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Original Article

# Incidence & Risk Factors for The Development of Transfusion-Associated Necrotizing Enterocolitis in Preterm Infants After Packed red Blood Cells Transfusion. A Prospective-Observational Study

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## Abstract

**Background:** Necrotizing enterocolitis (NEC) is a progressing inflammatory disease that is associated with high rates of morbidity and mortality in preterm babies. Transfusion-associated necrotizing enterocolitis (TANEC) is described as NEC where symptoms &/or signs start within 48 hours of blood or packed red blood cells (PRBCs) transfusion.

**Objective:** To determine the incidence of TANEC in preterms admitted to our neonatal intensive care unit & to identify the possible risk factors.

**Methods:** Sixty (60) preterms were conducted in this prospective observational study, they received packed red blood cells (PRBCs) transfusion due to different indications admitted to the NICU of the department of Pediatrics, Cairo University hospitals for a 6-months-duration and monitoring group of preterms who developed TANEC and compare all the possible risk factors.

**Results:** Out of the 60 preterms enrolled in the study, 13 (21.7%) preterms developed NEC within 48 hours after PRBCs transfusion. According to modified Bell´s staging for NEC: 7 preterms were diagnosed as stage I , 2 preterms were diagnosed as stage IIA, and 4 preterms in stage IIB, none of them required any surgical interventions, and no mortalities were detected among them. Low Apgar scores at 5 and 10 minutes & gestational age and low birth weight were highly statistically significant variants between both groups.

**Conclusion:** Keeping preterms receiving nothing per oral before, during & after PRBCs transfusion showed statistically significant protection against TANEC. The most significant alarming sign was the occurrence of episodes of apnea 12 hours after transfusion with a highly significant value.

**Key words**: Blood transfusion, preterm, necrotizing, enterocolitis

## Introduction

Numerous studies estimated that transfusion-associated necrotizing enterocolitis (TANEC) occurs after approximately 25–35% of transfusions. Multiple pathogenic mechanisms have been proposed [1].

In preterms, both anemia and RBCs transfusions can theoretically affect intestinal perfusion & induce injury. Possible mechanisms include splanchnic vascular bed immaturity, reperfusion injury in the anemic gut, and immune cascade similar to those seen in transfusion-related lung injury (TRALI) [2, 3].

Anti-HLA antibodies have been recognized in some preterms that developed TANEC [4].

Mucosal injury in the premature intestine presents a developmentally regulated proinflammatory dilemma with excessive immune responses to bacterial &/or nutritional antigens [5]. A decrease in NEC% was observed after initiating a protocol of withholding feeds during transfusions [6].

A meta-analysis aimed to determine the risk factors for NEC revealed significant prognostic factors for NEC: small for gestational age (SGA), low body weight (BW), low gestational age (GA), assisted ventilation, premature rupture of membranes (PROM), caesarean section (CS), black ethnicity, low Apgar scores at birth, sepsis, and hypotension [7].

**Aim of the Work:** To determine the incidence of occurrence of NEC in preterm neonates after PRBCS transfusion and to detect a correlation between the occurrence of NEC and the different feeding protocols applied.

## Patients and methods

This study was a prospective observational study, it was conducted on 60 preterms <36 weeks GA received PRBCs transfusion due to different indications in our neonatal intensive care unit (NICU), Cairo University hospitals for a 6-months-duration.

There were different causes of PRBCs transfusion including anemia of prematurity, hemolytic ABO or RH incompatibility, intracranial hemorrhage (ICH), and pulmonary hemorrhage. We excluded hemodynamically unstable neonates as persistent hypotension, persistent hypoxemia and acidosis in arterial blood gases, large doses of inotropes (Dopamine > 5 mic/kg/min &/or Dobutamine > 10 mic/kg/min), neonates with current or previous NEC or chromosomal abnormalities or severe congenital malformations.

Our 60 included preterms were divided into 2 groups according to the occurrence of NEC symptoms within 48 hours after PRBCs transfusion, (Group 1) developed NEC symptoms & signs within 48 hours after PRBCs transfusion, and (Group 2) with no NEC symptoms & signs developed after PRBCs transfusion till 1 week after transfusion.

Informed consent was taken from patients' guardians before enrollment with an explanation of the type of study.

The study design conformed to the requirements of the Revised Helsinki Declaration of Bioethics (2013) [8]. The study was authorized by The Scientific Ethics Committee of the Pediatrics Department, Faculty of Medicine, Cairo University, and the Higher Studies Research Committee of the Faculty of Medicine. Data were documented in the patients' files and on special excel sheets. Confidentiality in handling the database was guaranteed and the privacy of participants was ensured. The results of the research are used only in a scientific aim.

All the preterms included in the study were subjected to full history taking from their parents or caregivers including maternal history. Apgar scores at 1, 5, and 10 minutes were recorded. Data including a list of medications prescribed, feeding protocol that was ordered by NICU physicians, presence of central lines, positive blood culture, and associated complications of prematurity were recorded.

All preterms were subjected to the standard clinical evaluation and monitoring as per NICU protocol.

PRBCs transfusion was given, and we followed the guidelines of PRBCs transfusion in preterm infants according to the protocol we follow at our NICU [9].

Number, timing, and the cause of transfusions administered were obtained. All transfusions were irradiated, as in our NICU usually, the blood donation come from first or second-degree relatives which necessitate irradiation of blood (level of Evidence 2C) to prevent graft versus host disease (GVHD), type-specific or type O & Rh-compatible RBCs with depleted leucocytes, and they were transfused at 15 ml/kg intravenously for 3 hours. Irradiation, storage time, and age of RBCs were documented.

- *Before PRBCs transfusion*: Hemoglobin concentration (Hb conc.), hematocrite (Hct %) & C- reactive protein (CRP) were assessed.
- *During PRBCs transfusion:* The amount of packed RBCs transfused (cc/kg), duration of transfusion in hours, and the protocol of feeding were considered.
- *After PRBCs transfusion:* Hb concentration, Hct % & CRP were reassessed.

The protocol of feeding including the duration, type, volume, route, frequency, tolerance of feeding, and period of keeping nothing per oral (NPO) was documented before, during, and after PRBCs transfusion and was handled by the physician in charge in the NICU.

The preterms were monitored at 12, 24, and 48 hours after transfusion for any change in clinical status as apnea, episodes of bradycardia, abdominal distention, gastric aspirates, and feeding intolerance or increased oxygen requirements. Physical examination and review of medical records were done.

An X-ray abdomen erect was done to suspected cases of NEC. Documentation of NEC was performed using modified

Bell's criteria [10]. Preterms who did not develop NEC within 48 hours were kept monitored till 1 week after transfusion.

The level of respiratory support was documented before & after PRBCs transfusion.

## Ethical approval

Our research methods were in accordance with the international ethical standards and the Helsinki Declarations in this article. An informed consent was obtained from patients' parents/legal guardians.

## Statistical analysis

The data were coded and entered using the statistical package SPSS (statistical package for the social sciences) version 25. Data were summarized using descriptive statistical calculations. The mean, standard deviation (SD), median and interquartile ratio (IQR) were done to quantitative values, while qualitative variables were defined as numbers and percentages.

Comparisons between quantitative variables were done using the non-parametric Kruskal-Wallis and Mann-Whintney tests (Chan 2003). P-value less than 0.05 were considered statistically significant.

## Results

It was a prospective study, conducted on 60 preterms < 36 weeks; they were admitted to the NICU of the department of Pediatrics, Cairo University hospital & received PRBCs due to different etiologies. Some maternal diseases among studied preterms were observed, as 17(28.3%) mothers had pregnancy-induced hypertension (PIH), 2(3.3%) had diabetes mellitus (DM), 20(33.3%) had PROM and 22(36.7%) had antenatal steroid administration as demonstrated in table 1.

The median (IQR) of Apgar score at 1, 5 and 10 minutes was 3 (2-4), 6 (5 – 7), and 7 (6 – 8) respectively.

Thirty-five males were enrolled, representing (58.3%) of our studied preterms, while females were 25(41.7%).

The mean (±SD) GA among the studied preterms was 31.1± 2.5 weeks, the mean

of birth weight (±SD) was 1515.07 ± 491.13 grams and 41(68.3%) were born by cesarean section (CS) and only 19 (31.7%) were born vaginally. All the demographic characteristics are illustrated in table 2.

Fifty three (88.3%) needed mechanical ventilation, 13 (21.7%) needed surfactant administration and 24(40 %) had central line insertion. 54 preterms (90 %) received PRBCs transfusion due to anemia of prematurity.

The median (IQR) age at the time of PRBCs transfusion was 11 (6.5-16) days. The mean (±SD) of the transfused amount was 15.17 ± 3.18 cc/kg, the mean duration of transfusion was 2.16 ± 0.41 hours, and the mean storage time of PRBCs was 23.08 ± 4.36 days.

Only 5% of preterms had previous PRBCs transfusion & 16 preterms (26.6 %) had previous fresh frozen plasma (FFP) transfusion as shown in table 3.

The feeding protocol in our NICU was prescribed according to the unit protocol and handled by the physicians on charge. Sometimes we prescribe full term formula to preterms (34-36 weeks GA), if preterm formulas were not available in the unit at time of start of feedings and due to financial issues, it is saved for those with lower BW and lower GA.

Forty-four preterms (73.3 %) were receiving enteral feeds every 3 hours before PRBCs transfusion, with a median (IQR) volume of feeds 5 cc/kg (2 – 15) before PRBCs transfusion. 30 (50.0%) preterms received preterm formula, 7 (11.7%) received full-term formula and 7 (11.7%) received expressed breast milk.

Before transfusion, 16 (26.7%) received nothing per oral (NPO) and 22 (36.6%) were ordered to be NPO one feed after PRBCs transfusion according to the physician´s orders.

Before PRBCs transfusion, the mean (Hb) was 8.82 ±1.73 g/dl, (Hct) was 26.35 ±5.37 % and CRP median (IQR) was 26 (6-46) mg/L and after transfusion was 11.17 ± 1.85 g/dl for Hb, 34.83 ± 5.39 % for Hct and 59 (12 – 106) mg/l

for CRP; these laboratory indices are illustrated in table 4.

The level of respiratory support was the same before and after PRBCs transfusion.

Various drugs were administrated during the NICU stay, 26 out of 60 (43.3 %) of preterms received vancomycin, while gentamycin (aminoglycosides) was given to 22 preterms (36.7%), 12 preterms (20%) have received ciprofloxacin (fluoroquinolones) and 16 preterms (26.6%) received steroids regimens, whether for extubation from mechanical ventilation or as a bronchopulmonary dysplasia (BPD) regimen respectively.

Inotropes at small & moderate doses were added to 24 preterms (40%) of the preterms and caffeine citrate was prescribed to 54 preterms (90%) of the preterms included. Indomethacin was prescribed for 5 preterms (8.33 %) and oral ibuprofen was started for 3 preterms (5%).

Some complications of prematurity were experienced, as 13 (21.0%) preterms had ICH, 7 (11.7%) had BPD, 21 (35%) had hemodynamically significant PDA and 13 (21.7%) had culture-proven sepsis; as shown in figure 1.

We compared 2 groups, group (1): preterms received PRBCs transfusion with NEC symptoms &/or signs observed within 48 hours, and group (2): preterms received PRBCs transfusion with no NEC symptoms or signs observed within 48 hours & till 1 week after transfusion.

Thirteen preterms (21.7%) developed symptoms &/or signs of NEC within 48 hours after PRBCs transfusion as shown in figure 2. According to modified Bell´s staging: 7 preterms were diagnosed as stage I and 2 preterms were diagnosed as stage IIA and 4 preterms in stage IIB.

We monitored the transfused preterms at 12, 24, and 48 hours for apnea episodes, bradycardia, abdominal distension, and gastric residuals. Among them, apnea episodes had a higher significant incidence in the NEC group 12 hours after PRBCS transfusion ($p < 0.001$), where 5 preterms developed apnea after

12 hours in group 1(NEC) and none in group 2 (No NEC).

All the prenatal parameters did not show any statistical significance with the occurrence of NEC, such as antenatal steroids administration, maternal DM, PROM, and hypertension in the mothers and NEC occurrence (p>0.05).

In the group experienced NEC (number=13), 7 (53.8%) were males & 6 (46.2 %) were females with a non-significant (p>0.05). GA and birth weight (BW) had a highly significant correlation with NEC occurrence, where the mean GA was 29.25 ± 1.86 weeks in group 1(NEC) and 31.49 ± 2.40 weeks in group 2 (No NEC) with a (p<0.001) and the mean weights were 1095.31 ± 241.43 and 1631.17 ± 480.21 grams in group 1 and 2 respectively with (p<0.001).

The feeding protocol followed showed a statistically significant difference between cases with NEC and cases without NEC (p < 0.05). Keeping NPO before, during, and after PRBCs transfusion showed a statistically significant preventive factor for NEC occurrence as shown in table 5.

Volume of feeding was not a significant risk factor for NEC occurrence (P-value > 0.05), as before PRBCs transfusion in group 1(NEC), the median (IQR) of feeds was 5(3-12) cc/kg and in group 2 (No NEC) it was 5 (2-16) and after PRBCs transfusion was 5(4-14) and 6(3-16) in group 1 and 2 respectively with (p>0.05); as shown in table 6.

Low APGAR score at 5 and 10 minutes were significant risks factors for NEC occurrence, whereas, in group (1) NEC, the median (IQR) of Apgar score at 1, 5 & 10 minutes were 3(2-4), 5(4-6) and 7(6-8) respectively and in group 2 (No NEC) were 4(3-5), 6(5-7) and 8(7-9) respectively with (p<0.001). A comparison of the Apgar score between both groups is illustrated in figure 3. Surfactant administration, being on mechanical ventilation and central line insertion showed statistically non-significant differences between cases that

experienced TANEC and cases without TANEC (p >0.05).

The different causes for PRBCs transfusion do have not a statistically significant correlation with the occurrence of TANEC and also for previous PRBCs transfusion. All were statistically non-significant (p >0.05).

Amount & duration of transfusion were almost standardized for all preterms, with a non-significant P-value. All data regarding PRBCs transfusion are illustrated in table 7.

Preterms are better to receive fresh PRBCs with storage time <5 days, but when we started our study, it was a few months earlier before the settlement of our NICU blood bank and defining our policy in blood transfusion practice. We had to take the blood cell units from the general blood bank of the general hospital where we could not always be able to obtain fresh blood for preterms.

However, that mean storage time did not show a significance (p<0.05) in the occurrence of NEC.

There was no significant difference in Hb and Hct % between both groups. Before PRBCs transfusion, the mean of Hb (±SD) was 8.82 ± 1.58 in group1 (NEC) and 8.82 ± 1.79 in group 2(No NEC) & also their rise after transfusion was 11.09 ± 1.74 in group 1(NEC) and 11.19 ± 1.90 in group 2 (No NEC) had no statistical significance with the occurrence of NEC (p>0.05) and the same for Hct %.

The median (IQR) age at the time of PRBCs transfusion among our studied preterms was 11 (6.5-16) days. The median (IQR) age in group 1 (NEC) was 9(8-12) days and in group 2 (No NEC) was 11(5-18) days with *Mann Whitney t-test* value of -0.306 and a non-significant (p>0.05).

The level of respiratory support preterms received had no statistical correlation with the occurrence of NEC.

Hemodynamically significant patent ductus arteriosus (PDA) was a significant risk factor for NEC occurrence, it was detected in 8 preterms out of 13 (61.5%) in group 1(NEC) and 13 preterms out of

47 (27.7%) in group 2 (No NEC) with a significant ($p<0.001$). ICH and BPD had a higher incidence in the NEC group but there was no statistically significant difference; the associated complications of prematurity were illustrated in figure 4.

There was no statistically significant correlation with ($p >0.05$) between NEC occurrence and all the medications prescribed to our studied preterms during the NICU stay.

Risk factors that may be causes for increasing NEC incidence in transfused preterms were hemodynamically significant PDA, lower BW, lower GA, and low Apgar score at 5 minutes and feeding of preterm 3 hours before transfusion. Apgar score at 10 min and hemodynamically significant PDA were the most 2 predictors for NEC occurrence as shown in table 8

## Discussion

NEC can take a progressive course, starting from early subtle symptoms to full-blown disease and may be death within 24–48 h, so early diagnosis is crucial. Simple use of new terms is more applicable than applying the Old Bell´s staging, these terms are “medical NEC” to describe the condition with typical clinical symptoms in addition to radiologic signs (i.e., portal venous gas and definite pneumatosis intestinalis) and “surgical NEC” to describe definitive intestinal necrosis seen at surgery or autopsy [11].

A suggested cause for TANEC is reduced postprandial mesenteric tissue perfusion after PRBCs transfusion in neonates fed during transfusions, leading to an increased risk of mesenteric ischemia, compared with neonates who had feeds withheld [12].

Some studies hypothesized that TANEC may also share immunological mechanisms with transfusion-related acute lung injury (TRALI) [13].

The classic picture of NEC looks to be correlated to exaggerated inflammatory responses including serum cytokines & chemokines, specifically IL-8 markedly elevated. Other biomarkers include

claudin 3, intestinal fatty acid-binding protein, and fecal calprotectin [14].

Our study revealed that 13 preterms (21.7%) developed TANEC according to modified Bell´s staging, 7 preterms diagnosed in stage I , 2 preterms in stage IIA, and 4 preterms were considered in stage IIB, while 47 preterms (78.3%) did not develop any symptoms &/or signs of TANEC within 48 hours after PRBCs transfusion. None of them requires any surgical intervention and no mortality was reported among them.

Group 2 (No NEC), 47 preterms (78.33%), continued to follow up till 1 week after PRBCs transfusion and none of them developed NEC.

The most significant alarming sign was the occurrence of episodes of apnea 12 hours after transfusion with a highly significant value ($p<0.001$).

In our study, we found that the mean of GA was lower in the NEC group (mean of GA was 29.25 weeks in NEC group and 31.1 weeks in the No-NEC group with a highly significant ($p < 0.001$). Also, the mean of BW was lower in the NEC group (in the NEC group, the mean was 1095.31gms and in the No-NEC group mean was 1631.17 gms) with a highly significant ($p < 0.001$).

Many studies demonstrated that low birth weight is the most recognized important risk factor for NEC [15], [16].

All the maternal risk factors were not of statistical significance in our study, the most common maternal disease among NEC patients was PIH (28.3%).

Some studies stated that maternal preeclampsia is considered as an important risk factor for the development of NEC in preterms as NEC incidence & severity were found to be significantly higher in preterms born to mothers with PIH [17].

Generally, incidence of NEC seems to be higher in males [18]. Incidence of NEC among our studied preterms was 53.8% in males & 46.2% in females with a non-significant ($p>0.05$).

The median (IQR) age in group 1 (NEC) was 9(8-12) days in our study, other

studies stated that the median time for the development of NEC was 6 days of life [19], while others reported possible delay in the onset of NEC to > 14 days for preterms with lower GA [20].

Many studies showed a relationship between NEC & low Apgar score. [21]. There was a significant difference in Apgar score at 5 and 10 minutes between our 2 studied groups. The median of Apgar score was lower in the NEC group, so it is considered as a high-risk factor for development of transfusion-related NEC.

Several factors were claimed to be causes of TANEC, among them the storage time of PRBCs, receiving full enteral feeds during transfusion, and certain medications [22].

The mean (±SD) of storage time of RBCs was 21.83 ± 4.30 days in group 1 (NEC) and 23.44 ± 4.36 days in group 2 (no NEC) with a non-significant ($p>0.05$). The amount and duration were standardized among transfused preterms.

Many studies noticed that infants who were being fed in the 48-h period before transfusion was >8 times more likely to develop NEC than infants who were neither fed nor transfused [23], [24].

The WHEAT (WithHolding Enteral feeds Around packed red cell Transfusion) is a randomized controlled trial project, settled in the United Kingdom (UK) that compared 2 feeding protocols: continuing milk feeds (before, during, and after RBCs transfusions) and withholding milk feeds (for 4 hours before, during and for 4 hours after RBCs transfusions), with infants randomly assigned with equal probability, waiting for their results to be published [25].

A previous study mentioned that mesenteric tissue oxygenation during PRBC transfusion is not influenced by feeding status. However, neonates fed during PRBC transfusion had reduced postprandial mesenteric tissue oxygenation patterns for the upcoming

15 hours, compared with neonates not fed during RBC transfusion [26].

We reported a significant difference between being receiving NPO before, during & after PRBCs transfusion, where the incidence of NEC was significantly higher among preterms who were receiving feeds just before or after transfusion than those who were receiving NPO with ($p<0.001$), which suggests withholding feeds before, during & after transfusion.

Human breast milk showed protective evidence against NEC [27]. Among our studied preterms, the volume of feeds received and the type, whether preterm formula, full term formula or EBM did not show a statistical significance in our study in developing NEC, ($p > 0.05$), as before PRBCs transfusion group 1(NEC), the median (IQR) of feeds was 5(3-12) cc/kg and in group 2(No NEC) it was 5 (2-16) and after PRBCs transfusion was 5(4-14) and 6(3-16) in group 1 and 2 respectively with ($p >0.05$).

CRP has increasing sensitivity but remains a nonspecific marker for NEC [28]. However, CRP showed statistically non-significant difference among our 2 groups studied. Also, a positive culture was detected in only 1 preterm (7.7%) in group1 (NEC) and in 12 preterms (25.5%) in group 2(No NEC) with a non-significant ($p>0.05$).

Lower hematocrit is suggested to be associated with NEC. Severe anemia in a given week was associated with a 6-fold higher risk of NEC. Analyses among RBC transfused infants; each 1g/dl decrease in the lowest measured Hb in a given week was associated with a 65% increase in the risk of NEC [29]. In our study, both the Hb conc. & Hct % did not show up any significance, where the mean Hb conc. before PRBCs transfusion was 8.82± 1.58 in group 1(NEC) & 8.82 ± 1.79 in group 2 (No NEC) with ($p>0.05$). Also, the mean of Hct was 26.84 ± 5.47 in group 1(NEC) and 26.21± 5.40 with a non-significant ($p >0.05$).

PDA has an incidence of 40 -55 % in preterms, depending on the size of PDA and the volume of shunt patients may develop serious hemodynamic effects that increases the risk of complications such as NEC,BPD and IVH [30].

Presence of hemodynamically significant PDA, which is described as ductal size >1.5 mm, left-to-right shunting of blood and left atrial to aortic (LA: AO) ratio >1 [31].

In this current study, the incidence hemodynamically significant PDA among transfused neonates was 35%, 8 preterms (61.5%) in group 1(NEC) and 13 preterms (27.7%) in group 2 (No NEC) with a significant ($p<0.001$).

Some medications are well known to cause gastrointestinal adverse effects as steroids, some antibiotics, iron supplements and non-steroidal anti-inflammatory drugs (NSAIDs) [32] Other drugs are claimed to be risk factors for NEC as Indomethacin, aminophylline, vitamin A, gastric antacids and $H_2$ receptor blockers [33]. Also other drugs as oral probiotics seem to have a protective role against development of NEC [34].

In our study, none of the medications received by the studied preterms had any influence on occurrence of NEC. Caffeine citrate was the most commonly used among our studied preterms, followed by inotropes, then antibiotics and steroids.

We acknowledge some drawbacks as the small number of enrolled cases, further studies on larger scales are recommended as we have a high rate of admissions in our NICU. We did not standardize completely the feeding protocol in the unit as regards type or formula used, period of keeping NPO before or after PRBCs transfusion. We also faced missing of some data

## Conclusions

Incidence of TANEC in preterm neonates was 21.7 %. Other complications of prematurity were recorded where incidence of ICH, BPD and PDA were 21.7%, 11.7% and 35.0% respectively.

Risk factors that increased NEC incidence among our transfused preterms were manifesting PDA, lower BW, lower GA, and low Apgar score at 5 minutes and feeding of preterm 3 hours before PRBCS transfusion.

The most significant alarming sign was occurrence of episodes of apnea 12 hours after transfusion with a highly significant value ($p<0.001$)

**Abbreviations:**

BPD: bronchopulmonary dysplasia;
BW: body weight;
CRP: C- reactive protein;
CS: Caesarean section;
EBM: expressed breast milk;
FFP: fresh frozen plasma;
GA: gestational age;
Hct: hematocrit;
Hb: hemoglobin;
ICH: intracranial hemorrhage;
NEC: necrotizing enterocolitis;
NICU: neonatal intensive care unit;
NPO: nothing per oral;
PDA: patent ductus arteriosus;
PIH: pregnancy-induced hypertension;
PROM: premature rupture of membranes;
RBCs: red packed blood cells;
TANEC: transfusion-associated necrotizing enterocolitis;
TRALI: transfusion-related lung injury.

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**Author's contributions**

NA and ME: Conception and design of the work, revising all data and revising the article. AS: Patient Data collection, data analysis and interpretation. AS: Drafting the article, critical revision of the article and final approval of the version to be published.

**Conflict of interest**

The authors whose names are listed before certify that they have NO affiliations with or involvement in any organization or entity with any financial interest, or non-financial interest in the subject matter or materials discussed in this manuscript

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**Table (1): Maternal illnesses among the studied preterms**

| Variable | Percentage (Total No=60) |
|---|---|
| **Pregnancy induced hypertension** | 17 (28.3%) |
| **Diabetes Mellitus** | 2 (3.3%) |
| **Antenatal steroid administration** | 22 (36.7%) |
| **History of PROM** | 20 (33.3%) |

PROM= premature rupture of membranes

**Table (2): The Demographic Characteristics among the studied Preterms**

| **Total no. = 60** | | |
|---|---|---|
| **Gender** | **Male** | 35 (58.3%) |
| | **Female** | 25 (41.7%) |
| **Mode of delivery** | **CS** | 41 (69.5%) |
| | **NVD** | 18 (30.5%) |
| **Gestational age (weeks)** | **Mean ± SD** | 31.1 ± 2.5 |
| **Birth weight (grams)** | **Mean ± SD** | 1515.07 ± 491.13 |
| **Apgar score 1 min** | **Median (IQR)** | 3 (2 – 4) |
| **Apgar score 5 min** | **Median (IQR)** | 6 (5 – 7) |
| **Apgar score 10 min** | **Median (IQR)** | 7 (6 – 8) |

CS= Caesarean section; NVD= normal vaginal delivery

**Table (3): Data of PRBCs transfusion among the studied Preterms**

| | | |
|---|---|---|
| **Total Number = 60** | | |
| **Age at time of transfusion (days) median (IQR)** | | 11 (6.5 – 16) |
| **Cause of transfusion** | **Anemia of prematurity** | 54 (90.0%) |
| | **ICH hemorrhage** | 4 (6.7%) |
| | **External bleeding** | 1 (1.7%) |
| | **Unknown Couse** | 1 (1.7%) |
| **Amount (cc/kg) (mean ±SD)** | | 15.17 ± 3.18 |
| **Duration of transfusion in hours (mean ±SD)** | | 2.16 ± 0.41 |
| **Storage time of RBCs in days (mean± SD)** | | 23.08 ± 4.36 |
| **Previous PRBCs transfusion** | | 5 (8.3%) |
| **Previous FFP transfusion** | | 16 (26.6%) |

ICH= intra-cranial hemorrhage; FFP= fresh frozen plasma, PRBCs= packed red blood cells

**Table (4): Laboratory Indices before & after PRBCs transfusion**

| **Parameter** | **Before PRBCs transfusion** | **After PRBCs transfusion** |
|---|---|---|
| **Hb% (mean ±SD)** | 8.82 ± 1.73 | 11.17 ± 1.85 |
| **Hct (mean ± SD)** | 26.35 ± 5.37 | 34.83 ± 5.39 |
| **CRP median (IQR)** | 26 (6 – 46) | 59 (12 – 106) |

Hb= Hemoglobin, Hct= hematocrit; CRP= C-reactive protein

**Table (5): Feeding protocol in both groups**

| Feeding protocol | | Group 1(NEC) No. = 13 | Group 2(No NEC ) No. = 47 | P-value |
|---|---|---|---|---|
| **Before** | **NPO** | 0 (0.0%) | 16 (34.0%) | 0.031 |
| | **Preterm formula** | 11 (84.6%) | 19 (40.4%) | |
| | **Term formula** | 1 (7.7%) | 6 (12.8%) | |
| | **EBM** | 1 (7.7%) | 6 (12.8%) | |
| **During** | **NPO** | 13(100.0%) | 47 (100.0%) | ------ |
| **After PRBCs** | **NPO** | 0 (0.0%) | 16 (34.0%) | 0.031 |
| | **Preterm formula** | 11 (84.6%) | 19 (40.4%) | |
| | **Term formula** | 1 (7.7%) | 6 (12.8%) | |
| | **EBM** | 1 (7.7%) | 6 (12.8%) | |

NPO= nothing per oral; EBM= expressed breast milk; PRBCs=packed red blood cells

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

**Table (6): Volume of Feeds before and after PRBCs transfusion in both groups**

| Median (IQR) | Group 1(NEC) *(No. = 13)* | Group 2 (No NEC) *(No. = 47)* | P value |
|---|---|---|---|
| **Volume of feed before transfusion (cc/kg)** | 5 (3 – 12) | 5 (2 – 16) | 0.909 |
| **Volume of feed after transfusion (cc/kg)** | 5 (4 – 14) | 6 (3 – 16) | 0.718 |

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

**Table (7): PRBCs data among both groups**

| Item | | Group 1 NEC (n=13) | Group 2 No NEC (n=47) | P-value |
|---|---|---|---|---|
| Cause of transfusion | Anemia of prematurity | 10 (76.9%) | 44 (93.6%) | 0.056 |
| | ICH | 3 (23.1%) | 1 (2.1%) | |
| | External bleeding | 0 (0.0%) | 1 (2.1%) | |
| | Unknown cause | 0 (0.0%) | 1 (2.1%) | |
| Amount (cc\kg) | mean ± SD | 16.15 ± 3.63 | 14.89 ± 3.04 | 0.209 |
| Duration of transfusion (hours) | mean ± SD | 2.08 ± 0.49 | 2.18 ± 0.38 | 0.419 |
| Storage time of RBCs (days) | mean ± SD | 21.83 ± 4.30 | 23.44 ± 4.36 | 0.266 |
| Previous transfusion | No. (%) | 1 (7.7%) | 4 (8.5%) | 0.925 |

ICH= intracranial hemorrhage

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

**Table (8): Univariate & multivariate logistic regression**

| Variable | B | S.E. | Wald | P-value | Odds ratio (OR) | 95% C.I. for OR | |
|---|---|---|---|---|---|---|---|
| | | | | | | Lower | Upper |
| **Univariate logistic regression** | | | | | | | |
| **Apgar score at 10 min** | 1.875 | 0.847 | 4.900 | 0.027 | 0.153 | 0.029 | 0.807 |
| **Significant PDA** | 1.431 | 0.657 | 4.750 | 0.029 | 4.185 | 1.155 | 15.16 |
| **Multivariate logistic regression** | | | | | | | |
| **Apgar score at 10 min** | 1.697 | 0.888 | 3.650 | 0.056 | 0.183 | 0.032 | 1.045 |
| **Significant PDA** | 1.306 | 0.684 | 3.645 | 0.056 | 3.691 | 0.966 | 14.103 |

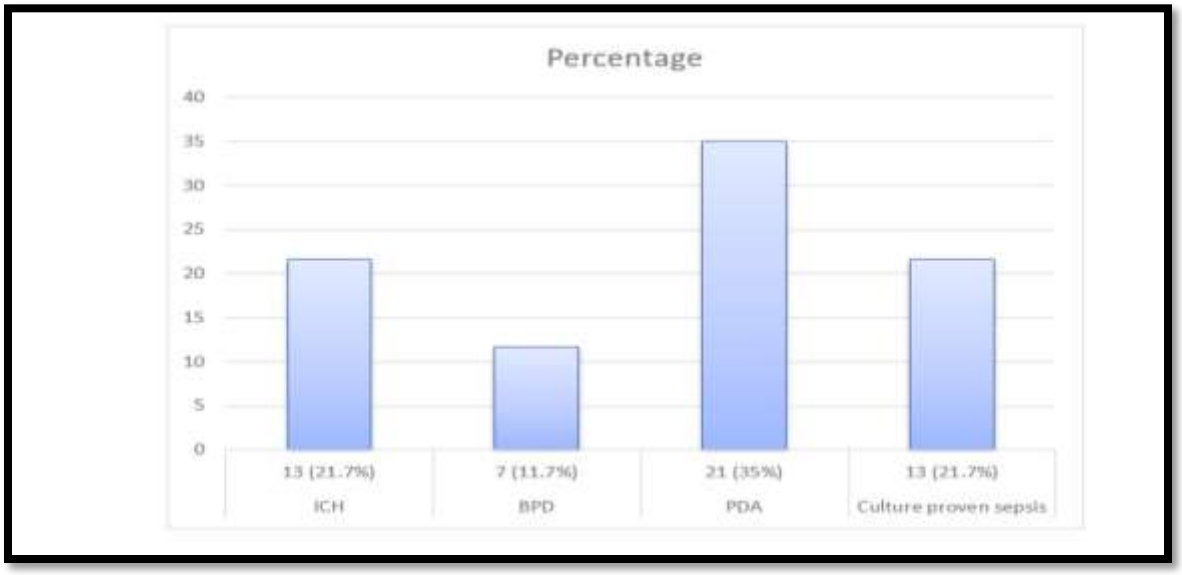


**Figure (1): Complications of Prematurity among the studied preterms**

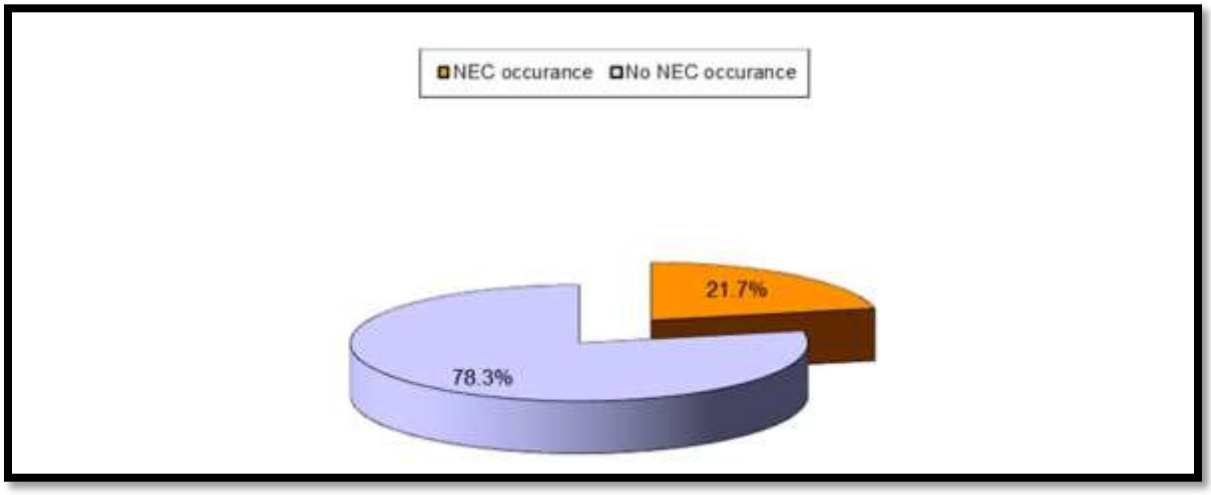


**Figure (2): Incidence of NEC within 48 hours after PRBCs**

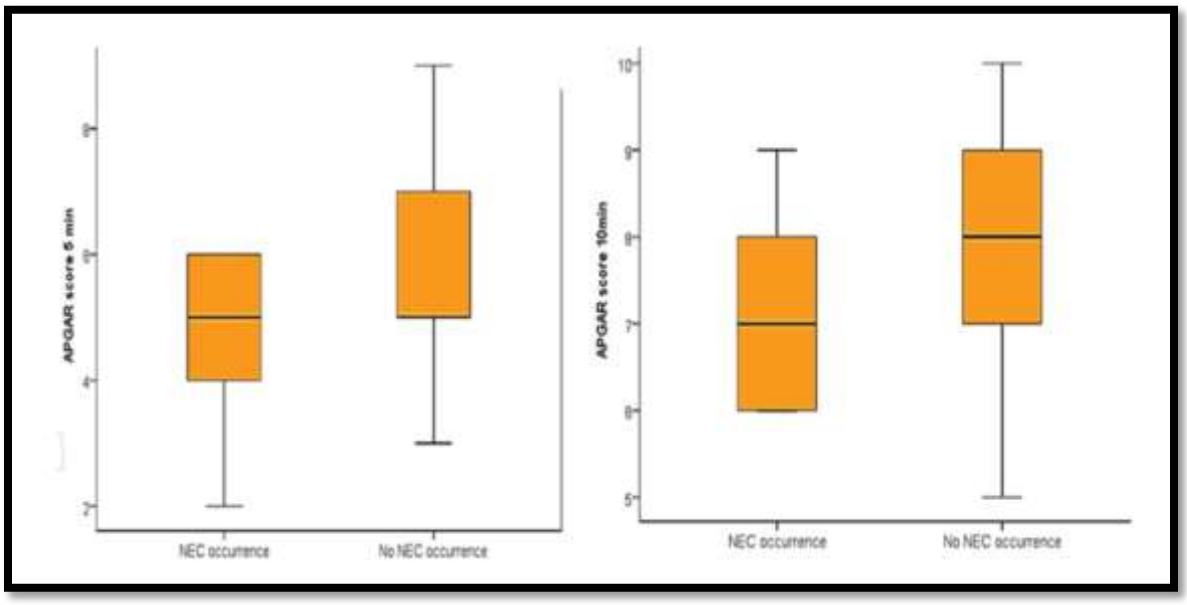


**Figure (3): Apgar Scores at 5 & 10 minutes among both groups**

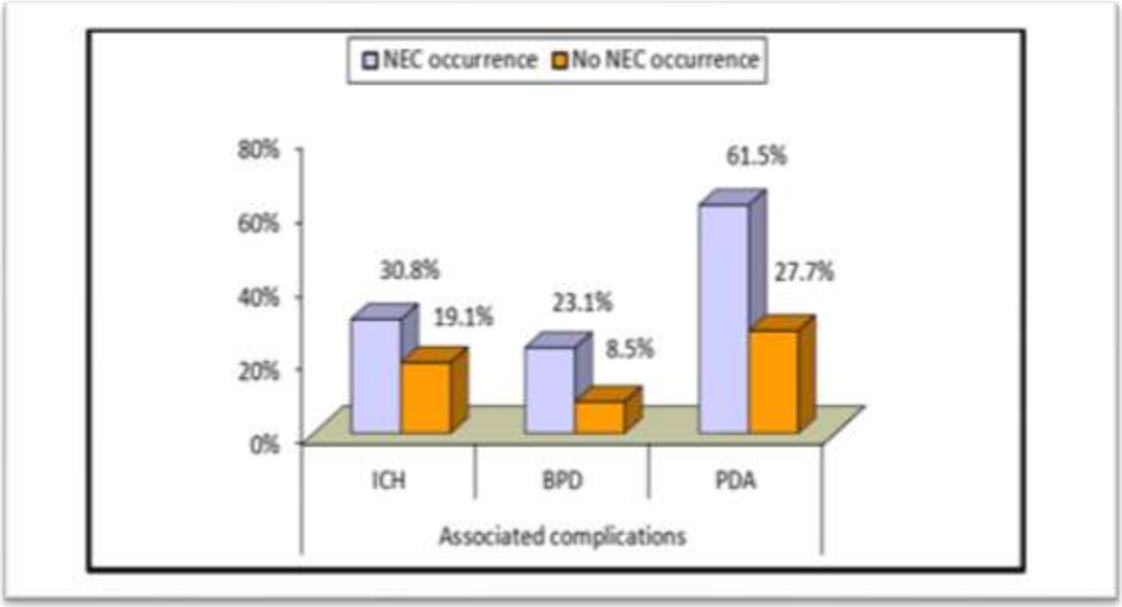


**Figure (4): Associated Complications of Prematurity in both groups**



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