Impact of Blood Transfusion on Vital Signs and Cardiac Functions in Neonates with Anemia

By

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ABSTRACT

Background: There is no clear objective hemoglobin or hematocrit (HCT) level below which blood transfusion is recommended in neonates. Moreover, hemodynamic measurements are not common in transfusion practice. The decision to transfuse is, therefore, frequently based on clinical signs and standard guidelines.

Objectives: To study the impact of blood transfusion on vital signs and cardiac functions in neonates with anemia

Patients & Methods: This cross-sectional study was conducted during the period from May 2023 to May 2024 on 40 preterm and full-term neonates less than 4 weeks of life of both sexes admitted to NICU at Al-Hussein University hospital Diagnosed as anemia and fulfilled the criteria of blood transfusion.

Results: The Results showed that the age ranged from 2 to 24 days with a mean of 8.7 ± 6.09 days. Gestational age ranged from 31 to 37 weeks with a mean of 33.5 ± 1.77 weeks. There were 14 (35%) males and 26 (65%) females. Weight ranged from 1.7 to 3.5 kg with a mean of 2.3 ± 0.41 kg. Length ranged from 41 to 50 cm with a mean of 44.6 ± 5.43 cm. Also, the causes of clinical instability of the studied patients were, 13 (32.5%) patients were subjected to continuous positive airway pressure with FiO2 >40% aged less than 7 days with Hb below 13 gm , 7 (17.5%) patients had early-onset sepsis with vasopressor support aged 8 to 14 days with Hb below 9 gm/dl,1 (7.5%) patients had late-onset sepsis with vasopressor support aged 20 days with Hb below 7 gm/dl , 12 (30%) patients were subjected to mechanical ventilation aged less than 7 days with Hb below 13 gm/dl, 5 (12.5%) patients had nasal catheter with vasopressor support aged 8 to14 days with Hb below 9 gm/dl, and 2 (5%) patients had surgery (imperforated anus) aged less than 7 days with Hb below 13 gm/dl. Respiratory rate before transfusion ranged from 45-63 breath\minute with a mean 53.2 ± 4.16 and after transfusion 45-60 breath\minute with a mean 51.8 ± 4 (P<0.001) , heart rate before transfusion ranged from 170-210 beat\minute with a mean 184.4 ± 6.81 and after transfusion from 140-163 beat\minute with a mean 154.7 ±5.83 (P<0.001), oxygen saturation before transfusion ranged from 91-96 % with a mean 93.7 ± 1.43 and after transfusion from 93-97 % with a mean 94.4 ±1.24 (P<0.001), MAP before transfusion ranged from 51_67 mmhg with a mean 59.3 ± 4.64 and after transfusion from 51-67 mmhg with a mean 60.3 ±4.36 (P<0.001), Ejection fraction before transfusion ranged from 51-69 % with a mean 60.2 ± 5.52 and after transfusion from 52-69 with a mean 61.4 ±5.61 (P<0.001), LVET before transfusion ranged from 170-239 ms with a mean 189.9 ± 20.82 and after transfusion from 162-264 with a mean 218.4 ±28.38 (P<0.001), stroke volume before transfusion ranged from 3.2-5.2 ml with a mean 4.3 ± 0.58 and after transfusion from 3.2-5.4 ml with a mean 4.4 ±0.57 (P<0.001), and fractional shortening before transfusion ranged 32-50% with a mean 37.1±2.85 and after transfusion from 35-41% with a mean 38.6 ±1.77 (P<0.001) , cardiac output before transfusion ranged from 0,61-0.97 L\m with a mean 0.8 ± 0.1 and after transfusion from 0.56-0.85L\m with a mean 0.7±0.08 (P<0.001)

Conclusion: The study revealed that Blood transfusion improves the clinical symptoms in neonates with anemia and showed Significantly higher oxygen saturation, MAP, lower heart rate and respiratory rate and significant effect on the heart function including; increase in EF, LVET, SV, Fs and decrease in cardiac output.

Key words: Blood transfusion, vital signs, cardiac function, Neonatal Intensive Care Units, neonates, anemia.

INTRODUCTION

All newborns are subjected to decline in hemoglobin levels in the first weeks after birth. In neonatology, this condition is often called physiological anemia of the newborn. In healthy term neonates, clinical signs or symptoms of anemia are absent; this normal decline in Hb is referred to as "physiologic" or "early anemia of infancy" **(Saito Benz etal., 2020)**

It was noted that the lowest value of hemoglobin in term neonates may fall below 10 gm/dL in age from 10 to 12 weeks; In contrast, anemia in preterm neonates (anemia of Prematurity) is the pathophysiological process with larger and faster drop in hemoglobin. Consequently, there is a need for blood transfusion and application of human recombinant erythropoietin. **(Laura and Thamires, 2021)**

The anemia experienced by neonates depends on the blood loss at birth, inadequate erythropoiesis, frequent blood sampling, rapid growth, hemorrhage and hemolysis. **(Saito Benz et al., 2019)**

The echocardiogram provides critical insights into how the neonatal heart compensates for anemia by evaluating parameters such as cardiac output, ventricular function, and stroke volume. **(Ilardi et al., 2021).** In anemic neonates, the heart often compensates by increasing cardiac output through a combination of higher heart rate and stroke volume **(Giesinger and McNamara,.2021).**

Echocardiography can measure these changes by assessing ventricular size, wall motion, and flow velocities. For instance, an increase in left ventricular end diastolic dimension may indicate volume overload, which is a common finding in anemic neonates as the heart attempts to increase stroke volume to compensate for reduced oxygen-carrying capacity **(Khot et al., 2023).**

Parameters such as left ventricular ejection fraction (LVEF) and fractional shortening (FS) can be particularly useful in determining the degree of cardiac stress in anemic infants **(Nestaas., 2022).**

AIM OF THE STUDY

The aim of this study is to find the impact of blood transfusion on vital signs and cardiac functions in neonates with anemia

PATIENTS AND METHODS

The sample size and power analysis were calculated using Epi-Info software statistical package created by World Health organization and center for Disease Control and Prevention, Atlanta, Georgia, USA version 2002. The criteria used for sample size calculation were as follows:

- Confidence limit 95%
- Accepted error 5%
- Power of the study 86 %

The sample size was found at N = 38 cases at least

Ethical consideration:

1. Approval of ethical committee in the pediatric department, college and university was obtained before the study.
2. written consent was taken from parents of each participant before the study.
3. The parents have the right to withdraw his or her newborn from the study at any time.

Postnatal age	Gestational age	Hemoglobin (hematocrit) thresholds For transfusion	
		Neonates With Clinical instability	Neonates Without clinical instability
0-7 days	Any	13 gm/dL (34%)	10 gm/dL (29%)
8-14 days	<35 weeks	12 gm/dL (32%)	8 gm/dL (24%)
	≥35 weeks	9 gm/dL (26%)	7 gm/dL (21%)
≥15 days	<35 weeks	10 gm/dL (28%)	7 gm/dL (21%)
	≥35 weeks	7 gm/dL (21%)	7 gm/dL (21%)

(Lacroix et al.,2007)

- Diagnosed as anemia and fulfill the criteria of blood transfusion according to the following criteria:

Clinical instability is defined by the presence of at least one of the following:

- Invasive mechanical ventilation Circulatory failure requiring inotropic/vasopressor support
- CPAP or other non-invasive positive pressure ventilation support with fraction of inspired oxygen >0.4
- Acute sepsis or necrotizing enterocolitis with hemodynamic instability requiring vasopressor support
- > 6 documented apneas requiring moderate intervention per 24 hours
- Undergoing major surgery (within or up to 48 hours after surgery (**Lacroix et al.,2007)**

Exclusion criteria

- Patient older than 4 weeks of age.
- Cardiac defects, severe congenital malformations, presence of other potential causes of bradycardia and/ or hypoxemia such as intracerebral hemorrhage, neonates with ongoing blood loss, severe alloimmune hemolytic disease of newborn **(Sawyer AA et al., 2017).**

Study procedure

• Patients with anemia were selected from NICU according to above mentioned inclusion and exclusion criteria and all neonates received packed RBC according to equation of volume of blood transfusion

$$\frac{\text{weight in kg x blood volume per kg x (desired HCT} - \text{observed HCT)}}{\text{HCT of blood to be given}}$$

over a period of 4-5 hrs, according to the usual transfusion procedure on the NICU. **(Padhi et al.,2015)**

All neonates included in the study were subsequently subjected to:

I. **Full medical history talking including:** age and sex, full perinatal history and gestational age, signs suggestive of anemia (e.g. desaturation, bradycardia, increase oxygen requirement, tachycardia and mottled skin).

II. **Complete clinical examination including:**

a. Vital signs were measured to detect any abnormality of vital signs (respiratory rate, heart rate, temperature, oxygen saturation, blood pressure, capillary refill time).
b. Assessment of gestational age according to Ballard and new Ballard score**. (Allan et al., 2009).**
c. Body weight and length according to ponderal index. **(Chard et al.,2012)**
d. Cardiac examination to detect any structural cardiac abnormality.
e. Echo-cardiograph was performed to cases under investigations.

III. **Laboratory evaluations included:**

Complete blood count (CBC) with our main interest concerning Hb. (g\dl), Hct and RBC counts and RBCs indices **(Gothwal et al., 2021).**, Mother blood group, Baby blood group, Rh factor, Blood film, Reticulocyte count **(Sakharkar et al.,2024)**, ESR and CRP. **(Elsayed et al., 2021)**.

IV. **Echocardiography:** Echo-Doppler examination was performed for all cases pre and 2hours post blood transfusions in a supine or left lateral position using Philips EPIQ7C (multi frequency transducer) according to the age of patient, having tissue velocity Imaging Capabilities.

V. All neonates underwent recording of vital signs (respiratory rate, heart rate, oxygen saturation and systemic blood pressure) before and after transfusion.

RESULTS

The result of our study will be demonstrated in the following tables:

Table (1): Demographic data of the studied patients

Variable	Number	Percentage %
Post-natal age (Days)		
Mean ± SD	8.7 ± 6.09	
Range	2 – 24	
GA (weeks)		
Mean ± SD	33.5 ± 1.77	
Range	31 – 37	
Sex		
Male	14	35%
Female	26	65%
Weight (kg)		
Mean ± SD	2.3 ± 0.41	
Range	1.7 - 3.5	
length (cm)		
Mean ± SD	44.6 ± 5.43	
Range	38 – 50	

This table shows: **Demographic data of the studied patients.**

Table (2): Causes of clinical instability of the studied patients

Variable	Number	Percentage %
RDS on CPAP with Fio2>40%	13	32.5 %
EOS with Vasopressor Support	**7**	17.5 %
LOS with vasopressor support	1	2.5 %
Patient with RDS on MV	12	30 %
Nasal catheter with vasopressor support	5	12.5 %
Surgery (imperforated anus)	2	5 %

This table shows: **clinical instability of the studied patients with predominance of babies with RDS on CPAP with Fio2 > 40%**.

Table (3): Clinical findings before and after transfusion of the studied patients

Variable	**Number**	**Percentage %**	
Temperature (◦C)			
Mean ± SD	37.4 ± 0.5		
Range	36.9 - 38.5		
Capillary refill time			
<3 sec	34	85%	
>3 sec	6	15%	
Variable	**Before Transfusion**	**After transfusion**	**P-value**
RR (breaths/min)			
Mean ± SD	53.2 ± 4.16	51.8 ± 4	**<0.001***
Range	45 - 63	45 - 60	
O2 saturation (%)			
Mean ± SD	93.7 ± 1.43	94.4 ± 1.24	**<0.001***
Range	91 – 96	93 - 97	
MAP (mmHg)			
Mean ± SD	59.3 ± 4.64	60.3 ± 4.36	**<0.001***
Range	51 – 67	51 - 67	
H.R (beat/min)			
Mean ± SD	184.4 ± 6.81	154.7 ± 5.83	**<0.001***
Range	170 - 201	140 - 163	

This table shows: statistically significant improvement of mean readings of RR, O2 saturation, MAP and heart rate.

Table (4): Echocardiographic data of the studied patients before and after transfusion

Variable	**Before transfusion**	**After transfusion**	**P-value**
Ejection fraction (%)			
Mean ± SD	60.2 ± 5.52	61 ± 5.61	**<0.001***
Range	51 – 69	52 - 69	
LVET (ms)			
Mean ± SD	189.9 ± 20.82	218.4 ± 28.83	**<0.001***
Range	170 – 239	162 - 264	
Stroke volume (ml)			
Mean ± SD	4.3 ± 0.58	4.4 ± 0.57	**<0.001***
Range	3.2 - 5.3	3.2 - 5.4	
Cardiac output (L/min)			
Mean ± SD	0.8 ± 0.1	0.7 ± 0.08	**<0.001***
Range	0.61 - 0.97	0.56 - 0.85	
Fractional shortening (%)	37.1 ± 2.85	38.6 ± 1.77	**<0.001***
Mean ± SD	32 – 50	35 - 41	
Range			

This table shows: statistically significant improvement of EF, LVET, SV, FS and decrease in CO.

DISCUSSION

This cross-sectional study was conducted on 40 neonates admitted at NICU at Al-Hussein University hospital diagnosed with anemia and fulfilled criteria of blood transfusion.

In the current study, regarding the causes of clinical instability of the studied patients, 13 (32.5%) patients were subjected to continuous positive airway pressure, with FiO2 40% 7 (17.5%) patients had early-onset sepsis with vasopressoer support, 3 (7.5%) patient had late-onset sepsis with vasopressor support, 12 (30%) patients were subjected to mechanical ventilation, 5 (12.5%) patients had nasal catheter with vasopressor support, and 2 (5%) patients had surgery (imperforated anus).

In accordance with us, **Qi and Li-na (2018)** found that among the 60 premature infants included, 18 premature infants required mechanical ventilation, and 5 (8%) premature infants 22 (37%) premature infants required nasal cannula or oxygen inhalation by mask.

In alignment with us, **Leipälä et al. (2004)** reported that out of 37 infants, 10 infants were breathing spontaneously, 5 were supported by nasal CPAP, and 22 were mechanically ventilated.

All the studied patients (40 neonates (100%)) had a decrease in heart rate and Respiratory rat after transfusion compared to before transfusion (P<0.001) while oxygen saturation was significantly higher after transfusion compared to before transfusion (P<0.001). The mean arterial blood pressure (MAP) was significantly higher after transfusion compared to before transfusion (P<0.001).

In accordance with us, **Qi and Li-na (2018)** found that respiratory rate decreased significantly within 24 h after blood transfusion (P<0.05. The body temperature was not statistically different in pre- and post-transfusion (P>0.05). They revealed that no significant improvement was noted in oxygenation following blood transfusion in preterm infants. The heart rate decreased significantly within 24h after blood transfusion (P<0.05) and the MAP was not statistically different in pre- and post-transfusion (P>0.05), this can be explained by nature of studied sample being homogenous group (preterm).

In agreement with our findings**, Ge et al. (2015)** showed that the heart rate and respiration rate of the neonates were significantly decreased within 4 hours after blood transfusion compared with before blood transfusion. The MAP increased after blood transfusion compared with those before blood transfusion. However, there was no statistically significant difference in MAP compared with that before blood transfusion.

In same line with us, **(Quante et al., 2013)** reported that heart rate decreased significantly after PRBC transfusion compared with that before blood transfusion (P<0.01). Respiratory rate, MAP, temperature, and oxygen saturation before transfusion were insignificantly different with that after transfusion.

According to our study, ejection fraction (EF), left ventricular ejection time (LVET), stroke volume (SV), and fractional shortening (FS) of the studied patients were significantly higher after transfusion compared to before transfusion (P<0.001) while cardiac output (CO) was significantly reduced after transfusion compared to before transfusion (P=0.003 and <0.001 respectively).

In difference with us**, Qi and Li-na (2018)** found that there was no significant difference in left ventricular output and SV after blood transfusion compared with that before transfusion, this can be explained by nature of studied sample being homogenous group (preterm)

In disagreement with our findings, **Ge et al. (2015)** showed that the LVEF, SV, CO, and FS showed no significant changes after blood transfusion compared with that before transfusion (P>0.05), this can be explained by nature of studied sample being homogenous group (preterm below than 34 weeks and VLBW.

In contrast with us, **(Quante et al., 2013)** reported that LVET before transfusion was insignificantly different from that after transfusion. However, COP on the right and left sides before transfusion was significantly lower compared with that after transfusion as the study made on preterm groups

In contrast with **Leipälä et al. (2004)** reported that left ventricular output, stroke volume and arterial pressures remained unaltered. Oxygen saturation after

the transfusion was lower than before the transfusion (94.0±3.8 versus 95.3±2.5%, P =0.014) despite unaltered oxygen supply, this can be explained by a very low gestational age of this group.

CONCLUSION

Blood transfusion could improve the clinical symptoms in neonates with anemia and showed significant effect on the heart function including; increase in EF, LVET, SV, and FS and decrease in cardiac output. Significantly higher oxygen saturation and MAP, and lower heart rate and respiratory rate were observed in newborns after blood transfusion.

RECOMMENDATIONS

- Larger sample size is recommended for more accurate results.
- Longer duration of follow up.
- Classification according to the degree of anemia is needed for more definite results.
- Differentiation between effects in preterm and term neonates.
- Further studies are required about our research topic.

Limitation of the study

- Relatively small sample size and short follow up period.
- No classification according to the degree of anemia.
- Lack of differentiation between effects in premature and mature neonates.
- Few studies were found about our research topic.

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