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INCIDENCE OF NASAL COLONIZATION BY COMMUNITY-ASSOCIATED METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (CA-MRSA) INFECTION DURING 2000 TO 2017

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ABSTRACT

Staphylococcus aureus (*S. aureus*) is a spherical microorganism, Gram-positive cocci, and common bacterial flora, considered an opportunistic human pathogen that can cause a large number of infections. The skin and nasal mucosa are the site concentrations of these bacteria in humans. *S. aureus* infections were treated with penicillin originally, however, new resistant strains emerged and beta-lactam, such as methicillin, was an antimicrobial of choice. However, multiresistance is a current reality and there are a lot of reports of methicillin-resistant *Staphylococcus aureus* (MRSA), followed by some reports of vancomycin resistant of *S. aureus* (VRSA). The occurrence of MRSA was restricted to the hospital (HA-MRSA), but with the emergence of resistant strains and the transport of bacteria by carrier individuals' nosocomial to community it started to colonize and infect health people in community. This study aims to correlate the incidence of nasal colonization and infection by community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) in the period of 2000 to 2017 through representative studies of current literature in order to bring new findings in the literature. The research was made in international databases of scientific articles from 2000 to 2017. In the present study, only nasal colonization incidence was selected. It was possible to observe that there was an increasing in the spread of this strain in the community in this period. Our data reinforce the hypothesis that the increase of CA-MRSA nasal colonization rates may contribute to the development of severe infection cases. However, more studies are necessary with a larger number of samples to prove and evaluate the causal association of this dissemination in the community and the incidence of nasal colonization and infection by CA-MRSA.

INTRODUCTION

The first clinical use of *Staphylococcus aureus* (*S. aureus*) was accidentally by Alexander Fleming in 1928, with the discovery of the fungus *Penicillium notatum* that inhibited the growth of *S. aureus* in cultures, indicating an antibacterial action (antimicrobial component activity that inhibits bacterial cell wall synthesis by preventing cross-links between peptideoglycan bands resulting in bacterial lysis) (Oliveira *et al.*, 2010; WHO, 2016; Murray, 2004).

S. aureus is considered an opportunistic human pathogen and it is frequently associated with infections acquired in the community and in the hospital environment. The most common infections involve the skin and wounds in several sites of the body. The severity of the diseases depends on the virulence of *S. aureus* strain and the affected region (Razera *et al.*, 2009). It could cause simple infections such as boils, acnes and cellulites to those serious, such as pneumonia, meningitis, endocarditis, toxic shock syndrome and septicemia (Masunari & Tavares, 2007; Santos *et al.*, 2007). The nasal mucosa are of particular importance in relation to other *S. aureus* colonization sites due to the large number of methicillin-resistant strains found in healthy and non-hospitalized individuals in this site, which demonstrates the pattern of dissemination of MRSA in the community (Masunari & Tavares, 2007). In the last decades, a pattern of antimicrobial resistance evolution from hospitals to the community has been observed (Palos *et al.*, 2006; Cambridge University Press, 2012; Gordon *et al.*, 2008; Ratti *et al.*, 2009).

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Nasia Safdar and Elisa Bradley (2008) did a systematic review to provide an overall estimate of the risk of infection following colonization with MRSA compared with colonization by MSSA. It was observed 10 observational studies with a total of 1,170 subjects (CI 95%), and they concluded that colonization by MRSA was associated with a 4-fold increase in the risk of infection (odds ratio 4.08, 95% confidence interval, 2.10-7.44), and nasal, axillary or inguinal colonization with *S. aureus* generally precedes invasive severe infections.

The present study is a mini review of the current literature regarding nasal colonization by CA-MRSA. It was used scientific articles indexed in databases, such as PUBMED/MEDLINE, Scielo, ISI Web of Science, Lilacs, EMBASE, EXCERPTA MEDICA. A total of 69 articles were used, however 14 were selected as a reference for discussion of the proposed topic due to its statistical and epidemiological relevance regarding the incidence of cases in the community of MRSA from nasal colonization. The small number of articles used for discussion revealed the difficulty in finding relevant articles with this site of colonization for CA-MRSA.

The objective of this mini review was to present the incidence of nasal colonization and CA-MRSA infection between the years of 2000 to 2017 in the current literature.

S. Aureus

S. aureus is a Gram-positive cocco that grows following a pattern that resembles bunches of grapes. This size is from 0.5 to 1µm diameter. The cytoplasmic components of staphylococci do not change from the general components of a bacterial cell; however some of them may contain flagella (Murray *et al.*, 2004). They are catalase and coagulase positive, facultative anaerobic, ferments mannitol, glucose, lactose and maltose, and resists to heat and dehydration and current disinfectants.

Table 1 Virulence factors of *S. aureus*.

Factors	Component	Action
Surface	Capsule	Classification of the samples into serotypes, based on the antigenic variability of the capsular polysaccharides (CP). The most frequent are serotypes 5 (CP5) and 8 (CP8).
	Peptiteoglycans and Teichoic Acids	They activate the alternative pathway of complement and stimulate the production of cytokines.
	Protein A	It prevents antibodies from interacting with phagocytes cells (protection against phagocytosis along with the capsule).
	Adhesins	They are proteins that bind to fibronectin, collagen and fibrinogen. They are anchored in peptideoglycan and promote tissue colonization by *S. aureus*.
Extracellular	Toxins	Alpha-toxin / alpha-hemolysin: It is a hemolysin with ability to form pores in the cell membrane of leukocytes, promoting cell content output, and cell death. This rupture of the membrane can release cytokines that contribute to the development of septic shock. Other hemolysins which cause red cell lysis are beta, gamma and delta. Leucocidin: It is present in 90% of the severe dermonecrotic lesions. Superantigens: TSST-1 (toxic shock syndrome toxin-1): this is the toxin responsible for staphylococcal toxic shock (STS). Enterotoxins (ES): they are the direct cause of staphylococcal food poisoning with the stimulation of T lymphocytes to release cytokines, which cause shock. Toxins that degrade adhesion molecules: Exfoliative toxins: exfoliatin and epidermolysin are responsible for the scalded skin syndrome, which consists of the separation of the epidermis from the dermis.
	Enzymes	Coagulase: It coagulates plasma by transforming prothrombin into thrombin which activates the formation of fibrin from fibrinogen. Fibrinolysin: It abilities to dissolve clots. Other enzymes: catalase, deoxyribonucleases (DNase), hyaluronidase, lipase, proteases and staphylokinase. The hydrolysis of different proteins and other molecules can generate nutrients that could be used by *S. aureus*, and facilitate their dissemination through the tissues.

The cell wall of staphylococci consists in capsule (layer of polysaccharides that protects bacteria by inhibiting chemotaxis and phagocytosis, and also facilitates adherence to synthetic materials); peptideoglycans (structural component composed of cross-linked glycan chains with peptides, which gives greater rigidity to the wall); protein A (it coats the surface of staphylococci and binds to the peptideoglycan layer, being effective in preventing the elimination of the microorganism by the immune system); teicoic acids (polymers containing phosphates bound to the peptideoglycan layer or to the plasma membrane and mediate the staphylococcal attachment to the mucosal surfaces); agglutination factor (protein that causes agglutination or aggregation of staphylococci); cytoplasmic membrane (complex of carbohydrates, proteins and lipids that act as an osmotic barrier and fixation site for enzymes) (Murray, 2004; Koneman, 2001; Trabulsi, 2002).

Virulence Factors

The main virulence factors of *S. aureus* are the cell surface components, toxins and enzymes (Table 1) (Murray, 2004; Cambridge University Press, 2012; Koneman, 2001; Trabulsi, 2002; Moreira *et al*., 1998).

Antimicrobial Resistance (MRSA)

The first antimicrobial used in the therapy of *S. aureus* infections was penicillin. It was effective until the 40's of last century when the first isolated cases of resistance began to emerge (Santos *et al.*, 2007; Gelatti *et al.*, 2009a; Mimica & Mendes, 2007). Molecular modifications occurred in the structure of the precursor of penicillin in order to resist of the action of beta-lactamases produced by the resistant strains, and the semisynthetic beta-lactams, such as methicillin and oxacillin, appeared against resistant *S. aureus* instead of penicillin (Mimica & Mendes, 2007; Gelatti *et al.*, 2009b). This pathogen has a high capacity to develop antimicrobial resistance, especially in the hospital environment, where antibiotics are widely used (Pereira & Cunha, 2009).

Methicillin and its analogue, oxacillin, are antimicrobials routinely used in hospitals for the treatment of infections caused by *S. aureus*. These drugs attach to penicillin binding

proteins (PBP's) preventing the formation of the cell wall and promoting bacterial lysis (Santos *et al.*, 2007; Stefani *et al.*, 2010; Gelatti *et al.*, 2009; Kobayashi *et al.*, 2009). However, this barrier was broken, resulting in methicillin-resistant *Staphylococcus aureus* (MRSA), with the need for new antimicrobials capable of containing a resistant infection, such glycopeptides as vancomycin and teicoplanin. But, strains of *S. aureus* resistant to vancomycin had already appears in Japan (1997), United States (2006) and Brazil (2000) hospitals (WHO, 2016, Anvisa, 2017).

The first documented cases of CA-MRSA infections occurred between Australian and Native American aborigines in Canada in the early 1990s. Subsequently, these infections spread throughout the world. In Brazil, the first isolates characterized as CA-MRSA were similar to the clone OSPC (Oceania Southwest Pacific clone) and came from a single city in the south of the country (Porto Alegre, RS, BrAzil) (Golin *et al.*, 2013; Rozembaum *et al*., 2009; Ribeiro *et al*., 2005).

The mechanisms that microorganisms may exhibit drug resistance are:

1. The production of enzymes that destroy the active drug;
2. The modification of their permeability to the drug;
3. The development of an altered structural target for the drug;
4. The development of an altered metabolic pathway that deviates from the inhibited reaction by the drug;
5. The development of an altered enzyme that still has the capacity to perform its metabolic function but is much less affected by the drug (Nicolini *et al.*, 2000; Flier e Fluit, 2003; Fortes *et al*., 2003).

This resistance was mediated by the acquisition of genes encoding enzymes, initially known as penicillinase and now called β-lactamases. In the 1950s, the production of penicillinase by *S. aureus* predominated in strains isolated from hospitalized patients. In 1960, methicillin was marketed as a therapeutic alternative for penicillinase-producing strains, since this drug does not undergo this enzyme action. However, as early as 1961, reports of methicillin-resistant strains have now been described and the so-called methicillin-resistant *S. aureus* (MRSA) have been identified (WHO, 2016; Cambridge University Press, 2012).

In 1959, the isolation of 6-aminopenicillanic acid (6-APA) made possible the production of semisynthetic penicillins. Modifications in the chain of this precursor of penicillin resulted in protection of the beta-lactam ring against the hydrolytic action of beta-lactamase. The first of these antimicrobial agents available for clinical use were oxacillin and methicillin, which temporarily solved the problem caused by resistance of *S. aureus* to penicillin. However, the use of these agents was rapidly followed by the emergence of resistant strains in 1961. Since then, resistance rates of *S. aureus* to methicillin have increased dramatically. Resistance to methicillin in *Staphylococcus aureus* is most often determined by the presence of a gene located in the chromosome, the mecA gene, which is responsible for the synthesis of penicillin-binding protein that replaces the other membrane binding proteins and have low affinity not only for methicillin but also for other beta-lactam antibiotics. The phenotypic resistance to methicillin is extremely variable and depends on the expression of the mecA gene. This variability is recognized as phenotypic heteroresistance and is characterized by the fact that all heterogeneously resistant bacteria populations carry the mecA gene (Mimica & Mendes, 2007).

Methicillin resistance occurs due to the lack of affinity between the antibiotic and the proteins that bind to the class of penicillins. The mechanism of resistance is related to the alteration of penicillin binding proteins (PBP), encoded by the mecA gene and unrelated to beta-lactamase production. The gene mecA and its regulatory gene are located in a mobile genetic element, Staphylococcal Cassette Chromosome mec (SCCmec), that encode the protein PBP2a, which is the responsible for the low affinity of methicillin and penicillinase-resistant compounds for the binding site in the pathogen. Some of these types of SCCmec are antibacterial multiple genes in addition to the beta-lactams, macrolides, lincosamides, streptogramins, tetracycline, ingsaminoglycosides leading a phenotype of multiple-resistance (McCulloch, 2006; Ito *et al.*, 2003).

Some strains of *S. aureus* present a bordeline resistance. It is a less common type of resistance to methicillin/oxacillin and it is not related to the presence of mecA gene. This mechanism of resistance may be due to the hyperproduction of β-lactamase, strains known as BORSA (borderline oxacillin-resistant *S. aureus*); modifications to penicillin binding proteins (PBPs 1, 2 and 4); and strains known as MODSA (modified penicillin-binding protein *S. aureus*) (Enrigth *et al.*, 2012).

MRSA is resistant to all β-lactam antibiotics, penicillins, cephalosporins, monobactams and carbapenems due to the low affinity of these antibiotics to the expressing receptors of the pathogen (Enrigth *et al.*, 2012). Thus, with the onset and spread of methicillin resistance, glycopeptides were the option for the treatment of this pathogen. Because of the high resistant of MRSA, the treatment of the infections caused by this resistant pathogen become complicated due to the limited number of therapeutic options. The therapeutic should consider the sensitivity to antibiotics of each isolated strain (Hanssen and Sollid 2006; Reinert, 2004). The glycopeptides vancomycin and teicoplanin are the classic drugs of choice for the treatment of MRSA infections in hospitalized patients, while sulfa and clindamycin are used for those who are not hospitalized. The prevalence of MRSA strains ranges from 40 to 80% in Brazil, and the SCCmec Type III is the most prevalent in nosocomial infections, which is resistant to aminoglycosides, chloramphenicol, lincosamides, macrolides, quinolones, sulphamethoxazole, tetracyclines, and trimethoprim (Gardella *et al.*, 2005; Sader *et al.*, 1993).

Vancomycin and teicoplanin are glycopeptide antibiotics used in the treatment of MRSA infections. Teicoplanin is a structural congener to vancomycin which has similar spectrum activity, but with a longer average duration (t½). Despite the slow oral absorption, these antibiotics are administered intravenously to infections in the body (system), with the exception of pseudomembranous colitis where vancomycin can be administered orally (Fiol *et al*. 2010).

Cases of resistance to glycopeptides have begun to appear since 2000 (Figure 1) and many of the new MRSA strains that were found showed antibiotic resistance even to vancomycin and

teicoplanin. Linezolid, quinupristin, daptomycin, tigecycline are the most current therapeutic additions, usually reserved for the most serious infections, which glycopeptides cannot respond to. Less serious infections can be treated with oral agents, such as linezolid, rifampicin + fusidic acid, pristinamycin, cotrimoxazole (trimethoprim + sulfamethoxazole), doxycycline, and clindamycin, especially used in no nosocomial patients (Hoefler *et al*, 2006; Holloway, 2003; Kampf *et al*., 1998; Fiol *et al*. 2010).

Chronology of resistant strains of S. aureus (MRSA, CA-MRSA and VRSA)

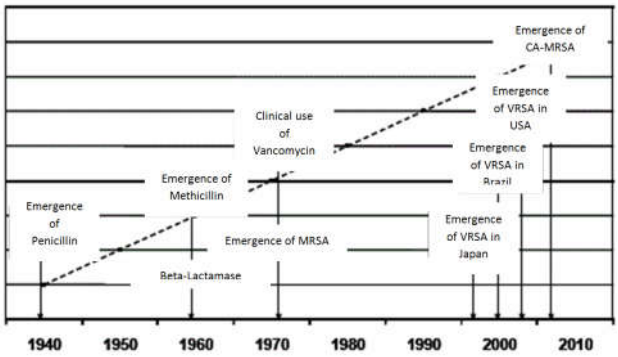

Figure 1 Emergence of *S. aureus* resistance to beta-lactams and vancomycin (Mimica & Mendes - adapted, 2007).

The mechanism of resistance of these strains to glycopeptides is due to the existence of an important thickening of the bacterial cell wall of *S. aureus*, which hinders the penetration of glycopeptides. No specific gene related to this resistance has been described. This mechanism of resistance is remained unclear until now, but studies suggest that this phenomenon can be mediated by accumulation of material or by changes in the cell wall (Anvisa, 2017). There are some options for vancomycin-resistant treatments through linezolid (WHO, 2016).

On May 8, 2006, the researchers from Merck Pharmaceuticals, according to Chem Med Chem Journal, reported that they had discovered a new type of antibiotic, called platensimicin, and demonstrated that it could be used to effectively combat MRSA. However, more studies are being doing for proving the results of this new antibiotic against MRSA (Häbich & von Nussbaum, 2006).

RESULTS AND DISCUSSION

In the present study, only studies related to the incidence of nasal colonization by *S. aureus* were selected, knowing that there is a higher incidence of this pathogen in this anatomical region. We considered 14 studies about the incidence of nasal colonization and CA-MRSA infection between 2000 and 2017, crossing information about nasal colonization by *Staphylococcus aureus* and *Staphylococcus* coagulase negative in the community and its resistance and sensitivity to methicillin (Tables 2 and 3) (Nilsson & Ripa, 2006; Oliveira *et al*., 2015; Pacheco, 2008; Santos, 2009; Tavares, 2000; Vandenesch *et al*., 2003) .

Table 2 presents the incidence of *S. aureus* and *Staphylococcus* coagulase negative in the study populations, showing a mean of 37.82% for *S. aureus* infection with nasal colonization site. These results demonstrate the importance of the pathogen and the nasal colonization as a site of infection when comparing with the great diversity of staphylococci and the other sites of infection. The Table 1 also shows that the nasal colonization is a place capable of spreading *S. aureus* in the community in health people, indicating that the colonization site plays an important role in the dissemination of the pathogen (Pacheco, 2008; Santos, 2009; Tavares, 2000; Vandenesch *et al*., 2003).

Table 2 Incidence of nasal colonization by *Staphylococcus aureus* and *Staphylococcus* coagulase negative in the community

Author	Samples	*Staphlylococcus aureus*	*Staphylococococus* negative coagulase
Santos, 2000	252	90 (36.0%)	162 (64.0%)
Bresolin, 2005	90	42 (46.7%)	48 (53.3%)
Menegotto, 2007	100	40 (40.0%)	60 (60.0%)
Leite, 2008	68	12 (17.6%)	56 (82.3%)
Pereira, 2009	109	30 (27.5%)	79 (72.5%)
Steffani, 2010	25	05 (20.0%)	20 (80.0%)
Correa, 2012	100	29 (29.0%)	71 (71.0%)
Nagat Sobhyl, 2012	50	38 (76.0%)	12 (24.0%)
Onofre, 2013	200	70 (35.0%)	130 (65.0%)
Ribeiro, 2014	102	39 (38.2%)	63 (61.8%)
Goulart, 2015	348	50 (14.3%)	298 (85.6%)
Albuquerque, 2015	55	19 (34.5%)	36 (65.5%)
Oliveira, 2016	977	929 (95.0%)	48 (5.0%)
Franchi, 2017	204	42 (20.6%)	162 (79.4%)
Total	2,680	1,435	1,245

Although three of the 14 articles selected did not present resistance or sensitivity to *S. aureus*, it was possible to trace a profile of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) and methicillin-susceptible *Staphylococcus aureus* (MSSA) due to the results obtained corroborate the current literature (Table 3). This profile showed a superiority of MRSA found in the community in relation of MSSA with a mean of 16.18% in the incidence of this pathogen in the community. The results present the importance of this pathogen in the community and its consequences related to public health because of the more easily of spreading MRSA strains between healthy people out-of-hospital population (Bustos-Martínez *et al*., 2006; Kluytmans *et al*., 1997; Gorwitz *et al*., 2008; Lowy, 1998; Fernandes *et al*., 2005; WHO, 2016).

Table 3 Incidence of *Staphylococcus aureus* and its resistance and sensitivity (CA-MRSA and CA-MSSA).

Author	*S. aureus*	MRSA	MSSA
Santos, 2000	90	-	-
Bresolin, 2005	42	-	-
Menegotto, 2007	40	03 (7.5%)	37 (92.5%)
Leite, 2008	12	01 (1.5%)	11 (16.2%)
Pereira, 2009	30	10 (30%)	20 (70.0%)
Steffani, 2010	05	0	05 (100.0%)
Correa, 2012	29	09 (31.03%)	20 (68.97%)
Nagat Sobhyl, 2012	38	18 (47.37%)	20 (52.63%)
Onofre, 2013	70	12 (17.14%)	58 (82.86%)
Ribeiro, 2014	39	-	-
Goulart, 2015	50	29 (42%)	21 (58.0%)
Albuquerque, 2015	19	04 (21.1%)	15 (78.9%)
Oliveira, 2016	929	52 (5.3%)	877 (94.7%)
Franchi, 2017	42	40 (95.23%)	02 (4.74%)
Total	1,435	178	1,086

The results of the studies presented in Tables 2 and 3 demonstrated an incidence of 20% to 40% of *S. aureus* carriers. The broad spectrum of MRSA resistance with the high

incidence rates of MRSA is a challenge to public health because of the change in the epidemiological pattern of MRSA infections occurred due to its extrapolation from the hospital environment to the community (Veronesi & Focaccia, 2015; Bannerman, 2003; Cruz, 2008; Fagon *et al*., 2002; Faria, 2009).

Santos *et al.* (2000) showed a 36% of incidence for positive samples of *S. aureus* in the nasal of healthy nursing students of Federal University of Ribeirão Preto, SP, Brazil. This study evidenced how the time of exposure to the hospital environment influenced in the nasal colonization of nursing students. Although the profile of antimicrobial susceptibility and resistance has not been done, the survey of the study confirmed what the current literature has revealed in relation to the nasal cavities as the site of higher frequency of *S. aureus* and MRSA.

Pereira *et al.* (2009) obtained 109 samples from nasal cavities in the students from Federal University of Ceará, CE, Brazil. This study presented 27.5% of the samples positive for *S. aureus* and 72.5% negative, and those positive for *S. aureus*, 30% were MRSA. Franchi *et al.* (2017) collected 204 samples from nasal cavities of individuals from public units of health in Botucatu, SP, Brazil, and 95,23% of the samples were MRSA, indicating a greater profile of resistance. Stefanni *et al.* (2010) presented a study with 25 individuals in the community who worked in intensive care units (UTI); however none was identified as MRSA.

Bresolin *et al.* (2005) obtained 90 samples from people in the community that worked in a food industry, and presented that 46.7% were positive for MRSA. There is a strong cross-correlation between MRSA contamination and MRSA colonization from the hospital to the community in the current literature, however, this study revealed that resistant strains of methicillin-resistant *S. aureus* are already prevalent in the community and not necessarily only spread through hospital to community, but also through person-to-person in the community among healthy individuals. This study emphasize the need for health control of food handlers, guidelines for strict hygiene and cleaning of the kitchens; cleaning of hands and nails and awareness of the danger of skin, nose and eye infections, and the importance of education, biosafety and awareness of the risk of large-scale food production and the critical factors that trigger the spread of this resistant strains.

Leite *et al.* (2008) obtained 68 samples in community and divided with subgroups of possible *S. aureus* carriers. After the analysis, 17.6% were considered as asymptomatic but nasal colonized carriers for *S. aureus*, and 1.5% of this was MRSA. Nagat *et al.* (2011) collected 50 samples from ambulatory patients attended at the Department of Dermatology in the School of Medicine of University of Alexandria, and identified a high percentage of positive samples (76%) and 47.37% of these positive were producers of penicillin binding protein 2a (PBP2a) and diagnosed as MRSA.

Goulart *et al.* (2011) collected 348 nasal swabs in order to investigate the frequency of colonization by *S. aureus* in hospitalized patients: 298 (85.6%) were negative for *S. aureus* and 50 (14, 3%) were positive, of which 29 (42%) had resistance to methicillin. After assessing the epidemiology of *S. aureus* colonization and risk factors, the author concluded that the detection of MRSA lineage circulating in health services may be signaling a route of cross-transmission of these microorganisms between hospitals and the community. Therefore, the development of effective prevention strategies to control the spread of MRSA in healthy people is crucial to stop and create a barrier to the increase of CA-MRSA.

Ribeiro *et al.* (2011) did an analysis of 204 samples of university students from Fortaleza, CE, Brazil, in which 102 of them were collected from nasal swabs, in which 39 (38.2%) were positive for *S. aureus* and 63 (61.8%) were *Staphylococcus* coagulase negative, reinforcing, however, that nasal colonization is the main site of the focus of the infection by *S. aureus*. This study showed the importance of the identification of who are the carriers that could act as vectors of the dissemination of *S. aureus* in the community.

Albuquerque *et al*. (2015) studied children with varicella in Goiania, Goiás, Brazil, and verified nasal colonization by *S. aureus* in 19 of 55 (34.5%) patients, in which 4 (21.1%) of them were MRSA. Of the total of these 55 patients, 29 (52.7%) were attended in daycare centers; 6 (10.9%) were hospitalized for more than 24 hours in the previous year; 3 (5.5%) had daily intimate contact with a relative who works in the health area; and 14 (25.5%) used beta-lactams antibiotics in the last 30 days preceding the interview. This analysis demonstrated a statistically significant association between *S. aureus* colonization and bacterial resistance, the problems related about the use of antibiotics, and the issues about family members who works in the health area. The author emphasizes the need for more studies with a larger number of samples in order to evaluate the causal association of the presence of CA-MRSA and its frequency and dissemination.

Correa *et al.* (2012) collected 100 pregnant women attended at the maternity hospital of Cartagena, Colombia. Thirty-four of them were colonized by *S. aureus*, in which 29 were in nasal site. This study corroborates with the current literature regarding the nasal mucosa as the largest site of *S. aureus* colonization. Although risk factors associated with colonization with MRSA strains during pregnancy have not been fully characterized, it is necessary to carry out prevention during pregnancy in order to identify the probable foci of infection, since during pregnancy the body of the mother undergoes important metabolic alterations, which can lead to the risk of developing severe infections.

Onofre *et al.* (2013) collected 200 samples of children in a nursery of Francisco Beltrão, Paraná, Brazil. Of these samples obtained, 70 were positive for *S. aureus* and 12 of them were MRSA. This study showed a high incidence of children colonized by *S. aureus*, indicating that they could be potential vectors of dissemination of MRSA in the community.

In a study with 100 nasal swab specimens randomly collected from non-hospitalized subjects in Rio Grande do Sul, Brazil, Menegotto *et al.* (2007) showed a population of 40% with nasal colonization by *S. aureus* without any reports of infection or hospital admissions, surgeries, dialysis or catheters. The study revealed a new scenario about CA-MRSA because there was no correlation between hospital environments and the specific community of samples collected. This study points to a predisposing factor for infections caused by *S. aureus* in asymptomatic carriers that usually act as reservoirs for infection.

Oliveira *et al.* (2016) collected 977 samples from volunteers of both genders in the community randomly. From all samples, 929 were positive for *S. aureus* and 52 MRSA, indicating the presence of the resistant strains in healthy subjects of community, nasal colonization as the largest site of infection, and no relation between de cross-relations linked hospital to community.

The origin of CA-MRSA strains is subject to debate and remains unclear until now. One of the possibilities is the offspring of hospital strains, which occurred through a vertical transformation. Other possibility is that community strains have emerged as a consequence of a vertical transfer of methicillin resistance genes; however, this transfer happens very rarely. CA-MRSA strains are the consequence of one of these rare events of transfer of the mec from a donor to a susceptible subject. However, all these hypotheses are still under study (Veronesi & Focaccia, 2015; Atique *et al*., 2012).

CONCLUSION

Despite the large number of studies related to CA-MRSA, few articles refer to colonization and nasal infection rates of CA-MRSA. Although the CA-MRSA incidence has been observed among the selected articles in this study, it is difficult to determine a reliable incidence or specific patterns of antimicrobial resistance in this population. More studies are needed in order to obtain a determinant CA-MRSA value for nasal infection and a specific antimicrobial resistance standard that can guide a specific treatment protocol.

Many studies pointed to the presence of CA-MRSA in healthy individuals who did not have prior contact with the hospital or health environment, however, the studies showed a cross-relation between hospital or health institutions environments and the spread of MRSA strains in community, which corroborate with current literature. However, other studies revealed that CA-MRSA is present in community in healthy subjects that do not have contact with health environments.

This mechanisms of adaptation of these resistant strains need to be studied in order to invest in the continuous education and periodic bacteriological control of people who work or move in hospitals or health settings to control or minimize the risks of such dissemination in the community.

The present study shows that *S. aureus* in the community grows markedly. Despite the limited size of our sample, which does not allow us to gauge the results for the entire population, the results obtained corroborate the incidence found in the current literature. Thus, the data reinforce the hypothesis that the increase in CA-MRSA colonization rates may contribute to the increase in the severity of infection cases for nasal colonization. However, more studies are necessary with a larger number of samples to prove and evaluate the causal association of this dissemination in the community and the incidence of nasal colonization and infection by CA-MRSA.

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