

**ASSESSMENT OF THE EFFECT OF DONOR
CHARACTERISTICS ON CLINICAL OUTCOMES IN
NEONATAL TRANSFUSION RECIPIENTS**



Thesis

Submitted to

All India Institute of Medical Sciences, Jodhpur

In partial fulfilment of the requirement for the degree of

Doctor of Medicine (MD)

(Transfusion Medicine and Blood Bank)

JULY 2020

AIIMS, JODHPUR

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DECLARATION

I hereby declare that the thesis titled “**Assessment of the effect of Donor characteristics on clinical outcomes in Neonatal transfusion recipients**” embodies the original work carried out by the undersigned at All India Institute of Medical Sciences, Jodhpur.

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CERTIFICATE

This is to certify that thesis titled '**Assessment of the effect of Donor characteristics on clinical outcomes in Neonatal transfusion recipients**', is the bonafide work of **Dr. Bodanapu Vinay**, carried out under our guidance and supervision, in the Department of Transfusion Medicine and Blood Bank, All India Institute of Medical Sciences, Jodhpur.

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ACKNOWLEDGEMENT

I want to start by thanking Dr. Archana Bajpayee, my guide, and teacher, for giving me the opportunity to do this thesis. Without her direction and frequent oversight, this study would not be completed in a timely manner. She has a remarkable ability to provide eminent patient care and inspire people around her with her remarkable leadership qualities.

I would like to thank Dr. Poonam Elhence for always supporting and encouraging us in our endeavors.

I owe a huge debt of gratitude to all of my co-guides, Dr. Neeraj Gupta, Dr. Anubhav Gupta, Dr. Arvind Sinha, and Dr. Suresh Kumar Sharma, for their input and encouragement throughout this study.

I'd want to convey my heartfelt gratitude to my teachers, Dr. Saptarshi Mandal and Dr. Siddharth Mittal, for assisting me in turning ideas into reality. I am grateful for their intelligent remarks and continual support, which helped to shape my research vision.

I cannot visualize finishing my thesis without the consistent assistance of Dr. Puneeth Babu Anne, Dr. Arun M, Dr. Pallavi Singh, Dr. Jaydyuti Mandal, and Dr. Vasanth Asirvatham, for whom I am incredibly thankful.

I'm incredibly appreciative of the insight and counsel provided by my seniors, Dr. Athik Khan, Dr. Rashmi Parashar, Dr. Pradip Banerjee, Dr. Richa Mishra, and Dr. Davood Bava.

I'd like to appreciate my juniors Dr. Arya V Nair, Dr. Subha P, Dr. Rajat Bansal, and Dr. Marthathi Aakarsh for their compassion and kindness during this difficult period.

I also sincerely acknowledge Mr. Bhavesh, Nursing Officer in NICU, Mr. Bharat Kumar Prajapat, and Ms. Kusum Prajapat for always helping with paperwork and file editing. I would also like to extend my gratitude to the department of transfusion medicine technical and non-technical personnel for encouraging the clinical residents to adhere to appropriate transfusion protocols at all times.

This project would not be possible without the help of the junior and senior residents from the Department of Pediatrics, Department of Neonatology, Department of Pediatric surgery, and the Department of Nursing at AIIMS, Jodhpur.

The finest teachers for a doctor are their patients. Additionally, I would want to thank all of the blood donors, patients and their guardians who enabled us to benefit from their experiences in order to advance medical knowledge. I am eternally thankful to all my teachers who inspired me at every stage of my life. I am thankful to AIIMS Jodhpur, for providing the resources and best facilities, and a wealth of knowledge on par with the world class.

Last but not the least, I want to express my gratitude to my parents who have had the most impact on my life: Mr. Bodanapu Prakash and Mrs. Bodanapu Rajeswari. Thank you for all your sacrifices and years of struggle to provide me with an education and make me worthy to stand on my own legs. I am truly blessed to have extremely kind-hearted parents and I owe all the accomplishments in my life to them.

A special thanks to my elder sister Mrs. Kalpana and My younger brother Mr. Bala Murali Krishna for their unconditional love and encouragement.

Dr. Bodanapu Vinay.

“Nothing in life is to be feared, it is only to be understood, Now is the time to understand more, so that we may fear less.”– Marie Curie

LIST OF ABBREVIATIONS

AABB	Association for the Advancements of Blood and Biotherapies
AGA	Appropriate for Gestational Age
BPD	Broncho-Pulmonary Dysplasia
BSH	British Society for Hematology.
CLD	Chronic Lung Disease
ELBW	Extremely Low Birth Weight
EPO	Erythropoietin
FFP	Fresh Frozen Plasma
HB	Hemoglobin
HIE	Hypoxic Ischemic Encephalopathy
HIV	Human Immunodeficiency Virus
IVH	Intra Ventricular Hemorrhage
LBW	Low Birth Weight
LOS	Length of NICU Stay.
NEC	Necrotising Enterocolitis
NHLBI	National Heart, Lung, and Blood institute
NICU	Neonatal Intensive Care Unit
NICE	National Institute for Health Care and Excellence
PBM	Patient Blood Management
PDA	Patent Ductus Arteriosis
QC	Quality control
RBC	Red Blood Cell
RDP	Random Donor Platelet
RDS	Respiratory Distress Syndrome
ROP	Retinopathy of Prematurity
SOP	Standard Operating Procedures
TACO	Transfusion-Associated Cardiac Overload
TRALI	Transfusion-Related Acute Lung Injury
TTI	Transfusion Transmissible Infections

LIST OF STUDIES

ARIPI	Age of Red Blood Cells in Premature Infants
ETTNO	Effects of Liberal vs Restrictive Transfusion Thresholds on Survival and Neurocognitive Outcomes in Extremely Low-Birth-Weight Infants
PENUT	Preterm Erythropoietin Neuroprotection Trial
PINT	Premature Infants in Need of Transfusion
PlaNeT-2	Platelet transfusion thresholds in premature neonates
REDS-III	Recipient Epidemiology and Donor Evaluation Study III
TOP	Transfusion of Premature
TOTAL	Tissue Oxygenation by Transfusion in Severe Anemia with Lactic Acidosis

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SUMMARY

Background: Neonates are a subset of pediatric patients who are less than 28 days old and have unique RBC transfusion needs not similar to adults and children. In NICU care, preterm with extremely low birth weights and newborns who needed surgery received the biggest share of the transfusions. The most common indications for red cell transfusions are severe anemia and preterm with respiratory distress, both of which are precipitated by iatrogenic blood loss during NICU admission. The safety of the donor and recipient is the key factor in contemporary blood product selection. The future is of precision medicine, and one aspect is improving blood donor selection, which can affect RBC product quality, as well as the focused selection and tailoring of red blood cell products for better neonatal outcomes. The determination of the ideal donor characteristics that may be related to the transfusion recipient outcomes may lead to the optimal blood donor and recipient matches.

Aims and objectives: The Aim of this study was to observe the relationship between blood donor characteristics (age, BMI, Smoking, Alcohol, Pre-donation hemoglobin, first-time donor vs repeat donors) and the clinical outcomes (mortality, HB increment, and morbidity) in neonates of post-red cell transfusion. The primary outcome is death and the secondary outcome is morbidity and HB increment.

Method: This was a Prospective observational cohort study conducted from January 2021 to August 2022 in our department and department of neonatology on NICU hospitalized newborn patients who underwent Red cell transfusion and were followed up to 28 days for mortality from birth or discharge and for transfusion-related short-term complications. The study started with baseline data collection from June 2019 to December 2020 retrospectively. The neonates were screened prospectively and were taken into the study after applying inclusion and exclusion criteria. The analysis of the collected data started in September 2022.

Results: A total of 73 neonates were qualified and included in the study and had 159 Red cell transfusions from 129 donors. The mean age of the donors is 29 years .126 (98%) were males only 3 (2%) were female donors. Nearly 100 (78%) of the donors fall under the overweight and obese category of BMI. Smokers and alcoholic donors were 19 (15%) and 21 (16%) respectively. The mean pre-donation hemoglobin is 14.05 and a standard deviation of 1.07.

Mortality with Red cell transfusion from the donor of age<35 years and >35 years has a P-value of 0.22 (statistically insignificant) and between sex-matched and sex-discordant red cell

transfusion p-value is 1. Mortality with Smoking Donors and alcoholic donors was a statistically insignificant p-value of 0.54 each. Mortality has no statistical significance with Donor's BMI p-value is 0.24. HB increment in neonatal recipients doesn't have statistical significance with Donor age (<35y & >35y) p-value of 0.23, donor's Rh status (negative & positive) p-value of 0.11, Donor ABO status (O group and non-O group) p-value of 0.36, smoking p-value 0.2 and alcoholic donors p-value 0.78. HB increment of 4.53 ± 4.87 (p-value-0.03) in neonatal recipients who received RBC from Donors with BMI <18.5 (underweight). A near statistical significance is seen with an HB increment of 2.26 ± 0.52 (p-value-0.05) in neonatal recipients who received RBC of Storage age less than 10 days. There is a positive association between the number of deaths and short-term complications occurring in exposure to the transfusion in neonates during NICU stay OD 8.4 (CI-4.2-16.5). and OD >1 respectively. The hazard rate of recipients with each additional donor exposure is HR 0.27 (95% CI -0.014-0.55, p-value 0.21) and the survival rate is SR 0.57 (95% CI 0.37-0.78, p-value 0.017). Odds of short-term complication in association with red cell transfusion exposure are like HIE (OD 3.63 CI 95% 1.52- 8.65), IVH (OD 6.83 CI 95% 2.84-16.43), ROP (OD 12.69 CI 95% 5.57- 28.9), PDA (OD 35.3 CI 95% 11.8-106.2), sepsis (OD 6.11 CI 95% 3.25-11.45), Bpd (OD 6.16 CI 95% 3.25-11.45).

CONCLUSION: The age, gender matching, BMI, smoking, and alcohol status of the donor are not relevant factors to consider when allocating blood because they were not associated with neonatal mortality. Multiple Red cell transfusions do cause mortality in neonates. Multi-donor exposure doesn't increase mortality. Apparently, more risk of sepsis, and no risk of short-term complications like BPD, HIE, ROP, and IVH with RBC transfusion. The age, ABO, Rh status, smoking, repeat or first-time donation, and alcohol status of the donors are not relevant factors to consider when allocating RBC because they were not associated with hemoglobin increment in neonates. Red cell transfusion in preterm can increase the length of NICU stay. Selection of RBC within 7 days for transfusion is preferable in neonates. RBC units from underweight Donors had better hemoglobin increment in neonates, and transfusion of fresh RBC within 10 days had better HB increment in neonates. The majority of the liberal transfusion went between 1-7 days of age.

INTRODUCTION

Infants up to 28 days after birth are considered neonates. These groups of patients are unique in their physiology, nutritive requirements, and total blood volumes. The need for NICU care in most sick neonates usually depends on their maturity at birth (Preterm/term), birth weights (ELBW, VLBW, LBW, AGA), and numerous factors that are not similar when compared to older children or adults.

Transfusion is considered one of the most common medical interventions in the management of NICU care, especially among those undergoing surgery or born prematurely. Extensive research regarding transfusion and its associated complications has been done in the past few decades, especially in adults and older children, whereas in neonates, whose life expectancy is considerably long post-transfusion, than adults this concept of understanding transfusion-associated complications and its expected outcomes are still in budding stages. Management of hospitalized neonates is both challenging and demanding requiring a different set of skills that are unique to this subset of patients. Hospitalized neonates are prone to anemia because of their small blood volumes and significant blood loss through various investigations and procedures performed throughout the hospitalization.

The causes of Anemia of prematurity like Immature hematopoiesis, physiological and non-physiological causes, frequent iatrogenic blood loss, and morbidity-related factors would make neonates an interesting group of patients with transfusion being the most commonly used medical intervention when compared to their small blood volume. Anemic patients in the NICU are mostly preterm infants because of their small size and small blood volume, but usually well tolerate the physiological anemia of prematurity which needs to be kept in mind before transfusion. Transfusion need arises mostly due to laboratory blood loss which accounts for most of the NICU transfusions that can be minimized.

Lacunae in the knowledge of transfusion triggers in neonates are evident. Disparities in the practices and variable transfusion triggers are preventing evidence-based practice. The safety of the blood unit is important given the long life ahead of neonates. Unnecessary blood transfusions not only have a risk of transfusion-related complications but also has a risk of infection, multiple donor exposure, TACO, TRALI, and metabolic problems which are usually underdiagnosed, especially in those neonates with prior respiratory complications. Transfusion requirements must be duly addressed and blood products should be selected and

tailored according to the condition and requirements of the neonates. Neonatal patient blood management (PBM) is a multidisciplinary approach where the cumulative efforts of neonatologists, laboratory physicians, and transfusion specialists interplay their respective important key roles in understanding the shortfalls related to transfusion and its alternatives. As a transfusion specialist following neonatal PBM poses its own set of challenges that are unique to neonates in terms of their transfusion needs, but in reality, most of the current blood transfusion guidelines are drawn from the studies done on adults.

Transfusion medicine researchers are particularly interested in the effects of blood donor demographic and genetic variables, component processing, and receiver parameters, on patients' clinical outcomes. A significant study has been concentrated on each of the following: blood donors, blood collection, component separation, storage of products, modifications, and optimal practices for transfusion. On the other hand, limited evidence is available about the efficacy of the practice of selecting fresh RBC units for transfusion, universal leukofiltration, removal of additive solutions, and irradiation in the case of neonates. Even further little studies are done on how the blood donor's health and characteristics affect the neonates if transfused.

The blood donor's safety during donation and the receiver's during transfusion are the main concerns of the present selection procedure. There are conflicting shreds of evidence regarding how blood donor health, age, sex, body stature, habits, and diet affect mortality among RBC transfusion recipients. According to recent research, the donor's traits may have an impact on the recipient's transfusion outcomes both in the short and long term.

The future is all about precision medicine, efforts are being made to adapt the delivery of medical treatment in order to maximize benefits in light of our growing awareness of the factors that affect both an individual's health and the health of the population as a whole. Improved blood donor selection is one of the main goals of current policies aimed at lowering risks for recipients since the features of these donors (health status, phenotypes) can have a significant impact on the quality of RBC products. Although one may readily compare solid organ or bone marrow transplantation to RBC transfusions (the "transplanting" of blood from a donor to a compatible recipient), there is a dearth of information about the influence of donor features on transfusion outcome. The determination of the ideal donor characteristics that may be related to the transfusion recipient outcomes may lead to the optimal blood donor and recipient matches.

HYPOTHESIS

In addition to the screening techniques implemented primarily to lower the risk of transfusion transmissible infections like HIV, Hepatitis B, Hepatitis C, syphilis, and Malaria, we postulate that donor demographics, genetic characteristics, smoking habits, and health may be related to the success of RBC transfusion in newborns.

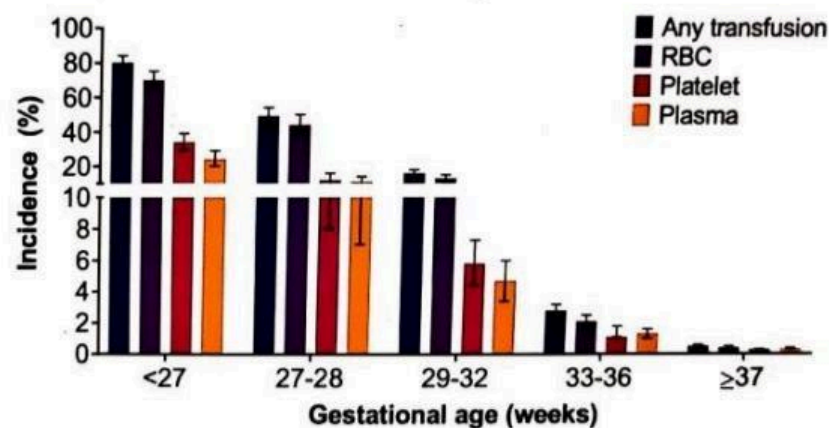
We performed a Prospective observational cohort study to observe the relationship between donor characteristics and recipient outcomes along with transfusion policy, decision-making, clinical outcomes of transfusion, and research in the field of Neonatal Patient blood management. This was done in light of the lack of published studies addressing the clinical impact of donor characteristics on RBC transfusion recipient outcomes in neonates.

REVIEW OF LITERATURE

RBC transfusion is one of the commonest medical prescriptions ordered as a part of NICU care for newborns, especially for those who were prematurely delivered or were having surgery. Hospitalized neonates are more prone to anemia in comparison to children and adults, particularly preterm immature babies and extremely low birth weight (ELBW) neonates who require at least a single episode of transfusion and may end up with multiple episodes of transfusions during their course of NICU stay⁽¹⁾

Preterm neonates under 1000 g are more likely to get transfusions due to the requirement for more intensive care, higher sampling losses relative to body weight, and hemodilution brought on by rapid development⁽²⁾

Incidence of transfusion based on Gestational Age



Retrospective cohort study using data from 7 geographically diverse US academic and community hospitals that participated in the National Heart Lung and Blood Institute Recipient Epidemiology and Donor Evaluation Study-III (REDS-III) from 2013 to 2016.

Figure 1. Incidence of transfusion based on Gestational age.

Image Source: REDS-III Study (NHLBI) (2013-2016).

Neonatal patients, in particular, have a different transfusion protocol than adult patients. There are few age-appropriate standards, and the majority of them are derived from adult studies and practice⁽³⁾

Neonates are not small adults with adjusted blood volumes. Different physiological changes occur during the transition from fetus to adolescent, including variations in blood volume, the maturation of the immune system, the development of hematopoiesis and coagulation, and

the physiological responses to hypovolemia and hypoxia that differ in heterogeneous populations⁽⁴⁾

Pediatric transfusion medicine in the past decade is the most discussed multidisciplinary approach among pediatricians, neonatologists, and transfusion medicine specialists and is considered to be the most exciting area to be explored with the advent of new technological advancements, yet certain gaps are to be addressed, such as (a) Age-defined definitions for anemia in neonates (b) Outcomes-based studies for RBC transfusion in neonates (c) Correlation between age of RBC units and adverse outcomes in neonates (d) Appropriate establishment of hemovigilance in neonates and infants (e) Correlation between donor characteristics and adverse outcomes in neonates (f) Effect of Restrictive vs liberal transfusion strategies on short term and long term complications on recipients⁽⁵⁾

Two randomized clinical trials (Lowa trial and PINT trial) evaluating transfusion protocols in preterm neonates, as well as other prospective studies, have defined severe anemia in neonates as hemoglobin levels of 8 g/dL or less^(6,7)

Following preterm birth, RBC transfusions are required in two stages: (a) early, for newborns who need major surgery or intensive care (NICU); and (b) later, throughout the duration of the physiological anemia associated with prematurity. Initial blood volume, the extent of iatrogenic blood losses related to the level of intensive care and length of NICU stay, and lack of erythropoiesis are all factors that affect transfusion in hospitalized neonates⁽⁸⁾

Transfusion is the most common medical intervention in NICU neonates. Indications for transfusion in this category have generally been based on the Hemoglobin concentration paired with the cardiorespiratory condition of the newborn (e.g. Necessity for oxygen or ventilatory assistance) and parameters such as weight gain, however, the evidence is poor⁽⁹⁾

Postnatal age	Suggested transfusion threshold Hb (g/L)		
	Ventilated	On oxygen/CPAP	Off oxygen
First 24 hours	<120	<120	<100
≤Week 1 (days 1–7)	<120	<100	<100
Week 2 (days 8–14)	<100	<95	<75–85 depending on clinical situation
≥Week 3 (day 15 onwards)		<85	

Table Source: BSH guidelines Transfusionguidelines.org

Figure 2: summary of the BSH recommendation for the Neonatal top-up transfusion

Instead of actually established recommendations, the great majority of newborn transfusions typically depend on professional clinical judgment. ⁽¹⁰⁾

Neonates have some specific adverse associations and outcomes that may be related to RBC transfusions, including the development of necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH) ^(11- 13), retinopathy of prematurity (ROP) ⁽¹⁴⁾, and chronic lung disease (CLD) ^(15, 16), as well as mortality.

Current guidelines for pediatric transfusion recommend blood component dosing of 10-15 mL/kg for red blood cells and fresh frozen plasma. Lower dosages of 5-10 mL/kg and 1-2 units/10kg are required for platelets and cryoprecipitate respectively. Top-up transfusions in excess of 20 mL/kg are not indicated due to the danger of transfusion-associated vascular overload (TACO) ⁽¹⁷⁾

Researchers in transfusion medicine is particularly interested in how patient clinical outcomes are impacted by component processing, receiver parameters, and demographic and genetic characteristics of blood donors. A substantial amount of research has been conducted on the following topics: blood donors, blood collection, component separation, product storage, changes, and optimal transfusion techniques. ^(18,19)

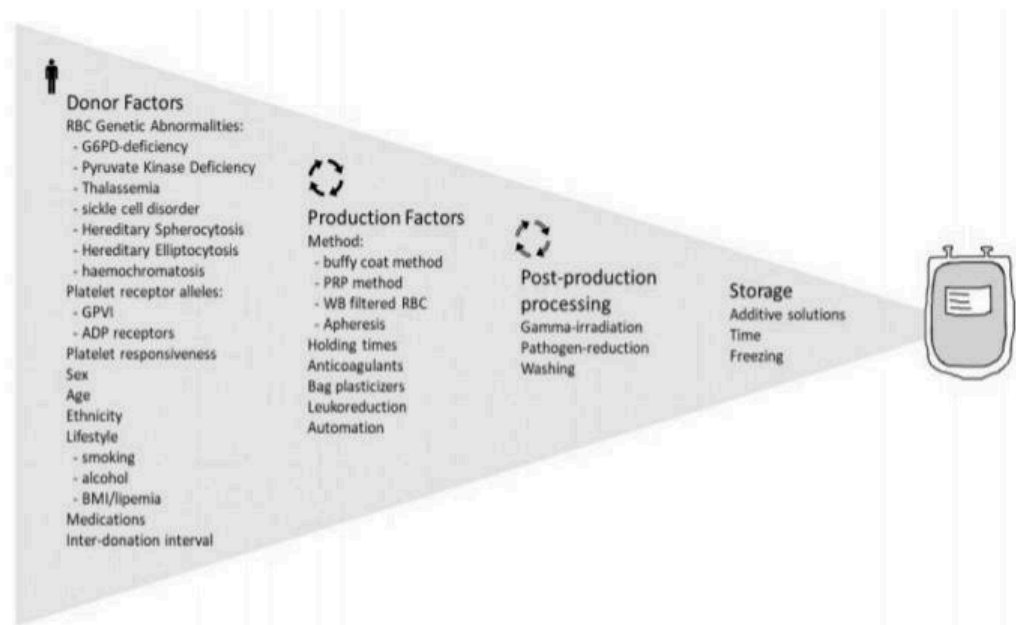


Figure 3: Factors affecting the quality of RBC products.

Image source: *Int. J. Mol. Sci.* **2021**, 22(8), 3943; <https://doi.org/10.3390/ijms22083943>,

Although it is recognized that the inherent variation in the blood donor population affects the quality of blood components, the effect on transfusion recipients' results is yet unknown. Moreover, variations in blood collection techniques (such as manual or apheresis), anticoagulants, and leukoreduction and storage solutions produce products with various physiological and biochemical properties (20,21)

Blood collection procedures, component manufacturing processes, and additive solution selection have all been proven to alter transfused product attributes and may influence product quality. Male-donor-derived RBC units have higher total hemoglobin content than female-donor-derived RBC units; nevertheless, rates of storage hemolysis are higher in male-donor-derived RBC units and vary with donor age in both sexes (22,23)

Tailoring the RBC units according to the needs of neonates and infants is the other area of interest in providing safe and optimal blood. Techniques like Gamma irradiation, leucocyte reduction, and washing of RBC units are already in practice for certain conditions in neonates and infants with satisfactory literature yet these practices are not uniform and need better studies to relate to outcomes in neonates ⁽²⁴⁾



Figure 4: Leukofiltration

Image source: AIIMS Jodhpur Blood center

Gamma irradiation and prolonged storage of RBC components have both been associated to an increase in vitro and in vivo hemolysis (25,26)



Figure 5: Irradiator

Image source: AIIMS Jodhpur Blood Center

Irradiation of blood products

It may be beneficial to administer aliquots from a single donor as needed in small, sick neonates if it is expected that blood components may be required more than once. Practically, this is accomplished by setting aside a bag of fresh RBC for a baby for up to 7 days and continuously extracting tiny aliquots from that bag into another bag of fresh blood while under laminar flow and utilizing a sterile connection device. The RBC bag may be used again for up to 7 days to draw comparable little amounts of blood by being immediately resealed under the laminar flow ⁽²⁷⁾

The washing of red blood cell concentrates and the donors' age and Rh blood type contribute to a significant increase in the recipient's post-transfusion hemoglobin. These variables might be used to predict changes in recipients' hemoglobin levels prior to transfusion ⁽²⁸⁾



Figure 6: Sterile connecting device, in making aliquots for neonates.

Image source: AIIMS Jodhpur Blood Center.

A sterile connecting device used for making aliquots as per the requirement of the neonate

The Age of RBC units in the ARIPI study, 7 days vs. 14 days, was discovered to be clinically equivalent in terms of outcomes in preterm infants ⁽²⁹⁾

Tissue Oxygenation by Transfusion in Severe Anemia with Lactic Acidosis (TOTAL) randomized clinical trial (290 children 6-60 months old) evidence in older children showed no difference in post-transfusion correction of mean lactate levels between young blood (median age of 8 days) versus older blood (median age of 32 days) ⁽³⁰⁾

In recent times two major studies published, TOP and ETTNO concluded that the current Hemoglobin trigger used in extremely low birth weight neonates does not fully represent the oxygenation status, various other factors like erythropoietin levels and physiology of anemia in preterm, etc should also be taken in to account before transfusion ^(31,32)

Recent research (PENUT) has shown encouraging results in reducing the need for RBC in ELBW infants by using early enteral iron administration with or without erythropoietin. Using an approach together with aliquots from a single donor blood component for repeated transfusions reduces the number of transfusions and donor exposures without the need for EPO medication. Even when transfusion standards are in place and properly followed, RBC transfusion rates are further lowered if anemia-prevention methods are used like following delayed cord clamping and using appropriate vacutainers⁽³³⁾.



Figure 7: Appropriate-sized pediatric Vacutainers

Image source: AIIMS Jodhpur, NICU

Appropriate Vacutainers to minimize iatrogenic blood loss.

The other less explored area of interest is examining the relationship between neonatal recipient outcomes and the use of donor RBC products. Selecting the RBC unit based on donor characteristics and the age of the unit and QC criteria by weighing the pros and cons of transfusion⁽³⁴⁾

Age, sex, blood groups, and other donor characteristics are frequently used to determine whether a particular organ may be suitable for transplantation, to choose the best recipient for a particular organ, and to improve follow-up of transplanted patients when some donor characteristics are not ideal, such characteristics may also affect RBC transfusion outcomes⁽³⁵⁾

To assess and create the best outcome-based strategies, donor and recipient-based research is required ⁽³⁴⁾. Additionally, it is essential to evaluate variation in donor attributes to properly assess the effects of "vein-to-vein" variability in donor characteristics on recipient outcomes. ⁽³⁵⁾

An emerging body of studies suggests that exposure to red blood cells may also be a factor in the higher mortality of transfused patients, even if their comorbidities may be the primary reason for this. RBCs from female donors, younger donors, and donor-recipient RBCs with sex-mismatched might make an already poor prognosis worse. ^(35, 36)

Through its sponsored REDS projects, the National Heart, Lung, and Blood Institute (NHLBI) has developed longitudinal databases that have the advantage of preserving contextual data on donor characteristics, the timing of transfusions, and delivery procedures.

This study has shed important light on vitally important features of adult RBC transfusion treatment but not infants ⁽³⁶⁾

Standardization of neonatal transfusion practices throughout the blood centers in India is the need of the hour. Identification of donor attributes linked to transfusion recipient outcomes may lead to improved blood donor selection and donor-recipient matching. For example, data indicate that contributions from certain donors have a deleterious impact on transfusion. The findings may result in revised donation practices, with such donors being excluded from the donor pool ⁽³⁷⁾

Various studies have given variable results regarding the blood donor and recipient association in the outcome. One study on Canadian blood donors stated that donors <45 years of age are associated with higher mortality and also stated that patients may benefit from receiving RBC transfusions from older donors who are sex-matched to their recipients ⁽³⁸⁾

The hemoglobin rise following transfusion of each packed red cell unit is one measure of transfusion effectiveness. Clinicians have long assumed that transfusion of a single RBC unit leads to a 1 g/dL rise in hemoglobin. However, there are few studies that look at the relative impact of the donor, component collection and manufacture, and receiver factors on transfusion outcomes ⁽³⁹⁾

Another study published by Ottawa hospital in Canada stated that male recipients who were transfused with blood from female donors have decreased survival. Donor antibodies, antigens, or infection may affect outcomes ⁽²⁵⁾ Younger donors under 20 years had a 3% shorter hospital duration of stay. There is no evidence of an association between blood donor variables and in-hospital mortality ⁽⁴⁰⁾

Table 1: Studies are done previously to evaluate the relationship between donor and transfusion recipient outcomes

Study	Year	Journal	Country	Sample size	Result
Association between blood donor sex and age on transfusion recipient mortality an exploratory analysis	2014	Canadian blood services	Canada	25,219	Donors<45 years of age are associated with higher mortality and also stated that patients may benefit from receiving RBC transfusions from older donors who are sex-matched to their recipients
Effect of donor, component, and recipient characteristics on hemoglobin increments following red blood cell transfusion ⁽³⁰⁾	2019	American Society of Hematology	United States	1,39,433	Individual donor, component, and recipient characteristics are significant in hemoglobin increments of transfusion recipients.
Effect of blood donor characteristics on transfusion outcomes, A	2014	Ottawa hospital	Canada	-	Male recipient transfused blood from Female donors has decreased survival. Donor antibodies,

systemic review, and meta-analysis					antigens, or infection may affect outcomes
Association of donor age, BMI, Hb, and smoking status within hospital, mortality, and length of stay among RBC transfused recipients	2019	NHLBI	United States	93,726	Younger donors <20 years of age are associated with a 3% lesser shorter hospital length of stay (p-value <0.001) No evidence of the association between blood donor factors and in-hospital mortality.

AIM AND OBJECTIVES

AIM

The major goal of this study was to examine the relationship between blood donor characteristics and the clinical outcomes after RBC transfusion in neonates.

OBJECTIVES

- 1) To study the association of donor characteristics (age, BMI, Smoking, Alcohol, Pre-donation hemoglobin, first-time donor vs repeat donors) with the mortality in neonates receiving RBC transfusions.
- 2) To study the association between RBC transfusion and its short-term complications in neonates.

Outcome

- 1) The primary outcome is in-hospital NICU mortality.
- 2) Secondary outcomes are RBC transfusion-related short-term complications (BPD/RDS, HIE, ROP, IVH, PDA,) HB increment, discharge without complications in neonates (morbidity) and length of NICU stay.

MATERIAL AND METHODS

STUDY DESIGN

A Prospective observational cohort Study

STUDY SITE

Department of Transfusion Medicine and Blood Bank, AIIMS, Jodhpur.

Department of Neonatology, AIIMS, Jodhpur.

Department of Pediatric Surgery, AIIMS, Jodhpur.

SAMPLE SIZE

73 Patients

DURATION OF STUDY

January 2021 to August 2022.

POPULATION

Inborn Neonates admitted to NICU requiring at least 1 RBC transfusion.

INTERVENTION

The impact of donor characteristics in relation to transfusion of RBCs in neonates

OUTCOMES

- 1) The primary outcome is in-hospital NICU mortality.
- 2) Secondary outcomes are the short-term complication (BPD, ROP, IVH, HIE, PDA and Length of NICU stay)

ELIGIBILITY CRITERIA

1. Inclusion criteria:

- a. Neonates under 28 days of age, who got at least one RBC or multiple RBC transfusions while being hospitalized in the NICU of AIIMS Jodhpur
- b. Preterm neonates are included.
- c. Extremely low birth weights and very low birth weight neonates are included.
- d. Neonates on ventilator support.
- e. Neonates in septic shock and respiratory failure.
- f. NICU patients who are admitted before 28 days of age are included up to an end point of discharge or mortality.

2. Exclusion criteria:

- a. Neonates born outside AIIMS Jodhpur Hospital.
- b. NICU patients who were not transfused.
- c. Transfusions limited to FFP and RDP.
- d. Neonates who had transfusion history outside of AIIMS Jodhpur
- e. Patients whom we were unable to follow up with or have incomplete missing details.

METHODOLOGY

We conducted a prospective observational study on neonates under 28 days of age, who got at least one RBC or multiple RBC transfusions while being hospitalized in the NICU of AIIMS Jodhpur between 1st January 2021 to 31st August 2022

Patients were followed up from the first transfusion until death, or discharge from NICU, or up to the end of follow-up i.e until 28 days from birth. All neonates who were born in AIIMS Jodhpur either by normal delivery or Caesarean underwent delayed cord clamping as a part of regular practice.

Algorithm-based transfusion protocol derived from AABB, BSH, and NICE guidelines was practiced.

Transfusion triggers are based on the following factors,

- Hemoglobin transfusion thresholds
- Postnatal age
- Respiratory support and Inotrope support.

The transfusion volume of the RBC unit was 15 ml/kg of body weight for top-up transfusions and for exchange transfusions, the total blood volume was estimated for preterm as 100ml/kg and for the term as 80ml/kg. All transfusions received by the neonates were crossmatched and compatible with the mother's plasma. Administration of erythropoietin is not practiced routinely.

Data collected from the inborn neonates admitted in NICU from initial admission throughout the 28-day postmenstrual age or discharge or death whichever is prior were included in this study.

Patients who got transfusions from outside sources, transfusions limited to FFP and RDP, and patients whom we were unable to follow up with were excluded from this study.

Clinical data from NICU records and laboratory data from the hospital's information system and RBC transfusion data from the blood center records of AIIMS jodhpur were used to identify and monitor eligible patients.

Details on the donor's sex, age, and pre-donation hemoglobin were obtained from the AIIMS Jodhpur blood center. The methodology used to prepare RBC units from whole blood is as per the SOP followed by AIIMS Jodhpur Blood center,

Every RBC unit that was transfused was collected as whole blood units into citrate-phosphate-dextrose, a component processed by buffy coat reduction method, and then kept in saline-adenine-glucose-mannitol solution at 1-6 C for a maximum of 42 days.

Post-collection modifications like leukofiltration and irradiation were done to the RBC units prior to exchange transfusions. Freshly prepared RBC units within 14 days from the collection were selected for transfusion.

we attempted to combine donor and RBC data with the specifics of the transfused Patients. The primary outcome is in-hospital NICU mortality. Secondary outcomes are short-term complications like the length of NICU stay, BPD/RDS, HIE, ROP, IVH, PDA, and discharge without complications.



Figure 8: workflow of the study

Baseline data collection

To establish baseline data the previous transfusion data were screened. A total of 303 blood requisition forms from June 2019 to December 2020, were screened for blood component requisitions in NICU patients, and 63% of blood requisitions were of RBC.

Crossmatch to transfusion ratio (CT ratio) of NICU was 1.46 suggesting a significant utilization of blood components

The primary indication for PRBC transfusion was anemia (56%), indication for PRBC transfusion was during surgery (19%), shock (11%), blood loss (10%), and pathological jaundice (0.05%) in decreasing order.

Table 2: Indications for RBC transfusion in NICU Patients of AIIMS Jodhpur from June 2019 to December 2020.

SNO	INDICATION FOR RBC TRANSFUSION IN NICU PATIENTS	PERCENTAGE
1	Anemia	56%
2	Surgery	19%
3	Shock	11%
4	Blood loss	10%
5	Pathological jaundice	11%

Male requisitions received outnumber female requisitions. Females received more transfusions (p-value 0.000, chi-square 16.2) with PRBC accounting for the majority of transfusions in terms of gender predisposition.

No significant association between transfusion requirement and maturity status (extreme preterm, very preterm, late preterm, and term patients) was seen (p-value 0.210).

ELBW neonates were more transfusion-dependent (Chi-square 18.8, p-value 0.000), and the most frequent blood component transfused was RBC.

In terms of clinical outcome, mortality was more in the extremely premature neonate. The association is significant when the frequency of transfusion is more than 2 and mortality was higher in late preterm neonates (p-value 0.004).

Screening and Selection

This study started in January 2021 after receiving ethical clearance from the institute.

Blood requisition forms were screened regularly and neonates admitted to NICU who were issued with RBC were followed back to NICU, after applying the inclusion and exclusion criteria, the selected patients were monitored for further up to 28 days from birth or discharge or death whichever is earlier.

Data regarding the following parameters were collected from NICU records

- Patient ID
- Patient Sex
- Birth Weight- ELBW, VLBW, LBW, AGA
- Gestational age- Preterm/ Term
- Date of Birth
- Date of NICU admission
- Place of birth: Inborn or outborn
- If outborn: Any transfusion history from Outside.
- Date of Discharge
- Admission Diagnosis
- Indication for Transfusion
- Pre-transfusion hemoglobin and post-transfusion hemoglobin.
- Outcome: Discharge/ Mortality/ Short-term complications.

The RBC unit transfused is temporally traced back to the donor who donated whole blood, and details of the donor's demographics and habits were obtained from donor screening records, the details regarding the whole blood unit collection, component separation, storage, and TTI record results were ensured to be as per the AIIMS blood center's sop.

Data regarding the following parameters were collected from Donor Screening records

- Donor ID
- Age
- Sex
- Blood group
- Date of donation
- Age of RBC unit at the time of issue
- Donor Weight
- Donor Height
- Number of times donated previously
- Systolic and Diastolic Blood pressure
- Pre-donation hemoglobin in gm/dl
- Smoking
- Alcohol

Any post-collection modification done to the RBC unit which is transfused to the patient is documented. The transfusion decision was made at the point of issuing the RBC unit, primarily following a restrictive transfusion approach as per guidelines laid in AABB, BSH, and NICE guidelines, exceptions were made in sick and critically ill neonates based on the expert clinical decision.

*Critical: on Ventilator or assisted breathing, on 1 or more inotropes or vasopressors.

Table 3: Transfusion thresholds for guiding RBC transfusion requirement based on Hemoglobin levels.

Age of neonate	Restrictive transfusion thresholds (Hemoglobin in gm/dl)		Liberal transfusion thresholds (Hemoglobin in gm/dl)	
	Critical	Non-critical	Critical	Non-critical
3-7 days	11	9	13	11.5
8-21 days	10	8	12	10
>27 days	9	7	11	9

Data regarding the following parameters of the RBC unit were collected from the records of the blood center.

- RBC unit number
- Aliquot Volume for transfusion in ml.
- Leukofiltered: Yes/No
- Irradiated: Yes/No
- Age of RBC unit at the time of issuing.
- Indication for transfusion
- Cross-match compatibility with the mother's sample as per SOP.

Observations & findings

After applying the inclusion and exclusion criteria, the selected patient is observed for further up to 28 days from birth or discharge or death whichever is earlier.

Data regarding the following parameters of the selected patient is collected from the hospital information system and NICU

- Pre-transfusion hemoglobin
- Post-transfusion hemoglobin
- Date of admission

- Admission Diagnosis
- Indication for transfusion
- Volume of transfusion
- Outcome on the follow-up- Death/ discharge
- Date of discharge/death
- Short-term complications length of NICU stay, BPD/RDS, HIE, ROP, IVH, PDA, and discharge without complications
- ✓ BPD/RDS- Yes/No
- ✓ HIE- Yes/No
- ✓ ROP- Yes/No
- ✓ IVH- Yes/No
- ✓ PDA- Yes/No
- ✓ DISCHARGE WITHOUT COMPLICATIONS- Yes/No

ANALYSE

After the end of August 2022, Donor data, RBC data, and clinical outcome data with the specifics of the transfused Patients were combined. Data is analyzed for the donor characteristics affecting the hemoglobin increment and patient outcome. The relation of RBC transfusion with the primary outcome i.e in-hospital NICU mortality and secondary outcomes like the length of NICU stay, BPD/RDS, HIE, ROP, IVH, and PDA were compared between transfused and un-transfused NICU admitted neonates.

STATISTICAL ANALYSIS

Data was entered in the excel spreadsheet. SPSS (Statistical Package for Social sciences) version 20. IBM SPSS statistics was used to perform the statistical analysis. To describe the data, descriptive statistics, frequency analysis, and percentage analysis were used for categorical variables, and the mean and SD were used for continuous variables.

For the number of transfusions and donor exposure group cohorts, the association between donor characteristics (previously pregnant, nulliparous, and male) and transfusion recipient survival, and hazard were analyzed using regression models. Regression results were reported as coefficients with 95% confidence intervals (CI) representing the mean hemoglobin increment following RBC transfusion for that variable.

To find the significance in categorical data Chi-Square test was used, Fischer exact test was also used when the expected frequency is less than 5. Two-sided p-values less than 0.05 were considered to be statistically significant. When appropriate, we provided pooled effect estimates as pooled log-odds ratios or risk ratios with 95% confidence intervals. For the number of transfusions and donor exposure group cohorts, the association between donor characteristics (previously pregnant, nulliparous, and male) and transfusion recipient survival was analyzed using regression models.

RESULTS

Donor demographic data

In our study, the 73 qualified neonates received blood from 129 donors. The average age of donors in our study was 29 years with a standard deviation of 7.1 (as shown in the table above). Of these 103 (79.8%) donors were aged ≤ 35 years and 26 (19.2%) donors had an age > 35 years. The majority of donors are in the first group (≤ 35 YEARS) with a mean age of 26 years and a standard deviation of 7.5, and the mean of the second age group (> 35 YEARS) is 41 years with a standard deviation of 7.1.

Table 4: DONOR VARIABLES -AGE

VARIABLES	Age groups	N	MEAN	Std. dev
DONOR AGE	≤ 35 YEARS	103 (79.8%)	26.72	7.57
	> 35 YEARS	26 (19.2%)	41.03	7.13
	TOTAL	129	29.61	7.13

Out of 129 donors included in this study, the majority of donors were males 126 (98%) and the remaining 3(2%) were females.



Chart 1: Gender distribution in Donors

39.5% (n=51) of the donors were overweight with a BMI between 23-26.9 followed by obese 38% (n=49) with a BMI above 27.

Table 5: DONOR VARIABLES- DONOR BMI

VARIABLES	CATEGORY(ASIAN)	BMI	N	(%)	MEAN	Std.Dev
DONOR BMI	UNDERWEIGHT	< 18.5	3	2.4%	18.02	3.10
	IDEAL	18.5-22.9	26	20.1%	21.70	4.43
	OVERWEIGHT	23-26.9	51	39.5%	24.78	4.38
	OBESE	>27	49	38%	30.66	4.34
	TOTAL		129	100%	26.24	4.44

In our study with a donor population of 129 donors, Smokers and non-smokers were 19 (14.7%) and 110 (85.2%) respectively. Alcohol consumers and non-consumers were 21(16.2%) and 108 (83.8%) respectively. Voluntary and replacement donors were 28 (21.7%) and 101 (78.3%) respectively. Indicates most of the donors were non-smokers, non-consumers of alcohol, vegetarians, and Replacement donors.

Table 6: DONOR VARIABLES- Smoking, Alcohol, Voluntary & Replacement donors, Dietary habits

VARIABLES	CATEGORIES	N	PERCENTAGE (%)
SMOKING	Smokers	19	14.7
	Non-Smokers	110	85.2
	Total	129	100
ALCOHOL	Consumers	21	16.2
	Non-consumers	108	83.8
	Total	129	100
TYPE OF DONATION	Voluntary	28	21.7
	Replacement	101	78.3
	Total	129	100

Pre-donation Hemoglobin of 129 donors was categorized into two groups of Hb less than equal to 15gm/dL and above 15 gm/dL with 90 donors (70%) and 39 donors (30%) respectively. The mean Hb of the first group is 14.04 gm/dL with a standard deviation of 1.07 and the Mean Hb of the second group is 15.8 with a standard deviation of 1.08.

TABLE 7: DONOR VARIABLES- Pre-donation Hemoglobin

VARIABLE	Pre-donation Hb (gm/dL)	N	%	Mean Hb (gm/dL)	Std.Dev
DONOR HEMOGLOBIN (Hb)	Hb \leq 15	90	70%	14.04	1.07
	Hb $>$ 15	39	30%	15.8	1.08
	Total	129	100%	14.05	1.07

Table 8: Overall variables of Donor (n= 129, 100%)

Characteristics		n	%
Age	18 - 25yrs	41	31.8
	26 - 35yrs	62	48.1
	36 - 45yrs	23	17.8
	45 -55 yrs	3	2.3
Gender	Male	126	97.7
	Female	3	2.3
Donor	Voluntary	28	21.7
	Replacement	101	78.3
No. of times donated	First time	30	23.3
	< 10 times	88	68.2
	> 10 times	10	7.8
Hemoglobin content	12.5 - 13	14	10.9
	13.1 - 14	33	25.6
	14.1 - 15	43	33.3
	15.1 - 16	26	20.2
	16.1 - 17	9	7.0
	> 17.1	3	2.3
Smokers	No	109	84.5
	Yes	19	14.7
Alcohol	No	108	83.7
	Yes	21	16.3
Diet	Vegetarian	93	72.1
	Non - Vegetarian	36	27.9

Recipient Demographic Data

During the study period from January 2021 to August 2022, a total of 802 neonates needed NICU care, out of which AIIMS born and outside born were 607 (75%) and 195 (25%) respectively. 38 (4.8%) outside-born neonates were transfused outside prior to admission. Most of the NICU admissions were of unborn babies. These were categorized to uniform the practice of delayed cord clamping and standard of delivery in selected neonates and standard of RBC product.

Table-9: NICU admissions from Jan2021to August 2022

Variable	Birthplace	N	Percentage	
NICU ADMITTED NEONATES	AIIMS born	607	75.7%	Total outside- born neonates n=195 (24.3%)
	Outside born and un-transfused	157	19.5%	
	Outside born and outside transfused	38	4.8%	
	Total	802	100%	

A total of 607 AIIMS-born neonates were categorized into un-transfused 484 (79.9%) and transfused 123 (20.3%).

Table 10: AIIMS-born neonates during the study period

VARIABLE	Transfusion status	N	PERCENTAGE
AIIMS BORN NEONATES	Un-transfused	484	79.7%
	Transfused	123	20.3%
	Total	607	100%

Out of 123 neonates who were AIIMS born and transfused exclusively from our blood center, 77 (63%) neonates were transfused with RBC products, and 46 (37%) were transfused exclusively with RDP, FFP, and other blood components. Out of 77, RBC transfused AIIMS-born neonates, 4 neonates (5%) were lost to follow-up.

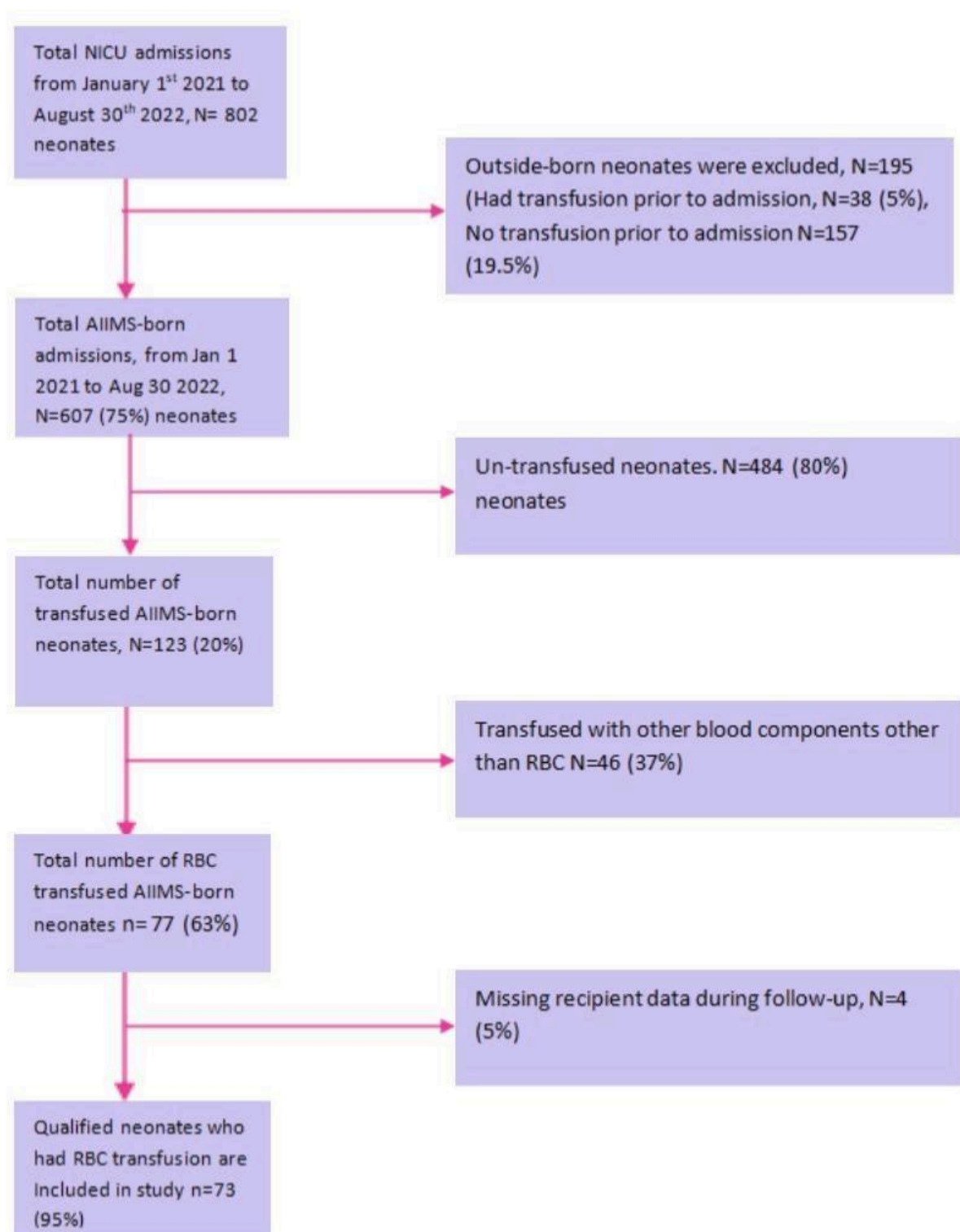


Figure 9: Flow diagram for applying inclusion and exclusion criteria

Table 11: Transfused AIIMS-born neonates with RBC transfusions during the study period.

VARIABLE	CATEGORIES	N	PERCENTAGE
TRANSFUSED AIIM-BORN NEONATES	RBC transfusion	77	63%
	Other components transfusion	46	37%
	Total	123	100%

The blood transfusion indices during the Study period indicate that for patients who sent requests for RBC were mostly crossmatched as indicated by blood utilization rates and transfusion index, and there was no significant blood wastage as indicated by CT ratio.

Table 12: Blood Transfusion Indices of NICU during the study period.

Variable	INCLUSION	N	%	Total	Excluded
Number of requests received from NICU during the study period (A)	Includes all AIIMS born who needed RBC transfusion (includes after a follow-up period of 28 days)	77	70%	N=115 (100%)	Excludes 1. AIIMS born and Outside born who never needed an RBC transfusion.
	Includes all Outside born who needed RBC transfusion	38	30%		
Number of units cross-matched for total NICU RBC requests received during the study period (B)	Same as above	411	-	411(100%)	Same as above

Number of RBC units Issued during the study period (C)	Same as above	268	-	268(100%)	Same as above
Number of patients transfused with RBC during the study period (D)	Same as above	115	-	115 (100%)	Same as above
Cross-match to transfusion ratio during the study period (CT RATIO)	Number of units crossmatched/ Number of units transfused (B/C)	1.53	The mean CT ratio for the study period is 1.7 (<2.5) indicating no significant blood wastage		
Blood utilization	number of units transfused/number of units crossmatched (C/B) X100	65%	>50% crossmatching is required in most cases		
Transfusion Index	number of units transfused/ number of patients transfused (C/D)	2.3	(>0.5 indicates crossmatch is required in most of the cases)		

A total of N=73 (60%) neonates qualified for the study out of 123 in-house transfused in-born neonates and 4 (3%) were lost to follow-up. Out of 73 qualified neonates, males were 44 (60%) and 29 (40%) were females, with a P-Value of 0.92 (not significant). Indicates episodes of transfusion are independent of the recipient's sex.

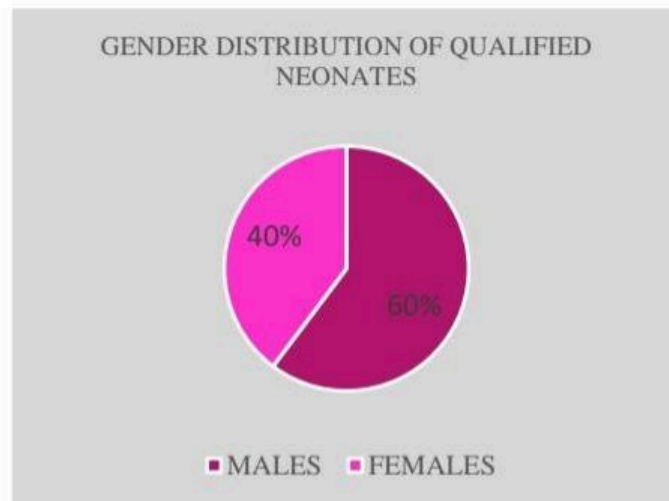


Chart 2: Gender distribution in Qualified neonates.

Out of 73 Qualified neonates with a mean gestational age of 32 weeks+3 days and standard deviation of 4.58 %, 59(81%) were qualified preterm with a mean gestational age of 30 weeks+2 days with a standard deviation of 4.58 and 14 (19%) were qualified term neonates 14(19%) with a mean gestational age of 39 weeks+1day and a standard deviation of 5. The majority of qualified neonates (73) who needed RBC transfusion were preterm 59 (81%)

Table 13: Gestational age distribution in NICU patients

VARIABLES	N=	GESTATIONAL AGE			
		TERM		PRETERM	
		N	%	N	%
UNQUALIFIED NEONATES	572	340	59.5%	232	40.5%
QUALIFIED NEONATES	73	14	19%	59	81%
TOTAL AIIMS BORN NEONATES	645	354	55%	291	45%

{Unqualified neonates include out-born neonates, outside transfused neonates, AIIMS born un-transfused neonates, lost for follow-up, and neonates who were transfused with other

blood products (other than RBC Products) (qualified neonates are the ones included in this study))

When we compared all the AIIMS-born, term, and preterm, we found 14 (4%) out of all terms n=354 admitted were transfused and the remaining 340(96%) were not transfused. We also observed a total of 291 Preterm were admitted to NICU during the study period and 59 (20%) of them needed RBC transfusion and the remaining 232 (80%) were not transfused.

Table 14: Gestational age distribution of Qualified Term and Preterm in NICU patients

GESTATION AGE	N	%	MEAN GESTATION AGE	Std.Dev
QUALIFIED TERM	14	19%	39w+1d	5.00
QUALIFIED PRETERM	59	81%	30w+2d	4.58
TOTAL QUALIFIED NEONATES	73	100%	32w+3d	4.58

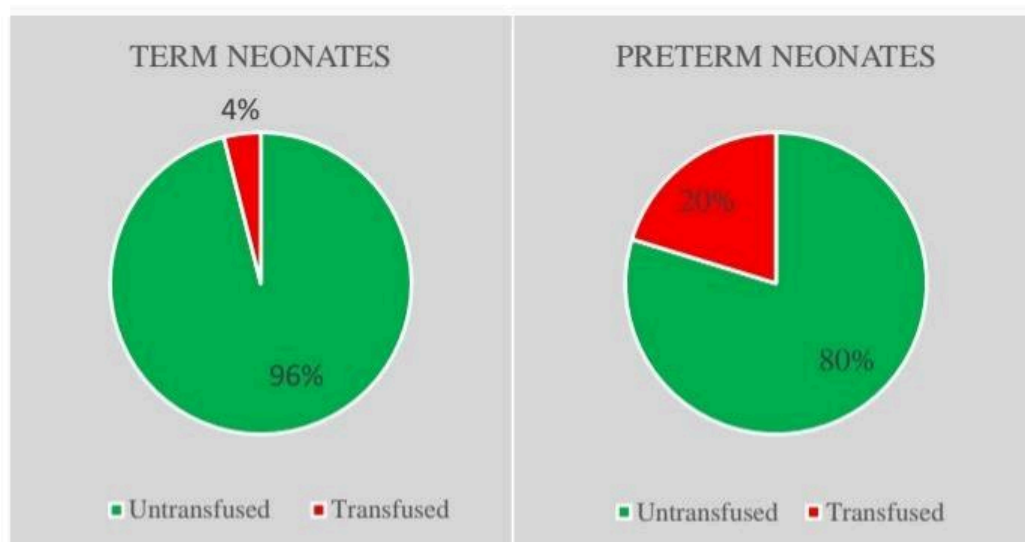


Chart 3: Term vs Preterm transfusion requirements in all AIIMS-born neonates.

We observed that 25 (65%) of qualified neonates were ELBW (extremely low birth weight) with mean birth weight of 795 gm, 15 (22%) and 17 (9%) were very low birth weight and low birth weight with mean birth weights of 1206 gm and 3210 gm respectively. It shows that

ELBW neonates needed more transfusions, next to them are VLBW. Lesser the birthweight from mean birthweight more is the transfusion requirement in neonates. ELBW neonates 25 (65%) out of 39 received RBC transfusion.

Table 15: BIRTH WEIGHT DISTRIBUTION IN AIIMS-BORN NEONATES

VARIABLES	N=	ELBW	VLBW	LBW	AGA
UNQUALIFIED NEONATES	572 (88%)	14 (35%)	53 (78%)	179 (91%)	326 (95%)
QUALIFIED NEONATES	73 (12%)	25 (65%)	15 (22%)	17 (9%)	16 (5%)
TOTAL AIIMS BORN NEONATES	645 (100%)	39 (100%)	68 (100%)	196 (100%)	342 (100%)

{Unqualified neonates include out-born neonates, outside transfused neonates, AIIMS born un-transfused neonates, lost for follow-up, and neonates who were transfused with other blood products (other than RBC Products) (qualified neonates are the ones included in this study)}.

Table 16: BIRTH WEIGHT DISTRIBUTION IN QUALIFIED NEONATES

QUALIFIED NEONATE'S BIRTH WEIGHT CATEGORIES	N	percentage	MEAN BIRTH WEIGHT
ELBW	25	34.3%	795gm
VLBW	15	20.5%	1206gm
LBW	17	23.2%	1920gm
AGA	16	22%	3210gm
TOTAL	73	100%	1670gm

It was observed that 37 (50%) of the qualified neonates who got RBC transfusions were admitted with respiratory distress next to it is hyperbilirubinemia 17 (23%)

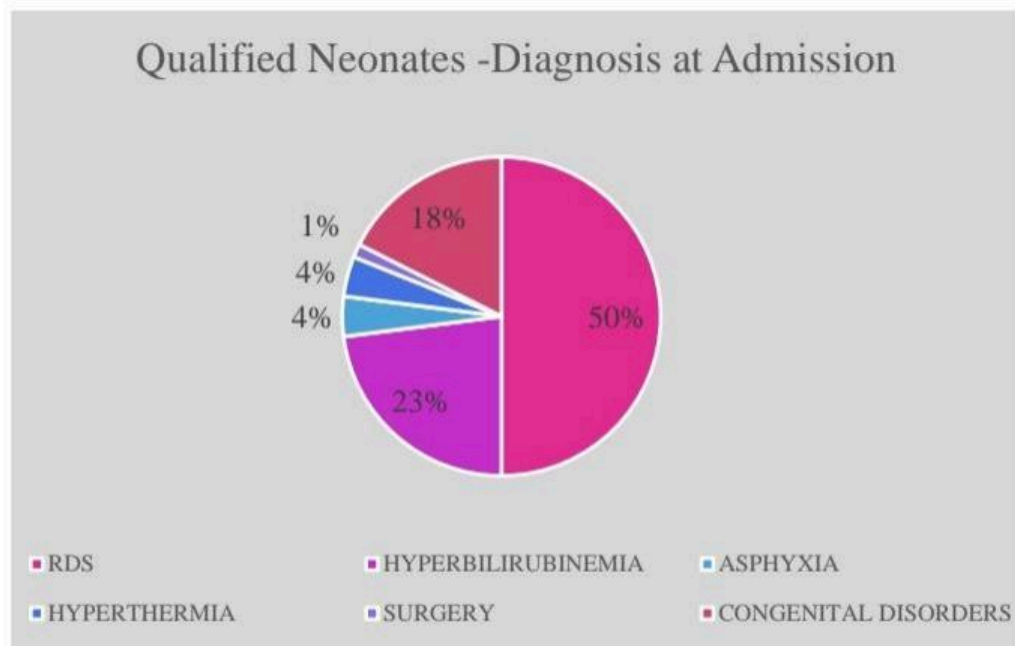


Chart 4: Distribution of qualified neonates as per Admission diagnosis

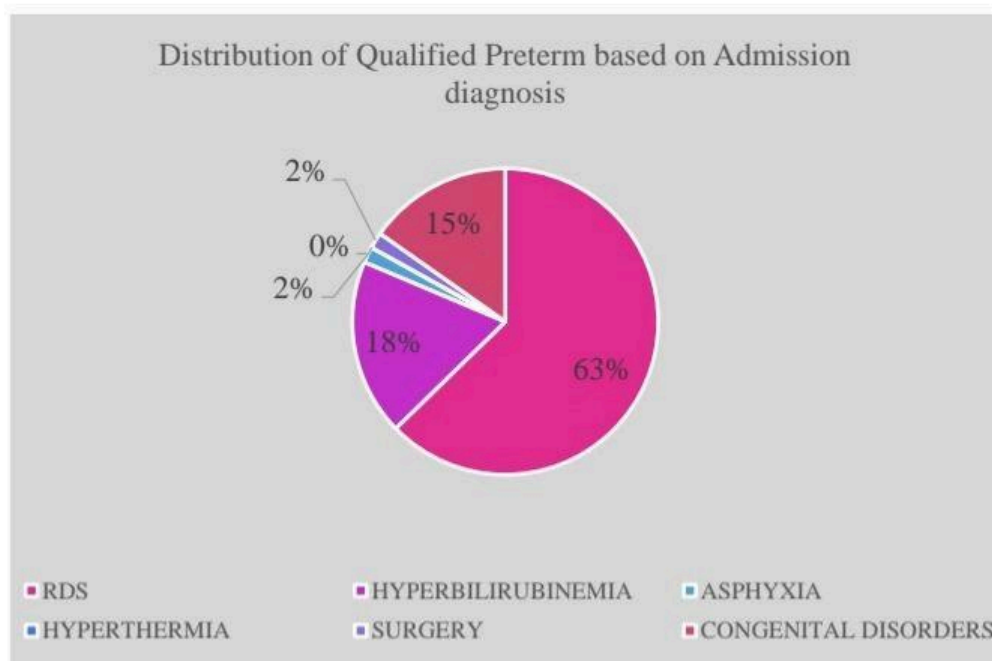


Chart 5: Distribution of qualified preterm as per Admission diagnosis

Qualified preterm 37(62.7%) were admitted with respiratory distress and received RBC transfusion, next to it is hyperbilirubinemia 11(17%).

Table 17: Recipient primary outcome -Mortality or Discharge

VARIABLES OF NEONATES	DEATH	%	DISCHARGE	%	-
TOTAL AIIMS BORN NEONATES(n=645)	42	7%	603	93%	-
UNQUALIFIED NEONATES(n=572)	26	4.5%	546	95.5%	P-value 0.00001
QUALIFIED NEONATES(n=73)	16	22%	57	78%	
TERM (n=14)	4 /16	25%	10	71.5%	P-value 0.50
PRETERM (n=59)	12 /16	75%	47	79.5%	

Total deaths of 42(7%) patients were seen in a total of 645 NICU patients. Out of 73 qualified neonates, 16 (22%) had an outcome of death. Out of all deaths in the qualified group, 16 (100%), 4(25%) were of term babies and the remaining 12 (75%) are of preterm babies.

To even out the confounding factor of multi-donor exposure in qualified neonates we only took single donor-exposed, i.e qualified neonates n=32 (44%) out of all qualified neonates exposed to 32 (25%) donors out of 129 donors to observe the association between donor and recipient outcome.

There is no significant association between donor age on recipient mortality as P-value is 0.22. Sex-matched or un-matched RBC transfusion has no association with the mortality as P-value is 1.0. Donor smoking and alcohol status has no significant association with mortality as the p-value is 0.54 for both. Donor's nutritional status (BMI) has no significant association with mortality as P-value is 0.24. Pre-donation hemoglobin and voluntary status of donation has no significant association with mortality as the P-value is 0.68 and 1.0 respectively. First-time donor and repeat donor status has no significant association with mortality as the P-value is 1.0

Table 18: P-values between the donor characteristics and recipient outcome

Blood Donor Characteristic		Recipient Outcome		p-value (FISCHER EXACT)
		Death (n=9)	DISCHARGE (n=23)	
Donor Age	≤ 35 yrs	5	18	0.22
	≥ 35 yrs	4	5	
Donor sex	Sex matched	5	14	1.0
	Sex mis-matched	4	9	
Donor smoking	Yes	0	3	0.54
	No	3	20	
Type of donation	VD	1	3	1.0
	RD	8	20	
Pre-Donation HB	≤15	7	15	0.68
	>15	2	8	
Donor BMI	Up To Ideal (<24.9)	2	11	0.24
	Overweight and obese (>25)	7	12	
Times of donation	First-time donors	2	4	1.0
	Repeat donors	7	19	
Donor's Alcohol status	Alcoholic			0.54
	Yes	0	3	
	NO	9	20	

Donor age does not have any significance over hemoglobin increment in the qualified neonates as P-value is 0.23. Donor ABO and Rh blood group does not have any significance over hemoglobin increment in the qualified neonates as the P-value is 0.11 and 0.36 respectively. Donor smoking status does not have any significance over hemoglobin increment in the qualified neonates as P-value is 0.2. Donor alcohol status does not have any significance over hemoglobin increment in the qualified neonates as P-value is 0.78. Age of RBC had near significance over hemoglobin increment in the qualified neonates as the P-value is 0.05. Donor BMI had no effect on hemoglobin increment in the qualified neonates as the P-value is (>0.05).

Table 19: Regression estimate for Haemoglobin Increment in qualified neonates

Blood Donor Characteristic	Hb Increment (g/dl) M with 95%CI	p-value (t-test)
<u>Donor Age</u>		
≤ 35 yrs	2.04 ± 0.55	0.23
≥ 35 yrs	1.54 ± 1.29	
<u>Donor Rh Status</u>		
Rh positive	1.74 ± 0.65	0.11
Rh negative	2.37 ± 0.79	
<u>Donor ABO Status</u>		
O group	1.85 ± 0.67	0.36
Non-O group	2.03 ± 0.84	
Blood Component Characteristic		
<u>Age of RBC</u>		
1 -10 days	2.26 ± 0.52	0.05
11 - 21 days	1.18 ± 0.54	
<u>Gamma Irradiation</u>		
Yes	2.06 ± 1.26	0.4
No	1.90 ± 0.56	
<u>Leuco filtration</u>		
Yes	2.06 ± 1.26	0.4
No	1.90 ± 0.56	
<u>Transfusion Volume</u>		
< 50ml	1.92 ± 0.65	0.5
≥ 50 ml	1.91 ± 0.84	
<u>Donor BMI</u>		
< 18.5 (Grp 1)	4.53 ± 4.87	Grp 1 -2 (0.03)
18.5 - 23 (Grp 2)	1.43 ± 1.41	Grp 1 - 3 (0.08)
23 - 27.5 (Grp 3)	2.30 ± 0.90	Grp 1 - 4 (0.06)
> 27.5 (Grp 4)	1.64 ± 0.65	Grp 2 - 3 (0.15)
		Grp 2 - 4 (0.39)
		Grp 3 - 4 (0.12)

<u>Donors</u>		
First-time donors	1.49 ± 0.59	0.09
Repeat donors	2.10 ± 0.69	
<u>Donors</u>		
<u>Smoking</u>		
Yes	2.55 ±0.53	0.2
NO	2.13 ±0.21	
<u>Donors</u>		
<u>Alcoholic</u>		
Yes	2.12 ± 0.44	0.78
NO	2.21 ± 0.22	

Table 20: P-vales for Qualified Neonates and Un-qualified Neonates with Outcomes

<u>Recipient Variables</u>	Qualified Neonates n	Un-qualified neonates n	P-value
<u>sex</u>	n=	n=	
Male	44	337	p-value- 0.82
Female	29	235	
<u>Gestational age</u>	n=	n=	
Term	14	340	p-value- 0.00001
Preterm	59	232	
<u>Birth weights</u>	n=	n=	
ELBW	25	14	p-value- 0.04
VLBW	15	53	
LBW	17	179	
AGA	16	326	
<u>Outcome</u>	n=	n=	
DEATH	16	26	p-value- 0.00001
DISCHARGE	57	546	
<u>Short-term</u>	n=	n=	

<u>complications</u>			
Yes	56	270	p-value- 0.00001
No	17	302	

Donor sex had no statistical significance with the occurrence of RBC transfusion as the P-value is 0.82. Gestational age has statistical significance with the occurrence of RBC transfusion as the P-value is 0.00001. Birthweight has statistical significance with RBC transfusion. Death in recipient had statistical significance with the RBC transfusion as the p-value is 0.00001. statistically, transfusion exposure is significant in the occurrence of short-term complications in recipients p-value is 0.00001.

The odds ratio for the short-term complications with the transfusion exposure. The odds ratio for HIE (hypoxic ischemic encephalopathy) is OD3.63 (CI 95%, 1.5-8.6). For IVH (intra-ventricular hemorrhage) is OD 6.83(CI 95% 2.8-16.4). For ROP OD is 12.69 (CI95%, 5.5-28.9), for PDA OD is 35.5 (CI 95% 11.8-106.2), for sepsis OD is 6.11 (CI95% 3.2-11.4%) and BPD OD is 6.1(CI 95%, 3.2-11.5). the odds of short-term complications in all the transfused neonates.

Table 21: Odds Ratio Between Qualified Neonates and Unqualified Neonates with Outcomes

(D wo C- Death without complications)

Outcomes	Qualified Neonates	Outcome Death/DischARGE	Un-qualified Neonates	Outcome Death/DischARGE	Absolute difference Confidence Interval (CI)	Odds ratio	P-correlation
Death Discharge	16 57	0.4	26 546	0.05	16.579 4.256	8.40	0.127
HIE (D wo C)	9 17	0.53	44 302	0.15	8.653 1.526	3.63	0.469
IVH	10	0.59	26	0.09	16.437 2.840	6.83	0.283

D wo C	17		302					
ROP D wo C	15 17	0.88	21 302	0.07	28.904 5.571	12.69	0.13 1	
PDA D wo C	12 17	0.71	6 302	0.02	106.207 11.88 6	35.53	0.11 1	
Sepsi s D wo C	33 17	1.94	96 302	0.32	11.450 3.257	6.11	0.16 1	
BPD /RD S D wo C	34 17	2.00	98 302	0.32	11.517 3.298	6.16	0.13 9	

Table22: Distribution of Short-term complications in AIIMS-born neonates

Short-term complications	Un-Qualified neonates n=572	%	Total qualified neonates n=73	%	Qualified Term n=14	%	Qualified Preterm n=59	%
BPD	95	16.6%	34	46.5%	3	21%	341	52.5%
HIE	44	7.6%	9	12.3%	2	14%	7	11.8%
IVH	26	4.5%	10	13.6%	1	7%	9	15.2%
ROP	21	3.6%	15	20.5%	1	7%	14	23.7%
PDA	6	1%	12	16.4%	1	7%	11	18.6%
Sepsis	96	16.7%	33	45.2%	4	13%	4	13%
Deaths	26	4.5%	15	20.5%	4	28.5%	12	20%
Discharge without complication	308	53%	17	23.2%	5	53.2%	12	20%

It is observed that all short-term complications of BPD, HIE, IVH, ROP, and SEPSIS were more in the qualified group compared with the unqualified group. Preterm is more affected by short-term complications after transfusions with BPD, IVH, ROP, and PDA with no difference between sepsis and low risk of HIE. Discharge without complications is same in term (53%) as compared to the untransfused group of 53%.

The median number of NICU stay is 4 days in the unqualified and 22 days in the qualified group with a significant P value-0.00001. The median number of qualified term neonates and qualified preterm is not statistically significant (p-value- 0.79).

Table 23: Number of NICU Days for Each Category

VARIABLES	n=	MEDIAN DAYS OF NICU STAY	Mann-Whitney test
TOTAL AIIMS-BORN NEONATES	645	5	
TOTAL AIIMS-BORN PRETERM	291	5	
TOTAL AIIMS-BORN TERM	354	5	
UN QUALIFIED NEONATES	572	4	P value-0.00001
QUALIFIED NEONATES	73	22	
UNQUALIFIED TERM NEONATES	340	3	
UNQUALIFIED PRETERM NEONATES	252	7	
QUALIFIED TERM NEONATES	14	5.5	p-value -0.79
QUALIFIED PRETERM NEONATES	59	31	

73 qualified neonates had a total of 159 RBC transfusions with a mean of 2.17 RBC transfusions and a standard deviation of 1.85. These 73 qualified neonates were exposed to 129 donors with a mean exposure of 1.76 and a standard deviation of 1.32.

Post-Hoc Analysis

Following are the findings found in addition to those planned in the protocol during the analysis. 59 qualified preterm had 133(83.6%) RBC transfusions with a mean of 2.25 and a standard deviation of 1.85 and were exposed to 106 (82%) donors with a mean of 1.79 and a standard deviation of 1.34.

Table 24: Number of RBC transfusions and donor exposure to the qualified recipients.

Study population	Variable	N	Mean	Std.Dev
Qualified neonates n=73	Number of RBC transfusions	159	2.17	1.85
	Number of Donor exposure	129	1.76	1.32
Qualified preterm n=59	Number of RBC transfusions	133(83.6%)	2.25	1.85
	Number of Donor exposure	106(82%)	1.79	1.34
Qualified term n=14	Number of RBC transfusions	26(16.4%)	1.85	1.61
	Number of Donor exposure	23(18%)	1.64	1.27

14 qualified term neonates had 26(16.4%) RBC transfusions with a mean of 1.85 and a standard deviation of 1.61 and were exposed to 23(18%) donors with a mean of 1.64 and a standard deviation of 1.27, Preterm had more mean number of RBC transfusions (2.25) and Donor exposure than the term (1.85).

Table 25: Hazard Rates In Relation to number of Transfusions

Qualified Recipient	No. of Tx per pt.	Hazard Rate	p-value
Males n=44	1	0.19	0.09
	2	0.33	
	3	0	
	4	0	
	5	0	
	6	0	
	8	0	
	10	0	
Females n=29	1	0.17	0.41
	2	0.22	
	3	1	

	4	0	
	8	0	
	10	0	
Term n=14	1	0.25	0.12
	2	1	
	3	1	
	4	0	
	5	0	
	6	0	
	8	0	
	10	0	
Pre-Term n=59	1	0.17	0.18
	2	0.21	
	3	0.63	
	4	0	
	5	0	
	6	0	
	8	0	
	10	0	

Qualified Male recipients who had more than 1 transfusion had a hazard rate of 0.33 with a p-value of 0.09. Sex-matched and mismatched RBC units in male recipients and female recipients had a P-value of 0.09 and 0.41 respectively. The number of transfusions in qualified preterm and term had no significant hazard rate as P-values are 0.12 and 0.18 respectively.

Exposure to the number of Donors had no statistically significant hazard rate as the P-value is 0.12.

Table 26: Hazard and survival rates in relation to the number of donors

Donors	Death	n	Survival rate	HR	p-value
1	9	41	0.69	0.22	0.12
2	3	6	0.67	0.5	
3	0	6	0.73	0	
4	0	2	0.67	0	
5	0	2	1	0	
6	0	3	1	0	
8	0	1	1	0	

For survival rate

R square	F	Significance F
0.7065	12.03	0.0178

	Coefficients	P-value	Lower 95% CI	Upper 95% CI
Intercept	0.5793	0.0008	0.3752	0.7835
X variable 1	0.0585	0.0179	0.0152	0.1019

Inference: p-value of the X1 variable is 0.017 which is < 0.05 . The association between the number of donors and the increase in the survival rate of NICU transfused patients is statistically significant.

For Hazard rate

R square	F	Significance F
0.292	2.06	0.210

	Coefficients	P-value	Lower 95% CI	Upper 95% CI
Intercept	0.2702	0.0589	-0.0149	0.555
X variable 1	-0.0338	0.2104	-0.0944	0.026

Inference: To confirm whether the number of donors for blood transfusion has any effect on the outcome of the NICU patients, Regression analysis was performed with hazard rate. The p-value of X variable 1 is 0.21 which is statistically insignificant

Age of RBC at the time of transfusion had no significant effect on mortality in both sexes of the recipients as the P value is 0.7 and 0.4 for male and female qualified recipients respectively. Age of RBC at the time of transfusion had a near to significant hazard rate (P-value-0.05) of 0.32 and 0.50 if the age is between 7 to 14 days and greater than 14 days respectively. The greater the age of RBC at the time of transfusion greater the likelihood of death in preterm within 28 days of NICU stay.

Table 27: Hazard Rate with respect to RBC storage duration

Qualified Recipients	Age of RBC at the time of transfusion	Deaths	Number of transfusions (n=159)	HR	p-value
Males	< 7 days	3	54	0.06	0.7
	7 - 14 days	2	22	1.00	
	> 14 days	3	8	0.38	
Females	< 7 days	4	38	0.11	0.4
	7 - 14 days	20	25	1.00	
	> 14 days	10	12	0.83	
Term	< 7 days	1	8	0.13	0.1
	7 - 14 days	5	14	0.36	
	> 14 days	8	10	0.80	
Pre-Term	< 7 days	6	64	0.07	0.05
	7 - 14 days	17	53	0.32	
	> 14 days	5	10	0.50	

Out of 159 RBC transfusions, 132 (83%) has pre-transfusion hemoglobin details which are included and 27 (17%) with missed Pre-hemoglobin details were excluded.

Table 28: Transfusion Appropriateness in NICU-admitted Qualified Neonates

CATEGORY	CRITICAL			NON-CRITICAL		
	n=	%	HB	n=	%	HB
Restrictive thresholds (n=110, 83%, 7.9±1.9)	75	87%	8.1±1.97	35	76%	7.3±1.99
Liberal thresholds (n=22, 17%, 11.3±2.0)	11	13%	12.9±2.3	11	24%	9.7±2.0
Total (132, 100%, 8.4±1.97)	86	64%	8.7±1.97	46	36%	8.0±1.99

(Critical – Neonates on ventilator support or vasopressors support)

Out of 132 RBC transfusions, 110 (83%) transfusions went according to restrictive thresholds (Hb- 7.9 ± 1.9) and 22(17%) transfusions went according to liberal thresholds (11.3 ± 2.0). 86 (64%) RBC transfusions went in Critical patients with a mean HB of 8.7 ± 1.97 and 46 (36%) went in non-critical patients with a mean HB of 8.0 ± 1.99 .

Maintaining the Restrictive transfusion threshold in critical patients was possible in 75 (87%) transfusions and the remaining 11(13%) followed liberal thresholds. Maintaining the restrictive transfusion thresholds in non-critical patients was possible in 35 (76%) transfusions and the remaining 11 (24%) followed liberal thresholds

Most of the transfusions followed restrictive transfusion thresholds i.e.110 (83%). Restrictive thresholds were maintained more strictly in critical patients 75(87%) than in non-critical patients 35 (76%). 64% of critical patients followed restrictive thresholds and 36% of critical patients followed liberal thresholds. 76% of non-critical patients followed restrictive thresholds and 24% of non-critical patients followed liberal thresholds. In critical patients only 13% needed liberal thresholds whereas in non-critical patients 24% needed liberal thresholds.

Out of 132 RBC transfusions, 37 (28%) went within 1-7 days of age from birth with a mean HB of 9.5 ± 1.98 , 32 (24%) went within 8-14 days of age from birth with a mean HB of 8.2 ± 1.97 , 41 (32%) went within 15-21 days of age from birth with a mean HB of 7.9 ± 2.04 , 41 (32%) went under 21 days of age from birth with a mean HB of 8.03 ± 1.97 . Out of 132 RBC transfusions, 75 (57%) of patients were critical and able to maintain restrictive thresholds with a mean HB of 8.1 ± 1.97 , whereas 11 (8.25%) of patients were critical followed liberal thresholds with a mean HB of 12.9 ± 2.3 & 35 (26.5%) patients were non-critical and able to maintain restrictive thresholds with a mean HB of 7.3 ± 1.99 and 11 (8.25%) patients were non-critical and followed liberal thresholds with a mean HB of 9.7 ± 2.0 .

Table 29: Age-wise transfusion thresholds in qualified neonates

CATEGORY	RESTRICTIVE THRESHOLDS (n=110, 83%, 7.9±1.9)				LIBERAL THRESHOLDS (n=22, 17%, 11.3±2.0)				Total (132, 100%, 8.4±1.97)		
AGE	CRITICAL (n=75, 68%)		NON-CRITICAL (n=35, 32%)		CRITICAL (n=11, 50%)		NON-CRITICAL (n=11, 50%)				
	n=	HB	n=	HB	n=	HB	n=	HB	n=	%	HB
1-7 DAYS	22 (59%)	8.8± 1.98	7 (19%)	7.5± 2.25	5 (14%)	14.3± 2.3	3 (8%)	11.2± 2.1	37	28%	9.5±1.98
8-14 DAYS	20 (62%)	8.3± 2.07	8 (25%)	7.6± 2.04	1(3%)	-	3 10%	8.7± 2.13	32	24%	8.2±1.97
15-21 DAYS	14 (64%)	7.7± 2.04	4 (18%)	6.9± 1.67	2 (9%)	10.2± 1.8	2 (9%)	9.1± 2.25	22	16%	7.9±2.04
>21 DAYS	19 (46%)	7.6±1.97	16(39%)	7.2±2.0	3(7.5%)	12.6± 2.3	3 (7.5%)	9.8±2.1	41	32%	8.03±1.97
TOTAL (132)	75 (57%)	8.1±1.97	35 (26.5%)	7.3±1.99	11(8.25%)	12.9± 2.3	11 (8.25%)	9.7±2.0	132	100%	

(Critical – Neonates on ventilator support or vasopressors support)

Interpretation

Most of the liberal transfusions were seen in neonates aged between 1-7 days (36%) with a mean HB of 14.3± 2.3 in critical patients and a mean HB of 11.2± 2.1 in non-critical patients. Restrictive Transfusion thresholds were best possibly followed in neonates aged >21 days n=35 (31%) with a mean HB of 7.6± 1.97 in critical patients and a mean HB of 7.2± 2.0 in non-critical patients.

DISCUSSION

In total 73 neonates were qualified and included in this prospective observational study and had 159 Red blood cell transfusions from 129 donors. The majority of RBC transfusions went to preterm i.e., 81% corresponds to the study done by Lin Jc “et al.” (2).

65% of all extremely low birth weight babies needed RBC transfusion in their NICU stay this corresponds with the study done by Valieva “et al.” that 50% to 80% of ELBW infants received 1 or more red blood cell transfusions (RBCs) during their hospitalization (41).

In addition, 22% of very low birth weight (VLBW) neonates received RBC transfusions during a NICU stay not corresponding to the study done by R F Maier “et al.” of about 60%. Change might be attributed to advancements in neonatology, improved point-of-care testing, and reduced iatrogenic blood loss.

The major indication for transfusion in 50% of neonates is anemia with Respiratory distress corresponds to our baseline data and Neonatal AABB guidelines (42)

A significant number of deaths are observed in 20% of the transfused neonates of which 75% were preterm. Most likely as already sick neonates were more often transfused as mentioned in the study done by Hume H “et al.” (4)

No significant association between the Donor age and the mortality in the recipient (neonates) with p-value-0.22 favours the findings in the study done by Chasse “et al.” i.e. no association between donor age and outcomes in the adult recipient (34) differs from findings of Heddle M “et al.” transfusions from older donors may benefit patients in adult recipients (38)

Donor recipient Sex-matched or sex-discordant RBC transfusions have no significant association with the recipient (neonate) mortality this part corresponds to the study done by Edgren G “et al.” states that no significance was found in sex-discordant donors with recipient mortality and sex-matched RBC transfusions had better outcomes statistically (43) and another study by Chasse “et al.” postulated sex of donor had no effect on mortality but the female donor has more safety for necrotizing enterocolitis and also stated sex-mismatched transfusion had better short-term outcomes.

No significant association between the donor's BMI, smoking, and alcohol status with the mortality in recipients (neonates) with P-values 0.24, 0.54, and 0.54 respectively corresponds to the study done by Roubinian NH "et al." (REDS-III study).

There is a positive association between the number of deaths occurring in exposure to the transfusion in neonates during NICU stay OD 8.4 (CI-4.2-16.5). there is a positive association between the short-term complications that occurred with transfusion exposure statistically (OD >1). observational findings showed more sepsis complications seen in transfused neonates (45%) than un-transfused (16%) with no difference between term (13%) and pre-term (13%). BPD, IVH, ROP, and PDA are more observed in transfused preterm and no difference is seen in sepsis and with less risk of HIE in transfused preterm when compared to the transfused term. Each short-term complication like HIE (OD 3.63 CI 95% 1.52- 8.65), IVH (OD 6.83 CI95% 2.84-16.43), ROP (OD 12.69 CI95% 5.57- 28.9), PDA (OD 35.3 CI95% 11.8-106.2), sepsis (OD 6.11 CI95% 3.25-11.45), Bpd (OD 6.16 CI95% 3.25-11.45) have shown a positive association with transfusion, however, this is a probing study and relationship with donor characteristics is difficult to establish due to the confounding factors and small sample size. Further large multicentric studies and robust hospital lab information systems with standardized co-morbidity index in NICU neonates are necessary.

The median number of NICU days was significantly associated with transfusion in neonates than in un-transfused neonates, donor characteristics had no association with the NICU stay is against the finding found by Roubinian NH "et al." (REDS-III study) (41) No statistical association was observed between the median number of NICU days and transfusion in preterm and term neonates a finding needs a further larger donor-recipient linked study to establish an association.

No significant association was found between Donor Rh status (p-value-0.11), Donor ABO group (p-value-0.36), and Donor alcohol status (p-value-0.78) with the hemoglobin increment in the recipient (neonates). Given the potential outcome benefits or risks observed in some studies, further, well-designed studies are needed to better evaluate if an improved selection of donors by their characteristics (age, sex, etc.) improves RBC transfusion outcome

Statistical significance was found between Donor BMI <18 (underweight) with Hb increment (p-value 0.03). Further study with a large sample size is needed to verify this finding.

A significant association was found between the days of RBC storage with recipient Hb increment (p-value-0.05). Age of RBC less than 10 days had more Hb increment than RBC age greater than 10 days of storage contradicts the finding of a study done by Roubinian NH “et al.” no association between the days of RBC storage with hemoglobin increment in adults (41)

There is no significant association between the donor smoking status with the hemoglobin increment of the recipient (p-value 0.2) corresponds to the study done by Roubinian NH “et al.” (REDS-III study) that no association variation of smoking on hemoglobin increment in adult recipients (41)

There is no significant association between the first-time donor or repeat donors with the hemoglobin increment of the recipient (p-value-0.09) a finding that needs to be analyzed further in large donor-recipient linked studies.

There is no significant association between the leukofiltration and irradiation modification on blood components with the hemoglobin increment of p-value 0.4 for both. Most of these modifications of RBC units were used for exchange transfusion deferring to the finding found in the study done by Roubinian NH “et al.” that irradiation had less Hb increment in adult recipients (41)

The hazard rate (HR) estimates for each additional transfusion episode from either single or multiple donors was Hr-0.33 in male recipients (1 as a reference at 95% CI, and p-value >0.05) and HR-0.22 in female recipients (95% CI, and p-value >0.05) explains no significant association between the number of RBC transfusions from either single or multiple donors with the risk of NICU mortality in neonates, this corresponds to the same finding in the study done by Edgren G “et al.” (43) done in adult patients and differs from the finding in the study done by Yu-Cheng Wang “et al.” i.e. RBC transfusion has a negative impact on survival in ELBW infants (14). The hazard rate for more than 3 transfusions was zero in both male and female recipients because of the small sample size needs further study with larger data to comment.

No significant association between the number of RBC transfusions in term and preterm transfused neonates with HR-1 & 0.63 respectively (95% CI, p-value >0.05). The hazard rate for more than 3 transfusions was zero in both term and preterm recipients because of the small sample size needs further study with larger data is needed to comment.

The estimate for the survival rates for each additional donor exposure from a transfusion episode is SR 0.57 (CI 95% (0.37-0.78) p-value-.0017). A significant association is observed between the number of donors exposed to RBC transfusion with the rate of survival in NICU stay. Whereas no significant association was found between the number of donors exposed to RBC transfusion with the mortality HR-0.27 (CI 95% 0.01-0.5, p-value-0.2) this corresponds to the same finding in the study done by Edgren G “et al.” done in adult recipients. i.e.no statistically significant associations between donor exposures and in-hospital mortality in the 3 cohorts (KPNC cohort, REDS-III cohort, SCANDAT cohort) (43).

A near to significant association between the age of RBC greater than 7 days at the time of transfusion to the mortality with a p-value of 0.05 in preterm neonates corresponds to ARIPI trial done by Fergusson D “et al.” RBCs stored for 7 days or less has decreased the harmful sequelae (44) and defers from the study done in adults by Roubinian NH “et al.” (41)

Regression estimates done on donor characteristics affecting recipient outcome showed no significant association between the Donor age and hemoglobin increment in recipients (neonates) p-value-0.23.

This study will also serve as an audit for neonatal blood transfusion therapy. Close adherence to neonatal transfusion policy and restrictive transfusion guidelines helped in reducing inappropriate use of blood products with a transfusion probability of 2.3 and CT ratio of 1.53 indicating no significant blood wastage especially observed in term and VLBW preterm corresponds to the study done by Shanmugha Priya RA “et al.” (45)

Most of the critical neonates at any day of age followed restrictive thresholds. This is backed up by the studies done by Franz “et al.” (31) that following restrictive transfusion thresholds doesn't affect mortality and individual short-term complication like BPD, ROP, IVH, or NEC. Most of the neonates (36%) who followed liberal thresholds belong to 1-7 days of age because of their small size and significant iatrogenic blood for initial investigations and procedures.

CONCLUSION

The age, gender matching, BMI, smoking, and alcohol status of the donor are not relevant factors to consider when allocating blood because they were not associated with neonatal death. Because the chance of receiving less common blood components is determined by the number of transfusions, any comparison of common and less common transfusion categories will ultimately be confusing. Previous positive findings regarding donor age and sex are most likely due to residual confounding factors affecting the outcome.

The age, ABO, Rh status, smoking, repeat or first-time donation, and alcohol status of the donors are not relevant factors to consider when allocating RBC because they were not associated with HB increment in neonates. RBC units from underweight Donors had better HB increment in neonates, and transfusion of fresh RBC within 10 days had better HB increment in neonates.

Multiple RBC transfusions do cause mortality in neonates. Multi-donor exposure doesn't increase mortality. Apparently, more risk of sepsis, and no risk of short-term complications like BPD, HIE, IVH, and ROP with RBC transfusion. RBC transfusion in preterm increases the days of NICU stay. Selection of Fresh RBC within 7 days for transfusion is preferable in neonates.

Prospective screening of blood requisition forms by transfusion medicine practitioners and immediate communication with neonatologists regarding any deviations made the practice of following restrictive transfusion thresholds more viable even in critical patients.

Liberal transfusions are seen more in noncritical patients when compared with critical patients. The reason may be because of more iatrogenic blood loss and patients may be in the recovery phase of a previously critical condition. Critical neonates irrespective of the day from birth can follow restrictive thresholds without any significant risk of mortality. Most of the neonates (36%) who followed liberal thresholds belong to 1-7 days of age.

STRENGTHS OF THIS STUDY

1. This study was done in the absence of no previous donor–recipient linked studies on neonates.
2. Long-term follow-up can be done for long-term complications like neurological development
3. This is a probing study directing further sub-analysis of each complication associated with donor characteristics in neonates.
4. Can serve as an audit for Neonatal transfusion practices in our blood center.
5. This study will help to determine the correlation between transfusion and the length of NICU stay in neonates.
6. Neonatal PBM is not routinely practiced in India and had shown multiple benefits in developed countries.

CHALLENGES FACED DURING THE STUDY

- Differences between practices and clinical decisions
- Lack of awareness of strategies for decreasing iatrogenic blood loss
- Incomplete, delayed, or unavailability of laboratory reports.
- Most of the neonates who received RBC transfusions were already sick making it difficult to adhere to restrictive transfusion thresholds.
- Male donors preferentially bleed more than female donors.
- We observed a selection bias in selecting large-volume RBC products to make aliquots for neonates which are usually collected from male donors.
- Older donors above 60 years were not eligible for blood donation in India
- The accuracy of clinical data is questionable in neonates whose clinical diagnosis is not supported by any laboratory or radio-diagnostic parameters
- The complicated manner in which neonates' exposure status changes over time and the issues associated with summarising exposure is one of the main hurdles in the analysis of these sorts of data.

LIMITATIONS

This study has several limitations. It is a prospective observational study and a single-centered study. All confounding factors in recipients cannot be addressed as the sample size is not big enough. Donor characteristics like smoking, BMI, and Alcohol were not typically used to select units for transfusion. Selection bias is observed in the selection of RBC units based on volume. No validated comorbidity index is available exclusively to NICU-admitted neonates. This study did not account for blood components other than red blood cells, which may have influenced the results. No long-term follow-up to further study the long-term neurological complications and developmental complications after transfusion in neonates.

Source of funding: No specific funding has been received for this study.

Conflicts of interests: None to declare.

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All India Institute of Medical Sciences, Jodhpur
संस्थागत नैतिकता समिति
Institutional Ethics Committee

No. AIIMS/IEC/2021/3563

Date: 12/03/2021

ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: AIIMS/IEC/2021/3398

Project title: "Assessment of the effect of donor characteristics on clinical outcomes in neonatal transfusion recipients"

Nature of Project: Research Project Submitted for Expedited Review
Submitted as: M.D. Dissertation
Student Name: Dr. Bodanapu Vinay
Guide: Dr. Archana Bajpayee
Co-Guide: Dr. Neeraj Gupta, Dr. Arvind Sinha, Dr. Poonam Elhence, Dr. Anubhav Gupta & Dr. Suresh Kumar Sharma

Institutional Ethics Committee after thorough consideration accorded its approval on above project.

The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:

- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

Please Note that this approval will be rectified whenever it is possible to hold a meeting in person of the Institutional Ethics Committee. It is possible that the PI may be asked to give more clarifications or the Institutional Ethics Committee may withhold the project. The Institutional Ethics Committee is adopting this procedure due to COVID-19 (Corona Virus) situation.

If the Institutional Ethics Committee does not get back to you, this means your project has been cleared by the IEC.

On behalf of Ethics Committee, I wish you success in your research.

Dr. Pooveen Sharma
Member Secretary

Member secretary
Institutional Ethics Committee
AIIMS, Jodhpur

PATIENT / GUARDIAN INFORMATION SHEET

Title of the Study: Assessment of the effect of Donor characteristics on clinical outcomes in Neonatal transfusion recipients.

Name of the principal investigator: Dr. Bodanapu Vinay

Tel no. (Mobile): - 8309002978.

Before you decide whether or not you wish to participate in this study, it is important for you to understand why this study is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish.

1) What is the purpose of this study?

The purpose of this study is to observe the association between the blood donor's characteristics and neonatal transfusion recipient along with the outcomes in terms of safety, effectiveness, adverse events, morbidity and mortality, and length of hospital stay, to implement effective neonatal transfusion practices in the future.

2) What if I don't want to participate or if I want to leave the study later?

Participation in this study is voluntary. It is completely up to you whether you want to participate. You may withdraw from the study at any time and for any or no reason. please tell the researcher That you want to discontinue.

3) What does this study involve?

This study will involve the collection of the Patient's basic information, laboratory investigation data, Intraoperative data, transfusion data, post-transfusion clinical outcome data, and hospital records for the duration of admission.

4) Will confidentiality be protected?

Yes, the information about the patient will be subjected to absolute anonymity.

Thank you for taking the time to consider taking part in the study.

This information sheet is for you to keep.

अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर

ट्रांसफ्यूजन मेडिसिन और ब्लड बैंक विभाग

रोगी / अभिभावक सूचना पत्र

अध्ययन का शीर्षक : नवजात रक्ताधान प्राप्तकर्ताओं में नैदानिक परिणामों पर दाता विशेषताओं के प्रभाव का अध्ययन।

प्रमुख अन्वेषक का नाम : डॉ. बोदनपु वनय

टेल नं. (मोबाइल): - 8309002978.

इससे पहले कि आप तय करें कि आप इस अध्ययन में भाग लेना चाहते हैं या नहीं, यह महत्वपूर्ण है आपको यह समझने के लिए कि यह अध्ययन क्यों किया जा रहा है और इसमें क्या शामिल होगा। कृपया समय निकालें

निम्नलिखित जानकारी को ध्यान से पढ़ने के लिए और यदि आप चाहें तो दूसरों के साथ चर्चा करें।

1) इस अध्ययन का उद्देश्य क्या है?

इस अध्ययन का अंतिम उद्देश्य आरबीसी दाताओं और नवजात आधान प्राप्तकर्ता के बीच सुरक्षा, प्रभावशीलता, प्रतिकूल घटनाओं, रुग्णता और मृत्यु दर के मामले में परिणामों के साथ संबंध का पालन करना है ताकि भविष्य में एक प्रभावी नवजात आधान प्रथाओं को लागू किया जा सके।

2) क्या होगा अगर मैं भाग नहीं लेना चाहता या अगर मैं बाद में अध्ययन छोड़ना चाहता हूँ?

इस अध्ययन की भागीदारी स्वैच्छिक है। यह पूरी तरह से आप पर निर्भर है कि क्या आप भाग लेना चाहते हैं। आप किसी भी समय और किसी भी कारण के लिए अध्ययन से आकर्षित के साथ हो सकता है। कृपया शोधकर्ता को बताएं कि आप बंद करना चाहते हैं।

3) इस अध्ययन में क्या शामिल है?

इस अध्ययन में जन्म के बाद 28 दिनों की अवधि के लिए रोगी की बुनियादी जानकारी, प्रयोगशाला जांच डेटा, इंटरऑपरेटिव डेटा, ट्रांसफ्यूजन डेटा, पोस्ट ट्रांसफ्यूजन नैदानिक परिणाम डेटा का संग्रह शामिल होगा

4) क्या गोपनीयता की रक्षा की जाएगी?

रोगी के बारे में जानकारी पूर्ण गुमनामी के अधीन किया जाएगा।

अध्ययन में भाग लेने पर विचार करने के लिए समय लेने के लिए धन्यवाद।

यह सूचना पत्र आपके लिए है।

CASE RECORD SHEET FROM NICU

Date:

Name:

Age/Sex:

Department:

Ward/Bed:

Diagnosis:

Date of birth:

Birth weight:

Date of transfusion:

Indication for transfusion:

Type of product transfused:

Quantity of product transfused:

Date	LAB Values	<u>HB</u>	<u>Haematocrit</u>	<u>TLC</u>	<u>CRP</u>	<u>S. Bilirubin</u>
	At admission					
	Before transfusion					
	After transfusion					
	At the time of discharge					
	Remarks					

Is the patient is prematurely born: yes/no

Does the patient require any blood product transfusion: yes/no

Was there any post-transfusion reaction:

Are there any following adverse outcomes after RBC transfusion:

none/sepsis/shock/respiratory failure/cardiac failure/neuro-cognitive dysfunction/NEC/IVH/Death/others(mention).

Remarks:

Signature of the Patient/Guardian

Signature of the investigator

DONOR RECORD FROM BLOOD BANK

Date:

Name:

Age/sex:

Department:

Diagnosis:

Date of transfusion:

Indication for transfusion:

Type of product issued:

Quantity of RBC product issued:

PRBC Unit no:

Segment no:

Neonate blood group:

PRBC unit blood group:

Age of PRBC unit issued:

Details if aliquot is used:

Compatibility of unit:

Date	Qc details of the unit	QB/Volume	Haematocrit	WBC Contamination	Haemolysis	Remarks

Donor details:

Donation number

Date of donation

Type of donation (voluntary/replacement/apheresis)

Age/Sex:

Total donation time

Any Relevant clinical history

Weight of donor

Blood pressure

Haemoglobin >12.5: yes/no

Signature of resident/Technician
investigator.

Signature of the principal

SNO	UNIT NO	AGE	SEX	WEIGHT	HEIGHT	BMI	BSA	VD/RO	TIMES	SBP	DBP	HB	SMOKING	ALCOHOL	DIET
1	21/355	30	M	96	172	32.45	2.14	RD	4	124	80	14.2	NO	NO	VEGETARIAN
2	21/769	32	M	100	171	34.20	2.18	RD	15T	130	80	13.7	NO	NO	VEGETARIAN
3	21/1204	19	M	90	172	30.42	2.07	VD	15T	112	74	14.8	NO	NO	VEGETARIAN
4	21/1410	47	M	96	176	30.99	2.17	RD	15T	130	80	15.1	NO	NO	NOM VEGETARIAN
5	21/1340	21	M	76	170	26.30	1.89	VD	15T	140	90	14.2	NO	NO	VEGETARIAN
6	21/1628	35	M	80	176	25.83	1.98	RD	1	1210	90	13.8	NO	NO	VEGETARIAN
7	21/1903	25	M	62	170	21.45	1.71	RD	15T	128	86	17.1	NO	NO	VEGETARIAN
8	21/2009	30	M	67	171	22.91	1.78	RD	1	128	76	16.1	NO	NO	VEGETARIAN
9	21/2204	34	M	96	178	30.30	2.18	RD	3	138	88	14	NO	NO	VEGETARIAN
10	21/2284	40	M	76	175	24.82	1.92	RD	1	110	80	13	YES	YES	NOM VEGETARIAN
11	21/2492	20	M	96	170	33.22	2.13	RD	15T	130	70	16	NO	NO	VEGETARIAN
12	21/2477	25	M	94	182	28.38	2.18	VD	5	140	80	15	NO	NO	VEGETARIAN
13	21/2603	40	M	95	170	32.67	2.12	RD	2	136	84	14.8	NO	NO	VEGETARIAN
14	21/2780	24	M	63	170	21.80	1.72	RD	15T	130	80	13	NO	NO	NOM VEGETARIAN
15	21/2867	36	M	70	170	24.22	1.82	RD	3	120	80	13.9	NO	NO	NOM VEGETARIAN
16	21/2843	19	M	75	175	24.69	1.91	VD	1	120	80	12.9	NO	NO	NO
17	21/3147	20	M	63	168	22.52	1.71	VD	15T	130	80	14	NO	NO	VEGETARIAN
18	21/3388	20	M	64	170	22.15	1.74	RD	15T	98	72	14.7	NO	NO	VEGETARIAN
19	21/3271	51	M	80	180	24.69	2.00	RD	1	140	80	17	YES	YES	VEGETARIAN
20	21/3387	19	M	76	176	24.54	1.93	RD	15T	116	78	15	NO	NO	VEGETARIAN
21	21/3681	32	M	90	178	28.41	2.11	VD	3	132	78	15.9	NO	NO	VEGETARIAN
22	21/3678	27	M	68	175	22.20	1.82	VD	7	126	70	15.2	NO	YES	NOM VEGETARIAN
23	21/3804	40	M	94	174	31.05	2.13	RD	15T	130	90	15.2	NO	YES	VEGETARIAN
24	21/3744	21	M	75	176	24.21	1.91	RD	3	120	80	14.7	NO	NO	VEGETARIAN
25	21/3782	31	M	71	181	21.67	1.89	RD	6	114	78	14	NO	NO	VEGETARIAN
26	21/4127	23	M	95	178	29.98	2.17	RD	15T	124	82	14.5	NO	NO	VEGETARIAN
27	21/4137	27	M	85	177	27.13	2.04	RD	15T	114	82	15.2	NO	NO	NOM VEGETARIAN
28	21/4162	30	M	70	176	22.60	1.85	RD	2	128	76	15	NO	NO	VEGETARIAN
29	21/4515	26	M	77	181	23.50	1.97	RD	2	134	72	16.2	NO	NO	NOM VEGETARIAN
30	21/4812	21	M	70	173	23.39	1.83	RD	15T	120	80	15.1	NO	NO	VEGETARIAN
31	21/4623	22	M	63	168	22.32	1.71	RD	3	120	78	14.4	NO	NO	NOM VEGETARIAN
32	21/4768	30	M	78	181	23.81	1.98	RD	4	122	70	14.9	YES	NO	VEGETARIAN
33	21/4873	23	M	77	178	24.30	1.95	RD	6	120	80	13.6	NO	NO	VEGETARIAN
34	21/5100	28	M	58	168	20.55	1.65	RD	2	110	70	16	NO	NO	NOM VEGETARIAN
35	21/5107	30	M	73	175	23.84	1.88	RD	8	120	80	14.7	NO	NO	VEGETARIAN
36	21/4982	47	M	64	182	19.32	1.80	RD	1	124	70	16.1	NO	NO	VEGETARIAN
37	21/5233	40	M	74	175	24.16	1.90	VD	4	110	70	16	NO	NO	VEGETARIAN
38	21/5203	28	M	76	174	25.10	1.92	RD	1	120	80	14.6	NO	NO	VEGETARIAN
39	21/5391	37	M	86	186	24.86	2.11	RD	50	120	80	147	YES	YES	NOM VEGETARIAN
40	21/5374	29	M	100	179	31.21	2.23	RD	5	128	84	15.2	NO	YES	VEGETARIAN
41	21/5370	25	M	78	182	23.55	1.99	RD	15T	130	80	16	NO	NO	VEGETARIAN
42	21/5563	21	M	69	168	24.45	1.75	VD	3	140	90	14.7	NO	NO	VEGETARIAN
43	21/5727	42	M	70	175	22.86	1.84	RD	7	130	70	14.3	YES	NO	VEGETARIAN
44	21/5711	27	M	80	178	25.25	1.99	RD	1	120	80	14.8	NO	NO	VEGETARIAN
45	21/5847	32	M	81	170	28.03	1.96	RD	25	120	80	13.1	NO	NO	NOM VEGETARIAN
46	21/6037	38	M	77	173	25.73	1.92	RD	7	120	80	14	NO	NO	NOM VEGETARIAN
47	21/5987	42	M	85	171	29.07	2.01	RD	6	120	80	13.8	NO	NO	VEGETARIAN
48	21/6098	29	M	74	168	26.22	1.86	RD	1	122	78	14	NO	NO	VEGETARIAN
49	21/6217	31	M	83	171	28.38	1.99	RD	1	112	78	15	NO	NO	VEGETARIAN
50	21/6084	30	M	80	175	26.12	1.97	RD	2	120	80	14.5	YES	YES	NOM VEGETARIAN
51	21/6294	20	M	66	175	21.55	1.79	VD	1	120	80	14.9	NO	NO	VEGETARIAN
52	21/6382	41	M	72	179	22.47	1.89	RD	30	118	80	13.8	NO	YES	VEGETARIAN
53	21/6314	39	M	76	174	25.10	1.92	RD	15T	130	90	15	NO	NO	NOM VEGETARIAN
54	21/6629	27	M	70	170	24.22	1.82	RD	1	120	80	14.2	NO	NO	NOM VEGETARIAN
55	21/6676	29	M	84	166	30.48	1.97	RD	1	120	80	15.1	NO	YES	NOM VEGETARIAN
56	21/6865	24	F	67	162	25.53	1.74	RD	5	116	70	13.8	NO	NO	VEGETARIAN
57	21/6970	24	M	84	182	25.36	2.06	RD	1	122	72	15.2	NO	NO	NOM VEGETARIAN
58	21/6727	37	M	67	170	23.18	1.78	RD	15T	110	78	13.2	NO	NO	VEGETARIAN
59	21/6878	32	M	95	168	33.66	2.11	RD	4	130	80	14	NO	NO	VEGETARIAN
60	22/125	24	M	86	170	29.76	2.02	RD	4	120	80	14	NO	NO	VEGETARIAN
61	22/226	29	M	96	175	31.35	2.16	RD	15T	120	80	14.5	NO	NO	VEGETARIAN
62	22/397	28	M	67	165	24.61	1.75	RD	20	110	70	13.9	YES	YES	VEGETARIAN
63	22/504	40	M	69	165	25.34	1.78	RD	15T	120	80	16	NO	NO	NOM VEGETARIAN
64	22/396	40	M	82	175	26.78	2.00	RD	1	120	80	13	NO	NO	VEGETARIAN
65	22/611	21	M	70	172	23.66	1.83	RD	1	110	70	15	NO	NO	VEGETARIAN
66	22/457	29	M	68	165	24.98	1.77	RD	1	120	70	13	NO	NO	VEGETARIAN
67	22/980	44	M	102	172	34.48	2.21	RD	5	130	80	15.7	NO	NO	VEGETARIAN
68	22/931	43	M	90	168	31.89	2.05	RD	19	120	80	14	YES	YES	NOM VEGETARIAN
69	22/1149	26	M	93	165	34.16	2.06	RD	4	130	80	15.2	NO	NO	VEGETARIAN
70	22/1190	31	M	60	169	21.01	1.68	VD	4	110	70	13	NO	NO	VEGETARIAN
71	22/1197	24	M	83	171	28.38	1.99	VD	6	120	80	13.6	NO	NO	NOM VEGETARIAN
72	22/1330	41	M	91	178	28.72	2.12	RD	15T	120	80	13.9	NO	YES	VEGETARIAN
73	22/1200	31	M	85	168	30.12	1.99	VD	5	120	80	12.9	YES	YES	VEGETARIAN
74	22/1448	31	M	83	172	28.06	1.99	RD	6	110	70	13.8	NO	NO	VEGETARIAN
75	22/1429	31	M	84	169	29.41	1.99	RD	3	120	80	14.6	NO	NO	VEGETARIAN
76	22/1593	26	M	88	172	29.75	2.05	RD	3	130	80	14.2	NO	NO	VEGETARIAN
77	22/1663	34	F	82	169	28.71	1.96	RD	3	120	80	13.4	NO	NO	VEGETARIAN
78	22/1707	30	M	88	162	33.53	1.99	VD	2	126	80	14.6	YES	NO	NOM VEGETARIAN
79	22/1823	31	M	66	173	22.05	1.78	RD	1	124	70	15.3	NO	YES	VEGETARIAN
80	22/1861	35	M	65	168	23.03	1.74	RD	2	130	90	13.1	YES	NO	NOM VEGETARIAN
81	22/2024	33	M	79	165	29.02	1.90	RD	5	130	90	13	NO	NO	VEGETARIAN
82	22/2040	22	M	68	169	23.81	1.79	RD	1	110	80	13.5	NO	NO	VEGETARIAN
83	22/2088	27	M	86	168	30.47	2.00	RD	3	120	80	13	NO	NO	VEGETARIAN
84	22/2085	23	M	62	172	20.96	1.72	RD	15T	140	80	13.5	NO	NO	NOM VEGETARIAN
85	22/2155	22	M	70	165	25.71	1.79	VD	3	110	70	12.9	NO	NO	VEGETARIAN
86	22/2404	22	M	83	168	29.41	1.97	VD	15T	126	80	14.5	NO	NO	NOM VEGETARIAN
87	22/2456	29	M	73	120	50.69	1.56	RD		120	80	13	NO	YES	VEGETARIAN
88	22/2437	22	M	82	172	27.72	1.98	VD	4	120	90	14.7	NO	NO	VEGETARIAN
89	22/2582	22	M	65	169	22.76	1.75	RD	1	122	82	14	NO	NO	VEGETARIAN
90	22/2625	21	M	64	165	23.51	1.71	VD	1	110	80	13.1	NO	NO	VEGETARIAN
91	22/2514	43	M	84	167	30.12	1.97	RD	2	120	94	15	NO	NO	VEGETARIAN
92	22/2695	30	M	91	178	28.72	2.12	RD	15T	120	80	14.2	YES	YES	NOM VEGETARIAN
93	22/2728	30	M	79	169	27.66	1.93	RD	15T	130	80	13.4	NO	NO	VEGETARIAN
94	22/2861	34	M	80	174	26.42	1.97	VD	15T	110	70	13	NO	NO	VEGETARIAN
95	22/2995	37	M	91	168	32.24	2.06	RD	10	110	60	13.2	NO	NO	NOM VEGETARIAN
96	22/3106	27	M	65	171	22.23	1.76	VD	10	130	86	13.5	YES	NO	VEGETARIAN
97	22/3198	26	M	60	169										

[illegible]

SNO	ADMS ID	SEX	T-1PT-1	OUTCOME	DATE OF TX	PRETRANSFUSION HEMOGLOBIN	POST TRANSFUSION HEMOGLOBIN	INC INCREMENT	UNIT NO	DONOR AGE	DONOR SEX	DONOR STATUS	DONOR RH STATUS	RBC STORAGE DURATION	VOLUME	GAMMA RADIATION N-Y UNRADIATION	LEUCOPHLETRATED N-Y UNLEUCOPHLETRATED	PRE DONATION RBC	SMOKING	HB INCREMENT	ALCOHOL	NO OF TIMES DONATED	
1	202104010011	M	PT	DISCHARGE	20/01/2021	11.3	12.7	1.4	210150	30	D	POSITIVE	5	30	NO		NO	14.2	12.4890	NO	1.4	NO	4
2	202104010014	M	PT	DISCHARGE	14/01/2021	11.7	13.7	2.0	210160	32	D	POSITIVE	8	30	NO		NO	13.7	14.1865	NO	0.4	NO	107
3	202104010002	F	T	DEATH	14/01/2021	6.6	6.9	0.3	210140	21	D	POSITIVE	11	30	NO		NO	14.2	16.2978	NO	2.0	NO	107
4	202104010002	F	T	DEATH	06/06/2021	8.2	8.3	0.1	210140	21	D	POSITIVE	8	30	NO		NO	15.1	16.9912	NO	0.1	NO	107
5	202104010002	F	T	DEATH	11/06/2021	7.8	8.3	0.5	210160	33	D	POSITIVE	7	30	NO		NO	13.8	17.8364	NO	0.4	NO	1
6	202104010002	F	T	DEATH	15/06/2021	6.3	7.8	1.5	210160	33	D	POSITIVE	9	30	NO		NO	13.8	20.8264	NO	1.5	NO	1
7	202104010002	F	T	DEATH	15/06/2021	7.8	8.3	0.5	210160	33	D	POSITIVE	8	30	NO		NO	13.8	20.8264	NO	0.5	NO	1
8	202104010011	M	PT	DISCHARGE	10/02/2021	7.7	9.7	2.0	210150	30	D	POSITIVE	14	15	NO		NO	15.6	17.9535	NO	2	NO	3
9	202104010002	F	T	DEATH	24/06/2021	6.7	6.7	0	210160	33	D	POSITIVE	18	30	NO		NO	15	25.8242	NO	2	NO	1
10	202104010026	M	PT	DISCHARGE	15/06/2021	8.1	10.9	2.8	210160	33	D	POSITIVE	8	30	NO		NO	17.1	31.4529	NO	4.1	NO	107
11	202104010000	F	PT	DEATH	25/06/2021	4.9	6.8	1.9	210160	34	D	NEGATIVE	10	30	NO		NO	15	16.9902	NO	2	NO	3
12	202104010000	F	PT	DEATH	03/06/2021	9.4	11.1	1.7	210160	34	D	NEGATIVE	6	165	YES	YES	12	16.9902	NO	1.0	NO	1	
13	202104010000	F	PT	DEATH	03/06/2021	8.3	9.3	1.0	210160	34	D	NEGATIVE	8	30	NO		NO	15	24.8113	YES	2.0	YES	1
14	202104010000	F	PT	DEATH	06/06/2021	6.5	9.4	2.9	210160	34	D	NEGATIVE	10	30	NO		NO	17	25.8113	YES	0.9	YES	1
15	202104010000	F	PT	DEATH	06/06/2021	6.3	8.8	2.5	210160	34	D	NEGATIVE	10	30	NO		NO	15	24.8113	YES	1.8	YES	1
16	202104010000	F	PT	DEATH	17/06/2021	8.1	10.9	2.8	210160	34	D	NEGATIVE	10	30	NO		NO	15	24.8113	YES	1.5	YES	1
17	202104010000	F	PT	DEATH	17/06/2021	8.7	10.2	1.5	210160	34	D	NEGATIVE	8	30	NO		NO	16	25.2190	NO	1.0	NO	107
18	202104010026	M	PT	DISCHARGE	15/06/2021	9.1	12.7	3.6	210160	35	D	NEGATIVE	11	125	YES	YES	17	38.7522	NO	5.6	NO	3	
19	202104010026	M	PT	DISCHARGE	15/06/2021	10.7	13.7	3.0	210160	35	D	NEGATIVE	8	314	YES	YES	16.8	32.8737	NO	5.0	NO	1	
20	202104010000	F	PT	DEATH	12/06/2021	9.1	10.8	1.7	210160	35	D	NEGATIVE	13	30	NO		NO	16	17.2190	NO	1.7	NO	107
21	202104010000	F	PT	DEATH	12/06/2021	9.1	10.8	1.7	210160	35	D	NEGATIVE	14	30	NO		NO	16	17.2190	NO	1.7	NO	107
22	202104010011	M	PT	DISCHARGE	20/06/2021	8.7	10.2	1.5	210160	35	D	POSITIVE	10	30	NO		NO	15	17.2190	NO	1.1	NO	107
23	202104010000	F	PT	DEATH	17/06/2021	8.7	10.2	1.5	210160	35	D	NEGATIVE	10	30	NO		NO	16	17.2190	NO	1.7	NO	107
24	202104010027	F	PT	DEATH	04/07/2021	8.8	11.8	3.0	210160	36	B	POSITIVE	13	20	NO		NO	13.9	24.2245	NO	5.2	NO	3
25	202104010011	M	PT	DISCHARGE	09/07/2021	7.6	14.7	7.1	210243	36	D	POSITIVE	14	20	NO		NO	12.9	24.4908	NO	7.1	NO	1
26	202104010027	F	PT	DEATH	09/07/2021	8.2	14.7	6.5	210243	36	D	POSITIVE	14	20	NO		NO	13.9	24.2245	NO	5.2	NO	3
27	202104010027	F	PT	DEATH	09/07/2021	8.2	11.6	3.4	210160	36	B	POSITIVE	14	27	NO		NO	13.9	24.2245	NO	7.8	NO	3
28	202104010011	M	PT	DISCHARGE	09/07/2021	8.7	14.7	6.0	210160	36	D	POSITIVE	14	27	NO		NO	14	24.2245	NO	1.9	NO	107
29	202107010001	M	PT	DISCHARGE	09/07/2021	12.4	11.3	-1.1	210160	36	D	POSITIVE	4	4	NO		NO	14.7	27.1271	NO	4.3	NO	107
30	202104010048	F	PT	DISCHARGE	21/07/2021	6.7	10.1	3.4	210271	37	D	POSITIVE	14	30	NO		NO	17	24.6910	YES	3.3	YES	1
31	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
32	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
33	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
34	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
35	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
36	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
37	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
38	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
39	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
40	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
41	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
42	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
43	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
44	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
45	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
46	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
47	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
48	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
49	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
50	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
51	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
52	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
53	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
54	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
55	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
56	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
57	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
58	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
59	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
60	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
61	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
62	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
63	202107010048	M	PT	LAMA	12/07/2021	6.3	11.3	5.0	210271	37	D	POSITIVE	6	30	NO		NO	15	24.1212	NO	4.0	NO	107
64	20210701004																						

