



# RISK FACTORS ASSOCIATED WITH PROLONGED HOSPITAL STAY IN NEONATAL INTENSIVE CARE: A CASE-CONTROL STUDY

FACTORES DE RIESGO ASOCIADOS A ESTANCIA HOSPITALARIA PROLONGADA EN CUIDADOS INTENSIVOS NEONATALES: UN ESTUDIO DE CASOS Y CONTROLES

Victorio Arribasplata Gladys Edith <sup>1,a,b</sup>, Román Víctor Hillary Marian <sup>1,c</sup>,  
Román Larrea Sergio Alfredo <sup>1,d,e</sup>

## ABSTRACT

**Introduction:** Identify neonatal pathologies or conditions that influence the prolongation of hospital stay in a Neonatal Intensive Care Unit (NICU). **Methods:** An observational, retrospective, case-control study was carried out; in neonates hospitalized in the NICU, during the period 2015-2019, considering their perinatal and postnatal diagnoses as factors to be evaluated, as well as hospital stay. Two groups were divided: cases (prolonged stay) and controls (non-prolonged stay). The collected data were processed in the SPSS v.23 program, obtaining the OR and the Binary Logistic Regression. **Results:** 361 neonates (91 cases and 270 controls) were included, finding significance in perinatal factors ( $p < 0.05$ ): Birth weight (1000g to <1500g, ORa 8.2: CI 3.1 - 21.2) and gestational age (28 to 31 weeks, ORa 18.6: CI 4.8-71.4; 32-33 weeks, ORa 8.1: CI 3.5 - 18.4); and postnatal factors ( $p < 0.05$ ): RDS (ORa 10.3: CI 4.8-22.2), PHT (OR 32.2: CI 1.8-559.0), sepsis (ORa 7.1: CI 3.1-16.0), Neonatal malnutrition (ORa 10.2: CI 4.7-22.1) and anemia of prematurity (aOR 8.3: CI 2.4-28.1). The following did not reach significance: asphyxia, transient tachypnea of the newborn, pneumonia, pneumothorax, bronchopulmonary dysplasia, meconium aspiration syndrome, patent ductus arteriosus, congenital heart disease, hyperbilirubinemia, hypoglycemia, necrotizing enterocolitis, and apnea of prematurity. **Conclusions:** Birth weight, gestational age, RDS, PHPT, sepsis, neonatal malnutrition and anemia of prematurity are risk factors for prolonged hospital stay.

**Keywords:** Length of stay; Neonatal disease; Neonatal ICU. (Source: MESH-NLM)

## RESUMEN

**Introducción:** Identificar las patologías o condiciones neonatales que influyen en la prolongación de la estancia hospitalaria en una Unidad de Cuidados Intensivos Neonatales (UCIN). **Métodos:** Se realizó un estudio observacional, retrospectivo, de casos y controles; en neonatos hospitalizados de la UCIN, durante el periodo 2015 - 2019, considerando sus diagnósticos perinatales y posnatales como factores a evaluar, así como la estancia hospitalaria. Se dividieron dos grupos: casos (estancia prolongada) y controles (estancia no prolongada). Los datos recolectados fueron procesados en el programa SPSS v.23 obteniendo el OR y la Regresión Logística Binaria. **Resultados:** Se incluyeron 361 neonatos (91 casos y 270 controles), encontrándose significancia en factores perinatales ( $p < 0.05$ ): Peso al nacer (1000g a <1500g, ORa 8.2: IC 3.1 - 21.2) y edad gestacional (28 a 31 sem., ORa 18.6: IC 4.8-71.4; 32-33 sem, ORa 8.1: IC 3.5 - 18.4); y factores posnatales ( $p < 0.05$ ): Síndrome de distrés respiratorio (ORa 10.3: IC 4.8-22.2), Hipertensión pulmonar persistente (OR 32.2: IC 1.8-559.0), sepsis (ORa 7.1: IC 3.1-16.0), Malnutrición neonatal (ORa 10.2: IC 4.7-22.1) y anemia del prematuro (ORa 8.3: IC 2.4-28.1). No alcanzaron significancia: asfisia, taquipnea transitoria del recién nacido, neumonía, neumotórax, displasia broncopulmonar, síndrome de aspiración meconial, conducto arterioso persistente, cardiopatía congénita, hiperbilirrubinemia, hipoglicemia, enterocolitis necrotizante y apnea del prematuro. **Conclusiones:** El peso al nacer, edad gestacional, Síndrome de distrés respiratorio, Hipertensión pulmonar persistente, sepsis, malnutrición neonatal y anemia del prematuro son factores de riesgo para estancia hospitalaria prolongada.

**Palabras claves:** Duración de la estancia; Enfermedad neonatal; UCI de neonatos. (Fuente: DeCS- BIREME)

<sup>1</sup> Hospital Santa Rosa, Av. Bolívar Cuadra 8 S/N Pueblo Libre, Lima.

<sup>2</sup> Hospital de Ventanilla, Av. Pedro Beltrán S/N Calle 3 Ventanilla, Callao.

<sup>a</sup> Master in Public Health.

<sup>b</sup> Degree in Nutrition.

<sup>c</sup> Surgeon.

<sup>d</sup> Pediatrician.

<sup>e</sup> Master in Health Management.

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## INTRODUCTION

Hospital stay (HS) is subject to a variety of factors that, to varying extents, impact the management of hospital units, altering costs, duration, and risks for the most vulnerable patients. It can be measured using different parameters, but it remains an indicator of the efficiency level of health services.

In the hospital setting, beds represent a critical resource for service delivery. As a result, there is a need for measures to prioritize this resource and achieve proper efficiency<sup>(1)</sup>.

Length of stay (LOS) in the ICU has been used as a measure of resource utilization because it is surprisingly consistent across most diagnoses<sup>(2)</sup>.

Studies estimate that between 22.1% and 48% of HS days were unnecessary. A study from Iran showed that over 20% of the HS was inappropriate, with 45.1% due to the hospital's internal procedures<sup>(3)</sup>.

Illness and hospitalization are critical events that a newborn might face, having a psychological impact on the entire family, often manifesting as stress frequently seen during admission due to severe health status<sup>(4)</sup>.

For deducing prolonged stay (PS) in the neonatal ICU, any stays beyond the 75th percentile of hospitalized neonates who were discharged alive that year have been used as a reference<sup>(5)</sup>.

Accurately predicting hospital LOS and time to discharge could aid in resource planning and management, stimulate quality-improving activities, and support physicians in advising parents<sup>(6)</sup>. Neonatal units manage significant resources due to their complex nature and are a focal point in each of their processes; among them is HS. When extended, it demands the identification of underlying causes to be addressed in favor of administrative efficiency, resulting in service improvements for patients. The aim of this research was to identify neonatal pathologies or

conditions representing a risk of extended stay in the neonatal unit of the institution under study. This initiative seeks to delve into various problems affecting hospital costs and consuming resources that could benefit patients.

## METHODS

### Type, design, and study area

An analytical case-control study was conducted.

### Study Area

Level 3 Hospital, "Santa Rosa."

### Population and sample

Population: Newborns hospitalized in the Intensive Care Unit of Neonatology, at Hospital Santa Rosa (HSR).

### Sample

A simple random sampling was conducted from the population of hospitalized newborns from 2015 to 2019, meeting the inclusion (hospitalized in neonatal ICU during the period, born at HSR, complete medical record) and exclusion criteria (deceased, referred, underwent surgery, social abandonment, genetic syndromes, or multiple malformations). Sample size was calculated using Epidat® 4.2, aiming for an odds ratio (OR) of 2<sup>(7)</sup>, with a proportion of exposed cases of 50% and exposed controls of 33%, a case-control ratio of 3:1, a confidence level of 95%, and a power of 80%. This resulted in a sample size of 91 cases and 270 controls. The exposure factor was neonatal pathologies or conditions identified in other studies.

### Variables and Instruments

-Dependent Variable:

Prolonged Hospital Stay (PHS): Prolonged stay was considered any stay exceeding the 75th percentile of the total hospital stay recorded for the registered newborns, equal to 20 days.

-Independent Variables:

Perinatal factors: Gestational age, birth weight, weight for gestational age, asphyxia.

-Postnatal factors: Neonatal respiratory distress syndrome, transient tachypnea of the newborn, neonatal pneumonia, pneumothorax, bronchopulmonary dysplasia, meconium aspiration syndrome, patent ductus arteriosus persistence, congenital heart disease, pulmonary hypertension, neonatal sepsis, neonatal malnutrition, hyperbilirubinemia, hypoglycemia, necrotizing enterocolitis, anemia, apnea of prematurity.

### Definition of cases and controls

-Cases: Neonates admitted to the neonatal ICU, with an HS longer than 20 postnatal days (> 75th percentile of neonate stays).

-Controls: Neonates admitted to the neonatal ICU, with an HS  $\leq$  20 postnatal days ( $\leq$  75th percentile of neonate stays).

### Data Collection Instrument

A validated instrument was used, based on expert judgment with the selected variables.

### Statistical Analysis Procedures

Data Analysis: Using SPSS v.23, descriptive statistics were conducted, calculating frequencies and percentages. Additionally, the Odds Ratio and confidence interval were obtained to assess the measure of association and the significance of the risk factors for hospital stay. Binary logistic regression analyzed the significance level and the influence of the various independent variables on the dependent variable.

### Ethical Aspects

The research was submitted to the ethical and research committee of Hospital Santa Rosa.

Ethical aspects were considered in accordance with the General Health Law N°26842 and the Public Official Law N°27815. In line with the Declaration of Helsinki on human research, confidentiality and privacy of the collected information were maintained, adhering to the objectives.

### Informed Consent

Not applicable, as this study used secondary sources.

### Data Collection Procedures

Information was collected from hospitalization books, identifying neonates and their respective medical records. Through the data collection instrument, the selection and recording of information were systematized using secondary sources, such as the medical records of patients hospitalized in the Neonatal ICU.

## RESULTS

Of the 700 registered neonates, 440 remained after applying the inclusion and exclusion criteria. Ultimately, based on the quality of the information, the number of studied neonates was reduced to 91 cases and 270 controls.

### Perinatal Factors

Table N°1 shows that the most marked differences in favor of cases versus controls are in gestational ages of 28 – 31 weeks (OR 23.486, CI 6.762-81.587) and 32 – 33 weeks (OR 9.556, CI 4.604-19.832), which reached risk value. According to birth weight, in the ELBW with very few neonates (OR 0.231, CI 0.191-0.279) and VLBW (OR 22.44, CI 9.899-50.869), the latter presented a risk value.

**Table 1.** Perinatal Risk Factors by NICU Hospital Stay.

Risk Factor	Cases (91)		Controls (270)			CI 95%	
	N	%	N	%	OR	Lower	Upper
<b>Gestational Age</b>							
<28 weeks	1	1.1	0	0	0.250	0.209	0.299
28 – 31 weeks	19	20.9	3	1.1	23.486	6.762	81.587
32 – 33 weeks	28	30.8	12	4.3	9.556	4.604	19.832



34 – 36 weeks	34	37.4	126	45.5	0.682	0.419	1.110
37 – 40 weeks	9	9.9	129	46.6	0.119	0.057	0.247
<b>Birth Weight (*)</b>							
< 1000 g (ELBW)	10	11	0	0	0.231	0.191	0.279
1000 g - < 1500 g (VLBW)	35	38.5	8	2.9	22.440	9.899	50.869
1500 g - < 2500 g (LBW)	36	39.6	100	36.1	1.279	0.787	2.077
2500 g - < 4000 g (Appropriate for GA)	9	9.9	150	54.2	0.084	0.040	0.174
> 4000 g	1	1.1	12	4.3	0.239	0.031	1.863
<b>(Macrosomic)</b>							
Small for Gestational Age	23	25.3	37	13.7	3.097	1.773	5.411
Appropriate for Gestational Age	65	71.4	211	78.1	0.553	0.329	0.930
Large for Gestational Age	3	3.3	22	8.1	0.125	0.017	0.943
Perinatal Asphyxia	14	15.4	28	13.7	1.571	0.787	3.136

(\*) ELBW: Extremely Low Birth Weight, VLBW: Very Low Birth Weight, LBW: Low Birth Weight, Appropriate for GA: Appropriate for Gestational Age.

For weight according to gestational age, the SGA (25.3% vs 13.7%) had an OR of 3.097, CI 1.773-5.411, indicating a risk value.

#### Postnatal Factor

In Table No. 2, it can be seen that the largest difference between the cases and controls was in neonatal sepsis (81.3% vs 33.6%; OR 8.285, CI 4.621-14.854), respiratory distress (81.3% vs 63%; OR 2.561, CI 1.431-4.583),

neonatal malnutrition (61.5% vs 12.6%; OR 10.743, CI 6.187-18.653), cardiovascular disease (26.4% vs 5.1%; OR 6.55, CI 3.214-13.348), necrotizing enterocolitis (9.9% vs 1.4%; OR 7.299, CI 2.191-24.318) and prematurity anemia (30.8% vs 2.9%; OR 14.556, CI 6.331-33.643), both of which reached a risk value. Within respiratory distress, the OR risk value was for the respiratory distress syndrome (16.486, CI 9.245-29.388).

**Table 2.** Postnatal Risk Factors Based on Hospital Stay in NICU.

Risk Factors	Cases		Controls		OR	95% IC	
	N(91)	%	N(270)	%		Lower	Upper
Sepsis	74	81.3	93	34.4	8.285	4.621	14.854
Neonatal Malnutrition	56	61.5	35	13.0	10.743	6.187	18.653
Respiratory Distress	74	81.3	170	63.0	2.561	1.431	4.583
Cardiovascular Disease	24	26.4	14	5.2	6.550	3.214	13.348
Hyperbilirubinemia	29	31.9	96	35.6	0.848	0.511	1.407
Hypoglycemia	38	41.8	110	39.7	1.043	0.644	1.689
Necrotizing Enterocolitis	9	9.9	4	1.4	7.299	2.191	24.318
Apnea of Prematurity	3	3.3	2	0.7	4.568	0.751	27.783
Anemia of Prematurity	28	30.8	8	3.0	14.556	6.331	33.643

<b>Respiratory Distress</b>	<b>N (74)</b>	<b>%</b>	<b>N (170)</b>	<b>%</b>			
Respiratory Distress Syndrome	62	84.9	31	18.3	16.483	9.245	29.388
Transient Tachypnea of the Newborn	7	9.6	113	66.9	0.116	0.052	0.260
Pneumonia	5	6.8	16	9.5	0.923	0.328	2.594
Pneumothorax	5	6.8	9	5.3	1.686	0.550	5.168
Bronchopulmonary Dysplasia	11	15	0	0	0.229	0.189	0.227
Meconium Aspiration Syndrome	0	0	6	3.6	0.744	0.700	0.790
<b>Cardiovascular Disease</b>	<b>N (24)</b>	<b>%</b>	<b>N (14)</b>	<b>%</b>			
Persistent Ductus Arteriosus	17	70.8	6	42.9	10.108	3.848	26.552
Congenital Heart Disease	5	20.8	7	50	2.184	0.676	7.060
Persistent Pulmonary Hypertension	4	16.7	1	7.9	12.638	1.364	12.134

In the risk evaluation, Persistent Ductus Arteriosus (OR 10.108, CI 3.848-26.552) ) and Persistent Pulmonary Hypertension (OR 12.638, CI 1.364-112.134) were significant.

**Table 3.** Binary Logistic Regression. Risk Factors for Prolonged Hospital Stay in NICU.

<b>RiskFactors</b>	<b>B</b>	<b>Standard Error</b>	<b>Wald</b>	<b>gl</b>	<b>Sig</b>	<b>Exp (B)</b>	<b>95% C.I. para Exp (B)</b> Lower Upper	
<b>Perinatal Factors</b>								
Birth weight 1000.1500	2.107	0.485	18.851	1	0.000	8.221	3.176	21.278
Gestational age 28 to 31 weeks	2.927	0.685	18.277	1	0.000	18.675	4.880	71.463
Gestational age 32 to 33 weeks	2.096	0.419	24.989	1	0.000	8.131	3.575	18.494
Small for Gestational Age	0.523	0.380	1.893	1	0.169	1.687	0.801	3.556
<b>Postnatal Factors</b>								
Respiratory Distress Syndrome	2.339	0.390	35.961	1	0.000	10.374	4.829	22.284
Persistence of the ductus arteriosus	0.345	0.665	0.269	1	0.064	1.411	0.384	5.192
Persistent Pulmonary Hypertension Neonatal Sepsis	3.471	1.457	5.679	1	0.017	32.177	1.852	559.016
Neonatal Malnutrition	1.961	0.417	22.070	1	0.000	7.103	3.135	16.095
Neonatal Necrotizing Enterocolitis	2.326	0.393	34.980	1	0.000	10.236	4.736	22.124
Premature Anemia	1.103	0.842	1.715	1	0.190	3.014	0.578	15.706
Premature Anemia	2.120	0.621	11.663	1	0.001	8.333	2.468	28.137

### Binary Logistic Regression

According to Table No. 3, the binary logistic regression shows that among the perinatal risk factors, a significant adjusted OR value was achieved ( $p < 0.05$  and  $aOR > 1$ ) for birth weight (1000g to <1500g and 1500g to <2500g) and gestational age (28-31 weeks and

32 to 33 weeks). Likewise, among the postnatal risk factors, it was achieved for: Neonatal respiratory distress syndrome, neonatal sepsis, persistent pulmonary hypertension, neonatal malnutrition, and premature anemia. This means that the mentioned factors have a significant association with prolonged



neonatal hospital stay.

## DISCUSSION

In our analysis, we identified birth weight as a significant risk factor, specifically the group ranging from 1000g to < 1500g. Although differing in the number of cases and methodology, birth weight has also been pinpointed by various authors as a primary factor. Lee, Henry et al. (2016), in their comparative study with 23,551 neonates and predictive models for the length of stay, recognized birth weight as a comparison factor, varying from 8 to 79 days<sup>(8)</sup>. Adebajji, Atinuke et al. (2015) in a retrospective study of 180 neonates, linked birth weight with length of stay<sup>(9)</sup>. Medina, Mareyke et al. (2015) in a case-control study analyzed risk groups based on birth weight in 447 cases and 1,341 controls, affirming birth weight as a factor<sup>(10)</sup>. Kurek, Meryem et al. (2017) in a retrospective study in the ICU involving 331 neonates born to mothers with preterm rupture of membranes, found significance in birth weight<sup>(11)</sup>.

Neonates with low birth weight often face respiratory, cardiovascular, hemorrhagic, septic, metabolic, and other complications during their stay; these, combined with immaturity, necessitate extensive care and delay hospital discharge due to the risks they pose. This also applies to extremely low birth weight neonates, but there were not enough cases for analysis. In our research, we noted significant factors such as birth weight (1000g to < 1500g; adjusted OR 8.22, CI 3.17-21.27) and gestational age (28-31 weeks; adjusted OR 18.67, CI 4.88-71.46 and 32-33 weeks; adjusted OR 8.13, CI 3.57-18.49). Various studies similarly emphasized the combination of birth weight and gestational age as significant.

Seaton, Sarah et al. (2016) in a systematic review of 9 selected studies found that factors like birth weight and gestational age allow for early and simple predictions of stay length<sup>(12)</sup>. Kurek, Meryem et al. (2016) in a retrospective observational study with 3,607 ICU neonates also highlighted the importance of gestational age and birth weight<sup>(11)</sup>. Marrugo-Arnedo et al. (2019) in a retrospective study of 947 neonates

with a length of stay > 5 days also identified gestational age and birth weight as key determinants<sup>(5)</sup>. Mendoza, Luis et al. (2014) in their case-control study of 555 neonates (111 cases, 444 controls) with a length of stay > 7 days, pinpointed birth weight < 2000g and gestational age < 36 weeks as influential factors<sup>(7)</sup>. Khasawneh, Wasim et al. (2021) in their retrospective study of 2,236 late preterm infants considering a stay > 3 days, identified gestational age < 35 weeks, small for gestational age, and birth weight < 2500 g as factors<sup>(13)</sup>. Sahiledengle, Biniyam et al. (2020) in a prospective follow-up study with a stay > 7 days in 438 ICU neonates found significance in gestational age < 37 weeks and low birth weight<sup>(14)</sup>. Murki, Srinivas et al. (2020) in a multicenter study of 3,095 preterm infants (25 to 33 weeks) in the ICU found that for each week decrease in gestational age, the stay increases by 9 days. They identified factors such as gestational age and low birth weight<sup>(15)</sup>.

Gestational age is directly linked to birth weight, and lower gestational ages express multiple complication possibilities based on the degree of immaturity. Given the level of complexity, most neonates admitted are  $\geq$  28 weeks gestational age and with birth weight  $\geq$  1000 grams, reflecting the complexity of problems and the time required for treatment.

In our study, sepsis was also found to be significant, reaching an adjusted OR of 7.103 (CI 3.13-16.09) with a  $p < 0.05$ . Neonates diagnosed with sepsis or those receiving antibiotics have been acknowledged by various authors. Ahlén, Katia et al. (2016) conducted a cross-sectional correlational study with 527 neonates and found that preterm infants treated with antibiotics had prolonged stays<sup>(16)</sup>. Kurek, Meryem et al. (2016) also identified sepsis and pneumonia as significant factors<sup>(11)</sup>. Khasawneh, Wasim et al. (2021) pointed to sepsis<sup>(13)</sup>, Sahiledengle, Biniyam et al. (2020) to hospital-acquired infections<sup>(14)</sup>, and Murki, Srinivas et al. (2020) to sepsis cases<sup>(15)</sup>. The use of various invasive interventions, mechanical ventilation, parenteral nutrition, handling, and the potential presence of highly resistant germs in the ICU make sepsis a common complication that can prolong the stay of the hospitalized neonate.

Respiratory Distress Syndrome (RDS), formerly known as Hyaline Membrane Disease (HMD), associated with pulmonary immaturity in preterm infants, achieved appropriate risk and significance values (OR 10.37, CI 4.82-22.28) with a p-value < 0.05. Its occurrence also represented an important factor confirmed in various studies. Donda Keyur et al. in 1,526,186 preterm infants <34 weeks, (RDS: 260/1000 live births), found an average stay of 38 days<sup>(17)</sup>. Khasawneh, Wasim et al. (2021)<sup>(13)</sup> and Murki, Srinivas et al. (2020)<sup>(15)</sup> also concluded that RDS is a highly influential factor in hospital stays. Once again, immaturity, in this case at the pulmonary level, plays an important role in the use of invasive methods or mechanical ventilation that can lead to complications extending the stay in the neonatal ICU.

Anemia is a silent but very common factor in the neonatal ICU due to the population of preterm neonates admitted, thus achieving significance as a risk factor for PS. The authors present results that also express its influence on HS. Li Jinrong et al. (2021) in a meta-analysis conducted in 1807 preterm infants to assess the efficacy and safety of cord clamping at birth, found that late clamping reduces anemia and HS<sup>(18)</sup>. Anemia in preterm infants is a common event that often prolongs and affects the oxygen quality, impacting the functional status of various organs and systems. The transfusion of blood packs to stabilize the neonate is not rare and responds to the consequences of blood monitoring and other factors such as hemorrhages, immaturity, or of a nutritional nature. Usually as a PS factor, it overlaps others and affects the neonate's condition.

Neonatal malnutrition is related to birth weight conditions but also to the ability to adapt to feeding and its progress rate. We evaluated this factor in a population of 223 preterm infants and identified its influence on PS (Adjusted OR: 10.23, CI 4.73-22.12). Macuartú Amanda (2017), studying 37 very low birth weight neonates, found an average HS of 43.8 days. Weight (37.8%), head circumference (40.6%), and discharge weight (54.1%) in <3 percentile<sup>(19)</sup>. Thabet Amina 2021, studied 60 preterm infants (30 – 34 weeks) and found that oral motor intervention reduces the HS of these patients by improving their feeding and

weight gain<sup>(20)</sup>. Maintaining adequate nutritional intake and developing conditions for successful breastfeeding are a significant challenge faced daily by neonatal units. Preterm infants, due to their immaturity and complications, require special attention in this regard, and their progress may require more days of hospitalization.

In this study, the factors of SGA and NEC were analyzed with the following risk values (OR 3.097, CI 1.77-5.4 and OR 7.29, CI 2.19-24.31 respectively), but with the adjusted OR in logistic regression, they did not achieve significance, possibly due to the number of cases and the small difference between cases and controls. Kurek, Meryem et al. (2017), identified NEC as a factor<sup>(21)</sup>. Murki, Srinivas et al. (2020)<sup>(15)</sup>, on the other hand, found significance in the SGA and NEC cases. When cardiovascular disease was assessed as a group, a risk value was found (OR 6.55, CI 3.21-13.34), but congenital heart disease was not identified as a significant factor, as the OR 2.184, 0.676-7.06, could not be confirmed in the adjusted OR (aOR: 1.41, CI 0.38-5.19, p > 0.05). The same happened with the PDA (OR, 10.108 CI 3.848-26.552) that in the adjusted OR (1.411, CI 0.384-5.5.192) did not achieve significance. Kurek, Meryem et al. (2017), on the contrary, obtained a significant risk for congenital heart disease and PDA. Individually, PPHN found significance with an adjusted OR value: 32.17 (CI 1.852-559.016) and p = 0.017 (< 0.05) (21). Lowe, Calvin et al. (2007), in a study conducted in 94 neonates with PPHN, in which they evaluated the use of Nitric Oxide during transport to the referral hospital to reduce the HS (38 days), found a reduction of the same in 17 days<sup>(22)</sup>. This coincides with our pointing it out as an important factor.

When assessing respiratory distress as a group, we found a risk value (OR: 2.561, 1.43-4.58), but individually these factors (NN: OR 0.92, CI 0.32-2.59; TTN: OR 0.11, CI 0.052-0.26; BPD: OR: 0.22. CI 0.189-0.22; PNx: OR 1.68, CI 0.55-5.16) did not show the same pattern. The most relevant factors found in different studies regarding their influence on neonatal PHS were: birth weight, gestational age, sepsis, and RDS; the same ones were also identified in this study. Reference values for PS were very variable, as well as the methodology of the studies. Few studies focused on the anemia of the preterm and neonatal malnutrition since they usually have a chronic course and their impact is projected in the long term.



The strengths of this study can be observed in the period of the collected data since a review of clinical records was conducted over 5 years, obtaining a significant number of neonates that exceeded the selection criteria. With the exclusion criteria, it was intended to eliminate confounding factors such as genetic syndromes, referrals (received or sent), deceased or surgically intervened. The review of records and clinical histories was meticulous to ensure the fidelity of the information.

Among the limitations of the study, it is worth noting that the diagnoses recorded in the histories were accepted as such since the study did not intend to apply specific criteria for such diagnoses. The number of cases of certain diagnoses such as extremely low birth weight and BPD are insufficient for a good analysis and may be absent in the results. Administrative, logistical, equipment, and personnel factors, among others, are not part of the study, but they can impact the stay of neonates. The patient selection was not optimal in that adequate matching was not achieved, but all available cases were taken.

## CONCLUSIONS

- a. Neonatal PHS is significantly associated with perinatal risk factors: birth weight (from 1000gr to <1500gr) and gestational age (28 to 31 weeks and 32 to 33 weeks).
- b. Neonatal PHS is significantly associated with postnatal risk factors: Neonatal respiratory distress

syndrome, persistent pulmonary hypertension, neonatal sepsis, neonatal malnutrition, and prematurity anemia.

c. The selected factors: asphyxia, transient tachypnea of the newborn, pneumonia, pneumothorax, bronchopulmonary dysplasia, meconium aspiration syndrome, persistent ductus arteriosus, congenital heart disease, hyperbilirubinemia, hypoglycemia, necrotizing enterocolitis, and prematurity apnea; did not achieve significant association with PHS in this study.

The identified risk factors are neonatal pathologies or conditions that require highly complex care. These accumulate over the days of hospitalization and demand considerable resources from the institution. In light of this, it is essential to delve into each factor, breaking down the various stages of their evolution and the processes involved, to implement any required changes or improvements, be they administrative or medical in nature. These should involve the various stakeholders in charge of the established or to-be-established processes for preventive or recuperative neonatal care, refining logistical and technological processes as well as human potential development.

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**Correspondence:** Gladys Edith Victorio Arribasplata.

**Address:** Hospital Santa Rosa, Av. Bolívar Cuadra 8 S/N Pueblo Libre, Lima.

**Telephone number:** 945076805

**Email:** [gvictorio@hsr.gob.pe](mailto:gvictorio@hsr.gob.pe)





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