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Review Article

# Methicillin Resistant *Staphylococcus aureus* (MRSA) a Challenge for Health Care- Professionals and Patients

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## Abstract

Following the first report in 1961, methicillin-resistant *Staphylococcus aureus* (MRSA) has progressively become a leading cause of nosocomial infections. In recent years, MRSA have become a truly global challenge. MRSA infections in hospital have obviously imposed a significant burden of morbidity and mortality, and strain on healthcare resources. The virulence of MRSA strains is increasing in both hospital and community settings highlighting the importance of their rapid identification in order to appropriately control infection, regular screening of carriers is required for the prevention of nosocomial infection.

Initial educational programs need to be followed by reinforcement and infection control staff should evaluate intrahospital compliance and identify lapses for further measures and education. Proper measures need to be undertaken to control infection rates by every available method; antibiotics alone may not be sufficient to win this war.

**Keywords:** MRSA; Staphylococcus aureus; Antibiotics

## Introduction

It is well known that infectious agents cause significant morbidity and mortality all over the world. In medical profession health team members are often exposed to different kind of health hazards. This is not limited to only health professionals but patients and their relatives also come under this risk. Thus, the question is; which kind of hazards are prevalent into hospital settings for example chemical hazards, such as carbon dioxide, nitrogen dioxide, acids, carbon mono oxide, etc which can affect through skin or inhalation and can cause skin allergies, cancers, or respiratory, disorders etc. The next is psychological hazards which includes organizational leadership, task and role demand, interpersonal intra departmental conflicts, life and career changes etc can leads to psychological disturbances and can be a cause of lack of motivation, fatigue, exhaustion. Environmental hazards like different noises, radiations, heat, air, ventilation etc. are also common into hospital surroundings which can cause genetic disorders, cancers, hearing loss, eye allergy, etc. The biohazards caused by bacteria, viruses, fungi, etc. are very common in hospital settings. The main focus of this paper is on biohazards due to bacteria called as Methicillin-resistant *Staphylococcus aureus* (MRSA). In recent years, MRSA have become a truly global challenge.

Hospital acquired infection or nosocomial infections such as "MRSA" is well known that contribute in morbidity and mortality at large. Methicillin-resistant *Staphylococcus aureus* (MRSA) is well recognized as a major cause of nosocomial infections worldwide and is associated with high morbidity and mortality rates with rapid development of resistance [1,2]. MRSA performs significant role in patient prolonged process and even in the deaths. Center for disease control and prevention (CDC) reported that "more than 90,000 life-threatening illness and nearly 19,000 deaths associated with MRSA occur yearly in the United States" [3]. Moreover, a survey report in Europe also showed 25,000 deaths each year by negative-gram infections [4]. It is also assumed that MRSA contribute not only in morbidity, mortality but also in long duration of stay, repeated admission in hospital, and cost burden as well. For example, "the death rate, length of stay, and cost of treating patients with MRSA are more than double than other hospital admissions" [5]. In fact, many health professionals and patient also felt it is a cause of stress and stigma for them, therefore MRSA plays a significant depressing role on the health professional and patient lives. It is mentioned in nursing action; "be aware that staff found to be MRSA carriers may experience stigma in the workplace" [3].

Moreover, a range of negative psychological and physiological effects as a consequence of source isolation have been reported, including psychological stress. In addition, for thousands of years those with infections were treated with dread and loathing; they were ostracized and excluded from general society [6]. Many studies have mentioned loneliness, anger, neglect, abandonment, boredom and stigmatization [7-12].

Therefore, the aim of this review paper is to provide the prevalence and the basic effective knowledge about MRSA. Furthermore, diagnosis, community care, prognosis and preventive measures will be the part of this review in order to understand the basic aspects of this dangerous organism.

## Background

*Staphylococcus aureus (S. aureus)* is a facultative anaerobic, gram-positive coccal bacterium also known as "golden staph" and Oro staphira. In medical literature, the bacterium is often referred to as *S. aureus. S. aureus* appears as grape-like clusters when viewed through a microscope, and has large, round, golden-yellow colonies, often with hemolysis, when grown on blood agar plates (Figure 1).

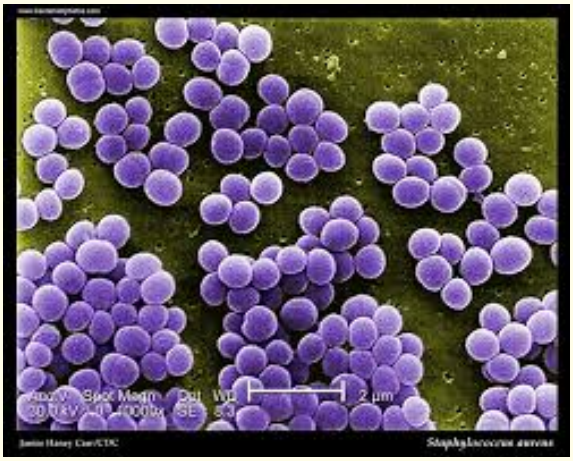


**Figure 1:** Electron micrograph of Staphylococcus aureus.

*S. aureus* is a key pathogen, which is implicated in nosocomial and community acquired infections [13,14].

Infection caused by *S. aureus* can be endogenous, where the infectious organism is found in the patient's body, or exogenous, where the organism is transmitted from an external source.

Methicillin-resistant *Staphylococcus aureus* (MRSA) first appeared in 1961 and since then there have been many reports of MRSA causing various infections throughout the world [15].

Methicillin resistance is clinically very important because a single genetic element confers resistance to the beta-lactam antibiotics, which include penicillin's, cephalosporins and carbapenems [16]. The age of penicillin saw the rapid emergence of resistance in *S. aureus* due to a plasmid-encoded penicillinase. This β-lactamase quickly spread to most clinical isolates of *S. aureus* as well as other species of staphylococci.

*S. aureus* resistance to methicillin and oxacillin is associated with integration of a mobile genetic element- "Staphylococcal cassette chromosome mec" (SCCmec) - into the chromosome of S.aureus t at contains resistance gene mecA. mecA gene encodes PBP2a protein, a new penicillin-binding protein, that is required to change a native staphylococcal PBP. PBP2a shows a high resistance to β-lactam antibiotics (they do not bind to β-lactams) and ensures cell wall synthesis at lethal β-lactam concentrations (Figure 2 and 3). Over the period of 20 to 30 years, MRSA strains have been present in hospitals, hospital-acquired MRSA (HA-MRSA); they have become a major cause of hospital-acquired infection. Community-acquired MRSA (CA-MRSA) emerged worldwide in the late 1990s [17].

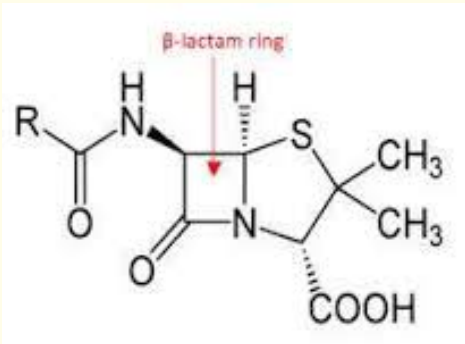


**Figure 2:** β-lactam ring.

Health care professionals, largely nurses working long in health institution are prone to get infected with MRSA. Thus, their unawareness about MRSA is greater risk in health institutions as they tend to spread MRSA infection to their patients because of

poor or malpractices of infection control. "Transmission of MRSA occurs primarily via the contaminated hands of healthcare workers who do not follow appropriate infection control measures" [18]. Moreover, Lindberg [19] said that "the multidrug-resistant bacteria (MDRB) Attitude Questionnaire showed that registered nurses do have knowledge deficiencies" and more than 85% of MRSA cases linked with healthcare settings [3] "health care workers' the hands are the most common vehicle for the transmission of healthcare-associated pathogens from patient to patients and within the healthcare environment" [20]. Staphylococci that are shed into the environment may survive for long periods in dust. Skin scales may contaminate if they become airborne - e. g, during activities such as bed-making, or if the affected person is heavily colonized or has a condition such as eczema which causes shedding of high numbers of organisms.

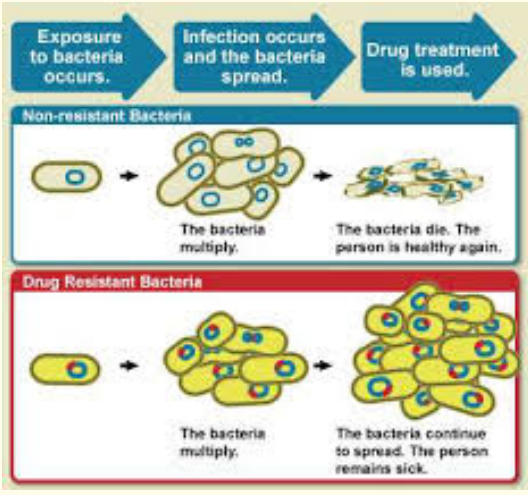


**Figure 3:** Antibiotic Resistance Mechanism.

Therefore, the hands of the health care workers are the predominant mode for patient to patient transmission. Thus, working with the life of clients; health professional should have to be accountable to sense their responsibility and understand the sensitiveness of MRSA not only on patient life but their own lives as well.

## Prevalence of MRSA among Healthcare Workers and Patients

It is also important to put light on the prevalence of MRSA among health care provider. Many studies showed that MRSA is prevalent among health care providers. "The increased prevalence of MRSA in health care settings poses an increased risk of exposure to MRSA among health care workers" [21].

Moreover, various studies reported prevalence rates of MRSA infection between 1% and 15% among health professionals [21-24]. MRSA infections have long been associated with health care setting such as clinical area and nursing homes. These settings are characterized by a sick general patient coupled with high antibiotic usage which selects from drug-resistance, are a perfect environment for MRSA strains to gain a grip [25]. Moreover, "mean nasal MRSA carriage in health-care workers was 4.1% in 104 studies (range 0-59%)" [26-29]. In addition, according to Thomas, 2004 [30], "The spread of antibiotic-resistant strains of micro-organisms such as methicillin-resistant Staphylococcus aureus (MRSA) represents an ever-increasing threat to the health of vulnerable people throughout the world who are obliged to spend extended periods in healthcare facilities. The organism is also responsible for increasing the financial burden placed on such centers and the wider community at large, with the result that precious financial resources are diverted from other areas of need to deal with the consequences of infection." It is difficult to get data related to prevalence of MRSA among health professionals from developing countries because no enough studies has been conducted on this issue or many cases remains unreported such as in developing countries, the use of unsafe equipments, syringes, medical devices, blood products, inadequate surgical procedures, deficient biomedical waste management and lack of resources result thousands of infections acquired not only from patient but from health care workers as well most of them unreported [31]. The other cause to increase the MRSA infections is shortage of staff and less knowledge about MRSA infection especially in developing countries as "understanding and low level of staff preparedness and knowledge are key factors leading to poor infection control in developing countries.

The WHO Health report [32] revealed that worldwide, 57 countries (all developing) currently have critical staff shortages, equivalent to a global deficit of 2.4 million physicians, nurses, and midwives. Giving this situation, the education and recruitment of infection control professionals is very far from being a realistic solution" [32]. These are the reasons that many health workers and patients get this kind of infections and remain mostly untreated and the rate of hospital acquired infections remains high. According to the report of World Health Organization (WHO), [33] estimates that the proportion of reused syringes and needles without sterilization is between 1.5% and 69.4% in developing countries. On the other hand, the prevalence of MRSA among health care workers and patient well presented in western countries "about

one-third of general population carry staphylococcal microbes [3]. Moreover, estimates of health care workers' carrier status range from 50% to 90%". MRSA prevalence is increasing.

In 1990 only 5% of all S. aureus bacteraemias (blood infections) were MRSA. Between 2001 and 2006 the proportion rose to around 40% [34]. Further, on exploring the different studies MRSA is also prevalent among the patients as well. A high prevalence of MRSA (22.3%) was reported in a study from Al-Kharj city of Saudi Arabia [1]. "The number of hospital admissions for MRSA has exploded in the past decade. By 2005, admissions were triple the number in 2000 and 10-fold higher than in 1995", [6] furthermore, in 1978, over a six-month period, 61 patients at a university hospital became colonized or infected with MRSA [35].

A cohort followed of 479 hospital patients colonized with MRSA and 53 patients (11.1%) subsequently developed 68% MRSA infections [36]. It was explored that, "Infections caused by community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) are being increasingly observed in patients who lack traditional risk factors. They described 8 postpartum women who developed skin and soft-tissue infections caused by MRSA at a mean time of 23 days (range, 4 - 73 days) after delivery. Infections included 4 cases of mastitis (3 of which progressed to breast abscess), a postoperative wound infection, cellulitis, and pustulosis" [26]. These studies indicate strong prevalence rates among health care workers and patients. Moreover, these prevalence rates also indicate that how much it will be stressful for the health workers and patients as well.

Antibiotic resistance is a global problem. New forms of antibiotic resistance can cross international boundaries and spread between continents with ease. Many forms of resistance spread with remarkable speed. World health leaders have described antibiotic resistant microorganisms as "nightmare bacteria" that "pose a catastrophic threat" to people in every country in the world. Each year in the United States, at least 2 million people acquire serious infections with bacteria that are resistant to one or more of the antibiotics designed to treat those infections. At least 23,000 people die each year as a direct result of these antibiotic-resistant infections. Many more die from other conditions that were complicated by an antibiotic resistant infection.

Antibiotic-resistant infections add considerable and avoidable costs to the already overburdened US healthcare system. In most cases, antibiotic-resistant infections require prolonged and/or costlier treatments, extend hospital stays, necessitate additional doctor visits and healthcare use, and result in greater disability and death compared with infections that are easily treatable with antibiotics. The total economic cost of antibiotic resistance to the US economy has been difficult to calculate. Estimated cost of antibiotic resistance has ranged as high as $20 billion in excess direct healthcare costs, with additional costs to society for lost productivity as high as $35 billion a year [37]. The use of antibiotics is the single most important factor leading to antibiotic resistance around the world. Antibiotics are among the most commonly prescribed drugs used in human medicine. However, up to 50% of all the antibiotics prescribed for people are not needed or are not optimally effective as prescribed. Antibiotics are also commonly used in food animals to prevent, control, and treat disease, and to promote the growth of food-producing animals. The use of antibiotics for promoting growth is not necessary, and the practice should be phased out. Recent guidance from the US Food and Drug Administration describes a pathway toward this goal [38].

The other major factor in the growth of antibiotic resistance is spread of the resistant strains of bacteria from person to person, or from the non-human sources in the environment, including food. There are four core actions that will help fight these deadly infections:

- Preventing infections and preventing the spread of resistance
- Tracking resistant bacteria
- Improving the use of today's antibiotics
- Promoting the development of new antibiotics and develop ing new diagnostic tests for resistant bacteria

Bacteria will inevitably find ways of resisting the antibiotics we develop, which is why aggressive action is needed now to keep new resistance from developing and to prevent the resistance that already exists from spreading.

## Impact of MRSA on Health Professionals and Patients

Impact of MRSA Infection from a resistant organism increases morbidity and mortality risk for the patient as well as healthcare costs. Compared to a methicillin-susceptible *S. aureus* (MSSA) infection, MRSA infections are associated with an increase in severity of disease (APACHE II Classification System), sometimes requiring additional specialized medical treatments (ventilation, surgical debridement, hyperbaric therapy, isolation, etc.), a decrease in options for antibiotic therapy that is more costly, often more toxic to the patient and sometimes not as effective, an increase in hospital length of stay, and sometimes outcomes with debilitating morbidity and even death [35, 40-42]. MRSA continues to remain a growing problem, within our healthcare facilities and in our communities. Surveillance data from the CDC National Nosocomial Infections Surveillance (NNIS) system report showed that from 1998 through 2002, 45% - 52% of *S. aureus* isolates collected from infections in ICU patients were MRSA. In 2003, 60% of those isolates were MRSA, representing an 11% increase in resistance in 2003 compared to the mean resistance over the previous five years. NNIS data from 1998 through 2004 revealed that of the number of *S. aureus* isolates tested, the pooled mean percent that were MRSA for ICUs was 53%, for Non-ICU inpatient areas was 46%, and for outpatient areas was 31% [42]. A recent study of MRSA hospitalizations reported an estimated 477,927 hospitalizations with a diagnosis of *S. aureus* infection annually in US hospitals. Of these, approximately 278,203 hospitalizations are related to MRSA [43].

In different studies [44,45] colonized or infected health-care workers were temporarily removed from patient care for varying durations until documentation of negative follow-up culture was obtained. Moreover, removal from patient care was implemented for longer period of time if result remains positive. If relapse occurred, or if clear breaches in infection control standards were observed, as was the case in a health-care worker with chronic sinusitis involved in an outbreak in an operating theatre [46,47]. One of the nurse positive with MRSA suspected presence of MRSA in her tonsils and had removed that because to be intact in healthcare work environment. Although it was uncertain whether MRSA was actually present in her organ or not but after surgery she became MRSA negative. Now the moral question is raised that how far health professionals will go as they have chosen to work in health care and do not allow a bacterium to interfere with their profession [48,49]. Therefore, Psychological or physiological effects leave its negative impact on health professionals. Nerys [50] said that "It emphasizes the importance of avoiding, feelings of guilt or stigma among colonized health care staff, and of not disrupting relationships between practitioners and the infection control team". Furthermore, psychological effects on patients such as, participants from three studies showed lack of visual contact, meaningless activities during isolation. Some of them make themselves busy such as watching TV, and cleaning rooms while others became attention seeking behaviour and anxious [7,51,52]. Further, patients also feel negative if treated as isolated such as "patients with MRSA are isolated and may have restricted access to treatments and services. The practice of isolation remains common and is considered by some as a vital control measure. However, there are complaints that these patients are treated as 'modern day lepers' and restrictions should be relaxed. Concerns are growing that patients with MRSA are socially isolated, denied access to services and subject to the stress of unfamiliar treatments and regimens" [48]. Patients also experience different kind of behaviour from health professional such as Eileen said, "*…sometime the doctors would come and open the door a crack and talk to me through the crack in the door, rather than having to put on apron, and mask and gloves… I would have preferred them to have come in and had their discussion*" [53]. Moreover, the experience of quarantined patients affected by sever acute respiratory syndrome, felt isolated, and lack of social contact with family and friends. A patient "Diane" admitted in hospital said about her friends that, *"when they come in they want to give me a kiss or a hug… I would say 'No, no you can't touch me because I might be contaminated or contagious,… and I wasn't sure how much of that could do",* [53]. These psychological effects also interrupt with the care and treatment of the patients. The central characteristics of patient experiences, and perceptions, 'Behind the Barriers', suggest that patients with MRSA isolation imposes barriers to the expression of own identity and normal interpersonal relationships, and impact on delivery of quality

care [53]. Further, few studies also report that "isolation can cause sensory deprivation, resulting in disorganized behavior and symptoms such as boredom, lack of coherent thinking, anxiety, fear and depression" [54,55]. Isolated patient had a statistically significant increase in anxiety and depression levels and the susceptibility and severity of altered mood states increased with length of isolation [11,51,56]. The other impact of MRSA creates problems for burns patients. MRSA is a particular hazard for burns patients and has the potential to cause significant morbidity and mortality in these patients because disruption of normal skin barrier and depression of immune system makes them more vulnerable to colonization and infection [57]. Moreover, "the presence of MRSA infection also reduces the chance of survival, particularly in association with lower respiratory tract infections, as the risk of mortality was three times higher in patients with MRSA than in those with Methicillin-sensitive *Staphylococcus aureus* [58]. The other impact is infections caused by MRSA are difficult to cure and result in increased mortality. The treatment cost also rises dramatically because of increased usage of antibiotic and prolong hospital stay, with the side effects that result from the use of more toxic antibiotics adding to the cost in human terms" [59].

### MRSA/VISA/VRSA *S.aureus:*

Future Considerations for MRSA, VISA, and VRSA *S. aureus* can be found all around us and is a part of our public health history. Based on current indications, the incidence and prevalence of MRSA will continue to rise. The risk groups and environments for HA-MRSA and CA-MRSA will intermix and soon the distinctions between the two may become blurred. The current epidemiology must be clearly defined and understood, so that the changing epidemiology can be tracked and described appropriately. Without this knowledge, effective intervention and prevention programs cannot be developed or implemented. We need evidence-based educational messages and control measures to keep transmission of this organism in check. Although the total number of reported VISA and VRSA cases currently remains low, new infections continue to be identified. The number of cases confirmed in Michigan has already raised concern. The dynamics of these cases must be defined and understood, so that further occurrences can be controlled and the possibility for transmission prevented. The serious threat of losing vancomycin as an effective antimicrobial agent increases as the number of VISA and VRSA cases climbs, taking us closer to the end of our current antibiotic lifeline.

For the treatment of VRSA only limited drugs are available. Quinupristin-dalfopristin and linezolid are two of the newer antimicrobial agents currently available with activity against drug-resistant staphylococci (including most VISA and VRSA strains *in vitro*). Though cross-resistance has not been noted for linezolid, isolates have known to develop resistance during therapy. Daptomycin, a bactericidal agent that damages the cytoplasmic membrane, is undergoing clinical trials [60]. Other agents in the pipeline include modified glycopeptides, carbapenems, oxazolidinones, quinolones and tetracyclines. But as they are still in the developmental stages, it will take almost a decade for new drugs to be launched.

Avoiding irrational use of antibiotics and having rational antibiotic policy is the only way forward till then.

### Investigations

- Rapid diagnosis of hospital-acquired infection is essential in order to start appropriate treatment early and also initiate procedures to prevent the spread of MRSA.
- Molecular testing methods (polymerase chain reaction (PCR) tests) are now available to identify MRSA within several hours. PCR from culture samples may be used to detect the mecA gene, confirming the presence of MRSA. Fully automated commercial tests are now available [13].
- MRSA DNA has now been decoded and a test based on two duplex reactions run simultaneously can detect MRSA, methicillin-resistant coagulase negative staphylococci and meticillin-susceptible *S. aureus* (MSSA) [61].
- A PCR-free test available at the point of care has been developed [62].

### Care in the Community

- While the risk of serious infection with MRSA is low in the community, it still exists. In 1996, the Department of Health issued guidelines for managing MRSA in nursing and residential homes. Further guidance was published by the British Society for Antimicrobial Chemotherapy Working Party on Community-onset MRSA Infections in 2008 and general guidance on prevention and control of infection in care homes was published by the Department of Health in 2013 [63,64].
- Standard infection control procedures are important. MRSA-positive patients should not be isolated in community homes; instead, patients should socialize as

normal. However, they should not share a room if they have a chronic open wound or invasive device, such as a urinary catheter.

- In the patient's own home there should be no restrictions to a normal life and people with MRSA can work and socialize as usual. They do not need to restrict contact with friends, children or the elderly. If they are admitted to hospital, where the risk of infection is increased, the ward should be informed so the patient is screened on admission and nursed appropriately.
- Community healthcare workers should practice standard infection control precautions, such as aseptic technique for wound care. They must decontaminate their hands before and after giving care, either by using soap and water or an alcohol hand rub.

## Prognosis

MRSA is no more dangerous or virulent than other varieties of *S. aureus* but it is much more difficult to treat because the range of antibiotics which are effective against it is reduced.

## Prevention

All patients going into hospital for a relevant planned procedure are now screened for MRSA beforehand.

## Healthcare Workers [65-67].

Guidelines vary for screening of healthcare workers for MRSA but it is essential that all healthcare workers closely follow local guidelines. It has been shown that healthcare workers are a significant source of MRSA on hospital wards, especially from nasal and hand colonisation. Hand hygiene is particularly important even when in contact with presumed 'low-risk' sources in the patient's environment such as medical notes and computers. Healthcare workers should therefore not work while known to be MRSA-positive, particularly if they are dressing wounds, treating surgical patients or dealing with physically vulnerable patients. To help prevent the spread of MRSA in a healthcare setting: [68,69].

- Hand cleansing using soap and water, alcohol gel or other hand cleansing solution should be carried out regularly.
- Topical treatments such as chlorhexidine should be applied to the skin of colonized patients.
- Keep the environment as clean and dry as possible [70].
- Wear gloves when managing wounds. After removing gloves, wash hands with soap and warm water, or use alcohol-based hand sanitizer.
- Carefully dispose of dressings and other materials that come into contact with blood, nasal discharge, urine, or pus from patients infected with MRSA.
- Clean surfaces in examination rooms, with commercial disinfectant or a 1:100 solution of diluted bleach.
- Equipment in regular use such as blood pressure cuffs can be a significant source of infection and should be cleansed regularly [71].
- Nasal carriage is usually transient, in some cases lasting only a matter of hours. Therefore, routine screening of staff for MRSA carriage is not recommended. Local guidelines may vary but there may be merit in screening staff for persistent colonization (including nasal, throat and groin swabs) as they come on duty [69].

Looking at the prevalent rate, feelings, experiences and impact of MRSA on health care workers and patients it is important for both of them (health professionals and Patients) that they should have the proper knowledge of MRSA. They also have to understand the consequences of MRSA, and have to adopt preventive measures to eradicate MRSA infection from hospital environment. In short, preventive measures are better than cure, because of being inexpensive and less difficult but only needs compliance and critical attention from both health care- workers and patients.

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