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INTEGRATIVE LITERATURE REVIEW

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Prognosis of Newborns in Neonatal Intensive Care Units: An Integrative Review

Prognóstico de Recém-Nascidos Internados em Unidades de Terapia Intensiva Neonatal: Revisão Integrativa

Prognostico de Recién Nacidos Internados en Unidades de Terapia Intensiva Neonatal: Revisión Integrativa

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ABSTRACT

Objective: The study's purpose has been to identify the scientific knowledge about the prognosis of newborns in Neonatal Intensive Care Units (NICUs). **Methods:** This is an integrative review that explored 11 articles from the following databases: PubMed/MEDLINE, CINAHL, Web of Science, LILACS, Science Direct, and SCOPUS. **Results:** Studies on the factors associated with the prognosis of newborns in NICUs and the interventions that influenced this prognosis were identified. The main clinical factors associated with the prognosis were low birth weight, prematurity, and asphyxia. These factors also influenced the mortality among newborns, which was the main prognosis evaluated by most of the studies. **Conclusions:** Low weight and prematurity were identified as the main factors leading to NICU admission. Weight gain was understood as means for improving the prognosis. Furthermore, prematurity and low weight associated with other pathologies worsened the prognosis, leading to the death of newborns.

Descriptors: Infant Mortality, Intensive Care Units, Newborn, Prognosis.

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RESUMO

Objetivo: Identificar na literatura evidências científicas acerca do prognóstico de recém-nascidos internados em Unidades de Terapia Intensiva Neonatal (UTIN). Métodos: Trata-se de uma revisão integrativa que explorou 11 artigos nas bases de dados: PubMed/MEDLINE, CINAHL, Web of Science, LILACS, Science Direct, SCOPUS. Resultados: Identificaram-se estudos que abordaram os fatores associados ao prognóstico de recém-nascidos internados em UTIN e as intervenções que influenciam o prognóstico do recém-nascido. Os principais fatores clínicos associados ao prognóstico foram o baixo peso, a prematuridade e a asfixia, esses mesmos fatores influenciaram a mortalidade, principal prognóstico avaliado pela maior parte dos estudos. Conclusão: Identificaram-se baixo peso e a prematuridade foram os principais fatores que levam à internação em UTIN. A melhoria do prognóstico é vislumbrada com o ganho de peso. Quando a prematuridade e o baixo peso estão associados a outras patologias há piora no prognóstico, tendo a morte neonatal como desfecho.

Descritores: Mortalidade Infantil, Unidades de Terapia Intensiva, Recémnascido, Prognóstico.

RESUMEN

Objetivo: Identificar en la literatura evidencias científicas acerca del pronóstico de recién nacidos internados en Unidades de Terapia Intensiva Neonatal (UTIN). Métodos: Se trata de una revisión integrativa que exploró 11 artículos en las bases de datos: PubMed / MEDLINE, CINAHL, Web of Science, LILACS, Science Direct, SCOPUS. Resultados: Se identificaron estudios que abordaron los factores asociados al pronóstico de recién nacidos internados en UTIN y las intervenciones que influencian el pronóstico del recién nacido. Los principales factores clínicos asociados al pronóstico fueron el bajo peso, la prematuridad y la asfixia, esos mismos factores influenciaron la mortalidad, principal pronóstico evaluado por la mayor parte de los estudios. Conclusión: Se identificaron bajo peso y la prematuridad fueron los principales factores que llevan a la internación en UTIN. La mejora del pronóstico es vislumbrada con la ganancia de peso. Cuando la prematuridad y el bajo peso están asociados a otras patologías hay empeoramiento en el pronóstico, teniendo la muerte neonatal como desenlace.

Descriptores: Mortalidad Infantil, Unidades de Cuidados Intensivos, Recién Nascido, Pronóstico.

INTRODUCTION

Nowadays, one of the greatest challenges for the Brazilian public health is reducing neonatal mortality through the implementation of public policies aimed at qualifying care. Thus, providing resolute care, from prenatal care to newborn care, leads to a reduction in injuries, which favors an increase in survival, especially for newborns at risk.¹

These newborns at risk require special care in neonatal units according to their needs. This special care is defined by the Legal Opinion No. 930 of May 2012 as Neonatal Intensive Care Unit (NICU), Conventional Neonatal Intermediate Care Unit (CNICU) and Kangaroo Neonatal Intermediate Care Unit (KNICU).²

Several biological, socioeconomic, and institutional circumstances are related to the newborn's hospitalization in these units. Also, the care delivered by health professionals have to be considered. Thus, the main reasons for this

hospitalization are: respiratory discomfort, low birth weight, congenital malformation and prematurity, which is the main cause.³⁻⁵

The aforementioned conditions can potentially cause irreversible side-effects, and many of them can be avoided by means of an appropriate care focused on the newborn's needs. This type of care, characterized by the use of high technology devices by qualified health teams, is required in NICUs. Nonetheless, NICUs are highly stressful environments, which expose the newborn to excessive light and noise, and to numerous manipulations and invasive procedures that generate pain and discomfort.⁶⁻⁷

Moreover, clinical factors also influence the prognosis of these newborns and allow us to know the main clinical conditions responsible their hospitalization, as well as the main reasons that lead to the deterioration their of health condition or recovery.

This study is based on the need to understand the clinical aspects of the care that influence the prognosis of newborns at risk, which is relevant to the actions aimed at reducing their morbimortality. Therefore, this study's objective has been to identify the scientific knowledge about the prognosis of newborns in NICUs.

METHODS

This is an integrative review of the literature carried out from October to November 2016 and guided by the following question: "What scientific knowledge about the prognosis of newborns in NICUs can be found in the literature?" Thus, we explored and analyzed 11 articles from the following databases: SCOPUS, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS) [Latin American and Caribbean Literature in Health Sciences], PUBMED/MEDLINE, Web of Science and Science Direct.

Data were collected by using matching descriptors obtained through synonym or equivalent descriptors combined with the OR and AND Boolean operators. As can be seen in Table 1, the descriptors obtained were: a) Health Sciences Descriptors (HeSD): "newborn", "neonatal intensive care units", "intensive care units for newborns", "neonatal ICC", "neonatal ICU", "prognosis", "neonatal mortality", and "survival rate"; b) Medical Subject Headings (MeSH): "infant", "newborn"; "neonate"; "intensive care units", "neonatal"; "neonatal ICU"; "newborn intensive care units"; "newborn ICU"; "survival"; "survival rate"; "prognosis"; "infant mortality"; "neonatal mortality"; and "postneonatal mortality"; c) CINAHL titles: "infant", "newborn"; "infant, "premature"; "infant", "hospitalized"; "infant", "high risk"; "intensive care units", "neonatal"; "intensive care units", "pediatric"; "intensive care units"; "survival"; "prognosis"; and "infant mortality".

Table I - Queries used during the database search.

Database	Ouery
PubMed/	((("Infant, Newborn"[All Fields] OR (neonate[All Fields] OR neonate"[All
MEDLINE	Fields] OR neonatesjāll Fields] OR neonates_[All Fields] OR neonateaālal Fields] OR neonateaaos[all Fields] OR neonateaalall Fields] OR neonatealall Fields] OR neonatesfall Fields] OR Newborn Icutality Fields Fields] OR Newborn Icutality Fields] OR Fie
	"humans"[MeSH Terms])
CINAHL	("Infant, Newborn" OR "Infant, Premature" OR " Infant, Hospitalizad" OR "Infant, High Risk") AND ("Intensive Care Units, Neonatal" OR "Intensive Care Units, Pediatric" OR "Intensive Care Units") AND (Survival OR PROGNOSIS OR "Infant Mortality")
Web of	((TS=("Infant, Newborn")OR TS=(Neonate*)OR TS=Newborn*)) AND
Science	[TS=("Intensive Care Units, Neonatal") OR TS=("Neonatal ICU") OR TS=("Newborn Intensive Care Units (NICU)") OR TS=("Newborn ICU")) AND (TS=(Survival") OR TS=("PROGNOSIS") OR TS=("Infant Mortality") OR TS=("Neonatal Mortalities"))
LILACS	[tw:['Recem-Nascido"]) ÁND [tw:[(tw:['Unidades de Terapia Intensiva Neonatal']) OR (tw:['Centros de Terapia Intensiva para Recem-Nascidos']) OR (tw:['CTI Neonatal']) OR (tw:['UTI Neonatal'])) AND [tw:[(tw:[prognóstico]) OR (tw:['Mortalidade Neonatal''])) AND (tw:[obrevida])) OR (tw:['Taxa de sobrevida'])) AND (inistance: 'regional') AND (flultext: ("1") AND db:['LILACS') AND limit:['humans'' OR "newborn''] AND la:['en'' OR "pt'' OR "es''] AND year_cluster: ("2014" OR "2012" OR "2013" OR "2015" OR "2010" OR "2000" OR "2000")
Science	(Intensive Care Units, Neonatal) and PROGNOSIS AND LIMIT-TO (yearnav,
Direct	" 2016,2015,2014,2013,2012,2011,2010, 2009,2008,2007,2006") AND LIMIT-TO (topics, "patient, neonate") AND LIMIT-TO (contenttype, "JL,BS", "Journal") AND LIMIT-TO(topics, "neonate".
SCOPUS	("Infant, Newborn") AND TITLE-ABS-KEY ("Intensive Care Units,
(Elsevier)	Neonatal") AND TITLE-ABS-KEY (prognosis*))

Source: Research data, 2017

The inclusion criteria were as follows: articles on the prognosis of newborns in NICUs, published from November 2006 to November 2016, and in Portuguese, English or Spanish. Articles not available in full, secondary studies or letters to editors, theses, dissertations, undergraduate theses and duplicate studies were excluded.

The Checklist for Measuring Quality was used for analyzing the content of the selected studies. After data collection, the inclusion and exclusion criteria and the Checklist for Measuring Quality were applied resulting in a sample of 11 articles: six from PUBMED/MEDLINE, three from LILACS, two from Web of Science, and one from SCOPUS (Figure 1).

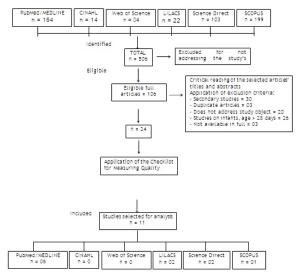


Figure 1: Flowchart for selecting articles.

In order to minimize systematic errors or bias, two researchers read the articles and applied the instruments independently for later comparison. All contradictions were solved through decisions based on discussions.

RESULTS AND DISCUSSION

The articles were distributed according to the year of publication, predominating the studies carried out in 2014 (45.45%), followed by those carried out in 2006 (18.18%). An equal number of articles were published in 2011, 2012, 2013 and 2015 (9.09%), but none in 2016.

The selected studies were carried out in London (1), China (1), Iran (1), Brazil (3), Uganda (1), Pakistan (1), Botswana (1), Nigeria (1), and Switzerland (1). From the 11 selected studies, two (18.2%) are written in Portuguese and nine (81.8%) in English.

Regarding the study design, three publications (27.27%) were longitudinal retrospective studies, two (18.18%) were longitudinal prospective studies, one (9.09%) was a case-control study, one (9.09%) was a cross-sectional study, two (18.18%) were prospective cohort studies, one (9.09%) was a retrospective cohort study, and one (9.09%) was a retrospective case-control study. These results are described in **Table 2**.

Table 2 - Characterization of the selected articles according to authorship, place, sample, study design, level of evidence, and evaluation score.

No.	Reference	Country	Study design	Level of evidence
1	Lopes PJ. et al. Uesophageal atresia: improved outcome in high-risk groups? Journal of Pediatric Surgery. 2006; 41(2): 331-334.	United Kingdom	Cohort study	2B
2	Chur CY et al. Metabolomic and bioinformatic analyses in asphyxiated neonates. Clinical Biochemistry. 2006; 39(2):203-209.	China	Case-control study	3B
3	Kadivar M., Parsaei R., Setoudeh A. The relationship between thyroxine level and short-term clinical outcome among sick newborn Infants. Acta Medica Iranica. 2011; 49(2):93-97.	Iran	Cross-sectional study	2C
4	Castro MP, Rugolo LMSS, Margotto PR. Sobrevida e morbidade em prematuroscom menos de 32 semanas de gestação na região central do Brasil. Rev Bras Ginecol Obstet. 2012; 34(5):235-242.	Brazil	Prospective cohort study	2B
5	Bezerra CTM, Cunha LCV, Libório AB. Defining reduced urine output in neonatal ICU: importance for mortality and acute kidney injury classification. Nephrol Dial Transplant. 2013; 28(4):	Brazil	Retrospective cohort study	2B
6	Sitva CF, Leite AJM, Almeida NMGS, Leon ACMP, Olofin I. Fatores associados ao óbito neonatal de recém-nascidos de alto risco: estudo multicêntrico em unidades neonatais de alto risco no nordeste brasileiro. Cad. Saúde Pública. 2014; 30(2):355-368.	Brazil	Case-control study	3B
7	Hedstrom A, Ryman T, Otal C, Nyonyintono J, McAdams KM, Lester D, Batra M. Demographics, clinical characteristics and neonatal outcomes in a rural Ugandan NICU. BMC Pregnacy and Childbirth. 2014; 14(327):1-9.	Uganda	Cross-sectional study	2C
8	Aslam HM et al. "Risk factors of birth asphyxia". Italian Journal of Pediatrics. 2014; 40(94):1-9.	Pakistan	Retrospective case-control study	3B
9	Zash RM et al. Risk Factors for Mortality among HIV-exposed and HIV-unexposed Infants Admitted to a Neonatal Intensive Care Unit in Botswana. J Paediatr Child Health. 2013; 50(3):189- 95	Botswana	Prospective Cohort Study	2B

10	Ekwochi U, Ndu IK, Nwokoye IC, bzemwosu UJ, Amadi UH, Usuorah DIC. Pattern of morbidity and mortality of newborns admitted into the sick and special care baby unit of Enugu state university teaching hospital, Enugu state. Nigerian Journal of Clinical Practice. 2014; 17(3):340-351.	Niger	Cohort study	2B
11	Steurer MA, Adams M, Bacchetti P, Schulzke SM, Roth-Kleiner M, Berger TM. Swiss medical centres vary significantly when it comes to outcomes of neonates with a very low gestational age. Acta Pædiatrica. 2015; 104(9):872-879.	Switzerland	Cohort study	2В

Source: research data, 2017

Table 3 shows that the main clinical factors associated with the prognosis are low birth weight, prematurity, and asphyxia. These factors also influenced the mortality, the main prognosis evaluated by most of the studies.

Table 3 - Characterization of the articles according to clinical factors, influencers and main neonatal prognoses hospitalized in NICUs.

No.	Clinical factors and influencers	Main prognostics
51	Esophageal atresia, low weight, and heart failure	Mortality
52	Asphyxia at birth, and presence of organic acids in the urine	Hypoxic ischemic encephalopathy, perinatal death
53	Low thyroxine level, gestational age < 34 weeks, and weight < 1,500 g	The thyroxine level returned at normal intervals and was not associated with any other clinical condition in the neonatal environment
54	Prematurity and low weight	High morbidity (O2 dependence), mortality
S5	Prematurity and low weight, reduced urine output, septic shock, perinatal asphyxia	
56	Low weight	Mortality
57	Infection, prematurity, respiratory discomfort, asphyxia, low birth weight	Mortality
58	Asphyxia, low birth weight, prematurity	Mortality and multiorgan complications
59	Prematurity, respiratory discomfort, sepsis, asphyxia	Mortality
\$10	Moderate neonatal asphyxia, severe neonatal asphyxia, neonatal sepsis, low birth weight, neonatal jaundice	Mortality
511	Sepsis, low birth weight, congenital malformation, prematurity	Mortality

Source: Research data, 2017

The critical analysis and the qualitative synthesis of the selected studies were carried out in a descriptive way according to the following analytical categories: "Factors associated with the prognosis of newborns in NICUs", and "Interventions that influence the prognosis of newborns".

Factors associated with the prognosis of newborns in NICUs

Knowing and monitoring the factors that determine neonatal mortality is an important step in identifying groups vulnerable to the different risk variables and the relationship with the progression to death, supporting the devices that stop this process from the prenatal period.

A study in Pakistan with 240 newborns showed that pre-eclampsia, gestational diabetes, breech presentation, umbilical cord prolapse, prolonged labor and premature membrane rupture were related to the risk of suffocation in newborns.¹⁷ As a result, cesarean delivery is considered a

protective factor against death in high-risk pregnancies, as reported in two studies. 11,15

These pregnancy and birth conditions lead to suffocation, involving the need for neonatal resuscitation and respiratory care procedures, which can be prevented or controlled by through quality prenatal care. Thus, fetal distress with/or signs of respiratory depression during childbirth usually require immediate resuscitation or respiratory support in NICUs. This was evidenced in one of the selected studies, which compared newborns who needed ventilatory support with those who did not.¹¹

Asphyxia is considered in another study as a risk factor for the incidence of hypoxic-ischemic encephalopathy, neurological examinations, and abnormal brain patterns.²¹ Respiratory discomfort in newborns is also found in cases of pneumonia and septicemia, considered a major cause of mortality when associated with prematurity and low birth weight.²² One study verified the etiologies of neonatal seizures and showed that a large number of newborns in NICUs were diagnosed with hypoxic-ischemic encephalopathy leading to their death.²³

Another factor associated with the need for resuscitation in the delivery room, and subsequent NICU care, was the gestational age (GA) related to pregnancy in adolescence, as discussed in one of the articles. Thus, the lower the GA, the greater the possibility that no resuscitation techniques will be available for the newborn, due to the characteristics that are intrinsic to prematurity.¹³ In a retrospective cohort study, it was observed that better glycemic control and modern management reduced the incidence of extremely preterm infants, reducing the neonatal mortality.²⁴

GA is directly related to low birth weight, that is, to the occurrence of preterm birth, thus being one of the main causes of morbimortality in newborns. According to two of the selected studies, birth weight was evidenced as one of the most important factors for the survival of newborns. Thus, the greater the weight, the better the neonatal prognosis. 10,13

Low birth weight and prematurity with GA < 34 weeks are also associated with sepsis, jaundice, and bilirubin levels, and low thyroxine levels. Nevertheless, despite NICU admission, one of the studies showed that these values remained at the baseline in newborns.¹²

The results of one study that evaluated newborns with GI < 32 weeks showed that lower GA groups were more prone to morbidities, oxygen dependence, and neurological disorders. Similarly, a study conducted in the Brazilian Northeast Region considered low birth weight as a predictor of mortality in NICUs. This is also presented in a study carried out in Uganda, where asphyxia, respiratory distress, prematurity, and infection stand out as the most common diagnosis. Low birth weight is also considered an important factor for neonatal mortality, as well as prematurity. Asphyxia leads to various systemic complications that can culminate in death. On the other hand, a study carried out in Switzerland found that low birth weight newborns who

had sepsis in the first week of life survived without severe neonatal morbidity. 20

Prematurity, Apgar score < 7 in the 1^{st} and/or 5^{th} minute, oligohydramnios and late enteral feeding were also considered according to a prospective cohort study as the main factors that contributed to neonatal mortality. Similar results were found in studies carried out in Enugu and Switzerland, which also included congenital malformation. $^{15,17,19-20}$

A study carried out in Brazil showed that the factors leading to low birth weight changed mainly due to socioe-conomic factors. Also, it showed that this reality occurs independently of purchasing power, mainly due to medical-surgical interventions. Low birth weight is a paradox among social classes, as the difference in the prognosis of mortality is evident since the low birth weight newborns' mortality rate is higher in places with low socioeconomic status.²⁵

Studies in Turkey and Camões showed that neonatal deaths were related to prematurity and its consequences, different heart diseases or genetic and congenital anomalies, infections, and asphyxia. Another study carried out in China found that newborns with congenital anomalies increased the odds of death by 50%, compared to those who did not have this anomaly.²⁶⁻²⁸

Prematurity was also observed in a study conducted in Africa, in which it was found that infants with GA < 32 weeks weighted much less and had lower survival rate when compared to preterm infants aged 32-36 weeks (MDELEMA et al., 2016).

There are several factors that lead to a good or bad prognosis of newborns in NICUs. Weight gain improves the newborns' condition, reducing their morbimortality. However, permanent neurological problems and mortality were the worst prognoses. Asphyxia at birth, very low GA, low birth weight and sepsis are among the greatest risk factors for newborns.

There are also other birth-related factors that influence the admissions in NICUs: the procedures performed by the doctors, such as cesarean delivery and other surgical complications, and the lack of adequate follow-up during prenatal care due to structure, work or management issues.

Among the factors that lead to the newborn's admission in NICUs are heart failure associated with esophageal atresia and the presence of organic acids in the urine. The latter factor was evaluated by a selected study that found that the presence of certain types of acids leads to the development of hypoxic-ischemic encephalopathy and perinatal death. 10-11

Considering the urinary output, a study of preterm and or low birth weight infants found that patients with reduced urine output were more likely to suffer septic shock, perinatal asphyxia, consequently delaying their discharge.¹⁴

Interventions that influence the prognosis of newborns

One of the greatest challenges of the Brazilian public health to reduce infant mortality is providing an appropriate,

integral, and quality care for newborns in all the health care units.

The use of surfactants stands as one of the crucial resources for the survival of neonates with respiratory failure. ²⁸ Therefore, lack of administrating antenatal corticosteroids is a risk factor because surfactants protect the extremely low birth weight neonates with respiratory distress syndrome, although it is favorable for the occurrence of bronchopulmonary dysplasia. ^{15,29}

Furthermore, other conditions contribute to the establishment of a poor prognosis such as bronchodysplasia, including newborns weighting less than 1,000 g, Apgar test performed at the $5^{\rm th}$ minute of their life and acute pulmonary diseases.³⁰

Newborns showing signs of respiratory discomfort tends to require immediate resuscitation as well as respiratory support, ¹¹ in which the lower the GA the greater the possibility of using positive pressure ventilation. ¹³ In addition, the death rates among newborns increase in the presence of endotracheal intubation and the time required for them to undergo mechanical ventilation. ¹⁵

Therefore, the use of antenatal corticosteroids by mothers is necessary considering the risk of preterm delivery, since it will help in the maturation of the fetal lung. Similarly, the use of surfactants after birth is extremely important to decrease pulmonary tension, improving survival chances, and decreasing the risk of complications in NICU care.

Another aspect addressed by the studies was the importance of early enteral feeding. Despite the weight, prematurity, and Apgar score of newborns, one of the causes of mortality was the late start of the first enteral feeding. ¹⁸

Thus, making a risk diagnosis from the beginning of prenatal care is important for the prognosis of newborns, since in this period actions for prevention and promotion can be effective in reducing comorbidities and mortality among them.

CONCLUSIONS

The studies analyzed in this review presented different objectives and methodologies. However, despite addressing the subject of newborns' health condition in NICUs in different ways, all emphasized the main clinical factors related to their prognosis.

It was observed that low weight and prematurity were the main factors that lead to the newborns' admission in NICUs. However, weight gain was a factor that improved this prognosis. When prematurity and low birth weight were associated with other pathologies, such as sepsis, neonatal asphyxia, heart and neurological diseases, and genetic and congenital malformation, the prognosis worsened, which may lead to neonatal death.

The main interventions that contributed to a good prognosis were the use of corticosteroids during pregnancy, the use of surfactant after birth and the interventions aimed at weight gain. Neonatal infections were treated as serious problems. However, the articles on this subject did not show the infectious disease etiologies, which could contribute to improve the quality of the care delivered not only by nurses but also the whole multiprofessional team. One of the shortcomings in developing this study was the lack of more accurate prognoses since most of the articles focused on the mortality outcome.

This paper aimed to contribute to the clinical practice based on evidence by discussing the main factors that influence the prognosis of newborns in NICUs. Therefore, health professionals who seek to increase their knowledge and improve the health care practices should use this study as scientific background.

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