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# Analysis of Incidence of Adverse Events of Neonatal Blood Transfusion in Sharqia Governorate

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## ABSTRACT

**Background:** The administration of blood products in neonates has greater risk of harm when compared to that in adults so we must weigh up the benefits and hazards of blood transfusion in this vulnerable age group.

**Objective:** To detect the incidence of adverse events of neonatal blood transfusion in Neonatal Intensive Care Unit (NICU) of Diarb Negm Central Hospital and Zagazig University Hospitals (Sednawi and Incident NICU).

**Subjects and Methods:** In this study sixty cases of neonates admitted to incubators of Diarb Negm Central Hospital and Zagazig University Hospitals (Sednawi and Incident incubator) and received any blood element transfusion e.g., packed RBCs, platelets and fresh frozen plasma and remained for at least 48 hours after transfusion. All studied neonatal cases were subjected to the following investigations before transfusion CBC, CRP, ABG, liver and kidney function tests, coagulation profile and electrolytes. Then after transfusion, only CBC was done for all cases except the case who developed complication.

**Results:** All cases received none previous blood transfusion. Majority of those neonates (75%) received packed RBC's transfusion followed by platelet (9%). RD in preterm and LBW was the most frequent disease in cases included in this study followed by congenital heart disease (13.3%) then bronchiolitis (11.67%) then sepsis (10%). Majority of cases were on CPAP (36.7%) followed by nasal catheter (28.3%)

**Conclusion:** Packed RBCs is the most blood component transfused in neonates especially preterm. Transfusion of blood components is associated with several adverse reactions, both acute and delayed.

**Keywords:** Adverse Events, Neonate, Blood Transfusion.

## INTRODUCTION

There is no doubt that blood transfusion is a lifesaving procedure in emergency conditions and a supportive treatment for patients suffering anemia and certain chronic diseases. Transfusion of whole blood and blood products (RBCs, platelets and plasma) are frequently needed for preterm neonates especially extremely low birth weight. The administration of blood products in neonates has greater risk of harm when compared to that in adults so we must weigh up the benefits and hazards of blood transfusion in this vulnerable age group. The World Health Organization (WHO) has set instructions for blood services in order to ensure safe blood transfusion. The WHO intensify that all aspects of blood transfusion from donor selection through to infection screening, blood grouping and blood storage to administration to patients must guarantee an effective quality [(1)].

Adverse events of blood transfusion include the following; the first is acute adverse reactions (occur within 24 hours of transfusion); acute hemolytic transfusion reactions (AHTRs): They occur due to accelerated RBC's destruction as a result of interaction between antigens on donor erythrocyte and recipient antibodies or antigens on recipient erythrocytes and antibodies in the donor plasma [(2)].

Febrile non hemolytic transfusion reactions (FNHTRs): They are the most frequent adverse events. They occur due to transfusion of cytokines accumulated during storage of blood components and the interaction between recipient antibodies and leukocyte antigen or leukocyte specific antigens on donor leukocyte. Allergic reactions are more common than anaphylactic reactions. They are considered as IgE-mediated type 1 hypersensitivity reaction. Transfusion transmitted infections: Either bacterial infection (gram-positive and gram-negative), protozoa, viral infection (HIV, HBV and HCV) [(3)]. The second is delayed adverse reactions (occur 48 hours or more after transfusion), which are immune in origin; delayed hemolytic transfusion reaction: It occurs as a result of immune response with development of alloantibodies to RBC's and/or platelets on exposure to donor blood cell antigens [(4)].

Post transfusion purpura: Due to platelet alloimmunization, macrophages engulf and destroy antibody coated platelets [(3)].

Transfusion related immunomodulation (TRIM): It is an immune suppression associated with transfusion of allogeneic leukocytes [(5)].

Transfusion associated graft versus host disease (TA-GVHD): It happens in immune-compromised individuals receiving transfusion with viable recipient T lymphocytes. These lymphocytes cause immune response against recipient cells [(6)].

We aimed in this study to detect the incidence of adverse events of neonatal blood transfusion in Neonatal Intensive Care Unit (NICU) of Diarb Negm Central Hospital and Zagazig University Hospitals (Sednawi and Incident NICU).

## SUBJECTS AND METHODS

This study was a prospective cohort study, which included sixty cases of neonates admitted to incubators of Diarb Negm Central Hospital and Zagazig University Hospitals (Sednawi and Incident incubator).

**Patient inclusion criteria:** All neonates were transfused with any blood element such as whole blood,



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packed RBCs, platelets or plasma and remained at least 2 days after transfusion.

**Patient exclusion criteria:**

Neonates didn't receive blood transfusion and those who died or were discharged within 2 days of transfusion.

Modified safety precautions during blood transfusion by Egyptian Neonatal Safety Training Network (ENSTN) were applied [7].

**All neonates included in the study were subjected to the following:**

1) **Full history taking** (prenatal, natal and postnatal history).
2) **Clinical examination**:
   - General examination.
   - Vital signs and Measurements.
   - C.N.S and C.V.S examination.
   - Chest and abdomen examination.
   - Umbilicus and genitourinary system examination.
   - Recording of any adverse events of blood transfusion and send hemovigilance notification to blood bank. The aim of hemovigilance is to collect all information of unexpected, undesirable, or serious adverse events in donors or in patient recipients of blood transfusion therapy in order to correct their cause, prevent recurrence, and improve the safety of blood collection and transfusion [8].

**Table (1):** Shows hemovigilance notification filled with our case [7]

| Symptoms and signs | Actions taken | Diagnosis for adverse events |
|---|---|---|
| Fever, tachycardia and jaundice | Investigations e.g., CBC and Reticulocyte count | DHTR |

**Investigations:**

All studied neonatal cases were subjected to the following investigations before transfusion: CBC, CRP, liver and kidney function tests, ABG, electrolytes as well as coagulation profile.

Then after transfusion, only CBC was done for all cases except the case who developed complication; he was subjected to the following investigations: CBC, CRP, Liver and Kidney function tests, ABG, electrolytes, coagulation profile as well as reticulocyte count.

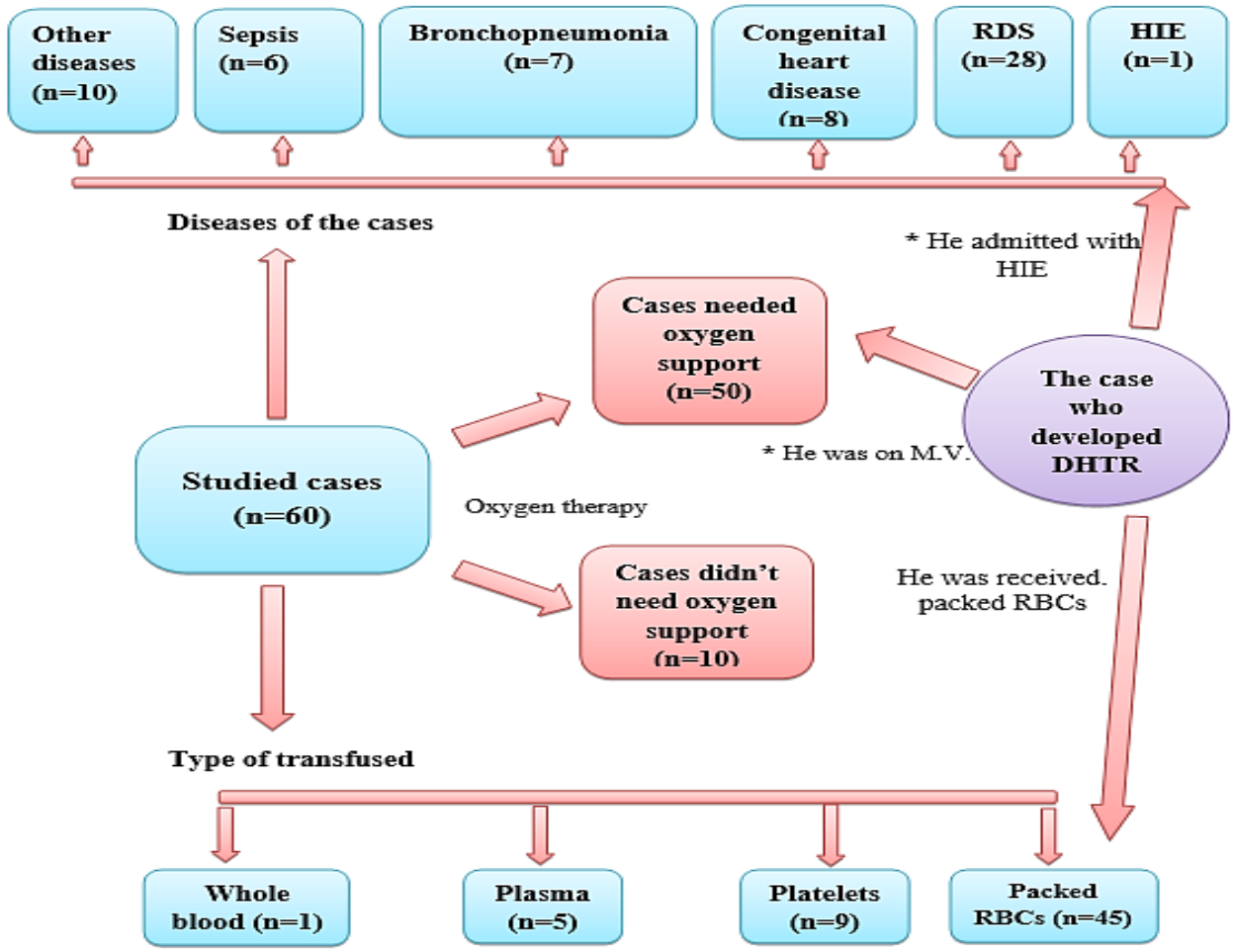


**Fig. (1):** Chart of transfusions done to different to cases

**Ethical consent:**

**This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Zagazig University. Written informed consent was taken from the caregivers of all the participants. The study was conducted according to the Declaration of Helsinki.**

***Statistical analysis***

Statistics by IBM SPSS, Windows edition, version 23.0. IBM Corp., Armonk, New York, was used for data collection, tabulation, and statistical analysis. Mean, standard deviation, median, and range were used to describe quantitative data, whereas frequency and percentage were used to describe qualitative data. Two sets of normally distributed continuous variables were compared using the t test. P< 0.05 was considered significant.

**RESULTS**

The personal, mode of delivery, and transfusion data of the studied patients are shown in table 1.

**Table (1) Age, sex distribution, and transfusion data of studied cases**

| | | Age (days) | GA (weeks) | Birth w (kg) |
|---|---|---|---|---|
| **Mean** | | 12.4333 | 34.7167 | 2.1008 |
| **Median** | | 5.0000 | 35.0000 | 1.8300 |
| **Std. Deviation** | | 16.96294 | 2.64954 | .67177 |
| **Minimum** | | 1.00 | 29.00 | 1.10 |
| **Maximum** | | 90.00 | 38.00 | 4.10 |
| | | **N** | **%** | |
| **Sex** | **Female** | 35 | 58.3 | |
| | **Male** | 25 | 41.7 | |
| | **Total** | 60 | 100.0 | |
| | | **N** | **%** | |
| **Mode delivery** | **C.S** | **43** | **71.7** | |
| | **N.V.D** | **17** | **28.3** | |
| **History of previous transfusion** | **-VE** | **60** | **100.0** | |
| **Type of transfused** | **Packed RBCs** | **45** | **75.0** | |
| | **Plasma** | **5** | **8.3** | |
| | **Platelet** | **9** | **15.0** | |
| | **Whole blood** | **1** | **1.7** | |
| | **Total** | **60** | **100.0** | |

Table (2) shows that majority of cases were on CPAP.

**Table (2):** Shows that type of respiratory support

| | | N | % |
|---|---|---|---|
| **Type of respiratory support** | **No** | 10 | 16.7 |
| | **CPAP** | 22 | 36.7 |
| | **Head box** | 1 | 1.7 |
| | **M.V.** | 4 | 6.7 |
| | **Nasal catheter** | 17 | 28.3 |
| | **NCPAP** | 6 | 10.0 |
| | **Total** | 60 | 100.0 |

Table (3) shows comparison between parameters of CBC pre and post transfusion. There was significant improvement after transfusion of all the measured parameters.

**Table (3):** Shows that CBC pre and post comparison

| | Pre | Post | P |
|---|---|---|---|
| **RBCs** (mcL) | 3.45±0.84 | 4.45±0.82 | <0.001** |
| **Hb** (g/dL) | 10.95±2.59 | 12.12±2.63 | 0.005* |
| **Hematocrit** | 30.78±6.54 | 37.58±6.54 | <0.001** |
| **Mean corpuscular hemoglobin** (pg) | 32.75±4.44 | 38.78±6.54 | <0.001** |
| **MCHC** (g/dL) | 35.29±1.97 | 39.21±9.73 | 0.008* |
| **Mean corpuscular volume** (fl) | 92.77±11.5 | 98.65±10.56 | <0.001** |
| **PLT** (mcL) | 229.61±56.32 | 265.25±64.43 | 0.024* |
| **WBCs** (mcL) | 15.51±3.41 | 17.65±4.21 | 0.0348* |

*: Significant, **: Highly significant

Figure (2) shows only one case had complication (**Delayed hemolytic transfusion reaction**). This case was a male and third child for mother from Hihya, 6 days in age with GA 38 weeks with birth weight 3.5 Kg, delivered by N.V.D, he was on M.V and received packed RBCs

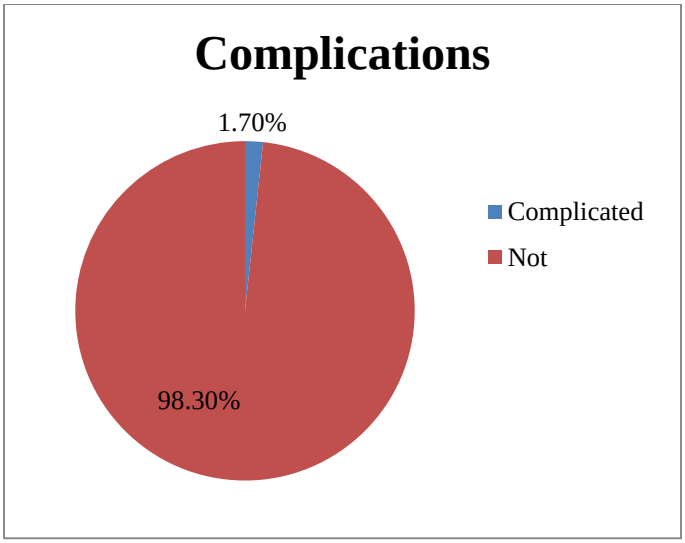


**Fig. (2):** Complications after transfusion among studied group.

Majority of neonatal cases with platelet transfusion had episodes of bleeding (all are minor bleeding in the form of petechial rash and oozing from venipuncture sites). Age of neonatal cases at platelet transfusion 1-10 days was higher than those >10 days (Table 4).

**Table (4):** Shows bleeding occurrence, and gestational age of neonatal cases with platelet transfusion

| | | N | % |
|---|---|---|---|
| **Bleeding** | **+ve** | 7 | 77.78 |
| | **-ve** | 2 | 22.22 |
| | **Total** | 9 | 100 |
| **Age at transfusion (days)** | **1-10** | 6 | 66.7 |
| | **>10** | 3 | 33.3 |
| | **Total** | 9 | 100 |

Table (5) shows that highest frequency of platelet transfusion was in neonatal cases with platelet count >50 $\times 10^9$/L.

**Table (5):** Shows platelet count for cases who received platelet transfusion

| | | N | % |
|---|---|---|---|
| **Platelet count ($\times 10^9$/L)** | **< 30** | 3 | 33.3 |
| | **30-50** | 2 | 22.2 |
| | **> 50** | 4 | 44.4 |
| | **Total** | 9 | 100 |

Table (6) shows that majority of the studied cases who received RBCs transfusion were on respiratory support.

**Table (6):** Shows the frequency of cases that needed respiratory support among those received RBCs transfusion

| | | N | % |
|---|---|---|---|
| **Respiratory support** | **+ve** | 36 | 80 |
| | **-ve** | 9 | 20 |
| | **Total** | 45 | 100 |

Table (7) shows that frequency of gestational age (28-34 weeks) among cases with RBCs transfusion was higher than gestational age >34weeks.

**Table (7):** Shows the gestational age among studied cases who received RBCs transfusion

| | | N | % |
|---|---|---|---|
| **Gestational age (weeks)** | 28-34 | 23 | 51.1 |
| | >34 | 22 | 48.9 |
| | Total | 45 | 100 |

Table (8) shows that the frequency of cases received RBCs transfusion had birth weight (>1.5 kg) was higher than those with birth weight (1-1.5 kg).

**Table (8):** Shows the birth weight of studied neonatal cases who received RBCs transfusion

| | | N | % |
|---|---|---|---|
| **Birth weight (kg)** | 1-1.5 | 10 | 22.2 |
| | >1.5 | 35 | 77.8 |
| | Total | 45 | 100 |

## DISCUSSION

Transfusion reactions may be acute or delayed. Transfusion reactions can also be classified based on the etiology into immunologic and non-immunologic subtypes [(9)].

Our study included 60 cases of neonates admitted to the incubator and received blood element transfusion. Mean age of whom in days was 12.43±16.9 with median 5 and range (1-90). Our study revealed that transfusion is more common in neonates (incidence among admitted cases during our study was 27%) and most of them receive at least single transfusion at some point of NICU stay. A retrospective single center study (blood component therapy in neonates in a neonatal intensive care unit of northern India from August 2014 to July 2015) agree with our study in this point [(10)].

GA of the studied cases ranged between 29-38 weeks with mean 34.71±2.64 weeks. In contrast to our result, GA in **Kirpalani *et al.*** [(11)] study was <31 weeks while in **Mukhopadhyay *et al.*** [(12)] study, GA was <34 weeks. This may because they are concerned with preterm infants only. Mean of birth weight was 2.1±0.67 kg. In contrast to our study the birth weight in **Bell *et al.*** [(13)] study was 0.5-1.3 kg.

Our study revealed that packed RBCs was the maximum component transfused (75%) followed by platelets (15%) then plasma (8.3%) and lastly whole blood (1.7%). A retrospective study done in the Department of Transfusion Medicine, Government Medical College, Jammu (from Jan 2014- Dec 2014) agrees with our study (regarding pediatric cases included in the study) [(14)]. While the study done in the NICU of northern India disagrees with our study (in which platelet was the maximum component to be transfused). This could be because of transfusing

packed RBCs on higher threshold level of hemoglobin in our study [10].

Majority of cases were on CPAP (36.7%) followed by nasal catheter (28.3%) and those who needed no oxygen therapy (16.7%). The rest of cases were on head box (1.7%), NCPAP (10%) and M.V (6.7%). In **Bell *et al.*** [13] study, cases required ventilation were (46% vs 34%), those were on NCPAP/Oxygen (38% vs 28%) while those need no respiratory support were (30% vs 21%). While in **Chen *et al.*** [15] study, cases required ventilation were (45% vs 35%), those required NCPAP/Oxygen were (40% vs 30%) and those need no respiratory support were (30% vs 22%). This difference may be due to usage of invasive oxygen support in their studies more than our study.

Comparison between distribution of CBC pre and post transfusion showed highly significant improvement after transfusion in RBCs, Hct, MCH and MCV ($P < 0.001$), while HB ($P < 0.005$) and platelets ($P < 0.024$) showed significant improvement. The following two studies, hemodynamic effects of differing blood transfusion rates in infants less than 1500 g [16], and a comparison of high and standard blood transfusion volumes in premature infants by **Wong *et al.*** [17] agree with our study.

Our study showed statistically significant increase of packed RBCs transfusion in cases on respiratory support (80% of cases were on respiratory support). Also 83.3% of cases received any blood component transfusion in our study needed oxygen therapy (either CPAP, NCPAP, Nasal catheter, Head box or M.V). This revealed that this condition is associated with higher transfusion needs which agree with an observational study of a cohort of very low birth weight infants by **Stefano Ghirardello and colleagues** [18].

In our study, 80% of cases received packed RBCs were at hemoglobin level ≥ 8 g/dl (high threshold) while percent of cases transfused packed RBCs at hemoglobin level < 8 g/dl (low threshold) was 20%. This agrees with **Ransome *et al.*** [19] study in which liberal HB threshold was 10 g/dl and restrictive threshold was 7 g/dl (<8g/dl).

In our study most of cases received blood component transfusion without developing any adverse events except one case who developed DHTR. This means that following precautions of Egyptian neonatal safety training network (ENSTN) during transfusion lead to decrease incidence of these adverse events and this is the aim of our study.

This case developed symptoms and signs (e.g., fever and jaundice) suggesting diagnosis of DHTR with a percent (1.7%). A retrospective study done in the Department of Transfusion Medicine, Government Medical College, Jammu (from Jan 2014- Dec 2014) revealed that the frequency of DHTR was 4.2% of total transfusion reactions occurred [14].

In our study, platelet transfusion was highly significant in neonatal cases aged 1-10 days (66.7%) than those age > 10 days (33.3%). A prospective observational study and implications for use of platelet transfusions (Severe thrombocytopenia and patterns of bleeding in neonates) by **Muthukumar and colleagues** agrees with our study in that the majority of neonates with severe thrombocytopenia (ST and platelet count < $60 \times 10^9$L) bleed and need platelet transfusion and this mostly develop in first 10 days of birth [20].

Most of studied cases received platelet transfusion had GA > 34 weeks (55.56%). The highest percent of platelet transfusion was in neonatal cases with platelet count > 50 $\times 10^9$/L (44.4%) followed by cases with platelet count < $30 \times 10^9$/L (33.3%) and lastly those with platelet count 30-50 $\times 10^9$/L (22.2%). A survey of platelet transfusion practices among US and Canadian neonatologists agrees with our study in this point [21].

There were no statistically significant differences in adverse events among cases transfused with platelets at platelet count ≥ $50 \times 10^9$/L versus those received platelets at < $50 \times 10^9$/L (restrictive). A randomized trial of platelet transfusion thresholds in neonates (PlaNeT-2 study) agrees with this point [22].

The majority of neonatal cases with platelet transfusion had episodes of bleeding (all were minor bleeding in the form of petechial rash and oozing from venipuncture sites) (77.78%). A prospective multicenter observational study by **Stanworth and colleagues** (PlaNeT-1 study) agrees with our study in this point [23].

In our study majority of cases received platelet transfusion at platelet count > $50 \times 10^9$/L and this disagree with the prospective multicenter observational study performed in the United Kingdom (transfusion is done at median platelet count $27 \times 10^9$/L) [24]. This may be because we were not concerned with platelet count only but also with clinical condition of neonates who developed bleeding.

A policy of routine coagulation screening is inappropriate as results are difficult to interpret in neonates and routine testing may lead to increased transfusion of FFP without benefit [25]. So, we couldn't compare our results on cases received plasma transfusion with other research articles also in foreign countries where they transfuse according to deficient coagulation factor.

## CONCLUSION

Packed RBCs is the most blood component transfused in neonates especially preterm. Transfusion of blood components is associated with several adverse reactions, both acute and delayed. Following safety precautions of ENSTN leads to decrease incidence of these adverse events. Recording any adverse events occurred during blood transfusion and reporting them (Hemovigilance) helps in prevention of recurrence and improvement of the safety of blood collection and transfusion.

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