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Effectiveness of disinfectants against methicillin resistant *Staphylococcus aureus* (MRSA) contamination in hospital: a review

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ABSTRACT

Methicillin-resistant *Staphylococcus aureus* (MRSA) contamination is still widely reported in various hospital areas. Despite routine cleaning and preventive measures in places such as hospitals, the prevalence of MRSA is still increasing worldwide, especially in Asia. This review aimed to evaluate the effectiveness of disinfectants against MRSA contamination in hospitals. Articles were searched from PubMed, ScienceDirect, Cochrane, and Google Scholar databases using specific keywords and boolean operators. Journal selection from these databases was based on inclusion criteria, exclusion criteria, and PICOS framework. Studies that did not fit the topic or study design and had paid access and duplication were excluded. A total of five valid and reliable articles found that some disinfectants, such as JUC Polymer, a combination of hydrogen peroxide (H_2O_2) and silver cations (Ag), have effectiveness in eradicating germs or inhibiting the growth of MRSA germs. The application of disinfectants in MRSA also showed benefits in terms of cost. However, the use of disinfectants needs to be considered because they can cause tolerance and resistance. In conclusion, MRSA disinfectants are still proven effective with various methods and precautions. In addition, disinfectants are beneficial in terms of prevention and health financing.

ABSTRAK

Kontaminasi *Methicillin-resistant Staphylococcus aureus* (MRSA) masih banyak dilaporkan di berbagai area rumah sakit. Meskipun pembersihan rutin dan tindakan pencegahan dilakukan di berbagai tempat seperti rumah sakit, prevalensi MRSA masih terus meningkat di dunia terutama di Asia. Tinjauan ini bertujuan untuk mengetahui efektivitas disinfektan terhadap kontaminasi MRSA dan dampaknya. Artikel dicari dari database PubMed, ScienceDirect, Cochrane, dan Google scholar menggunakan kata kunci tertentu dan operator boolean. Pemilihan jurnal dari database ini didasarkan pada kriteria inklusi, kriteria eksklusi, dan kerangka PICOS. Studi yang tidak sesuai dengan topik atau desain studi serta memiliki akses berbayar maka tidak termasuk. Sebanyak lima artikel yang valid dan reliabel melaporkan bahwa beberapa disinfektan seperti JUC Polimer, kombinasi hidrogen peroksida (H_2O_2) dan kation perak (Ag) mempunyai efektivitas dalam membasmi kuman atau menghambat pertumbuhan kuman MRSA. Penerapan disinfektan pada MRSA juga menunjukkan manfaat dari segi biaya. Namun penggunaan disinfektan perlu diperhatikan karena dapat menimbulkan toleransi dan resistensi. Kesimpulan, disinfektan MRSA masih terbukti efektif dengan berbagai metode dan kehati-hatian. Selain itu, penggunaan disinfektan bermanfaat dalam hal pencegahan dan pembiayaan kesehatan.

Keywords:
disinfectant;
effectiveness;
hospital;
MRSA;
resistance

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INTRODUCTION

Staphylococcus aureus is one of the main microorganisms that cause infections in humans. These microorganisms can spread in various places, such as at home or in hospitals. Currently, *S. aureus* shows increasing resistance to different antimicrobial agents.[1] Methicillin-resistant *S. aureus* (MRSA) is one of the *S. aureus* strains that are resistant to β-lactam antibiotics, except cephalosporins and new β-lactams under development.[2,3] Recent studies showed ceftaroline fosamil, which is a fifth-generation cephalosporin antibiotic, to be effective in treating various MRSA infections, including in patients with complicated conditions such as bacteremia and pneumonia.[4-6]

A study reported that MRSA can contaminate patients and objects in the hospital environment for an extended period.[7] Such contamination contributes to the spread of MRSA, especially from infected patients, through direct or indirect contact.[8] Among the hospital areas that are often contaminated with MRSA are 20-50% intensive care unit (ICU), 60-80% burn unit, and 5-15% general ward.[9-11] Moreover, in acute hospital wards, the disease can be isolated in up to 27% of MRSA-positive patient room surfaces.[12]

Methicillin-resistant *S. aureus* is associated with worse clinical outcomes than methicillin-sensitive *S. aureus* (MSSA).[13] It can cause cross-infection, which can occur through healthcare workers' hands or contaminated surfaces, causing problems in the healthcare environment. Therefore, infection control measures such as hand hygiene, screening, decolonization, and environmental cleaning are essential to reduce cross-transmission.[14]

The problem of MRSA is increasing worldwide, and Asia is reported as the continent with the highest incidence rate.[1,15] Most hospitals in Asia are MRSA endemic, with varying proportions: 28% in Hong Kong and Indonesia to over 70% in Korea.[1] The Regional Resistance Surveillance (RSS) program aims to monitor antimicrobial resistance in various regions. In 2011, the RSS Program was held in the Asia-Pacific (APAC) region in four countries, namely China, Indonesia, the Philippines, and Thailand. This program is carried out in an observational manner using primary data in the form of microbial sampling and then observation at the central laboratory. The RSS revealed the proportion of MRSA in clinical isolates of *S. aureus* ranged from 28% in Indonesia to 59% in the Philipines.[16]

A study conducted at Dr. Soetomo General District Hospital, Surabaya, Indonesia showed that the MRSA rate in the nose and throat of its patients was 8.1%.[17] Respectively, patients admitted to surgical and non-surgical wards were 8.2% and 8.0% found to be MRSA positive.[18] This finding also aligns with previous reports on patients discharged from hospitals in Malang in 2014, which recorded a 16-fold increase since the first study.[17,18]

Over time, several strategies have been implemented to minimize MRSA transmission. Hand hygiene strategies, with or without the role of water, were implemented to reduce nosocomial infection rates.[19] In addition, due to its ability to contaminate the environment, MRSA-infected patient rooms require strict disinfection of furniture, bedside tables, handrails, sinks, floors, and any healthcare equipment used during patient care (e.g. stethoscopes, thermometers, tensimeter cuffs).[13] Eventhough, routine cleaning and precautions are still being taken in places such as hospitals, the prevalence of MRSA is still increasing, as described. This raises a fundamental question: are disinfectants still effective in treating MRSA? So far, there has been no review in this regard. Therefore, we aimed to investigate the effectiveness of disinfectants against MRSA contamination in hospitals and its indirect impact.

MATERIAL AND METHODS

Data sources and searches

This systematic review was conducted by searching for studies on the effectiveness of disinfectants in managing MRSA and related indirect effects. The literature search used three databases [PubMed, ScienceDirect, Cochrane, and Google Scholar] to collect journals. The keywords used in the search were (Disinfectant or Hand sanitizer or Contact lens solution) AND (Methicillin-resistant *Staphylococcus aureus* or methicillin-resistant *Staphylococcus aureus*) AND (Hospital or Hospital medicine) AND (Contamination or Equipment Contamination) according to MeSH Terms in NCBI database. We used Mendeley to write and organize references. All methods in this study follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Network Meta-Analyses (PRISMA)[20]. The PRISMA is shown in FIGURE 1.

Eligibility criteria

The article search process used boolean operators. We used the PICO (Populations, Interventions, Comparisons, and Outcomes) framework. The populations in this article are MRSA-positive patients, furniture, and medical objects that surface in hospitals. The interventions in this study are any disinfectant and outcomes are decreased bacterial growth, increased incidence, and other related impacts. The article included a study that completed the following inclusion criteria: experimental research, publications in the last 15 years (2008 - 2023), and written in English. Furthermore, some publications were excluded due to topic differences (n = 51), differences in study design (n = 23), inability to access the full text (n = 4), and duplication of articles (n= 9). Finally, the total number of articles used in this systematic review was five.

RESULTS AND DISCUSSION

Five experimental articles that met the inclusion criteria discussed the effectiveness of disinfectants against MRSA. The characteristics and summary of the five valid studies are summarized in the following table (TABLE 1)

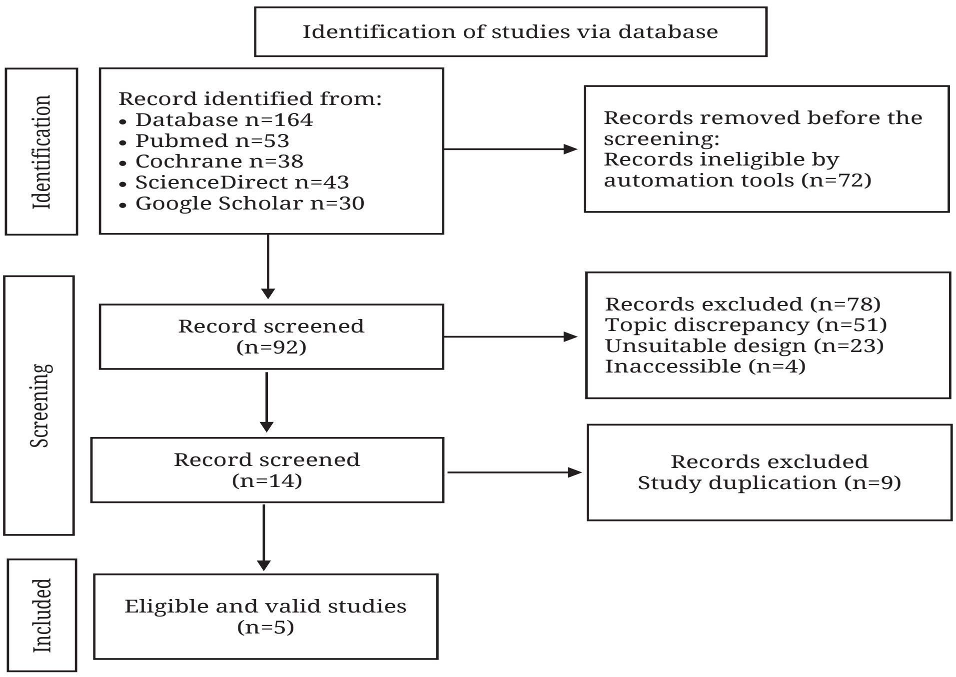

FIGURE 1. The PRISMA used in this study

TABLE 1. Summary of study characteristics

Author (Year)	Countries	Sample	Center	Intervention	Result	Conclusion
Yuen *et al.*,[12] (2015)	Hong Kong	Elderly patient (mean age 77.3 yo with CNS/ MSSA/ MRSA (n=36))	Teaching hospital in HongKong with a capacity of >1500 beds	JUC spray: organosilicon quaternary ammonium chloride (OrganoSi QAC) (n=18)	Decreased MRSA contamination on the surface of objects	MRSA contamination at the bedside was shown to be effectively reduced by the use of JUC OrganoSiQAC-based surfactant as an antimicrobial layer. This JUC demonstrated long-lasting antimicrobial activity for at least 4 hours after application. JUC spray is an environmental decontamination method that can stop the spread of MRSA disease throughout hospital wards.
Bartels *et al.*,[8] (2008)	Denmark	MRSA germs isolated from furniture in experimental hospitals (n=2), experimental hospitals (n=1), experimental households (n=1)	Experimental hospitals (n=2), experimental hospitals (n=1), experimental households (n=1)	Dry-mist-generated hydrogen peroxide (sterinis)	Growth of MRSA bacteria on furniture	MRSA can survive on hospital furniture and fabrics for at least one month, so using Sterinis has proven effective in eradicating MRSA on hospital furniture and sofas used by patients. Sterinis can be recommended as a final cleaning supplement for MRSA isolation rooms. Sterinis is not recommended in domestic settings.
Yang *et al.*[21] (2021)	China	*S. aureus* was isolated from Fourth People's respiratory tract samples of the geriatric psychiatric unit	Hospital of Chengdu. Tiongkok.	Effervescent chlorine disinfection tablets	Detection rate of MRSA in sputum samples from the respiratory tract	Frequency of disinfectant also contributes to the increase in MRSA infection Disinfectants containing high concentrations of chlorine are not recommended because they can make bacterial resistance
Gagné *et al.*[19] (2010)	Canada	Patients with nosocomial MRSA infection	250-beds community hospital, Centre Hospitalier Pierre Le Gardeur, Terrebonne, Québec, Canada	70% ethyl alcohol and 0.5% chlorhexidine gel without water rinsing	MRSA infection incidence per 1000 admissions and cost-benefit analysis	The predominant transmission of MRSA is through the hands. Patient and relative hand hygiene strategies are considered efficient and inexpensive preventive measures against nosocomial MRSA transmission.

TABLE 1. Cont.

Author (Year)	Countries	Sample	Center	Intervention	Result	Conclusion
Rahmi *et al.*[25] (2019)	Indonesia	HA-MRSA isolates with SCCmec type III isolated from patients with MRSA infection	Dr. Soetomo District General Hospital Surabaya, Indonesia	Benzalkonium chloride with 0.625, 1.25, 2.5, 5, and, 10 μg/mL concentration	The MIC of benzalkonium chloride was 5 μg/mL and it is considered active eradicating bacteria	HA-MRSA isolated from Dr. Soetomo Distric General Hospital Surabaya is still sensitive to benzalkonium chloride Benzalkonium chloride can be implemented to eradicate MRSA not only at the Dr. Soetomo District General Hospital Surabaya but also at another hospital

Disinfectant to eradicate MRSA

Health-associated methicillin-resistant *S. aureus* (HA-MRSA) is a strain of *S. aureus* bacteria that is endemic in hospitals. Over the years, many strategies have been conducted to minimize the spread of this bacteria. These strategies include a campaign to reintroduce hand washing, targeted nasal screening of high-risk patients, hand sanitizers, cohorting of MRSA-positive patients in hospitals, and using antibiotics and disinfectants.[19] Several studies discuss the application of disinfectants against MRSA.[8,21] One of these studies conducted by Yuen *et al.*[12] which shows that applying JUC polymer spray can reduce bacterial concentrations from 78 to 11% within 4 hr. JUC is a disinfectant formulated with quaternary cationic organocyclone ammonium chloride with nanoscale technology (OrganoSiQAC).[12]

QACs are membrane-active substances interacting with yeast's plasma membrane and bacteria's cytoplasmic membrane. It also works well against viruses that contain lipids because of its hydrophobic properties.[22] Additionally, QACs bind to DNA and engage with intracellular targets.[23] JUC spray has also been shown to work well for treating skin abscesses associated with MRSA. The use of JUC polymer on the surfaces of critical medical items has been shown in other recent trials to reduce bacterial counts. Among these is evident in urinary catheters, which have a much lower infection rate.[12]

Other research conducted by Barthel *et al.*[8] shows that silver cations (Ag^+) in combination with hydrogen peroxide (H_2O_2) dispersed by the dry mist have the potential to eradicate MRSA from both hospital and residential settings.[8] The highly bactericidal hydroxyl radicals and iron ions are the products of the classic Fenton reaction, which involves hydrogen peroxide and iron ions. According to several studies, the combination of H_2O_2 and PVA-AgNP at low concentrations causes a rapid decrease in bacterial viability over time, ultimately leading to total death of *S. aureus* and *E. coli* after 45 and 60 min. In addition, this combination can also cause a bactericidal effect.[24]

Different things shown in the study by shows MRSA detection rates in sputum samples increased with higher disinfection concentrations and frequencies (1,000 or 500 mg/L twice daily since January 2020 vs. 500 mg/L two to three times per week in the previous four years). Suppose chlorine-containing disinfectants are used in poorly ventilated environments, such as large areas with high concentrations. In that case, they may adhere to the mucosa of open channels, such as the human respiratory tract, for a long time. This can damage the microecological balance in the channel. This is the mechanism underlying the increase in MRSA with increasing concentrations and frequency of disinfectants. Initially implanted in patients' upper respiratory systems, MRSA eventually proved resistant to chlorine-containing disinfectants and eventually emerged as the dominant bacteria in MRSA samples.[21]

Based on research by Rahmi *et al.*[25] benzalkonium chloride is used as a disinfectant to eradicate HA-MRSA with SCCmec type III. The concentrations used varied from 0, 0.625, 1.25, 2.5, 5, and 10 µg/mL to know the minimum inhibitory concentration (MIC) benzalkonium chloride against for eradicating HA-MRSA. After treatment on bacterial growth media, it was found that the minimum inhibitory concentration was at a 5 µg/mL concentration because bacterium that had been inoculated in the media with this concentration died.[25]

Benzalkonium chloride is a quaternary ammonium compound (QAC) that acts as a disinfectant by breaking down the phospholipid double layer of bacterial cells. Once inside the cell, it denatures essential proteins and inactivates enzymes that the organism needs for metabolism.[25] According Weber *et al.*[26] disinfectants work by lysing enzymes and proteins in cells, thus causing the death of bacteria. Treating patients with nosocomial infections due to HA-MRSA with drugs will be challenging because the bacteria resist β-lactam antibiotics.[26] Therefore, nosocomial infections due to methicillin-resistant bacteria can be avoided by using benzalkonium chloride at the recommended concentration.[25]

The mecA gene, which produces a penicillin-binding protein with reduced affinity for b-lactam antibiotics, is a source of methicillin resistance. MecA is a mec "staphylococcal cassette chromosome" (SCC) component, which is part of the genetic elements. SCCmec is flanked by chromosomal recombinase genes (ccrA/ccrB or ccrC) that enable horizontal transmission intra-SCCmec and between species.[27] Environmental factors and regular use of disinfectants encourage MRSA gene mutations, which results in antibiotic resistance.[28]

Methicillin-resistant *S. aureus* strains growing under various conditions usually show different resistance patterns to different antibiotics and disinfectants.[29] Based on research by Rahmi *et al.*[25] HA-MRSA with SCCmec type III was proven to be resistant to methicillin because it carries the mecA gene, which in all MRSA strains codes for methicillin resistance. However, it is not resistant to benzalkonium chloride.[25] In addition, resistance to ampicillin, penicillin, and erythromycin is also caused by mutations in the qac gene.[28] The resistance mechanism of MRSA bacteria to various types of disinfectants and antibiotics, especially benzalkonium chloride, can be caused by several gene mutations, not only one gene.[29]

Incidence of MRSA Infections

Methicillin-resistant *S. aureus* strains are a novel pathogen that can infect humans and animals with moderate to severe illnesses. In humans, the majority of infections caused by this disease range from mild to fatal and include soft tissue and skin infections, including staphylococcal scalded skin syndrome (SSSS), pustules, impetigo contagiosa, abscesses, and papules; serious infections include pneumonia and TSS.[30] Twenty percent of people with MRSA infections per year pass away. Adults, the elderly, and children receiving hospital treatment are common populations for HA-MRSA infections.[30]

Research conducted by Gagne *et al.*[19] A team was formed to meet all visiting patients and their relatives. The team's duties include teaching visitors the importance of good hand hygiene, cleaning hands twice a day on weekdays with an alcoholic gel rinse, and providing brochures about nosocomial infections. Based on the research findings, there was a decrease in the ratio between the total number of cases of nosocomial MRSA infection (acquired at home) and the number of MRSA-positive cases (carriers who were infected and did not show symptoms), from 51% in the comparison year (108 of 210 cases were positively infected) to 37 % (48 of 130 infected cases) in the study year.[19]

Methicillin-resistant *S. aureus* infection rates decreased as a result of increasing hand hygiene compliance in healthcare settings and empowering patients and hospital staff to maintain their safety through education and awareness of nosocomial infections. As a result, from 10.6 to 5.2 instances per thousand admissions, the rate of MRSA nosocomial infections fell by 51%.[19]

Cost benefits

The increase in MRSA cases also has an impact on hospital costs. This is related to the health services needed by patients, starting from screening, isolation, follow-up, contact tracing, cleaning, treatment, and the placement of additional staff because MRSA can be transmitted between patients, patient families, or even health workers.[31] According to a study in the US, *S. aureus* infections resulted in seven million hospital admissions in the country, highlighting the significant harm caused by HA-MRSA. The estimated annual loss from these infections is $2.7 million, a substantial loss of 12,000 deaths per year, and puts the nation's economy under the financial stress of more than $9.5 billion. First, MRSA is primarily associated with healthcare services, and the risk factors contributing to its spread are well-known.[21]

According to research conducted by Kim *et al.*[32] the entire project cost (including salaries and equipment) was estimated at Can$170,000. Additional expenditure (2001 assessment) for infected cases without septicemia was Can$14,360. Bloodstream infections cost 27,083 Canadian dollars. Assuming that MRSA incidence in the comparison year would not have changed, this intervention could have avoided 51 infections, 10 of which would have resulted in septicemia.[32] This resulted in savings of Can$858,843. In addition, MRSA infections can be avoided by using appropriate disinfectants, thereby reducing costs.[31]

Limitation and recommendation

Some studies found that the research was not controlled or conducted at only one centre, so researchers cannot guarantee that annual fluctuations do not affect the research results. The second limitation is that some studies state that further research is needed to investigate the mechanism of MRSA tolerance to chlorine-containing disinfectants in experimental animals.

We recommend that future research be designed with controlled studies, employing proper controls and randomization to minimize the impact of confounding variables. This will help establish cause-and-effect relationships and improve the reliability of the results. Designing and conducting animal model experiments to investigate the mechanisms of MRSA tolerance, particularly concerning chlorine-containing disinfectants. This can provide valuable insights into the underlying mechanisms.

CONCLUSION

In conclusion, there are various ways to eradicate MRSA through disinfection, such as quaternary ammonium organosilicon cations (OrganoSiQAC), hydrogen peroxide (H_2O_2), benzalkonium chloride, silver cations (Ag), or those containing chlorine. The application of disinfectants plays a role in preventing MRSA infections, benefiting both patients and hospitals in terms of reducing the incidence of cases and hospital expenses. However, the use of disinfectants should not be excessive, as it can reduce their effectiveness and lead to tolerance.

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