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## Characterization of transfused neonates in a hospital institution in Medellín, Colombia. Cases series.

### Caracterización de neonatos transfundidos en una institución hospitalaria de Medellín, Colombia. Serie de casos.

Yulis Fernanda Lobo-Salas,<sup>a</sup> Lina Maria Martínez-Sánchez,<sup>b</sup> Lucelly López-López,<sup>c</sup> Ana Paulina Pamplona-Sierra,<sup>d</sup> Laura Isabel Jaramillo-Jaramillo,<sup>e</sup> Juan Diego Villegas-Álzate,<sup>f</sup> Mabel Dahiana Roldan-Tabares,<sup>g</sup> Alejandro Hernandez-Martinez,<sup>h</sup> Laura Herrera-Almanza,<sup>i</sup> Juan Pablo Orozco-Forero<sup>j</sup>

#### Abstract

**OBJECTIVE:** To characterize clinical and epidemiological aspects of transfused neonates in Intensive and Special Care Units of a high-complexity Institution in Medellín, Colombia.

**MATERIALS AND METHODS:** Retrospective descriptive study that included hospitalized neonates in intensive or special care units between 2017 and 2018 who received transfusions during their hospital stay. For data collection information from medical records was used. The data analysis was done in the SPSS software, average and standard deviation were calculated for quantitative variables, and for qualitative variables, proportions were estimated. This study had ethical approval.

**RESULTS:** 175 patients were included, with an average gestational age at birth of 31 weeks and an average weight of 1610 grams. 52.9% of the population was female. The main diagnoses were prematurity 127 (72.6%), respiratory distress syndrome 93 (53.1%), sepsis 75 (42.8%), and unspecified anemia 53 (30.3%). 94.4% of the neonates were hospitalized in the intensive care unit, with a median hospital stay of 35 days. Discharge was the main outcome with 83.7%, followed by death with 11.6%.

**CONCLUSIONS:** Red blood cell transfusion in the neonatal population was frequently used in those admitted to intensive and special care units, this intervention showed favorable results but the lack of data in the medical records as a retrospective study limits the establishment of further associations.

**KEYWORDS:** Newborn infant, Blood transfusion, Premature infant, Newborn infant diseases.

#### Resumen

**OBJETIVO:** Caracterizar clínica y desde la perspectiva epidemiológica a los neonatos transfundidos en la Unidad de cuidados intensivos y especiales de una institución de alta complejidad en Medellín Colombia.

**MATERIALES Y MÉTODOS:** Estudio descriptivo retrospectivo que incluyó neonatos hospitalizados en servicios de cuidados intensivos o especiales entre 2017 y 2018, que durante su estancia hospitalaria hayan recibido transfusión de algún hemoderivado. Para la recolección de información se emplearon datos de la historia clínica. El análisis de los datos se realizó en el programa SPSS, a las variables cuantitativas se les calculó el promedio y la desviación estándar y a las cualitativas se les estimaron proporciones. Este trabajo contó con aprobación ética.

**RESULTADOS:** Se incluyeron 175 pacientes, el promedio de edad gestacional al nacimiento fue de 31 semanas y un peso de 1610 gramos. El 52.9% de la población fue de sexo femenino. Los principales diagnósticos subyacentes fueron prematuridad 127 (72.6%), síndrome de dificultad respiratoria 93 (53.1%), sepsis 75 (42.8%) y anemia no

#### ORDICID

<http://orcid.org/0000-0002-0500-9405>  
<http://orcid.org/0000-0002-9555-0843>  
<http://orcid.org/0000-0002-1534-520X>  
<https://orcid.org/0000-0001-5042-626X>  
<http://orcid.org/0000-0002-2123-0847>  
<http://orcid.org/0000-0002-7544-9801>  
<http://orcid.org/0000-0001-5226-2393j>  
<http://orcid.org/0000-0001-6577-9666>  
<http://orcid.org/0000-0003-1898-1268>  
<http://orcid.org/0000-0002-4166-4773>

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#### Correspondence

Yulis Fernanda Lobo Salas  
[yulis.lobos@upb.edu.co](mailto:yulis.lobos@upb.edu.co)

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especificada 53 (30.3%). El 94.4% de los neonatos estuvo hospitalizado en la unidad de cuidados intensivos, con una mediana de estancia hospitalaria de 35 días. El alta fue el desenlace principal con un 83.7% seguido de muerte con un 11.6%.

**CONCLUSIONES:** La transfusión de glóbulos rojos fue muy usada en la población neonatal admitida a unidades de cuidados intensivos y especiales, esta fue una intervención que mostró ser una intervención favorable, pero como estudio retrospectivo la falta de datos en la historia clínica limita realizar más asociaciones.

**PALABRAS CLAVE:** recién nacido, transfusión de componentes sanguíneos, recién nacido prematuro, enfermedades del recién nacido.

## INTRODUCTION

Transfusion of blood components, especially red blood cells, is one of the most common "life-saving" interventions in clinical practice, and neonatal services are no exception.<sup>1-3</sup> Neonatal patients, with their relatively lower blood volume and immature hematopoietic system, are among the most transfused populations.<sup>4,5</sup> The smaller the newborns, the more likely they are to receive transfusions, with 50% to 94% of very low birth weight infants (birth weight <1500 g) and up to 95% of extremely low birth weight infants (birth weight <1000 g) reported to receive at least one transfusion, with an average of up to 8 to 10 transfusions during their hospital stay.<sup>6,7</sup>

Transfusion rates differ over time and between populations due to variation in clinical practice and transfusion criteria at each institution. For example, in New South Wales (Australia), neonatal transfusion is performed in approximately 5.4 per 1000 births, and red blood cell transfusion rates remain constant at 4.8 per 1000 of them.<sup>8,9</sup> On the other hand, in Colombia, current information on the number of transfusions in this population is limited, however, in the bulletin of the blood network in Bogotá for 2017, they reported a total of 3796 transfused patients in neonatal intensive

care units, corresponding to 5% of all newborns hospitalized during that year.<sup>10</sup>

The blood components that are regularly transfused are red blood cells, platelets, fresh frozen plasma, and cryoprecipitate; red blood cells concentrate being the most frequently used component in neonatal intensive care units.<sup>11-13</sup> The indication for red blood cell transfusion will depend on the goals to be achieved, the patients underlying pathology and clinical status, however, the main indications are hyperbilirubinemia and anemia of prematurity, followed by hemorrhagic events. As for platelet transfusion the main cause is thrombocytopenia which can be a common hematologic disturbance in neonates, especially in those born preterm result of multiple factors such as fetal growth restriction, neonatal sepsis or be the only manifestation of alloimmune thrombocytopenia.<sup>14,15</sup> Finally, fresh frozen plasma and cryoprecipitate are mainly used in coagulopathies.<sup>16</sup>

The highest incidence of transfusions occurs in the first 14 days of life, with a second peak after 28 days of age, probably due to late complications and special conditions in the preterm group of newborns.<sup>17</sup> Each transfusion may produce a transfusion reaction that most of the time is as

expected according to its indication, however, a small number of patients, 0.5% to 3.0%, may experience some adverse effect that may be immediate or delayed.<sup>18</sup>

Premature infants who receive multiple transfusions are not only exposed to different donors but also the risk of exposure to infections and iron overload from blood product components, increasing the risk of retinopathy of prematurity, necrotizing enterocolitis, metabolic and hydro electrolytic disorders, among others.<sup>3,19,20</sup>

## OBJECTIVE

To characterize clinical and epidemiological aspects of transfused neonates in the intensive and special care unit of a high complexity institution in Medellín, Colombia.

## MATERIALS AND METHODS

### Design and study population

An observational, cross-sectional, descriptive case series study was conducted including medical records of patients who met the following eligibility criteria: newborn patients hospitalized in intensive or special care services who during their hospital stay had received some type of blood product, in the period from January 2017 to December 2018. A non-probabilistic sampling of consecutive cases was performed.

### Data collection process

The source of the information was secondary, through clinical records. For the collection, a form was designed by the research group where the clinical, sociodemographic, and laboratory variables were collected to comply with the objectives.

### Statistical analysis

The information collected was entered into a database with variable validation to reduce possible biases. A periodic review of the records was carried out to verify the quality of the information obtained. The analysis was carried out using the SPSS Version 24 software, estimating absolute and relative frequencies for qualitative variables, and mean with deviation or median with interquartile ranges for quantitative variables, as appropriate.

### Ethical considerations

According to resolution 008430 of 1993 of the Colombian Ministry of Health, this work constitutes research without risk, since no interventions were performed on the study sample. In addition, ethical approval was obtained from the participating hospital for the execution of this research.

## RESULTS

A total of 175 neonates were included in this study, with a female predominance of 52.9% (92). The median of gestational age was 31.5 weeks, with a 25th percentile (P25) of 29 weeks and a 75th percentile (P75) of 36 weeks. Regarding weight, the median was 1610 grams with a P25 of 1110 grams and a P75 of 2620.

Concerning the general condition of the neonates, 34.3% (60) and 58.8% (103) had a normal APGAR at 1 minute and 5 minutes, respectively.

In relation to the most frequent clinical characteristics of the neonates who received transfusions, 72.6% (127) of the patients were premature, 68.6% (120) had anemia, and 53.1% (93) presented respiratory distress syndrome.

Among other clinical characteristics identified in the population, the blood type and Rh found

were 52.6% (96) O positive, followed by 33.1% (58) A positive, and 8% (14) B positive.

As for the records, structural congenital anomalies with 38.3% (67) and ventilatory support with 48% (84) were the most frequent, follow by history of surgical intervention with 17.1% (30) and history of bleeding with 10.9% (19); it is worth noting that these findings are non-exclusive.

Regarding hospitalization, 94.9% (166) were in the neonatal intensive care unit (NICU), 4% (7) in the neonatal special care unit (NSCU), and 1.1% (7) in the neonatal basic care unit; the median number of hospitalization days was 35 days with a P25 of 18 days and a P75 of 58 days.

The main diagnoses that the neonates had were unspecified anemia with 32.6% (57) followed by hyaline membrane disease with 14.3% (25), bronchopulmonary dysplasia with 13.7% (24), and thrombocytopenia with 9.7% (17). These diagnoses were not exclusive and there were others with non-representative percentages. **Table 1** shows the hematological variables evaluated in these patients.

A total of 539 transfusions were reported in the 175 patients included, with a median of 5 transfusions per neonate, finding that the 25th and 75th percentile was 1 to 4 transfusions; the maximum range of transfusions received was between 18 and 22, this only occurred in one patient for each case (2.9%).

The main indications for transfusion were low Hb and/or HCT levels with 70.3% (396) and coagulopathy with 14.9% (84), followed by hypovolemic shock with 3% (17), and other causes represented the remaining percentage (they are not exclusive, with a total of 563 indications). Fluid overload was the most common early complication, see **Table 2**.

As to the first transfusion of the patients included in this study, the frequency of use of each blood

product was: 160 times the packed red blood cells, 6 times fresh frozen plasma, 9 times platelets. In most cases the transfused volume was below 40 cubic centimeters (cc) in 147 occasions and above 40 cc only in 28.

The most frequently used dose was 30 cc for any of the blood products, followed by 10 cc.

For the total number of transfusions (539), packed red blood cells were the most frequently used blood products with 82.5% (444), followed by platelets 12.2% (66) and fresh frozen plasma with 5.3% (29). The use of cryoprecipitate was not reported.

About the clinical outcomes, 83.7% (144) of the patients were discharged, 11.6% (20) died, 2.9% (5) were referred to another institution and 3 patients, corresponding to the remaining 1.7%, did not have this information in their medical records because this was a retrospective study.

## DISCUSSION

Blood transfusions are an important part of modern medicine and neonates are the most fragile and labile patients facing changes, so among their treatments are the transfusion strategies of packed red blood cells for the treatment of neonatal anemia.<sup>5</sup>

In the study carried out by Bowen et al in Australia in neonates admitted to the NICU who received some blood product, the male sex predominated with 55.4% (2952), compared to the present study in which the female sex predominated with 52.9% (92), in a similar population.<sup>8</sup>

In relation to gestational age, the median age was 31.5 weeks, with a median birth weight of 1610 g, compared to the study conducted by Escolan and Eguigurems in which they reported a gestational age of 37 weeks and a mean weight in grams of 2257.<sup>12</sup> While in the study performed

**Table 1.** Hemoleucogram before the blood product transfusion

Parameter	Median	25 <sup>th</sup> percentile	75 <sup>th</sup> percentile
Erythrocyte count 10 <sup>6</sup> /μL	3.1	2.7	3.5
Hemoglobin (Hb) g/dL	10.5	9.5	11.8
Hematocrit (HCT) %	30.3	27.5	33.8
VCM <sup>†</sup> fL	101.8	96.3	107.8
HCM <sup>‡</sup> pg	35.6	33.8	37.1
CHCM <sup>§</sup> g/dL	34.9	34.1	35.7
ADE <sup>†</sup> %	17.2	16.0	18.8
Leukocyte count 10 <sup>3</sup> /μL	11.0	8.3	15.1
Neutrophils 10 <sup>3</sup> /μL	4.7	2.5	7.7
Neutrophils %	44.3	31.6	57.5
Eosinophils 10 <sup>3</sup> /μL	0.29	0.13	0.54
Eosinophils %	2.6	1.2	4.6
Basophils 10 <sup>3</sup> /μL	0.020	0.010	0.040
Basophils %	0.2	0.1	0.4
Lymphocytes 10 <sup>3</sup> /μL	3.9	2.3	5.2
Lymphocytes %	33.5	23.7	48.9
Monocytes 10 <sup>3</sup> /μL	1.5	1.0	2.1
Monocytes %	14.3	10.8	17.8
Platelets 10 <sup>3</sup> /μL	213	138	312

<sup>†</sup> Mean corpuscular volume

<sup>‡</sup> Mean corpuscular hemoglobin

<sup>§</sup> Mean corpuscular hemoglobin concentration

<sup>†</sup> Red blood cell distribution width

**Table 2.** Complications after transfusion

Early	n (%)	Delayed	n (%)
Fluid overload	64 (11.8%)	Delayed hemolysis	1 (0.2%)
Metabolic complications	22 (4.1%)	DIC <sup>†</sup>	1 (0.2%)
Acute lung injury	5 (0.9%)		
Cardiac arrest	3 (0.6%)		
Non-hemolytic febrile reaction	2 (0.4%)		
Hypothermia	2 (0.4%)		
Infection	2 (0.4%)		
Allergic reaction	1 (0.2%)		

<sup>†</sup>Disseminated Intravascular Coagulation

by dos Santos et al in Brazil in 126 neonates with a mean gestational age of  $29.0 \pm 2.8$  weeks, they reported a mean weight of  $1046 \pm 288$  g.<sup>21</sup>

With respect to APGAR in the Australian study performed by Bowen et al they obtained values  $<4$  at 1 minute in 24.5% (1305) and  $<7$  at 5 minutes in 26.7% (1263), compared to the data of the present study of 18.22% (32) and 23.3% (41) for 1 minute and 5 minutes, respectively.<sup>8</sup>

Dos Santos et al reported respiratory distress syndrome in 82.1% of the study population and sepsis in 41.9%, lower data were found at the present study in which 53.1% and 42.8% were reported for both pathologic states, respectively.<sup>21</sup>

In the present study, Hb levels before transfusion had a median of 10.5 g/dL, compared to the study by Ghirardello et al that reported a median of 9.6 g/dL.<sup>22</sup>

In this study, a total of 539 transfusions were reported in the 175 patients included, giving a median of 5 transfusions per neonate, compared to the study by dos Santos et al with 126 neonates in which the median number of transfusions was 2.<sup>21</sup>

In a study carried out in Honduras by Escolan and Eguigurems, they reported that the most used blood product was red blood cell concentrate in 50% of the cases, followed by platelets with 33.3% and plasma with 14.7%, data comparable with the present study in which the packed red blood cells, platelets and fresh frozen plasma were used in 82.5%, 12.2% and 5.3%, respectively.<sup>12</sup>

The main indication for transfusion was low Hb and/or HCT levels with 70.3%. De Leon and Szallasi in a study carried out in the United States reported that 96% of the indications were low Hb/HCT levels.<sup>18</sup>

As for mortality in the present study a figure of 11.6% was reported (20), while Ghirardello et al for this same variable reported 9%.<sup>22</sup>

The main limitation of this retrospective study is the lack of information in the medical records, which prevents the analysis of some clinical variables that may be important in the management of transfused neonates. In addition, there is evidence of the need to develop standardized management guidelines to obtain better clinical results with the use of blood products in this population.

## CONCLUSION

In neonates admitted to intensive and special care units was frequently used the red blood cells transfusion, this intervention showed favorable results and was used on numerous occasions in each patient. However, as a retrospective study the lack of data in the medical records limits the establishment of a cause-effect association, for which reason it is suggested that new studies needs to be carried out.

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