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Risk factors Associated with Lower Respiratory Infection due to Mechanical Ventilation: Systematic Review

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Abstract:- The main objective of this study was to determine the risk factors associated with lower respiratory infection due to mechanical ventilation. Methodology: Systematic review that consisted of the observation and deepening of a series of realities and theoretical reflections, the search engines of Pubmed, Medigraphic, Scielo, Elsevier, Dialnet, Medline were used, 25 articles were selected and the published ones were used as inclusion criteria between 2015-2020 in English, Portuguese and Spanish whose keywords were: risk factors, lower respiratory infections, NAVM, mechanical ventilation. Results: The average age of the patients in the studies was 60 years; In relation to the associated factors, the number of days with MV stands out, which on average in the studies was 8, the most common microorganisms P. aeruginosa with 77% and Klebsiella pneumonia with 62%. Conclusions: The risk factors are multiple, they manifest in each case according to the characteristics of the patients, so that lower respiratory infections are effectively associated with mechanical ventilation, but the level of complication is manifested from the conditions specific to each patient such as age, associated comorbidities and exposure to mechanical ventilation.

Keywords:- *Mechanical Ventilation, Lower Respiratory Infection, Risk Factors, Pneumonia.*

I. INTRODUCTION

Mechanical ventilation (MV) has been conceived since its genesis as a life support for extraordinary cases that require this procedure in order to artificially replace the function of the respiratory system when this is not possible naturally, which is common in patients with acute diseases. Although the use of this technique favors the survival of many patients whose diseases are of a high level of severity, the reality warns that this technique generates multiple complications among them the appearance of lower respiratory infections that constitute one of the most common in-hospital infections in Intensive Care Units in the world.

Worldwide, this type of nosocomial infections has constantly increased between 5 and 15% in hospitalized patients, representing 10 to 30% of all nosocomial infections, of which pneumonias and tracheobronchitis are the most common.1 Thus, up to 70% of intubated patients or those with acute respiratory disorders develop this type of conditions associated with artificial respirator. In Ecuador, the Ministry of Public Health warns that between 24% and 75% of annual mortality in hospital establishments (before the pandemic) was due to pneumonia associated with mechanical ventilation(5Alvarado), which has increased significantly since COVID-19, reaching a total of 89,338 by the year 2020(2).

According to the Forum of International Respiratory Societies, this type of respiratory disease annually claims the lives of at least 3 million people worldwide (representing the third leading cause of death worldwide) and affects an estimated 65 million people, especially children under 5 years of age. 3

However, the use of modern techniques and equipment has generated a series of complications due to the fact that they are very invasive for the condition of certain patients, which is added to the use of antimicrobials for a period of time that is counterproductive, as in the case of prolonged use of mechanical ventilators.4 This occurs because when an airway is invaded artificially, the sterility of the lower airway is lost a few hours after intubation, which can generate from an animate or inanimate focus to a susceptible host.5

Pneumonia and tracheobronchitis are among the major manifestations of this type of lower respiratory tract infections and their risk factors are characterized by maximization at the extremes of life (early age and adulthood) and in developing countries where poverty, access to health care and sanitary conditions favor the appearance of this type of affections.6 Therefore, it is one of the most common nosocomial infections in patients who undergo this method of respiratory assistance, which has a significant impact on the increase in mortality and the costs derived from hospital stay.7

This type of infection can occur early or late, depending on the number of days the patient has undergone this type of mechanism. In the first case, it occurs after 4

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days of intubation and mortality is low; however, as the number of days of use of mechanical ventilation increases, the risk of mortality increases; therefore, after more than 5 days with this type of mechanism (mechanical ventilation) it is necessary to be aware of what is known as late-onset VAPM which is the product, in most cases, of superinfection due to multidrug-resistant strains.8

In the case of mechanical ventilation, it is directly related to this type of in-hospital conditions and is the result of a complication that occurs in those patients to whom this technique is applied for more than 48 hours and who are exposed to a series of microorganisms that cause, among other things, pneumonia.9

In this context, the high prevalence of this type of disease generates a significant health burden for the health care system; likewise, the incidence and severity of respiratory failure make it necessary for health care personnel, physicians and nurses to know the different protocols for the use of procedures that allow dealing with this type of pathology in such a way as to minimize risks and reduce costs associated with the misuse of equipment and resources.

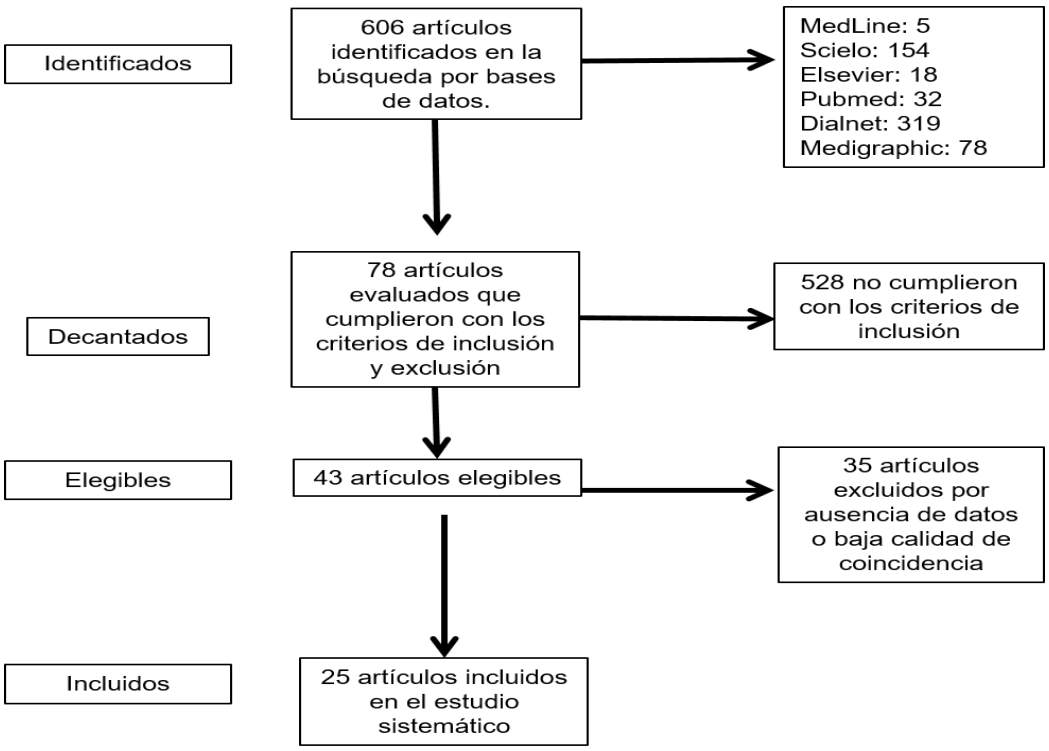
Consequently, there are various risk factors associated with lower respiratory infection due to mechanical ventilation, hence the interest in this study in recognizing their incidence, how they are produced and how they can be prevented.

II. METHODOLOGY

A systematic review was carried out which consisted of the observation and deepening of a series of realities and theoretical reflections that allowed us to investigate and interpret diverse information in relation to the subject of this study: Risk factors associated with low respiratory infection due to mechanical ventilation. Bibliographic sources were found through the following databases: Pubmed, Medigraphic, Scielo, Dialnet, Elsevier and Medline.

In this context, a search strategy was established that began with the determination of the inclusion and exclusion criteria, which were:
- *Inclusion Criteria:* Year of publication between 2015 and 2021, published in English, Portuguese and Spanish, that share at least one of the key words, scientifically validated international journals, web pages of official sites, laws, texts and works that deal with risk factors associated with low respiratory infection by mechanical ventilation.
- *Exclusion criteria:* Articles published prior to 2015, in a language other than Spanish, English or Portuguese, bibliographies and degree theses, information from sites not authorized for scientific studies such as, for example: Wikipedia, El Rincón del Vago or similar. Blogs and newspapers are also excluded from this research.

After specifying the inclusion and exclusion criteria, the following keywords were determined: risk factors, mechanical ventilation, lower respiratory infections, pneumonia. At first, the inclusion criteria were applied to make a preliminary selection based on the key words and the research topic (606 articles), then the review was deepened in order to discard those whose content was not significant for the study through the inquiry in the summary and objectives of each study; finally, the articles whose results and conclusions were important for this review were selected for this research, which in total were: 25



III. RESULTS

The results show a total of 25 reviewed studies of which 32% were published in 2019, 24% in 2018, 16% in 2020, 8% in the years 2015-2016-2017 and 4% in 2021. For their part, most of the articles correspond to descriptive studies (56%), followed by review articles (16%), Case Studies (12%) and, finally the other types of studies total 16%. In this order of ideas, 100% of the articles reviewed addressed the subject of lower respiratory infections, 76% of which were pneumonia and 24% other types of infections. Likewise, 88% of the studies dealt with mechanical ventilation as the main associated risk factor (Table 1) and the other 12% referred to other risk factors associated with VAPNM.

Table 1 Articles selected for systematization

N	YEAR	AUTHOR	TITLE	TYPE OF STUDY	OBJECTIVE	KEYWORDS
1	2019	Barletta et al.7	Clinical and microbiological characterization of patients with ventilator-associated pneumonia, Cienduegos 2015-2017.	Descriptive study	To describe the clinical and microbiological characteristics in patients with ventilator-associated pneumonia.	Pneumonia, hospital infection, ventilator.
2	2020	Camejo et al.4	Risk factors of acquired infections in Bayamo Pediatric Intensive Care Unit. 2018-2019.	Case analysis	Identify the risk factors for the appearance of this disease.	Infection and risk factors
3	2021	Céspedes and Others8	Pneumonia associated with mechanical ventilation in children and adolescents.	Descriptive study	To clinically and epidemiologically characterize children and adolescents with ventilator-associated pneumonia pneumonia associated with mechanical ventilation, according to selected variables.	Pneumonia and mechanical ventilation
4	2019	Cieza L, Coila E.18	Mechanical ventilation-associated pneumonia in the pediatric intensive care unit of a Tertiary Hospital. 2015-2018.	Descriptive study	To know the characteristics of VAP, determine infection rates, isolated germs, antibiotic sensitivity and mortality.	Ventilator-associated pneumonia, infections
5	2018	Cornistin and Others10	Pneumonia associated with mechanical ventilation. Update and inter-society recommendations, Sociedad Argentina de Infectología.	Original Article	Establish recommendations based on the literature and local expert opinion on the diagnosis, treatment and prevention of VAP, establishing clear algorithms. and prevention of VAP, establishing clear algorithms.	Pneumonia, ventilator
6	2017	Durán et al11	Behavior of ventilator-associated pneumonia in adult intensive care.	Descriptive study	To assess the behavior of VAP as an indicator of quality of care.	Ventilator-associated pneumonia, artificial mechanical ventilation, artificial mechanical ventilation.
7	2018	Garay and Others25	Impact of ventilator-associated pneumonias on mortality in an adult intensive care unit.	Descriptive study	To determine the incidence, isolated microorganisms and mortality in patients with ventilator-associated pneumonia.	Pneumonia associated with mechanical ventilation

8	2018	Maldonado and Others27	Consensus Document: Prevention of Pneumonia associated with mechanical ventilation in adults.	Consensus Document	To elaborate recommendations of national scope for nursing work in priority and cross-cutting clinical areas such as the care of patients on mechanical ventilation.	Pneumonia associated with mechanical ventilation
9	2019	Miranda R.[22]	Pneumonia associated with artificial mechanical ventilation	Descriptive study	To determine the clinical-epidemiological behavior of ventilator-associated pneumonia in an intensive care unit. pneumonia associated with artificial mechanical ventilation in an intensive care unit.	Ventilator-associated pneumonia, risk factors.
10	2019	Perez et al19	Nosocomial infections and antimicrobial resistance	Descriptive study	Describe the behavior of nosocomial infections and antimicrobial resistance.	Nosocomial infections
11	2018	Pezo M, Menoscal K, García A.23	Pneumonia associated with mechanical ventilation in patients admitted to the ICU: Etiology and risk factors.	Review article	To deepen on ventilator-associated pneumonia (VAP) in patients admitted to the intensive care unit (ICU), its etiology ventilator-associated pneumonia (VAP) in patients admitted to the intensive care unit (ICU), in addition to its etiology and risk factors.	Pneumonia, mechanical ventilation
12	2019	Ramírez C, Palma O.[28]	Mortality of patients subjected to noninvasive mechanical ventilation.	Case reports	To establish whether patients with respiratory pathology subjected to noninvasive mechanical ventilation presented a statistically significant benefit in mortality.	Artificial respiration
13	2020	Rego and Others13	Pneumonia associated with mechanical ventilation in patients cared for in an intensive care unit.	Descriptive study	To characterize the patients with mechanical ventilation, admitted to the Intensive Care Unit No. 2 of the Intensive Care Unit No. 2 of the Hospital General Docente Abel Santamaría during 2018.	Ventilator-associated pneumonia.
14	2016	Rocco and Others16	Incidence of respiratory infections in tracheostomized patients in a mechanical ventilation weaning and rehabilitation center.	Case studies	To describe the incidence of respiratory infections (RI) in tracheostomy patients (TQT) admitted to a mechanical ventilation weaning and rehabilitation center (CDVMR). and rehabilitation center (CDVMR). To identify risk factors (RF) for the development of RI.	Pneumonia, tracheostomy.
15	2020	Rodriguez et al17	Characterization of mechanical ventilation in patients with chronic obstructive pulmonary disease.	Descriptive study	To characterize the behavior of patients with acute exacerbation of chronic obstructive pulmonary disease admitted to the intermediate care unit of the Hospital Universitario "General Calixto García".	Artificial ventilation

16	2015	Rodríguez R, Pérez R, Roura J, Basulto M.15	Pneumonia associated with mechanical ventilation in a multipurpose intensive care unit.	Descriptive study	To describe the clinical and epidemiological characteristics of pneumonia associated with mechanical ventilation in the intensive care unit of the Hospital Provincial Docente Clínico Quirúrgico Manuel Ascunce Doménech, from February 2012 to February 2014.	Pneumonia associated with mechanical ventilation
17	2019	Valverde F. [9]	Risk factors for mechanical ventilator-associated pneumonia in pediatric patients in the intensive care unit of the National Institute of Child Health. April 2018 February 2019	Cross-sectional restrospective study	To determine the main risk factors in children for developing ventilator-associated pneumonia in the PICU of the Instituto Nacional de Salud del Niño (Breña, Lima - Peru).	Mechanical ventilation, risk factors.
18	2016	Male and Others20	Tracheobronchitis and ventilator-associated pneumonia in intensive care units in Latin America: epidemiology, clinical course and outcomes.	Multicenter Study	To describe the epidemiology, diagnostic methods used, microbiology and outcomes of patients with HAT or VAP in Intensive Care Units (ICU) in Latin America.	Ventilator-associated pneumonia
19	2019	Vásquez et al.24	Pneumonia associated with mechanical ventilation	Review article	To develop the most relevant aspects related to VAPM.	Infections; Tracheostomy;
20	2015	Viera et al. 14	Lower respiratory infection associated with mechanical ventilation.	Descriptive study	To determine the incidence of low respiratory infection associated with mechanical ventilation in adults admitted to the intensive care unit of the Isle of Youth.	Respiratory infections associated with mechanical ventilation; tracheobronchitis; pneumonia.
21	2017	Yañez et al. 21	Acute lower respiratory infections: description of discharges from roberto del rio hospital in 2016.	Descriptive study		Acute lower respiratory infection.
22	2018	Zamora and Others. 5	Prevalence and risk factors of pneumonia in patients subjected to mechanical ventilation at the verdi Cevallos Balda Hospital during 2017.	Descriptive Study	To determine the prevalence risk factors in VAPM	Pneumonia, mechanical ventilation, risk factors
23	2020	Moreno and Miliar[26]	Pneumonia associated with mechanical ventilation: an area of opportunity in Intensive Care Units.	Bibliographic Review		Pneumonia associated with mechanical ventilation
24	2018	Asensio et al29	Infections in the critically ill patient	Review Article		Device-related infections
25	2019	Lam and Others. 12	Epidemiological characterization of nosocomial infections in IESS patients.	Descriptive study	"Characterize nosocomial infections through epidemiological surveillance in order to assess the quality of medical care in the (IESS). "	Nosocomial infection, risk factors

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In relation to the characteristics of the samples used in the articles reviewed, the average age stands out, which is divided into two groups: those investigations carried out in adults, whose average age was 60, and those carried out in pediatric patients, whose average age was 4 (Table 2). Likewise, the average number of days that the patients who took part in the study used mechanical ventilation was 8 days.

Table 2 Characteristics of the study sample, microorganisms, and days with MV.

N°	Age	Microorganismo	Days VM	Type of MIC.
1	70-79 (75)	A. baumannii		
2	children 5 years old	P. aeruginosa	7	Gram negative
3	children 5 years	Klebsiella pneumoniae	7	Gram positive
4	children 2 - 2 years	Staphylococcus aureus (Granpositivas)	9,8	
6	60 +		5	Gramnegative
7	49	Klebsiella pneumoniae	16,7	Gramnegative
9	70 +	P. aeruginosa		Gram negatives
10	60	Enterobacter cloacae		Gram positive
12	55	A. baumannii	1	Gram negative
13	70-79 (75)	Stenotrophomona Maltophilia	14	Gram negative
14		P. aeruginosa	2,22	Gram negative
15	69	Staphylococcus	7 14	Gram positive
16	20-80 (50)	Klebsiella pneumoniae	12,5	
18	55	A. baumannii	1	Gramnegative
20		P. aeruginosa	12,8	Gram positive

The most common microorganisms detected in the studies were 100% Gram-negative and 36% Gram-positive, as shown in Table 3. Among them, P. aeruginosa stands out with 77% and Klebsiella pneumonia with 62% as the most common microorganisms in this type of infections.

Table 3 Type of microorganism identified in the reviewed studies

Microorganism	n	%
A. baumannii	4	31
P. aeruginosa	10	77
Klebsiella pneumonia	8	62
Staphylococcus aureus	8	54
Enterobacter cloacae	4	31
Maltophilia	1	8
Stenotrophomona	1	8
Acinetobacters	2	15
E. Coli	2	15

IV. DISCUSSION

Determining the risk factors associated with lower respiratory infection by mechanical ventilation makes it possible to identify the actions that are counterproductive in improving the health status of a patient, since the use of this mechanism in cases of severe and acute illness often leads to a series of complications that can even result in the death of the patient. Thus, the findings obtained from the review of various studies that addressed this issue have made it possible to recognize the impact that this type of infection has on the health of hospitalized patients.

In this context, several studies 5 agree that the lethality of ventilated patients when exposed to this mechanism for more than 48 hours is 20 to 25%, with an additional 1% incidence for each additional day of mechanical ventilation (MV), which increases the risk of acquiring pneumonia 21 times more compared to patients who do not undergo this type of ventilation. 5

Thus, prolonged time on mechanical ventilation is directly linked to the level of risk of generating complications, since patients who are more exposed to this type of ventilation are more prone to elements that interfere with the respiratory system, such as the endotracheal tube.8 These studies coincide with the results obtained in this study, where 83% of the cases analyzed used mechanical ventilation for more than 4 days and the average number of days they used it was 8 days. Therefore, mortality

attributable to VAPM is highly debated among specialists due to the variability of vulnerability of patients in critical care units.10

Hence, the high incidence of infection in the first week is generally associated with the time of instrumentation and inadequate endotracheal suctioning technique, as well as manipulation after instrumentation, which causes what is known as bacterial translocation, since it can generate the entry of bacteria into the bloodstream.11

In this order of ideas, a great diversity of pathogens have the faculty to cause this type of infections, in studies it is estimated that 90% of the infections are produced by bacteria: Staphylococcus aureus (S. aureus), Streptococcus sp. Acinetobacter sp., Staphylococcus coagulase negative (S. coagulase negative), Pseudomonas aeruginosa,12 which were found in most of the studies reviewed in this research. In this way, studies13 have identified negative germs according to Gram stain, which coincides with the present investigation where 100% of the cases of studies reviewed reported this type of germs, which shows the highest prevalence in all the wards according to the microbiological mapping of the hospital. Likewise, these findings show that the microbiota of each institution is different.13

Likewise, studies14 show that tracheobronchitis is presented as an independent entity that significantly affects, but with less prevalence than pneumonia, the hospital stay of patients with artificial mechanical ventilation.

The associated risk factors vary from one study to another; however, most clinical cases agree that patient age, days of artificial mechanical ventilation, associated comorbidities and organ failure are the most common risk factors for this type of infection.

This and other studies have indicated that the age group most affected by this type of infection is the elderly, due to the susceptibility that characterizes them not only to contract this type of respiratory infection but also to the comorbidities they present that require the use of this type of artificial assistance that are invasive procedures, which corresponds to the findings of the present study where the average age of the samples of the studies reviewed was 60 years.7

Thus, the most common comorbidities in this type of patient are arterial hypertension, diabetes mellitus and ischemic heart disease according to the admission diagnosis presented in various studies.15 Likewise, TQT has been identified as a risk factor for the development of VAPM due to the fact that the treatment required to treat it is prolonged mechanical ventilation.16

Therefore, the duration of mechanical ventilation has an impact on the development of this type of disease, as shown in some descriptive studies17 in which patients with some degree of malnutrition predominate, which is a case in which the risk of developing VAPM is increased. Among the extrinsic factors, multiple studies have linked a longer duration of mechanical ventilation of 5-11 days, and some consider this to be the greatest risk factor for VAP, occurring in 94% of cases in the first week of MV.18 Patients with a prolonged stay and with polymicrobial infections left the service deceased.19

Likewise, it is revealed that in Latin America there is a tendency to perform tracheal aspiration and then bronchoalveolar lavage20 , which represents another risk factor associated with this type of disease.

The low detection of bacteria as an etiological agent could also be related to the low sensitivity of the diagnostic methods used.21 In this context, research associated with this study4 shows that mechanical ventilation favors aspiration of gastric contents and constitutes an important factor in the pathogenesis of nosocomial pneumonia, since in this type of patients who use MV the risk of becoming ill increases at least 10 times.

Microorganisms associated with the epidemiological characteristics of each hospital and the conditions of critical areas such as Intensive Care Units8 are also considered risk factors for lower respiratory infections where tissue injury makes bacterial adherence possible.

In this order of ideas, previous antibiotic use, selective pressure, cross transmission and colonization of ICU environmental sources also influence as risk factors due to which resistant germs are produced.18 Thus, patients with VAPVM have a higher prevalence of associated chronic diseases. They are at increased risk for nutritional deficiencies.22

Airway care and patient management in the intensive care unit are fundamental factors for the development of this type of infection, since bacterial colonization and the alteration of local defensive barriers in the airway are factors associated with this type of infection.23

Other studies24 show that other factors associated with this disease include: the use of neuromuscular relaxants in the first 48 hours, malnutrition, tracheostomy, transport outside the Intensive Care Unit (ICU), emergency reintubation, prone position (or ventral decubitus).

However, in recognizing the factors associated with this type of infection, the need arises to determine the actions that can prevent lower respiratory infection associated with mechanical ventilation. In this regard, it is suggested8 to consider pneumonia and tracheobronchitis as the first diagnostic option as complications associated with mechanical ventilation, especially in patients who have not received prophylactic antibiotics.

Likewise, it is necessary for medical and specialized personnel to maintain high standards in the performance of the endotracheal suctioning technique, as well as to prepare the necessary elements for the execution of the technique, which requires both physicians and nurses to perform it with

a high scientific rigor that allows it to be initiated and concluded without interruptions.11

Other recommendations made in the studies reviewed to prevent this type of infection include the use of broad-spectrum antimicrobials and less invasive procedures, as well as preventive measures that include: hand hygiene, use of gloves, daily assessment to determine in a timely manner when a patient can stop using assisted ventilation in order to ensure the minimum use of ventilation duration or replacement by noninvasive ventilation, raising the bedside to avoid unscheduled reintubation, use of orotracheal intubation, and cleaning and disinfection of respiratory equipment.25

It is important to understand that the treatment of VAP involves two simultaneous approaches, one supportive and the other as anti-infective therapy, so it is necessary to use verification packages as part of quality improvement actions in a way that studies26 have shown to significantly reduce morbidity and mortality rates of VAP.

To this end, the education and training of specialists in airway manipulation is essential, so that a targeted training plan and protocolization in airway manipulation has become an action to prevent this type of disease. In relation to the general aspects of endotracheal tube handling, the studies reviewed agree that aseptic technique should be maintained during intubation, preventing self-extubation and reintubation.27

Another preventive suggestion is the use of noninvasive mechanical ventilation (NIV), which is a ventilatory support therapy modality in patients with acute or chronic respiratory failure that is applied more frequently in Intensive Care Units because it is a service where the indication criteria are better managed and applied earlier; this is an alternative that allows early detection of complications, which reduces the mortality rates associated with this type of infection.28-29

V. CONCLUSIONS

The high incidence rate of VAPV and TQT was high in most of the studies reviewed, as well as the appearance of isolated Gram-negative microorganisms, with a predominance of A. baumannii, P. aeruginosa and K. pneumonaie, Streptococcus sp. Acinetobacter sp. and Staphylococcus, which presented high multiresistance, showing that there are different microorganisms that depend to a great extent on the epidemiological conditions within the hospital.

Thus, although the risk factors are multiple, they are manifested in each case according to the characteristics of the patients, so that lower respiratory infections are indeed associated with mechanical ventilation, but the level of complication is manifested from the conditions of each patient such as age, associated comorbidities and exposure to mechanical ventilation. Therefore, prevention is found in the diagnostic phase and in timely procedures that adhere to protocol parameters which, although they seem to be basic, constitute the best alternative to prevent complications that lead to this type of infections that have a significant prevalence and incidence in mortality rates worldwide.

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