

RISK FACTORS ASSOCIATED WITH NOSOCOMIAL PNEUMONIA IN ADULT PATIENTS

FACTORES DE RIESGO ASOCIADOS A NEUMONÍA NOSOCOMIAL EN PACIENTES ADULTOS

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ABSTRACT

Objective: The objective of this article is to conduct a systematic review of several scientific publications about the risk factors associated with nosocomial pneumonia in adult patients. **Methods:** The review was conducted through an electronic search of several scientific articles related to this topic. We used the following PEO question: Is there an association between risk factors and the development of nosocomial pneumonia in adult patients? The search sources were PubMed and Scielo. The keywords used to search were: "nosocomial pneumonia", "hospital - acquired pneumonia" in combination with "risk factors"; "neumonía nosocomial", "neumonía intrahospitalaria" together with "factores de riesgo". Articles published from January 1, 2014 to December 10, 2018 were selected. **Results:** Of the 101 articles found, 77 were discarded for not meeting our inclusion and exclusion criteria, leaving 24 articles for this review. Significant risk factors for NN were: Age (OR= 1,742, p=0,000), consciousness disorder (HR: 2.0, P < 0.005), CKD (OR: 2,194; P<0.002), COPD (OR: 3.52; p=0.001), emergency tracheal intubation (OR 1,511; P<0.024) and mechanical ventilation (HR: 8.2, P < 0.005), etc. **Conclusion:** Several intrinsic and extrinsic risk factors are associated with the acquisition of nosocomial pneumonia in adult patients: age, consciousness disorder, CKD, COPD, endotracheal intubation, mechanical ventilation and other factors.

Key words: Nosocomial pneumonia; Hospital – acquired pneumonia; Risk factors. (source: MeSH NLM)

RESUMEN

Objetivo: El objetivo de éste artículo es realizar una revisión sistemática de diversas publicaciones científicas acerca de los factores de riesgo asociados a neumonía nosocomial en pacientes adultos. **Métodos:** La revisión se realizó a través de la búsqueda electrónica de diversos artículos científicos relacionados con el tema. Se utilizó la pregunta PEO: ¿Existe asociación entre los factores de riesgo y el desarrollo de neumonía nosocomial en pacientes adultos? Las fuentes de búsqueda fueron PubMed y Scielo. Las palabras clave fueron: "nosocomial pneumonia", "hospital - acquired pneumonia" en combinación con "risk factors"; "neumonía nosocomial", "neumonía intrahospitalaria" junto con "factores de riesgo". Se seleccionaron los artículos publicados desde 1 de enero de 2014 hasta 10 de diciembre de 2018. **Resultados:** De los 101 artículos encontrados se descartó 77 por no cumplir con nuestros criterios de inclusión y exclusión, quedando 24 artículos para ésta revisión. Los factores de riesgo significativos para NN fueron: Edad (OR= 1.742, p=0.000), trastorno de conciencia (HR: 2.0, P < 0,005), ERC (OR: 2.194; P<0.002), EPOC (OR: 3.52; p=0.001), intubación traqueal de urgencia (OR 1.511; P<0.024) y ventilación mecánica (HR: 8.2, P < 0,005), etc. **Conclusión:** Diversos factores de riesgos intrínsecos y extrínsecos se asocian a la adquisición de neumonía nosocomial en pacientes adultos: Edad, trastorno de conciencia, ERC, EPOC, intubación endotraqueal, ventilación mecánica y otros factores más.

Palabras clave: Neumonía nosocomial; Neumonía intrahospitalaria; Factores de riesgo. (fuente: DeCS BIREME)

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INTRODUCTION

Nosocomial pneumonia (NN) is the infection that affects the lung parenchyma (alveoli) that manifests after 48 hours or more of admission from the patient to the hospital, evidenced by a new infiltrate on the chest radiograph, and that during the income was not present or in the period of incubation. Also if pneumonia is associated with a diagnostic or therapeutic intervention is considered nosocomial, even though it occurs within these 72 hours, for example after endotracheal intubation. Pneumonia associated with the use of mechanical ventilation (VAP) appears after 48 - 72 hours after intubation endotracheal in the patient. It is pertinent to highlight that many patients with nosocomial pneumonia are treated outside the intensive care unit (ICU) and do not require mechanical ventilation⁽¹⁻³⁾. The NN is one of the most common hospital infections common, occurring with a frequency of 5 or more of 20 cases per 1000 hospital admissions, and is one of the main causes of death, morbidity, and use of resources in hospitalized patients.

Furthermore, the highest number of cases of NN occurs in conventional hospital wards, with an incidence of 3 to 7 episodes per 1000 admissions⁽¹⁾. On the other hand, the distribution of infections in nosocomial is not homogeneous and, although only 5 - 10% of patients admitted to a hospital are in ICU, 20 - 25% of all acquired infections in the hospital occur in these units; being nosocomial pneumonia the diagnosed infection more frequently in ICU. To be able to develop effective strategies to prevent NN in the ICU, first, you need to correctly identify the factors that increase the risk of acquiring infection⁽⁴⁾. This is also relevant for all conventional medical inpatient units or surgical. The objective of this article is to review of the published literature on risk factors associated with nosocomial pneumonia in adult patient.

METHODS

In this systematic review work, we used articles in English and Spanish published from 1 January 2014 to December 10, 2018, at PubMed and Scielo. The PEO question was used: Is there an association between risk factors and the development of nosocomial pneumonia in adult patients? Population: Adult patients Exposure: Factors risk Result: Nosocomial pneumonia the keywords were: "risk factors" (MeSH Term) in combination with "nosocomial pneumonia" and "hospital-acquired pneumonia"(used in PubMed);

"Nosocomial pneumonia", "intra-hospital pneumonia", "Risk factors" (used in Scielo). Work is found in the health priorities "Diseases communicable: intra-hospital infections, Respiratory infections, Pneumonia". According to "National Priorities for Health Research 2015-2021 ".

Inclusion criteria:

- Articles published in the last 5 years. Articles that include any of the following combinations of keywords in title or abstract: pneumonia nosocomial or in-hospital pneumonia together with risk factors; "Nosocomial pneumonia" or "hospital-acquired pneumonia "together with" risk factors ".

Exclusion criteria:

- Studies including patients with community-acquired pneumonia (CAP)
- Pediatric patients.
- Studies that are not directly related to our topic.
- Articles that do not state an author or Digital Object Identifier System (DOI).

RESULTS

Of the 101 articles found, it was discarded 48 articles for not complying with any of our keyword combinations in the abstract, also withdrew: 7 articles from pediatric patients, 7 articles that included patients with pneumonia acquired in the community, 3 descriptive studies, 1 article without an author, 1 article without DOI and 11 articles for not having a direct relationship with the review topic. In total, 77 articles were discarded, therefore there were 24 articles for this bibliographic review. Of the 24 selected articles, 21 had results research and 3 were considered for aspects theoretical conceptual that are related to the objective of this study: Risk factors in nosocomial pneumonia (NN).

The risk factors associated with the development of pneumonia in non-ventilated and ventilated patients have some similarities. Thus, they may have in common the presence of intrinsic risk factors, i.e. that are related to the host itself as chronic diseases. They can also be exposed to extrinsic risk factors such as the use of antibiotics that can increase risk colonization of the oropharynx; and risk factors that increase the likelihood of aspirating secretions oropharyngeal in the lower respiratory tree⁽¹⁾. In other words, extrinsic risk factors are diagnostic and therapeutic procedures that increase the possibility of developing a disease⁽⁴⁾.

Prospective studies found the following:

The case-control study by Sopena and collaborators had the objective of determining the associated risk factors and prognosis of nosocomial pneumonia in hospital wards in general. Adult patients aged ≥ 18 were included years, hospitalized between January 2006 and April 2008; from internal medicine wards, hemato-oncology, cardiology and other specialties medical; in addition to surgery services: general, thoracic, trauma, neurosurgery, and others. I know defined diagnosed patients as cases with NN and two controls were randomly assigned (matched by age, sex, and date of admission) by each. Also, patients who acquired pneumonia in the ICU. The study group was 119 cases and 238 controls. The results found that the incidence of NN in hospital wards overall was 2.45 cases per 1000 admissions. The distribution of NN cases was 62.2% in the wards of clinical medicine and 37.8% in surgery services. The mean age of the cases was 70 ± 14.46 years, 73% were male. In multivariate analysis, he found; that malnutrition (OR: 3.41, $p = 0.01$), chronic kidney disease (OR: 3.14, $p = 0.008$), anemia (OR: 2.08, $p = 0.02$), disorder of consciousness (OR: 2.14, $p = 0.04$), the Comorbidity Index of Charlson ≥ 3 (OR: 1.91, $p = 0.04$) are risk factors independent intrinsic associated with NN; While than hospital admission in the previous month (OR: 3.24, $p = 0.008$), and thoracic surgery (OR: 6.03, $p = 0.02$) are independent extrinsic risk factors associated with NN. Besides, it was determined that clinical complications occurred in 57.1% of the cases, the most frequent of these were: insufficiency respiratory (52.9%), septic shock (10.1%), renal failure acute (7.6%). Finally, 32.7% of patients died and 27.7% of these deaths were attributed to pneumonia⁽⁵⁾.

The cohort study by GuzmánHerrador B. et al., Aimed to identify the intrinsic and extrinsic factors that independently increased the risk of developing NN in the ICU. All patients have included adults admitted at least 24 hours to the ICU of a Spanish hospital from January 2006 to December 2009. The total number of patients studied was 4427, of which 66% were men, the mean age was 58.8 years. The average stay in ICU was 8.1 days (SD = 10.6). Besides, 233 patients developed NN while they were admitted to this unit. The incidence cumulative number of patients with NN was 5.3 for every 100 admissions. The average length of stay in ICU before the diagnosis of NN was 7.4 days (SD = 8.8). The results of the multivariate analysis found that the factor that most influenced the acquisition of NN was exposure to mechanical ventilation (HR: 8.2, $P < 0.005$). The use of a nasogastric tube, another factor extrinsic, was also significantly associated with NN (HR:

2.3, $P < 0.005$). The intrinsic factors significantly related to NN were: The decreased level of consciousness on admission (HR: 2.0, $P < 0.005$) and the APACHE II index (HR: 1.018, $P < 0.005$)⁽⁴⁾.

Ewan et al. Conducted a study of cohorts, to investigate the association of NN with dental and microbiological risk factors. Therefore, a series of swabs were obtained from the throat and tongue of patients aged ≥ 65 , with lower limb fractures. The reaction was used in the polymerase chain to detect bacteria. Of the 93 patients, 44 had simple ($n = 22$) or mixed pathogens ($n = 22$). Of 51 colonization events, the colonization with *S. pneumoniae* was the most common, ($n = 27$), followed by *H. influenzae* and others. Microorganism's colonizers were first detected 72 hours after admission, in 90% of cases. The NN was not associated with dental factors. The NN is associated with being a previous oral carrier of *E. coli* / *S. aureus* / *P. aeruginosa* / MRSA ($p = 0.002$; OR: 9.48).

The incidence of NN in those carriers of microorganisms potentially pathogenic was 35% (4% in patients without these germs). The NN was associated with a longer duration of hospital stay with a 30-day excess average. In univariate analysis NN was significantly associated with *S. aureus* / MRSA / *P. aeruginosa* / *E. coli* detected on day 5 (OR: 4.39) or 14 days of hospitalization (OR: 6.69). The NN is associated with a higher Charlson index ($p = 0.005$; OR: 1.46; 95% CI), having been admitted from a hospital ($p = 0.048$; OR: 4.18), having active cancer ($p = 0.001$; OR 17.11) or having had an aspiration episode ($p = 0.004$; OR 33.86)⁽⁶⁾.

The research carried out by Toledo C. and collaborators sought to characterize the risk factors early perioperative for complications postoperative pulmonary disease (POPC) in patients who undergo non-cardiac surgeries. Of the total POPC, 10% were NN, the majority of late occurrence. A logistic regression analysis found that a low functional capacity (RR: 4.6, 95% CI: 2.1 a 10.0), major surgery (RR: 3.6, 95% CI: 1.2 to 10.7), preoperative hemodynamic instability (RR: 3.4; CI 95%: 1.1-10.6), alcoholism (RR: 3.3, 95% CI: 1.0-10.7), unplanned surgery (RR: 2.3, 95% CI: 1.0-5.2), the SOFA score (RR: 1.1, 95% CI: 1.0- 1.2) and increased central venous pressure (RR: 1.1; 95% CI: 1.0-1.1) were independent predictors of POPC.7 Hinduja A. et al. studied the prevalence, risk factors, and test results of nosocomial infections in patients with bleeding spontaneous intracerebral. Nosocomial infection the most frequent in this study were pneumonia (18%).

In the multivariate regression analysis, the only significant predictor of nosocomial infection was intraventricular

hemorrhage (OR: 5.4, 95% CI: 1.2-11.4, $P = 0.02$) 8. Verelst S. and colleagues investigated whether overcrowding in the emergency department is independently associated with the risk of in-hospital death and morbidity. The results obtained by multivariate analysis indicated that overcrowding in the emergency department was not independently associated with mortality (OR: 0.94; 95% [CI] 0.74-1.19; $p = 0.6$), but it tended to be associated with a higher incidence of NN (OR 1.24; 95% CI: 0.96 to 1.62; $P = 0.09$)⁽⁹⁾.

In retrospective studies, the following results were found:

Uvizl R. et al. Conducted a study where processed information from all older patients of 18 years admitted consecutively to ICU from 2011 to 2015. The objective was to evaluate the factors of risk that contribute to the development of NN. A total of 2229 patients. Of which 65.9% were men and 34% women. The median age was 63 years. The average length of stay in ICU was 5.9 days. Total mortality independent of diagnosis was 24%. The criteria for NN were met by 310 patients (13.9%). Of this group, 14.5% had NN of early-onset and 85.5% NN of a late start. The non-modifiable risk factors that were significantly associated with NN were failure multiple organic (OR: 13.733; $P < 0.0001$), heart disease (OR: 2.255; $P < 0.0001$), and chronic kidney disease (OR: 2.194; $P < 0.002$). Also, risk factors modifiable that were significantly associated with NN were: intolerance to enteral nutrition ($P < 0.0001$), emergency tracheal intubation (OR 1,511; $P < 0.024$), reintubation (OR 1.851; $P < 0.001$) and bronchoscopy (OR 2.558; $P < 0.0001$)⁽¹⁰⁾.

Stenlund M. et al. Conducted a study predictive in order to determine the incidence and potential risk factors for pneumonia acquired at the hospital in a department of emergency surgery for admitted patients by acute abdomen and trauma. The medical records of 165 patients, of which 90 were cases and 75 controls matched by age. The NN was diagnosed in 0.9% of all patients and there was a significantly higher proportion in males ($p = 0.025$). Potential risk factors obtained by simple logistic regression were suspected or verified aspiration (OR: 23.9, $p < 0.001$) which was approximately 2 times greater than the immobilization (OR: 11.2, $p < 0.001$). Likewise, COPD / Asthma (OR: 3.7, $p = 0.05$), abdominal surgery (OR: 3.2, $p < 0.001$), vomiting / gastric retention (OR: 2.2, $P = 0.012$), were risk factors for NN⁽¹¹⁾.

Minakuchi et al. Conducted a study of cases and controls, to determine the factors of the risk associated with NN due to aspiration in patients hemodialysis.

An incidence of 5.4% was found of NN per aspiration. Multivariate analysis revealed that risk factors for getting pneumonia aspiration include: age ($p = 0.0056$, $\beta = 0.267$) index body mass ($p = 0.0312$, $\beta = -0.486$), levels of serum creatinine ($p = 0.0021$, $\beta = -1.050$), decrease monthly creatinine ($p < 0.0001$, $\beta = 4.890$). Further it was identified that albuminemia ($p = 0.0413$, $\beta = -4.659$), baseline total cholesterol ($p = 0.0306$, $\beta = -0.486$), the albumin reduction rate ($p = 0.0055$, $\beta = 18.161$) and creatinine ($p = 0.0280$, $\beta = 211.79$) and the duration of aspiration pneumonia ($p = 0.0001$, $\beta = 6,436$) were independent risk factors for mortality⁽¹²⁾.

Zuo M. et al. Also studied factors the risk associated with nosocomial pneumonia in hemodialysis patients. A case design was used and controls, patient data were analyzed between January 2008 - December 2015. Risk factors significant in the multivariate analysis were: age of the patient (OR: 2.029, $p = 0.024$), the healing time baseline (OR: 1.960, $p = 0.005$), a disorder of consciousness (OR: 1.616, $p = 0.000$), underlying diseases (OR: 10.484, $P = 0.001$) organic failure (OR: 2.154, $p = 0.002$) the Charlson comorbidities index (OR: 1.278, $p = 0.008$) and the APACHE II index (OR: 1.186, $p = < 0.001$)⁽¹³⁾. Zhu et al. Conducted a study cases and controls in order to identify if the atrial fibrillation (AF) is an independent factor which increases the risk of NN. Of patients with FA 25.64% had NN while only 3.66% of the controls suffered it. In multivariate analysis, found AF to be an independent risk factor for NN (OR = 13.386, $p = 0.000$). The increase in the risk was also associated with arterial hypertension (OR = 4,695, $p = 0,000$) heart failure (OR = 2,854, $p = 0.000$) and age (OR = 1.742, $p = 0.000$)⁽¹⁴⁾.

Total mortality was 8.8% which it was directly attributed to lung infection. The multivariate analysis identified that age older than 60 years (OR: 2.34; $p = 0.001$), being a smoker (OR: 9.48; $p = 0.001$), COPD (OR: 3.52; $p = 0.001$), surgery of urgency (OR: 2.48; $p = 0.001$), general anesthesia (OR: 3.18; $p = 0.423$), the duration of surgery ≥ 120 min (OR: 5.79; $p = 0.001$), the length of stay in the ICU ≥ 7 days (OR: 1.23; $p = 0.001$), the duration of ventilation mechanical assisted ≥ 4 days (OR: 5.93; $p = 0.001$) and the post-surgical hospitalization time ≥ 15 days (OR: 1.20; $p = 0.001$) are predictive risk factors and independent who are associated with the development of NN postsurgical⁽¹⁵⁾.

Kim T et al. Conducted a study of cases and controls to determine the risk factors for NN caused by bacteria Gram-negative carbapenem-resistant (CRGNB), critically ill adult patients were included from 8 tertiary level hospitals. 82 patients with 86 CRGNB isolates were

the cases, while the control group recruited 122 patients with NN due to Gram-negative bacteria sensitive to carbapenems. In multivariate analysis were significant ($p < 0.05$): age ≥ 70 (OR 0.46), diabetes mellitus (OR: 2.77), previous use of carbapenems (OR: 4.87), and radiological score ≥ 5 (OR: 3.63) were independently associated with the NN caused by CRGNB⁽¹⁶⁾. The study of Wang Z. and collaborators investigated the factors of risk related to postoperative NN in patients with stage I - III lung cancer a. The incidence of postoperative pneumonia in these patients with lung cancer was 2.9% (15 cases). Furthermore, the multivariate analysis revealed that advanced age (> 60 years) (OR 5.813, $p = 0.018$) and the histopathological type of squamous carcinoma (OR 5,831, $p < 0.001$) were also risk factors independent statistically significant for the postoperative pneumonia⁽¹⁷⁾.

The Divani AA Study. and collaborators had the objective of identifying associated risk factors a NN in patients with intracerebral hemorrhage spontaneous. 19.6% occurrence of NN was observed in the population studied. The results obtained using multivariate analysis indicated that: aspiration in the hospital (HR: 3.03, $p = 0.0003$), the intubation (HR: 2.31, $p = 0.01$), independently from where it was performed, either outside the hospital, in the emergency department or neuro - ICU; and the tracheostomy (HR 2.37, $p = 0.001$), were predictors significant of NN. In surviving patients, the mean hospitalization for those with NN was of 20 days and in the group, without this disease, it was 4 days⁽¹⁸⁾. Li YJ et al. Investigated the factors risk, clinical characteristics, and results in symptoms of NN caused by infection with *Acinetobacter baumannii* extensively resistant to medications (XDRAB). Most of the 52 strains of *A. baumannii* ($N = 37$, 71.2%) were collected in the ICU. Using the diffusion disk, he classified the isolated strains in 17 multi-resistant strains and 35 extensively resistant. The APACHE II score (OR: 1.17; $P: 0.034$), COPD (OR: 7.25; $P: 0.012$), and heart disease (OR: 6.94;

$p: 0.016$) were identified as factors of independent risk for the acquisition of XDRAB⁽¹⁹⁾.

In the study by Liu C et al. the risk factors associated with resistance to imipenem in patients with NN due to *Achromobacter xylosoxidans*. COPD and coronary artery disease were factors of independent risk according to multivariate analysis⁽²⁰⁾.

The study by Dudau D et al. Had the goal of identifying predictive factors early stages of NN recurrence after a lung or heart-lung transplant. Of the transplant patients, 47% acquired NN in the ICU. 40% of patients with NN had recurrence by NN. The severity of the disease (score SOFA) and lung injury (score value radiological) were the two risk factors of the recurrence of NN⁽²¹⁾. SánchezEncinales V and collaborators investigated the association from an overproduction of membrane protein A external (OmpA) of *Acinetobacter baumannii* with pneumonia, bacteremia, and mortality.

The analysis multivariate in the two cohorts studied showed that OmpA overexpression is a risk factor independent of pneumonia (OR: 4.81, $P < 0.001$), bacteremia (OR: 2.41, $P: 0.005$), and death (OR: 1.62, $P: 0.049$)⁽²²⁾. Buendgens et al. conducted a study retrospective in ICU patients where they found that there was no significant association between proton pump inhibitors and NN⁽²³⁾. Article of review by Bardou M et al: Two ECCA meta-analyzes of 2012 and 2013 that compared prophylactic drugs of stress ulcers did not provide evidence of an increased risk of NN attributable to PPIs. Also, the meta-analysis comparing prophylaxis with placebo or no prophylaxis did not indicate an increased risk of nosocomial pneumonia in the prophylaxis group (RR 1.16, 95% CI 0.84 to 1.58). An ECCA carried out from 2010 to 2011 found a significant increase in the incidence of pneumonia in patients who used pantoprazole⁽²⁴⁾.

Table 1. Titles, authors and design of research works related to nosocomial pneumonia and its risk factors.

AUTHORS	TITLE	YEAR	COUNTRY	POPULATION	DESIGN
Guzmán-Herrador B, Díaz Molina C, Farouk Allam M, Fernández-Crehuet Navajas R.	Independent risk factors associated with hospital-acquired pneumonia in an adult ICU: 4-year prospective cohort study in a university reference hospital	2015	España	4427	Prospectivo, Cohortes
Uvizl R, Kolar M, Herkel T, Vobrova M, Langova K	Possibilities for modifying risk factors for the development of hospital-acquired pneumonia in intensive care patients: results of a retrospective, observational study	2017	República Checa	2229	Analítico, Retrospectivo, Observacional
Sopena N, Heras E, Casas I, Bechini J, Guasch I, Pedro-Botet ML, et al.	Risk factors for hospital-acquired pneumonia outside the intensive care unit: A case-control study	2013	España	357	Prospectivo, Casos y controles
Stenlund M, Sjödah R, Pia Yngman-Uhlin RN.	Incidence and potential risk factors for hospital-acquired pneumonia in an emergency department of surgery	2017	Suecia	210	Retrospectivo, Casos y controles
Evaristo-Méndez G, Rocha-Calderón CH.	Factores de riesgo para neumonía nosocomial en pacientes con cirugía abdominal	2015	México	942	Analítico, Transversal
Divani AA, Hevesi M, Pulivarthi S, Luo X, Souslian F, et al.	Predictors of Nosocomial Pneumonia in Intracerebral Hemorrhage Patients: A Multi-center Observational Study	2014	E.E.U.U.	591	Analítico, Retrospectivo
Ewan VC, Sails AD, Walls AW, Rushton S, Newton JL	Dental and Microbiological Risk Factors for Hospital-Acquired Pneumonia in Non-Ventilated Older Patients	2015	Inglaterra	90	Analítico, Prospectivo, Cohortes
Minakuchi H, Wakino S, Hayashi K, Inamoto H, Itoh H.	Serum Creatinine and Albumin Decline Predict the Contraction of Nosocomial Aspiration Pneumonia in Patients Undergoing Hemodialysis	2014	Japón	335	Analítico, Retrospectivo
Zuo M, Tang J, Xiang M, Long Q, Dai J	Characteristics and factors associated with nosocomial pneumonia among patients undergoing continuous renal replacement therapy (CRRT): A case-control study	2018	China	1160	Retrospectivo, Casos y controles
Zhu J, Zhang X, Shi G, Yi K, Tan X.	Atrial Fibrillation Is an Independent Risk Factor for Hospital-Acquired Pneumonia	2015	China	8657	Retrospectivo, Casos y controles
Wang Z, Cai XJ, Shi L, Li FY, Lin NM.	Risk Factors of Postoperative Nosocomial Pneumonia in Stage I – IIIa Lung Cancer Patients	2014	China	511	Analítico, Retrospectivo
Sánchez-Encinales V, Álvarez-Marín R, Pachón-Ibáñez ME, Fernández-Cuenca F, Pascual A, et al.	Overproduction of Outer Membrane Protein A by <i>Acinetobacter baumannii</i> as a Risk Factor for Nosocomial Pneumonia, Bacteremia, and Mortality Rate Increase.	2017	España	346	Post hoc analysis of uncenter cohort and a multicenter cohort
Kim T, Chong YP, Park SY, Jeon MH, Choo EJ, et al.	Risk factors for hospital-acquired pneumonia caused by carbapenem-resistant Gram-negative bacteria in critically ill patients: a multicenter study in Korea	2014	Korea	320	Retrospectivo, Casos y controles, Multicéntrico
Li YJ, Pan CZ, Fang CQ, Zhao ZX, Chen HL	Pneumonia caused by extensive drug-resistant <i>Acinetobacter baumannii</i> among hospitalized patients: genetic relationships, risk factors and mortality	2017	China	52	Retrospectivo, Casos y controles
Liu C, Guo J, Yan W, Jin Y, Pan F, et al.	Hospital-acquired pneumonia due to <i>Achromobacter xylosoxidans</i> in the elderly: A single-center retrospective study in Beijing	2017	China	41	Retrospectivo, Casos y controles
Dudau D, Camous J, Marchand S, Pilorge C, Rézaiguia-Delclaux S, et al.	Incidence of nosocomial pneumonia and risk of recurrence after antimicrobial therapy in critically ill lung and heart-lung transplant patients	2014	Francia	79	Analítico, Retrospectivo
Toledo C, Nacul FE, Knibel MF, Silva NB, Rezende E, et al.	Pulmonary complications after non-cardiac surgeries: temporal patterns and risk factors	2017	Brazil	885	Prospectivo, Cohortes, Multicéntrico
Toledo C, Nacul FE, Knibel MF, Silva NB, Rezende E, et al.	Nosocomial infections in patients with spontaneous intracerebral hemorrhage	2015	E.E.U.U.	202	Analítico, Prospectivo
Verelst S, Wouters P, Gillet JB1, Van den Berghe G.	Emergency department crowding in relation to in-hospital adverse medical events: a large prospective observational cohort study	2015	Bélgica	108 229	Prospectivo, Cohortes

Table 2. Importance, strengths and weaknesses of research work related to nosocomial pneumonia and its risk factors.

REVIEW ARTICLE		WEAKNESSES	
TITLE	IMPORTANCE OF WORK	STRENGTHS	WEAKNESSES
Independent risk factors associated with hospital-acquired pneumonia in an adult ICU: 4-year prospective cohort study in a university reference hospital	Risk factors that independently increase the probability of developing NN in the ICU were identified. Although the severity of the patient's condition during admission and the alteration of consciousness predispose to NN, the strongest association was found in therapeutic interventions such as mechanical ventilation and the use of nasogastric tube.	The prospective cohort design and the 4-year follow-up duration. The number of patients studied. The use of multivariate analysis to determine the associated factors	Other recognized risk factors for acquiring nosocomial infections were not included, such as: hand hygiene, competencies of health personnel, the ratio between patients and health workers.
Possibilities for modifying risk factors for the development of hospital-acquired pneumonia in intensive care patients: results of a retrospective, observational study	The highest risk for NN in the ICU is caused by factors related to the patient: multiple organ failure, chronic kidney disease and heart disease; as well as extrinsic factors urgent tracheal intubation, reintubation, bronchoscopy, and intolerance to enteral nutrition. Additionally, stress ulcer prophylaxis was an independent risk factor for NN.	The sample size was considerable. Modifiable and non-modifiable risk factors was considered. The use of multivariate analysis to determine the associated factors.	The retrospective design does not allow evaluating temporality and generates less important results with respect to prospective studies. It also does not allow to evaluate cause-effect relationship.
Risk factors for hospital-acquired pneumonia outside the intensive care unit: A case-control study	The development of NN in the general wards tends to have a late onset and is more frequent in medical wards and in patients with severe comorbidities. PAH outside the ICU prevailed in patients with malnutrition, chronic renal failure, anemia, impaired consciousness, recent hospitalization, and thoracic surgery. NN has high morbidity and mortality; it is also associated with an increase in the length of stay in the hospital	Study the patients of the general hospitalization units; since most of the evidence for this group is extrapolated from ICU studies.	Some of the cases of NN were not detected by the surveillance methodology of the present investigation. The study was conducted in a single institution and the number of patients with NN was relatively small
Incidence and potential risk factors for hospital-acquired pneumonia in an emergency department of surgery	Verified or suspected aspiration was the dominant risk factor for NN, but immobilization was also frequently associated with NN. Therefore measures to prevent aspiration can be prophylactic for NN.	Study an emergency surgery department since the evidence in this high risk group for infections is scarce.	Smoking and postoperative weight gain due to intravenous fluid overload were excluded due to inadequate documentation.
Factores de riesgo para neumonia nosocomial en pacientes con cirugía abdominal	Age over 60 years, smoking, COPD (OR, emergency surgery, general anesthesia, duration of surgery \geq 120 min, ICU stay time \geq 7 days, duration of assisted mechanical ventilation \geq 4 days and post-surgical hospital stay \geq 15 days are independent predictive factors that increase the risk of developing postsurgical NN.	Address postoperative pneumonia, which is the cause of high morbidity and mortality, high costs, and a long hospital stay. The subsequent use of the data to propose sanitary measures.	The transversal design. Inclusion of some cases that probably fell into the category of health care-associated pneumonia.
Predictors of Nosocomial Pneumonia in Intracerebral Hemorrhage Patients: A Multi-center Observational Study	The onset of symptoms from arrival at the hospital, aspiration, intubation, and tracheostomy were identified as independent factors associated with NN.	The inclusion of six tertiary care hospitals for the study and the number of patients studied.	The retrospective design. The use of written documents to determine which patients had pneumonia.
Dental and Microbiological Risk Factors for Hospital-Acquired Pneumonia in Non-Ventilated Older Patients	NN was significantly associated with two or more <i>S. aureus</i> , MRSA, <i>E. coli</i> , or <i>P. aeruginosa</i> positive samples at any time, and specifically on days 5 and 14 after admission. Patients with a higher-scoring Charlson index or active cancer are at higher risk for NN.	The analysis of microbiological risk factors by using PCR. The use of serial samples to determine the influence of hospitalization on oral flora.	The results of this study are not directly generalizable to clinical medicine services because the study patients underwent fracture, anesthesia, and surgery.
Serum Creatinine and Albumin Decline Predict the Contraction of Nosocomial Aspiration Pneumonia in Patients Undergoing Hemodialysis	Decreased serum creatinine or albumin was identified as new clinical markers for contraction or death due to aspiration NN.	It was emphasized that nutrition is important to prevent aspiration NN in hospitalized hemodialysis patients.	Inclusion of a small number of patients with aspiration NN.

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Characteristics and factors associated with nosocomial pneumonia among patients undergoing CRRT	Modifying risk factors, such as: providing adequate nutrition, early treatment of underlying diseases and control of organ failure; the risks associated with nosocomial pneumonia can be reduced.	The Charlson index and APACHE II were shown to be predictive risk factors for NN in hemodialysis patients.	The retrospective design. The role of hand hygiene, which is considered an important factor in hemodialysis patients with NN, was not studied.
Atrial Fibrillation Is an Independent Risk Factor for Hospital-Acquired Pneumonia	Atrial fibrillation was shown for the first time to be an independent risk factor for NN. It was also concluded that high blood pressure and heart failure are risk factors associated with NN.	The research provides valuable information for use in the prevention of NN.	Further research is needed to validate the new finding of AF as a risk factor.
Risk Factors of Postoperative Nosocomial Pneumonia in Stage I – IIIa Lung Cancer Patients	It was concluded that being elderly (> 60 years), the histological type of squamous cell carcinoma, and the long duration of the operation are risk factors for postoperative pneumonia in patients with lung cancer.	A rarely investigated topic is studied despite the fact that lung cancer is one of the most common malignant neoplasms.	Conducting the study in a single institution does not allow generalization of the results. The retrospective design and the small sample size.
Overproduction of OmpA by Acinetobacter baumannii as a Risk Factor for Nosocomial Pneumonia, Bacteremia, and Mortality Rate Increase.	The overexpression of porin Omp A is a factor associated with pneumonia, bacteremia, and death caused by Acinetobacter baumannii.	Data from two single-center and one multicenter studies were analyzed.	The small sample size used, which is why some risk factors could not be included in the multivariate analysis.
Risk factors for hospital-acquired pneumonia caused by carbapenem-resistant GNB in critically ill patients: a multicenter study in Korea	To reduce the risk of NN caused by carbapenem-resistant Gram-negative bacteria, carbapenems and fluoroquinolones should be used with caution.	It is the first multicenter epidemiological study on this topic carried out in Korea.	The results are confined to the reality of Korea where resistant pathogens in nosocomial infections are prevalent. The retrospective design.
Pneumonia caused by extensive drug-resistant Acinetobacter baumannii among hospitalized patients: genetic relationships, risk factors and mortality	Pneumonia caused by extensively resistant Acinetobacter baumannii is strongly related to systemic diseases and the APACHE II score.	Carrying out the research in three teaching hospitals. The use of molecular biology techniques to analyze Acinetobacter baumannii.	The retrospective design. The difficulty of applying the results to populations other than the one studied.
Hospital-acquired pneumonia due to Achromobacter xylosoxidans in the elderly: A single-center retrospective study in Beijing	COPD and coronary artery disease are risk factors associated with NN.	Multivariate analysis was used to determine risk factors	A small sample was used, and the findings may not be accurately reflected in other populations.
Incidence of nosocomial pneumonia and risk of recurrence after antimicrobial therapy in critically ill lung and heart–lung transplant patients	The severity of the disease and lung injury are the two main risk factors for recurrence of NN	The prospective design and the follow-up period from January 2008 to June 2010	The study was conducted in a single unit particularly dedicated to transplantation of patients with pulmonary hypertension.
Pulmonary complications after non-cardiac surgeries: temporal patterns and risk factors	Low functional capacity, major surgery, preoperative hemodynamic instability, alcoholism, unplanned surgery, the SOFA score, and increased central venous pressure are independent risk factors associated with postsurgical pulmonary complications, such as pneumonia.	The homogeneous population of high-risk surgical patients admitted to ICUs from different regions of Brazil included in the cohort, and the prospective nature of the study.	The severity of postoperative pulmonary complications was not studied.
Nosocomial infections in patients with spontaneous intracerebral hemorrhage	Spontaneous intraventricular hemorrhage on admission was the only independent predictor of infectious complications such as pneumonia.	Multivariate analysis was used to determine independent risk factors.	The retrospective nature of the study that may cause bias. The relatively small number of patients in the sample.
Emergency department crowding in relation to in-hospital adverse medical events: a large prospective observational cohort study	Overcrowding in the emergency department is associated with the development of NN and other causes of morbidity.	The prospective design and the considerable number of patients studied.	The study was conducted in a single hospital in Belgium. As a result, care must be taken in generalizing our findings to other hospitals or countries.

DISCUSSION

Through the present systematic review, it was observed that there are risk factors for NN that were demonstrated by various authors. Also, various articles found different risk factors, since it is because not all the articles coincided with the variables studied or because they were not significant in statistical analysis. This can be explained by heterogeneity between studies concerning type of population (ICU patients, surgery, clinical medicine, with neoplasms, hemodialysis) designs (prospective, retrospective), countries (Europe, Asia, America), types of bacteria studied, and sample size. The facts significant risk factors that coincided in more number of studies were mostly intrinsic to the patient and therefore with less potential to be modified to prevent the development of NN. The risk factors highlighted by this review, considering the number of studies and the level of evidence is Age, which was a risk factor for NN in 6 of 2,112-17 studies, the reasons for which aging would favor NN could be explained because cognitive impairment, dementia, and delirium (which are common in this age group) favor the micro or macro aspiration of oropharyngeal secretions containing the bacteria pathogens of NN⁽³⁾. Also, immune function suffers from a functional impairment that is associated with diseases in the elderly⁽¹³⁾. The disorder awareness, an associated factor in 3 out of 21 studies^(4,5,13) (2 prospective), also increases the probability of aspiration of microorganisms from the oropharynx⁴ and generates inability to mechanically clean the oral secretions causing greater colonization by nosocomial bacteria⁽³⁾. Kidney disease chronic disease was associated with NN in 2 of 21 studies^(5,10) the immune impairment seen in its stages more advanced predisposes to infections; Besides, the anemia that increases the risk of NN⁽⁵⁾, occurs more frequently in CKD. Lung disease

The chronic obstructive disease was a factor associated with NN in 4 of 21 studies^(11,15,19,20), however, two of these studies were about specific germs. The APACHE score II was a risk factor in 3 of 21 studies^(4,13,19), this would favor the NN because it is a measure of the underlying severity of the disease⁽⁴⁾. For the so many more studies of the utility of this scale concerning

the acquisition of NN. Regarding the extrinsic risk factors mechanical ventilation (in 2 studies)^(4,15) and endotracheal intubation (in 2 studies)^(10,18) proved to be risk factors for NN. The presence of an artificial airway such as the endotracheal tube is recognized as the main risk factor for microaspirations because eliminates normal ejection mechanisms respiratory tract secretions. Besides the guides prevention standards recommend reducing the number of days on mechanical ventilation and the use of non-invasive ventilation⁽⁴⁾. A limitation of the present review is not having found national studies, which could lead to bias.

CONCLUSION

Various intrinsic and extrinsic risk factors, potentially modifiable or not, are associated with the acquisition of nosocomial pneumonia in adult patients: Age, a disorder of consciousness, CKD, COPD, smoking, endotracheal intubation, mechanical ventilation, bronchoscopy, aspiration, catheter nasogastric, intolerance to enteral nutrition, score APACHE II, Charlson index, heart disease, fibrillation atrial hypertension, immobilization, anemia, malnutrition, multiple organ failure, major surgery, duration of surgery, previous hospitalization and others more factors. More studies are still required, especially multicenter and national to better characterize the risk factors for NN in adults.

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