistant Staphylococcus aureus among dental students: An in vivo study	400	Nasal	18.5
Renushri, (2014) Karnataka30	Screening for Methicillin Resistant Staphylococcus aureus carriers among individuals exposed and not exposed to the hospital environment and their antimicrobial sensitivity pattern	119	Nasal, throat, Palm	11.8

NA: not available MRSA: Methicillin Resistant *Staphylococcus aureus* MSSA: Methicillin Sensitive *Staphylococcus aureus*

The total population included in the meta-analysis of MRSA colonization was 2,359. The population consisted of doctors, nurses, nursing orderlies, auxiliary nurses, health science students such as medical students, nursing students, dental students, technicians and housekeeping staff (Table 1). Most of the articles were published in recent years (2 articles published in 2017, 4 articles in 2016, 2 articles in 2015 and 1 each in 2014, 2013 and 2012). The key features of included studies are given in Table 1.

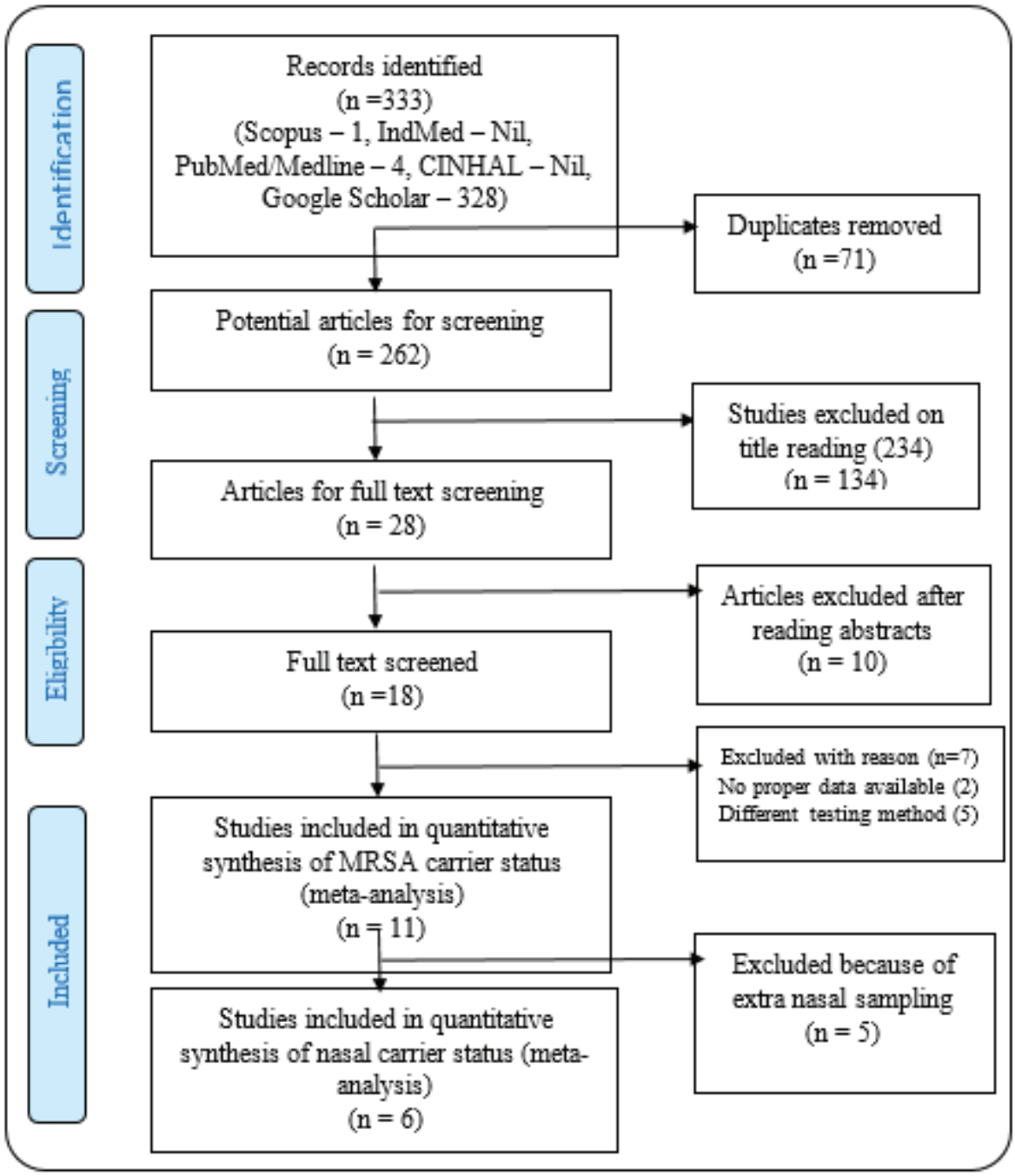

Figure 1: PRISMA Chart Detailing Study Selection for the Review

The forest plot (figure 2) on MRSA colonization among Indian healthcare workers shows the overall pooled prevalence of MRSA colonization with 95% confidence interval was nine percent (6%, 13%; p=0.001, I^2 91.68%).

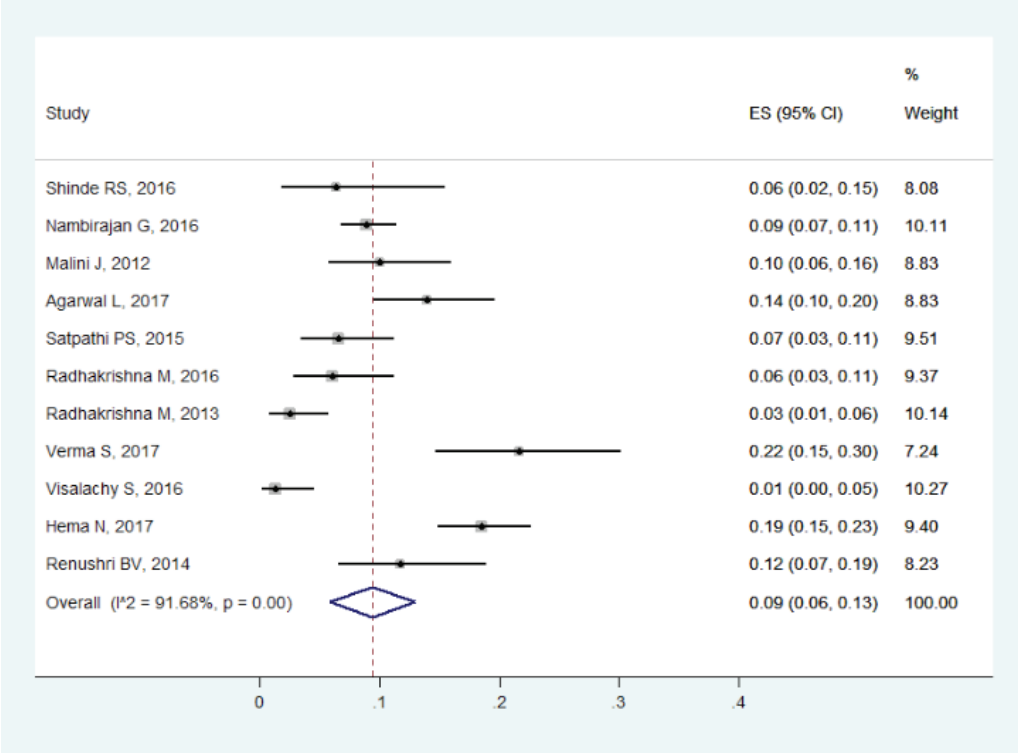

Figure 2: Forest plot of prevalence of MRSA carriage among Indian healthcare workers

From the 11 studies included in the meta-analysis, six studies have investigated nasal carrier status and rest five studies have multiple sampling from palm, finger tips, web spaces, axilla, etc. Therefore, six studies[10,24-28] were further analyzed for estimating the prevalence of nasal carrier status of MRSA. A total of 1,251 healthcare workers were included for the meta-analysis (Table 1). The prevalence of MRSA colonization in nasal cavity alone is given in figure 3. The pooled prevalence of nasal carrier is 11% (5%, 17%; p=0.001, I^2 93.3%).

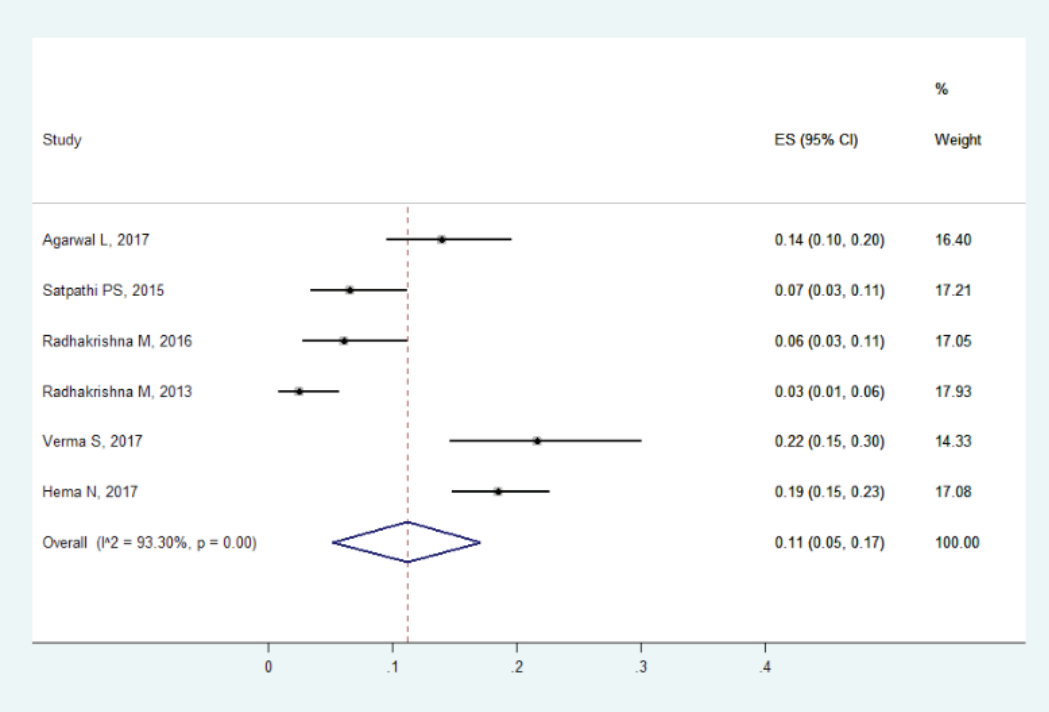

Figure 3: Forest plot of prevalence of nasal carriage status of MRSA among Indian healthcare workers.

Discussion

HCWs can spread infection to patients, as they are closely associated with them in the hospital. Doctors and nurses regularly encounter their patients in a hospital setting during patient care activities. The hands of HCWs are the common transportation for the hospital-associated organisms to cross contaminate between the patients and the hospital atmosphere[31]. Therefore, testing the carrier status and decolonizing the healthcare workers becomes essential to reduce MRSA infection in the hospital. Frequent screening with six months to one-year gap helps in reducing carrier status among HCWs[32].

A meta-analysis empowers greater precision by summarizing the results of all the significant studies conducted in different areas in a specified time. The meta-analysis presented here includes 11 published studies regarding MRSA colonization among healthcare workers from different hospitals of India. We observed more number of studies published in recent years (2016, 2017). However, MRSA can be screened at different locations such as nose, armpit, groin, throat, web spaces of hand and palm and fingertips, most of the studies have included nasal screening. It is also evident that nasal colonization of MRSA is more common than other location in human body[20,30].

But, nasal colonization of MRSA is not homogenous globally[33-37]. In the present meta-analysis, the prevalence of MRSA is nine percent among HCWs. A meta-analysis from Iran shows 32.8% (95% CI: 26.0-40.4) MRSA[39]. In Egypt, a review revealed that the prevalence of nasal carriage of *Staphylococcus aureus* among Egyptian HCWs was 22.9%, in which 58.8% was MRSA[36]. In Ethiopia, 28.8% HCWs were colonized with *Staphylococcus aureus* and 44% of them was MRSA[36]. In China, the prevalence of *Staphylococcus aureus* was 21.6%, in which 4.7% was MRSA[32]. 8.9% HCWs were nasal carriers in Ireland non-acute care health facilities[39]. MRSA carriage among HCWs in Europe and the United States was 1.8%[40]. A meta-analysis reported the average MRSA prevalence among HCWs was 4.6% globally[8]. This different rate among the countries may be due to sampling and sampling technique, sample size, the location of sampling, test performed to detect MRSA, and compliance to infection control policies in hospitals[34,41].

Healthcare workers have higher rate (11.8%) of MRSA carrier status compared to people not exposed (4%) to hospitals[30]. A study has noticed that the postgraduates in a hospital have higher rate of MRSA carriage than that of interns[10] indicating longer the exposure to hospital, higher the rate of colonization. MRSA is detected in the hospital environment such as stethoscopes, aprons, neck ties and frequently touched surfaces like computer monitors, tap and door handles[42,43] and have the ability to survive on abiotic surfaces up to 12 days[44].

Mupirocin is the most frequently used topical antibiotic of choice to combat MRSA colonization among HCWs. It can be used to treat isolated cases as well as during institutional outbreaks[45]. The use of nasal mupirocin is advisable twice daily for five days for decolonization.

MRSA is a global burden and one of the leading cause of hospital-associated infection. Screening every patients who visit hospital may not be feasible in India as we have a highly dense population. At the same time, the high risk of HCWs transmitting the infection to their patients cannot be ignored. Therefore, periodic screening of HCWs is recommended and there should be a mandatory policy on screening of HCWs. The other measure that can bring about reduction in transmission of infection from HCW to patient is by proper hand washing[2].

Noncompliance to hand hygiene, lack of knowledge on infection control measures and its importance, antibiotic abuse, under resourced hospital facilities are the causes of increased MRSA carrier status among HCWs[38]. Few healthcare workers have sufficient knowledge, and they also claim that they are practicing infection control measures during patient care. However, their actual practice of infection control was low[46]. Hence, newer method of hand hygiene monitoring system need to be implemented for the better compliance.

Infection control is considered as one of the quality indicators of a hospital. Most of the hospitals in India have formulated Hospital Infection Control Committee (HICC) striving hard to bring down Hospital Associated Infections (HAI). Screening of HCWs during recruitment is not a routine practice in many of the Indian hospitals. However, HCWs are screened during outbreaks or when

needed. A well formulated hospital policy may address these problem.

This systematic review has few limitations. The representation of the studies were not available from entire geographical regions in India. Hence, the generalizability of the calculated rate must be used cautiously. This review has included published articles only. The reviewed articles have included varied subjects such as doctors, nurses, technicians, students and housekeeping staff. Therefore, additional studies are necessary to find the prevalence rate in each categories of healthcare workers to formulate the policy on periodic screening and decolonization to reduce MRSA burden in the country.

Conclusion

Exposure to infection is an inherent risk of contracting varied infections among healthcare workers. It is an immense challenge as HCWs have frequent contact with patients and may transmit MRSA more frequently. Therefore, screening and decolonizing the healthcare workers becomes significant in reducing MRSA infection. No systematic review on MRSA colonization among healthcare workers was available. This study helps in understanding the burden of MRSA colonization and may be used in policy development on periodic screening and decolonization of healthcare workers. Perhaps, further systematic reviews and meta-analysis are needed among different cadres of healthcare workers to recognize the problem and implement preventive measures.

Ethical Clearance - Permission was obtained from institutional research committee.

Source of Funding- Self

Conflict of Interest - Nil

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