JOURNAL of Nursing
Revista de Enfermagem
UFPE On Line
JNUOL
ISSN: 1981-8963

INTEGRATIVE REVIEW ARTICLE

INFECTION BY RESISTANT *STAPHYLOCOCCUS* AUREUS IN INTENSIVE CARE UNITS: INTEGRATIVE REVIEW
INFECÇÃO POR *STAPHYLOCOCCUS AUREUS* RESISTENTE EM UNIDADES DE TERAPIA INTENSIVA: REVISÃO INTEGRATIVA
INFECCIÓN POR STAPHYLOCOCCUS AUREUS RESISTENTE EN UNIDADES DE CUIDADOS INTENSIVOS: REVISIÓN INTEGRADORA

Daniele Martins de Sousa[1], Álvaro Francisco Lopes de Sousa[2], Aline Raquel de Sousa Ibiapina[3], Artur Acelino Francisco Luz Nunes Queiroz[4], Maria Eliete Batista Moura[5], Telma Maria Evangelista de Araújo[6]

ABSTRACT

Objective: discussing from the national and international scientific production, the aspects related to the reported prevalence of resistant Staphylococcus aureus in Intensive Care Units and the associated risk factors. *Method:* an integrative review, in order to answer the guiding question << *What is the prevalence of hospital infections caused by resistant Staphylococcus aureus in intensive care units, and its associated risk factors?* >>. It was held in the databases LILACS and Science Direct, between 2004 and 2014, considering the inclusion and exclusion predetermined criteria. *Results:* there were selected in all eight articles. The associated risk factors were invasive procedures performed, previous exposure to antibiotics, the patient's own predispositions before his pathological condition, immunosuppression, endogenous contamination of professionals and patients, as well as length of stay in the ICU. *Conclusion:* the Staphylococcus aureus is a major problem in hospital infection control. *Descriptors:* Staphylococcus Aureus; Methicillin-resistant Staphylococcus Aureus; Hospital Infection; Intensive Therapy.

RESUMO

Objetivo: discutir a partir da produção cientifica nacional e internacional, os aspectos relacionados à prevalência relatada de *Staphylococcus aureus* resistentes em Unidades de Terapia Intensiva e os fatores de risco associados. *Método*: revisão integrativa, com vistas a responder a questão norteadora << *Qual a prevalência das infecções hospitalares causadas por Staphyloccocus aureus resistente em unidades de terapia intensiva, e seus fatores de risco associados?* >>. Foi realizada nas bases de dados LILACS e Science Direct, entre 2004 e 2014, considerando-se os critérios de inclusão e exclusão pré-estabelecidos. *Resultados*: foram selecionados ao todo oito artigos. Os fatores de risco associados foram procedimentos invasivos realizados, exposição prévia a antibióticos, predisposições do próprio paciente diante a sua condição patológica, imunossupressão, contaminação endógena dos profissionais e pacientes, bem como tempo de internação nas UTIs. *Conclusão*: o *Staphylococcus aureus* resistente representa um grave problema no controle de infecção hospitalar. *Descritores*: Staphylococcus Aureus; Staphylococcus Aureus Resistente a Meticilina; Infecção Hospitalar; Terapia Intensiva.

RESUMEN

Objetivo: discutir, desde la producción científica nacional e internacional, los aspectos relacionados con la prevalencia de Staphylococcus aureus resistente en Unidades de Cuidados Intensivos y los factores de riesgo asociados. *Método:* esta es una revisión integradora, con el fin de responder a la pregunta principal << *¿Cuál es la prevalencia de las infecciones hospitalarias causadas por Staphylococcus aureus resistente en las unidades de cuidados intensivos, y sus factores de riesgo asociados?* >>. Se celebró en la bases de datos LILACS y Science Direct, entre 2004 y 2014, teniendo en cuenta los criterios de inclusión y exclusión predeterminados. *Resultados:* fueron seleccionados en los ocho artículos. Los factores de riesgo asociados fueron procedimientos invasivos realizados, la exposición previa a antibióticos, predisposiciones del propio paciente antes de una condición patológica, la inmunosupresión, la contaminación endógena de los profesionales y de los pacientes, así como la duración de la estancia en la UCI. *Conclusión:* el Staphylococcus aureus resistente es un problema significativo en el control de la infección hospitalaria. *Descriptores:* Staphylococcus aureus; Staphylococcus aureus resistente a la meticilina; Infección Hospitalaria; La Terapia Intensiva.

[1]Nurse. Master's Student of Nursing at the Federal University of Piaui/UFPI. Teresina (PI), Brazil. Email: danielemartinss@hotmail.com; [2]Student, Graduate Nursing, Federal University of Piaui/UFPI. Teresina (PI), Brazil. Email: sousa.alvaromd@gmail.com; [3]Nurse, Master's Student of Nursing at the Federal University of Piaui. Teresina (PI), Brazil. Email: alineraquel8@hotmail.com; [4]Student, Graduate Nursing, Federal University of Piaui/UFPI. Teresina (PI), Brazil. Email: aacelino@hotmail.com; [5]Nurse, Post Doc. Graduation, Teaching at the Graduate and Postgraduate Nursing Program UFPI. Teresina (PI), Brazil. Email: mestradosaudedafamilia@uninovafapi.edu.br; [6]Nurse, Professor, Graduate and Postgraduate Diploma in Nursing, Federal University of Piaui/PPPGENF/UFPI. Teresina (PI), Brazil. Email: telmaevangelista@gmail.com

INTRODUCTION

The intensive care unit (ICU) is considered a critical environment in health care as a result of intense scientific and technological advances, the increasing recognition of new infectious agents and resurgent infections. In this environment patients have 5 to 10 times more probability of contracting infection, so that it holds approximately 20% of hospital infections. This environment provides greater patient risk of infection due to human factors involving endogenous and environmental conditions, such as clinical conditions and variety of invasive procedures that are routinely subjected. The length of hospital stay also favors a wide proliferation of microorganisms, because the longer the stay in the hospital more exposed to risk factors become the patients.[1-2]

The increases in infection rates Related Assistance to Health (HAIs) caused by the stay in the intensive care units, are directly related to the risks they are subject to these patients and their vulnerability arising from invasive methods employed.[3] The main risk factors related to infections include generally over the age of 60, use of corticosteroids, previous use of antibiotics, prolonged hospitalization and the presence of invasive medical devices.[4-5]

Infections Related Assistance to Health (IRAS), are configured in one of the main diseases that threaten patient safety, especially in the hospital setting. They are characterized as any infection acquired after the patient's admission to hospital. The IRAS may also manifest during hospitalization or after discharge, provided they are related to hospitalization or procedures performed during hospitalization.[6]

Based on recent data from the World Health Organization (WHO) estimated that 1.4 million infections occur at any time in developed countries as well as developing countries. In the US, it is estimated that about 2 million HAIs occur annually, resulting in between 60 and 90 thousand deaths and a cost of at least 17-29 billion dollars. On average, 5% to 15% of all hospitalized patients develop IRAS. In Brazil, it does not have precise estimates in the absence of databases. Thus, it is appropriate to state that the IRAS stand as one of the most important public health problems in the world.[7]

The ICU has recorded high rates of HAIs, including the occurrence of multi-drug resistant microorganisms. Research worldwide, reveal concern with regard to multidrug resistance in the ICU, and has noted that this issue has threatened society, particularly the pharmaceutical industry, which is no therapeutic response.[2]

This is justified by the fact that indiscriminate use of antibiotics, in turn, promotes the resistance that occurs when bacteria acquire genes that allow interference with the antibiotic mechanism of action by mutation. There is a considerable decrease in the therapeutic arsenal making the cure time consuming and expensive, and sometimes unattainable.[8] Thus, the microorganisms colonizing patients remain part of environmental microbes, becoming the subsequent infections agents.

Bacterial resistance is currently a major public health problem worldwide. For health care professionals has become a growing challenge to the extent that therapeutic options for the treatment of some infections caused by resistant microorganisms (MR) are becoming stricter.[9]

The Staphylococcus aureus is the pathogen with the highest mortality rate due to its high virulence and high prevalence in health institutions becoming a serious therapeutic problem because of this resistance of bacteria in ICU patients, their susceptibility to developing infections. Knowing that the rates of Staphylococcus aureus resistant strains in Brazilian hospitals are significant (40-80%), it is important to recognize the prevalence of this pathogen in ICU patients for proper implementation of an active microbiological surveillance program aimed at reducing these infections.[10]

Based on the above objective, it was to discuss from the national and international scientific production the aspects related to the reported prevalence of resistant Staphylococcus aureus in intensive care units and the associated risk factors

METHODOLOGY

To achieve the objectives of this study, we used the integrative literature review. The choice of method is made by the same enabling gather and synthesizing the results of multiple studies published on delimited theme in a systematic and orderly manner, contributing to the research theme of deepening. Moreover, it is considered an important evidence-based practice tool.[11] For the development of the review, it ran through six stages: preparation of the guiding research question; relevance of test preparation, searching the scientific literature for primary school; data extraction; evaluation of primary studies; analysis and synthesis of the results

and presentation of the review.[11-12] The guiding question was elaborated by the PICO strategy (P: patient, I: intervention, C: comparison and O: outcomes or outcome) as follows: "What is the prevalence of hospital infections caused by Staphylococcus aureus in intensive care units, in the literature, and their risk factors?" So we tried to identify prevalence and risk factors.

Defined the object of study, searches were carried out in the databases, by two trained researchers. The bases were: Latin American and Caribbean Health Sciences (LILACS); and SciVerse Science Direct (Elsevier), using a combination of controlled descriptors, registered in the Descriptors in Health Sciences (DeCS): "Staphylococcus aureus" [and] 'Staphylococcus aureus resistant to methicillin, "[and]" hospital infection "[and]" "intensive care"; with its variations in the Portuguese, English and Spanish, ensuring rigor in selection of articles process.

Thus, if employed as inclusion criteria: only primary studies that had directly link the theme; it is available in full and to understand the time frame proposed for the study, 2004 to 2014. As an exclusion criterion of articles that addressed neonatal or pediatric ICUs, which were repeated in the databases, opinion pieces, reflection and editorials.

In the next stage, a relevant test was applied, in which it addressed the year, language, methodology and applicability of the results in practice. After reading the titles and abstracts evaluated the methodological rigor of the studies measured the interventions and the findings, study type and level of evidence: 1 - systematic reviews or meta-analysis of relevant clinical trials; 2 - evidence of at least one randomized controlled clinical trial clearly delineated; 3 - well-designed clinical trials without randomization; 4 - cohort studies and well-designed case-control; 5 - systematic review of descriptive and qualitative studies; 6 - evidence derived from a single descriptive or qualitative study; 7 - authorities of opinion or expert committees including information not interpretations based on research.[12]

Thus, it obtained a total of 405 publications in LILACS and 217 in SciVerse Science Direct, 08 articles, as established criteria. The analysis and synthesis of primary studies were performed in a descriptive way, allowing the reader a summary of each study included in the RI and comparisons highlighting differences and similarities between the studies.

RESULTS

From the articles that met the inclusion criteria there were obtained in the sample eight articles produced between 2006 and 2013, and in 2006 three publications, in 2013 with two publications and in 2007, 2011 and 2012 with a publication each, five in the Portuguese, two in English and one in Spanish, as shown in Figure 1.

Figure 1 presents data on the articles analyzed by the year, database, title and magazine publishing. Regarding the indexation of six related publications were found in LILACS and two in Science Direct. The most related to periodic disclosures of the research were the American Journal of Infection Control with two publications.

Sousa DM de, Sousa ÁFL de, Ibiapina ARS et al.   Infection by resistant *staphylococcus aureus*...

Order	Level of evidence	Publishing journal	Database /Year	Article's title	Objectives
A1	II	*American Journal of Infection Control*	*Scienc Direct 2006*	Risk factors for ICU-acquired methicillin-resistant Staphylococcus aureus infections[13]	Investigation of the risk factors for MRSA infections acquired in intensive care.
A2	II	*Infectio*	LILACS 2006	Prevalence of staphylococcus aureus resistant to Methicillin in staff of the Bolivarian university clinic, Medellin 2004 intensive therapy unit [14]	Determining the prevalence of Staphylococcus aureus resistant nasopharyngeal and throat in ICU staff.
A3	II	Brazilian Journal of Epidemiology	LILACS 2006	Comparative study of the prevalence of Staphylococcus aureus imported into the ICU of a university hospital of Pernambuco, Brazil.[15]	Checking the prevalence and factors associated with nasal and skin colonization by MRSA and MSSA, if imported into the ICU at the Hospital studied.
A4	II	Brazilian Journal of Intensive Care	LILACS 2007	Prevalence of Nosocomial Infection in intensive care units of Rio Grande do Sul [16]	Determining the prevalence of infections acquired in INTENSIVE CARE and the risk factors for these infections, to identify infectious organisms more prevalent, evaluate the relationship between ICU-acquired infection and mortality.
A5	II	Acta Paulista of Nursing	LILACS 2011	Methicillin-resistant Staphylococcus aureus on surfaces of an intensive therapy[17]	Evaluating the presence of MRSA in areas close to the patients admitted to a General ICU.
A6	II	USP Nursing School Journal	LILACS 2012	Colonization by Staphylococcus aureus in nursing professionals of a teaching hospital of Pernambuco.[18]	Identifying the prevalence of colonization by Staphylococcus aureus in nursing professionals of a university hospital.
A7	II	*American Journal of Infection Control*	*Science Direct 2013*	Risk factors for and impact of methicillin-resistant *Staphylococcus aureus* nasal colonization in patients in a medical intensive care unit.[19]	Investigating the impact and predictive factors of MRSA.
A8	II	Science, Care and Health	LILACS 2013	Prevalence and profile of Staphylococcus Aureus isolates in patients and nursing staff.[20]	Determining the prevalence of carriers of S. aureus among patients and members of the nursing staff of an ICU of a general hospital.

Figure 1. Characterization of the articles, according to year of publication, database, title and publication journals. Teresina (PI), 2014.

It is observed that studies in general, stopped to identifying the prevalence of Staphylococcus aureus in Intensive Care Units; determine the percentage of these infections in this environment and the factors associated with colonization by this agent.

Figure 2 presents the main results of the studies found.

Order of the Articles	Main results of the studies
A1	Found a prevalence of Methicillin-resistant Staphylococcus aureus of 8,4%, among the 249 patients studied, being the largest number of involvement by bloodstream infections (47%), followed by pneumonia (38%) and surgical site infection (14%). The period of stay in the ICU, intra-abdominal diseases and orthopedic, mechanical ventilation, insertion of central venous catheter, total parenteral nutrition, prior use of antibiotics, Surgical ICU hospitalization, MRSA nasal colonization, and the presence of more than two patients with nasal colonization in the same ICU were significant for MRSA.
A2	The prevalence of Methicillin-resistant Staphylococcus aureus was 6,7%. The anatomical region in which obtained the largest number of isolates corresponded to his nostrils. There were no reported risk factors.
A3	The prevalence of s. aureus was 37,7%, and 13% Methicillin-resistant and 24,8% of Methicillin-sensitive. There was no significant association between origin and colonization by s. aureus, regardless of the strain, and between previous relocation and presence of Methicillin-resistant s. aureus.
A4	The Staphylococcus aureus was the most prevalent microorganisms. Risk factors: central vascular access, urinary catheter, tracheal intubation for extended time (> 4 days), chronic illness, trauma and prolonged hospitalization in intensive care (> 30 days).
A5	76.19% of the samples were positive for Staphylococcus aureus, and 60.4% were Methicillin-resistant. The results suggest that the areas around the patients constituted an important threat, since they represent secondary reservoirs of MRSA.
A6	The MRSA prevalence of 25.8% was obtained. Among the variables studied, the age and the amount of EPI were associated with colonization by the micro-organism. All the forty-two strains, only five (11,90%) showed Methicillin-resistance.
A7	There were identified MRSA-positive patients 06 and 07 MRSA-negative patients. Univariate analysis advanced age, Diabetes Mellitus, acute kidney disease, congestive heart failure, surgery performed to 03 months and admission to the ICU, as important risk factors for colonization by MRSA.
A8	The prevalence of Staphylococcus aureus among patients was 54,76% and among employees 59,04%. The main risk factors observed in the study were the presence of isolated microorganisms on the hands and foyers of professionals and patients nasal, previously beds occupied by patients colonized by s. aureus and the lack of adherence to standard precautions measures by the members of the nursing staff in addition to staying in the hospital environment, contact with patients.

Figure 2. Detailing the articles analyzed according to authors and key considerations identified in the studies. Teresina (PI), 2014.

The results of the articles mainly show the relationship between the prevalence of infections related to methicillin-resistant Staphylococcus aureus in intensive care units, and the presence of invasive procedures, listed as major risk factors.

DISCUSSION

There are notorious the findings of the high prevalence of infections by methicillin-resistant Staphylococcus aureus (MRSA) in intensive care units as well as associations with invasive procedures, and they are considered risk factors for the development of MRSA in this environment. The types of infections caused by these microorganisms there was a predominance of bloodstream infections, ventilator-associated pneumonia, surgical site infections and soft tissue and urinary tract infections.[13-20]

Staphylococcus aureus is considered one of the highest incidences of infections by microorganisms in hospitals and has been pointed out, these units as one of the pathogens that most closely relates to the high morbidity and mortality. The spread can occur among individuals by direct or indirect contact, especially in hospitals with greater susceptibility in critical units, it is remarkable colonization of this bacterium, both patients and health professionals.[4,18-20]

Despite the different forms of dissemination of the pathogen contamination in hospital environments is basically to what worries scholars. Staphylococcus aureus have acquired a prominent role to be an emerging pathogen in both skin infections, and systemic and his quickness in acquiring resistance to antibiotics.[4] Microbial resistance is seen as an important factor in the spread of multi-resistant bacteria and its serious complications, mainly due to the indiscriminate use of these, which stands out as a major factor in ICUs where patients are severely ill and therefore more vulnerable to acquire infectious processes.[15]

Resistance occurs at the time that the bacteria acquire genes that nurture the interference with the antibiotic mechanism of action by spontaneous DNA mutation or transposition and transfer of resistant plasmids, enabling the accumulation of mutations and the development of multidrug resistance. There is a significant decrease in therapeutic arsenal making the cure time

consuming and expensive, and sometimes unattainable.[8]

In the study conducted in ICUs in southern Brazil, there are the infections acquired in these environments as a result of contamination by resistant bacteria, with a predominance of gram positive cocci, particularly S. aureus, with insulation 43% of cases, and of these 63% were methicillin-resistant strains (MRSA). In the studies analyzed were highlighted as major risk factors for infection the presence of urinary and central venous catheters, tracheal intubation for prolonged periods (> 4 days), chronic illness, trauma and prolonged ICU stay (> 30 days).[16]

Therefore, it is important to note that infection and its consequences are the major causes of death in ICU and that prevention is extremely important, requiring a thorough understanding of the prevalence of infections in this environment, type and nature of the infection and pattern of the causative organisms. Recognizing the risk factors for the development of infection, especially when acquired in the ICU, and its relationship with mortality is crucial.[18]

The literature shows a high prevalence of S. aureus among patients always associating hospital origin and colonization. Therefore, such origin is considered a risk factor to carry MRSA.[21-22] Porting MRSA is an important factor for the development of infections during hospitalization in intensive care units and the consequent increased risk of mortality.[4,15-18.]

The threat of MRSA infection in the ICU is the fact that patients are usually severely ill and undergo an extensive antibiotic therapy, which would facilitate the MRSA infection. The evidence that the use of antibiotics is the main source for the development of bacterial resistance comes to the strengthening studies[23-25] the target of numerous observations. The resistance rates are worrying more intense consumption contexts of these drugs, which corroborates the fact that this issue be addressed dramatically in the hospital, because the health care professionals are faced with the constant concern to maintain the well being of his patient. Thus, the risk of casual resistance can be regarded as secondary or even undervalued.[26]

The doctor-patient relationship in hospital service predisposes expressively the spread of microorganisms when it is found that the lack of use of standard precautions practices by members of the nursing staff together with the stay in the hospital environment, the

contact with hospitalized clients, makes these professionals are subject to colonization by placing them on condition bearers and disseminators of infection, contributing to the occurrence of serious outbreaks and often irreparable.[18,27]

Moreover, contamination by MRSA in ICUs may be through the surfaces close to the patient and health care team, since the spread is mainly through the hands of professionals or direct contact with patients. The incidence of the microorganism in the bed railings, handles, bedside table, infusion and surgical gowns buttons contribute to the transmission resulting from health care, possibly through cross transmission between professionals and patients.[28-29]

Regarding topographic distribution, there was the nosocomial MRSA infection is commonly reported in upper respiratory tract infections, this is justified by the fact that Staphylococcus aureus mainly colonize regions of the oropharynx and trachea.[30]

Among the forms of resistance displayed by MRSA stands out that mediated by the MecA gene, intrinsic to oxacillin. Other resistance mechanisms include alterations in membrane permeability, microbial and enzymatic degradation of change in the active site. The vancomycin is one of last drug developed for the treatment of MRSA infections. In this microorganism infections empirical use of oxacillin is an option of choice, like vancomycin resistance because of the sharp oxacillin.[10]

CONCLUSION

The prevalence of methicillin resistant Staphylococcus aureus remains a serious problem to be faced in the dynamics of hospital infection control, as the presence of indexes strains in ICU evidenced in national and international studies are considered high.

Mortality rates point to a strong relationship with MRSA contamination present in ICU patients. The associated risk factors involving a range of invasive procedures performed, previous exposure to antibiotics, the patient's own predispositions before his pathological condition and immunosuppression, endogenous contamination of professionals and patients, as well as length of stay in the ICU.

In this sense, it is valid to deploy and expand mentoring programs in the institutions for the prevention and control of HAIs in ICUs, because health professionals need to constantly update forward to this issue, which may favor the use of measures to reduce the

incidence these factors as environmental decontamination, triage patients, performing cultures, active surveillance and contact precautions.

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Corresponding Address

Daniele Martins de Sousa
Universidade Federal do Piauí
Campus Universitário Ministro Petrônio Portela, Bl. 12
Bairro Ininga
CEP 64049-550 – Teresina (PI), Brazil