BLOOD AND BLOOD COMPONENTS TRANSFUSION PRACTICES IN THE NEWBORN UNIT, KENYATTA NATIONAL HOSPITAL.

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DECLARATION

This project is my original work and has not been presented for a degree in any other University.

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LIST OF ABBREVIATIONS AND ACRONYMS

ABG	Arterial blood gas
BPD	Bronchopulmonary Dysplasia
CI	Confidence Interval
DIC	Disseminated Intravascular Coagulopathy
ELBW	Extremely Low Birth Weight
ETTNO	Effects of Transfusion Threshold on Neurocognitive Outcomes of extremely low birth weight infants
FFP	Fresh Frozen Plasma
Hb	Haemoglobin
INR	International Normalized Ratio
IVH	Intraventricular Haemorrhage
KNH	Kenyatta National Hospital
LBW	Low Birth Weight
NBU	Newborn Unit
NEC	Necrotizing Enterocolitis
NICU	Neonatal Intensive Care Unit
OR	Odds Ratio
PINT	Premature Infants In Need of Transfusion
PlaNET	Platelet for Neonatal Thrombocytopaenia
PPT	Partial Prothrombin Time
PT	Prothrombin Time
PRBC	Packed red blood cells
RBC	Red Blood cells

RCT	Randomized Clinical Trial
ROP	Retinopathy of Prematurity
SSPS	Statistical Package for Social Sciences
TACO	Transfusion-associated Circulatory Overload
TA-GVHD	Transfusion-associated Graft versus Host Disease
TANEC	Transfusion-associated Necrotizing Enterocolitis
TOP	Transfusion of Prematures Trial
TRALI	Transfusion-associated Lung Injury
VLBW	Very Low Birth Weight

OPERATIONAL DEFINITIONS

Blood: Whole human blood collected from a donor and processed either for transfusion or for further manufacturing.

Blood Components: The therapeutic constituents of human blood (e.g. red blood cells, white blood cells, platelets and plasma) that are prepared by various methods.

Blood products: Are therapeutic substances derived from human blood and include whole blood, blood components and plasma derivatives such as albumin, coagulation factors and immunoglobulins.

Blood transfusion: Is a medical procedure in which blood or blood components from one person (the donor) are put into the bloodstream of another person (the recipient) through a vein.

Extremely low birth weight (ELBW) babies: Are babies born with a weight below 1000g.

Low birth weight (LBW) babies: Are babies born with a weight below 2500g.

Preterm babies: Are babies born before 37 completed weeks of gestation. These are further sub-categorized into:

Extremely preterm babies: Babies born before 28 weeks gestation.

Very preterm: Babies born between 28 to 32 weeks gestation.

Moderate or late preterm: Babies born between 32 to 37 weeks gestation.

Very low birth weight (VLBW): Are babies born with a weight below 1500g.

ASTRACT

Introduction: Blood transfusion is a commonly used supportive therapy in neonatal units worldwide. There are significant differences in blood transfusion practices among countries, newborn units and clinicians. Data on blood transfusion practices in neonatal units in Kenya is scarce.

Objective: To determine the prevalence of transfusion, pretransfusion haematological parameters, and transfusion practices of blood and various blood components in the Newborn Unit (NBU) of Kenyatta National Hospital (KNH).

Methods: A descriptive cross-sectional study. Medical records of 330 neonates admitted over a 3-months' period were reviewed. A survey was then conducted among 19 clinicians in the NBU.

Data analysis: Statistical Package for Social Sciences (SPSS) version 21.0 was used for data analysis. Nominal data was summarized using counts and percentages and continuous variable using measures of central tendency and dispersion. Data was presented using tables, pie charts and bar graphs.

Results: The prevalence of blood transfusion was 10.9%. The most commonly used blood component was packed red blood cells (PRBC) accounting for 66.7% of all transfusions, followed by platelets, 27.8%, while fresh frozen plasma (FFP) accounted for only 5.5% of transfusions. The mean pre-transfusion Hb was 10.8g/dl, and was highest in neonates who were on O_2 via nasal prongs (13.4g/dl) and those who were transfused in the 2^{nd} postnatal week (11.3g/dl). The median pre-transfusion platelet count was 14 $x10^9$/l. All neonates who received FFP had deranged coagulation profile and active bleeding. There was a wide variation in Hb thresholds for PRBC transfusion among clinicians and suboptimal monitoring of neonates during blood transfusion.

Conclusion: The current PRBC prescribing patterns and the overall monitoring of neonates on blood components transfusion in the KNH NBU are suboptimal and do not align with the current available evidence. Implementation of quality improvement activities to address the identified gaps is recommended.

CHAPTER ONE

1.0 INTRODUCTION

Neonates, especially those who are premature, have very low birth weight (VLBW) and are critically sick are one of the patient categories that are transfused the most (1). Ninety percent of very preterm neonates hospitalized in neonatal intensive care unit (NICU) will need a minimum of one transfusion of red blood cell (RBC) in the course of their NICU stay, while approximately 10% of them will need a transfusion of platelets (2, 3). Although data to support decisions for neonatal transfusions has been expanding, there is still no universal agreement on transfusion indications and ideal criteria (3). As a result, there are significant differences in blood transfusion practices between and within nations, as well as between doctors and neonatal units (3, 4).

In an international survey conducted by Guillen et al. (5), nearly half of the NICUs assessed lacked clear RBC transfusion guidelines, and clinicians reported a wide range of haemoglobin levels used for transfusion in newborn who were extremely preterm. In an assessment of the practice of platelet transfusion among Canadian and American neonatologists by Josephson et al. (6), the usage of platelet cutoff of 50 x 10^9/l for transfusion was reported by most physicians. This practice was inconsistent with the best available research at the time. Robust evidence on fresh frozen plasma (FFP) use in newborns is lacking with a recent review by Sokou *et al.* (7) showing that most transfusions of FFP in neonates are given “prophylactically”, without any signs of active bleeding.

Blood transfusions may be lifesaving, but they also carry a risk of side effects, such as haemolytic, febrile nonhaemolytic and allergic transfusion reactions, infections, graft versus

host disease and acute lung injury (8). In addition, neonates may be at risk of circulatory overload, hemodynamic instability, hypothermia and hyperkalaemia (9).

Although the cause-effect relationship is still unclear, recent research suggests a connection between transfusion with RBC and unfavorable outcomes specific to preterm newborns, including severe germinal matrix haemorrhage, chronic lung disease, necrotizing enterocolitis and retinopathy of prematurity (10-15).

Recent clinical trials in neonates comparing the risk-benefit ratio of restrictive/conservative transfusion strategy (where RBCs and platelets are transfused at a lower haemoglobin (Hb) level and lower platelet count cut-offs, respectively), versus liberal transfusion (where RBCs and platelets are transfused at a higher Hb level and higher platelet count cut-offs, respectively), seem to favour the restrictive transfusion strategy (16-18). Two sizable trials published in the year 2020, the TOP (Transfusion Of Prematures) and ETTNO (Effects of Transfusion Thresholds on Neurocognitive Outcomes of ELBW infants) trials compared lower and higher Hb cutoffs for transfusing ELBW infants and reported that restrictive/conservative transfusion strategy for RBC transfusion can be used safely without any detrimental effect on neurodevelopment or survival (16,17).

In the ETTNO trial, infants in the liberal and the restrictive groups did not have any statistically different rates of mortality or neurocognitive deficits by 2 years of age (44% versus 43%, OR 1.05 [CI 0.80-1.39] p value 0.72)(16). Similarly, in the TOP trial, neither the infants assigned to the group with liberal transfusion treshold nor those assigned to the group with restrictive transfusion threshold experienced significant rates of mortality or survival with disability (50.1% versus 49.8% , ARR 1.00 [CI 0.92-1.10] p value 0.93) (17). On the other hand, a large multicentre randomized trial in premature neonates with low platelet counts, the PlaNET-2 (Platelets for neonatal Thrombocytopenia) trial revealed that neonates assigned to the group

that was given platelets at higher transfusion cutoff ($50x10^9$/l), as opposed to the group that was given platelet transfusion at lower cutoff ($<25x10^9$/l), had statistically higher rates of severe haemorrhage or mortality (26% versus 19%; OR 1.57 [CI 1.06- 2.32] p 0.02) (18).

There is currently no data on blood transfusion practices in the newborn unit of Kenyatta National Hospital. This study will therefore provide insight on current transfusion practices and, potentially influence change in practice going forward if more liberal transfusion thresholds are found to be in use.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Prevalence of blood and blood components transfusion in neonates

There is scarcity of data on transfusion practices in term and late preterm neonates (19). A single-centre cohort study in a Canadian NICU that involved term neonates reported a 12.5% transfusion rate of any blood product (20). Transfusions are more common in preterm neonates, with up to ninety percent of ELBW infants receiving a minimum of one transfusion of RBC and ten percent a platelet transfusion during their NICU stay (2, 3). Other blood products used in neonatal units include plasma and whole blood, though the use of the former is reducing in many countries.

The usage of blood and blood components varies greatly among neonatal units and countries, and is inversely proportion to the postconceptional age and weight of the neonates. Fabres et al (21) in a single-centre review of RBC transfusions in premature infants hospitalized in a Level III NICU in United Kingdom, reported that 85% of infants needed at least one transfusion of RBC. Similarly, Valieva et al. (22) reported a 78% rate of RBC transfusion for ELBW neonates hospitalized in a NICU in the United States.

Studies conducted in low and middle-income countries also report variable blood transfusion rates in newborn units. Dos Santos *et al.* (23) in a multicentre prospective study conducted in Brazil, reported that about 56% of VLBW infants were transfused RBC atleast once. Kaur et

al (24) in a retrospective single centre study in a Northern India NICU found that 34.3% of all neonates admitted were transfused a minimum of one blood component during their hospitalization with about 12.2% of them needing more than one type of blood component. In that study, the most commonly used blood component was platelet concentrates, accounting for 54.7% of all transfusions followed by packed RBC (24.5%). In contrast, Dogra et al (25) in a NICU in India reported an overall rate of 21.1% of any blood transfusion among hospitalized neonates, with 32.7% of them receiving PRBCs.

In Africa, data on rates of blood transfusions among neonates is limited, with most of the available data coming from studies conducted in Nigeria. Joel-Medewase et al. (26) in a retrospective study conducted in Southwest Nigeria reported that 11.7% of neonates admitted had a blood transfusion, with 87.7% having received RBCs and 9.4% plasma transfusion. Higher transfusion rates of 30.8% and 27.9% among hospitalized neonates were reported in Southwest Nigeria (27, 28). Table 2.1 below shows a summary of studies on rates of blood and blood components transfusion among neonates.

Table 2.1: Summary of studies on rates of blood and blood components transfusion

Author	Year	Country	Blood/ blood product transfusion rate			
			Any	RBC	Platelets	Plasma
Villeneuve et al (20)	2014	Canada	12.5%			
Fabres et al (21)	2006	UK		85%		
Valieve et al (22)	2009	USA		78%		
Dos Santos (23)	2010	Brazil		55.9%		
Kaur et al (24)	2015	India	34.3%			
Dogra et al (25)	2018	India	21.1%			

Joel-Medewase et al. (26)	2019	Nigeria	11.7%			
Ayede at al (27)	2011	Nigeria	30.8%			
Ogulensi et al. (28)	2011	Nigeria	27.9%			

2.2 Blood and blood components transfusion practices and current evidence

2.2.1 RBC transfusion practices and current evidence

In neonates, the most regularly transfused blood components are RBCs (29). Neonatal RBCs are generally given as 'top-up' transfusions (30). RBC transfusions are also administered in cases of sudden blood loss or in cases where there are surrogate indicators of anaemia, such as slow growth, or an increase in apnea episodes (30, 31).

Due to frequent blood sampling for laboratory investigations, low endogenous erythropoetin synthesis, lower Hb at birth and concomitant diseases including sepsis amd cardiorespiratory illness, preterm neonates are at a significant risk for anaemia and subsequent RBC transfusions (1). Nearly 50% of RBCs administrered to premature neonates are given in the first two postnatal weeks (30).

The question of whether to use liberal (high Hb cutoff) or restrictive/conservative (low Hb cutoff) transfusion strategies in neonates has been debated over the years. The benefits and hazards of RBC transfusion using the two strategies were assessed in two randomized controlled studies, the Iowa (33) and PINT (Premature Infants in Need of Transfusion) trials (34) published in the year 2005 and 2006 respectively, with Hb treshholds for RBC transfusion as shown in table 2.2.

The Iowa trial (33) reported a significantly higher number of infants who experienced severe adverse brain events in the conservative group, 6 versus 0 in the liberal group (p value 0.012), even though the difference in proportion of infants who were not transfused was not significant (12% versus 10% ; p value 1.0). On the other hand, Kirpalani et al. in the PINT trial (34) reported more RBC transfusions in the liberally transfused group than those in the conservative group (95% versus 89%, p value 0.037). However, the difference between the rates of mortality or life with ROP, BPD or brain damage in the restrictive/conservative and liberal transfusion groups was not statistically significant (74.0% versus 69.7% ; p value 0.25).

Table 2.2: Hb tresholds for RBC transfusion in the Iowa and PINT randomized trials

Trials	Strategy			
	Restrictive		Liberal	
	Lower	upper	Lower	Upper
Bell et al 2005 (33) Iowa Trial	7.3	11.3	10.0	15.3
Kirpalani et al 2006 (34) PINT Trial	7.5	11.5	8.5	13.5

Thresholds are haemoglobin levels (g/dL).
PINT, premature infants in need of transfusion.

Subsequent post hoc analysis of both trials reported possible neurological repercussions of maintaining the Hb at various levels (35, 36, 37). Secondary analysis of data of the PINT trial infants at 18-21 month revealed that the restricted group had a higher prevalence of cognitive delay (44.9% versus 33.9%;AOR 1.81 [95% CI i.12-2.93]; p value 0.016), suggesting that libersl transfusion may have an advantage in terms of cognitive development (35). In contrast, post hoc analysis of the Iowa trial found that liberally transfused preterm performed worse than those in the restrictive transfusion group at school age on some

cognitive tests (36) and had reduced brain volumes compared to controls at 12 years of age (t83=1.72; p=0.09) (37).

Due to the contradictory findings of the previous studies, two large randomised trials (the TOP and ETTNO trials) with over 2,800 study participants were undertaken to further investigate the effects of transfusion on neurodevelopmental in ELBW neonates (16,17). In both trials which were published weeks apart in the year 2020, neonates were randomly assigned within the first 72 hours after delivery to lower or higher Hb transfusion cutoffs (Table 2.3.). In both studies, the risk of mortality or disability at 24 months was not different between the liberally-transfused and the restricted group. Evaluation at school-going age of infants enrolled in the TOP trial is currently ongoing to determine whether early Hb trnasfusion cutoffs have any long-term impacts.

Table 2.3: Hb thresholds for RBC transfusion in ETTNO and TOP trials

Study	ETTNO trial (17)			TOP trial (16)			
Transfusion threshold group							
Higher		Lower		Higher		Lower	
Severity stratum							
*Critical	Non-critical	Critical	Non-critical	Resp. support	No resp. support	Resp. support	No resp. support
Haemoglobin threshold, g/dl							
Week 1							
13.7	11.7	11.3	9.3	13.0	12.0	11.0	10.0
Weeks 2–3 (ETTNO) or 2 (TOP)							
12.3	10.3	10.0	8.0	12.5	11.0	10.0	8.5
Week >3 (ETTNO) or ≥3 (TOP)							
11.3	9.3	9.0	7.0	11.0	10.0	8.5	7.0

*Critical was defined as an infant having at least 1 of the following criteria: invasive mechanical ventilation, continuous positive airway pressure with fraction of inspired oxygen >0.25 for >12 hours per 24 hours, treatment for patent ductus arteriosus, acute sepsis or

necrotizing enterocolitis with circulatory failure requiring inotropic/vasopressor support, >6 nurse-documented apneas requiring intervention per 24 hours, or >4 intermittent hypoxemic episodes with pulse oximetry oxygen saturation <60%.

Based on the findings from the TOP and ETTNO trials, Bell (38) proposed that practitioners should feel at ease utilizing transfusion Hb cutoffs within the ranges of these two trials (Table 2.3), unless data from the ongoing assessments at school-going age indicate otherwise. Although there's little data on term infants, several experts and authors support using the same cutoffs or trasfusion as for preterms without haemorrhage (39). Table 2.4 summarizes RCTs on RBC transfusion thresholds and key findings.

Table 2.4: Summary of randomized trials on RBC transfusion thresholds and key findings

Authors Year	Country	No. of participants	Key findings
Kirpalani et al (34) 2006 PINT trial	Canada, USA, Australia	451	-Greater number of RBC transfusions in the liberally transfused group. -No difference in the rate of primary outcome between the groups
Bell et al (33) 2005 Iowa trial	USA	103	-No difference between the groups in the % of infants who avoided transfusions. -More infants in the restrictive group suffered severe adverse brain events.
Whyte et al (35) 2009	Canada, USA, Australia	421	-Cognitive delay was more prevalent in the restrictive transfusion group.
McCoy et al 2011 (36)	USA	103	-Liberally transfused preterm had poorer neurocognitive tests compared to those in the restrictive transfusion group.
Nopoulos et al 2011 (37)	USA	44	-Liberally transfused preterm subjects had reduced brain volumes compared to controls at 12 years of age
Kirpalani et al 2020 (16) TOP trial	USA	1823	-No difference between the two groups in the rate of death or survival with impairment
Franz et al (17) 2020 ETTNO	Germany	1013	-No difference in the rates of death or neurodevelopmental impairment by 24 months in both groups.

The typical packed RBCs transfusion volume in neonates is 10 to 20 millilitres per kilogram, given at an infusion rate of 5 to 6 millilitres per kilogram per hour (40, 41). Most preterms tolerate 20 millilitres per kilogram well, have a greater increase in Hb and fewer exposures to donors (42).

2.2.2 Neonatal platelet transfusion practices and current evidence

Thrombocytopenia is a frequent finding in NICU, particularly in ELBW neonates (43). As a result at least ten percent of preterms are transfused platelets during their stay in NICU, with some centres administering platelets to approximately a quarter of VLBW infants (3,44).

Preterm infants typically receive platelet transfusions 'prophylactically', (that is as indicated by a predetermined platelet cutoff) to reduce the potential risk of major bleedings such as IVH, pulmonary haemorrhage or gastrointestinal bleeding (3). In a minority of cases, platelet transfusions are given 'therapeutically' in the event of an active large bleed (3).
A survey conducted by Josephson et al. (6) on neonatal transfusion practices among American and Canadian neonatologists found significant practice diversity with most nonbleeding neonates with platelet counts $>50x10^9$/L receiving platelet transfusions. Stanworth et al. (45) in the PlaNeT-1 (Platelets for Neonatal Thrombocytopenia), a prospective observational study conducted among preterm neonates in seven tertiary-level NICUs in England, found that 81% of platelet transfusions were given prophylactically.

There is no convincing evidence that low platelet count causes bleeding, or whether infusion of platelets prevents bleeding (46). A study by Stanworth et al. (45) reported that 91% of enrolled neonates did not experience a significant haemorrhage, despite having thrombocytopenia of $<20x10^9$ platelets per litre in one-third of them. In this study, it was

discovered that infants with severe, small, or no haemorrhage all had similar nadir platelet count.

In the PlaNeT-2 study, a large multicentre trial, 660 neonates with severe thrombocytopenia who were delivered at < 34 weeks of gestation were randomly assigned to get platelet infusions at a platelet cutoff of 50 x 10^9/litre (liberal or high threshold group) or at a cutoff of 25x 10^9/L (restrictive/ low threshold transfusion group) (47). These authors found that neonates in the high threshold group had rates of mortality or new major haemorrhage that were higher than the low threshld group (26 % versus 19%; OR: 1.57;CI: 1.06–2.32; p 0.02). The rate of BPD was also found to be higher in neonates in the liberal than restrictive group (63% vs 54% (OR: 1.54; 95% CI: 1.03–2.30) (47).

Fustolo-Gunnink *et al.*(48) in a secondary analysis of the PlaNeT-2 trial reported that lower compared to higher platelet transfusion threshold was beneficial in all subgroups of premature infants (risk difference 4.9% to 12.3%). Another randomized clinical trial (RCT) by Kumar et al. (49) showed that liberal platelet transfusions strategy may be more harmful than the restrictive platelet transfusions strategy. The authors found that infants that mantained platelet counts above 100 × 10^9/L had higher rates of intracranial haemorrhage than the group counts above 20 × 10^9/L (41% versus 9%; p 0.034). Table 2.5 provides an overview of studies on neonatal platelet transfusion along with major conclusions.

Recent RCTs show that a lower platelet transfusion cutoff of 20 to 25 × 10^9/litre is beneficial for preterm infants (47- 49). Zerra et al. (50) in an article published in the journal of Clinics in Laboratory Medicine stated that the reasonable course of action is to transfuse platelets in neonates if the counts are < 25,000/millilitre and they are not bleeding, are older than seven

days, and not scheduled for a procedure within the next 24 hours. Neonatal platelets are typically administered at volumes of 10 to 20 millilitres per kilogram, at an infusion rate of 10 to 20 millilitres per kilogram per hour (31). In the PlaNeT-2 research, Curley et al. (47) used 15ml/kg of platelet for transfusion.

Table 2.5: Summary of studies on platelet transfusion

Authors	Study design	Country	Key findings
Stanworth et al. (45) PlaNeT-1	Observational study	UK	- 81% of platelet transfusions were given prophylactically. -Although one third of enrolled neonates developed thrombocytopenia of $<20x10^9/l$, 91% of them did not develop major haemorrhage.
Curley et al (47) PlaNeT-2 study	Multicentre RCT	UK, Netherlands, Ireland	Neonates who received platelet transfusions at a platelet-count threshold of $< 50x10^9/L$ had a significantly higher rate of death or new major bleeding within 28 days after randomization than those in the group that received transfusion at platelet counts $< <25x\ 10^9/L$
Fustolo-Gunnink et al. (48)	Follow up secondary sub-analysis of PlaNeT-2 study	UK, Netherlands, Ireland	Lower compared to higher platelet transfusion threshold was beneficial in all subgroups of preterm neonates, with the highest-risk infants gaining the greatest benefit (absolute risk difference of 12.3%).

Kumar et al. (49)	RCT	India	Significantly higher rate of IVH in neonates randomized to maintain platelets >100 × 10^9/L versus 20 × 10^9/L (41% vs 9%; p = .034).

2.2.3 Plasma transfusion practices in neonates and current evidence

After RBCs and platelets, FFP is one other commonly used blood products in NICUs, being administered to up to 11% of preterm neonates (29). With limited data to guide practice, there is increasing concerns on appropriateness of the use of the FFPs in neonates. Motta et al. (51) in a multicentre study in Italy found that up to six in ten transfusions of FFP in neonates were based on no evidence. A similar audit in UK by Stanworth *et al*. (45) revealed that 42% of neonatal received FFP infusions were prophylactic.

Haemorrhage and/or prolonged Prothrombin Time (PT) and activated Partial Prothrombin Time (aPTT) are the most utilized criteria for FFP transfusions (52). However, because newborn coagulation profiles differ from those of adults and depend on gestational and postnatal age, interpreting coagulation tests in neonates can be rather difficult (53). Moreover, studies have shown that these tests are poor predictors of clinical haemorrhage (51) and that abnormal coagulation test findings without symptoms or a risk of haemorrhagic complication do not warrant the transfusion of FP (31). The recommended volume of FFP in neonatal transfusion is 15-20 mls/kg, infused at 10-20mls/kg/hour (54).

2.3 Available guidelines on neonatal blood and blood components transfusion

2.3.1 Available guidelines on neonatal RBC transfusion

While transfusions of RBCs remain the main mode of treatment for anaemia in neonates, there is no international agreement on ideal Hb cutoff for RBC transfusions (3). Consequently, postulated Hb cutoffs for transfusions differ greatly and, sometimes, the

decision to transfuse is based on the clinician's judgement, irrespective of national or local guidelines (3, 30). Table 2.6 shows a summary of some international guidelines and RBC transfusion thresholds available in online, while Table 2.7 shows local (Kenyan) guidelines on RBC transfusion in neonates (57).

Table 2.6: Summary of some international guidelines and Hb cutoffs for RBC transfusions

	British Committee for Standards in Haematology-2016* (55)			Australian National Blood Authority-2016 (40)		Canadian Blood Services -2017 (56)	
	Haemoglobin threshold in g/dl						
Postnatal Wk	Ventilated	On O_2, CPAP or HFNC	Off O_2 and Resp. Support	Resp. Support Eg O_2, HFNC,CPAP, Ventilated	No Resp. support	Resp. Support (ventilated or requiring O_2 > 25%	No Resp. Support
Wk 1	<12	<10	<10	11-13	10-12	11.5	10
Wk 2	<10	<9.5	<7.5**	10-12.5	8.5-11	10	8.5
Wk ≥3	<10	<8.5	<7.5**	8.5-11	7-10	8.5	7.5

*The table applies for preterm infants (<32 weeks); for late preterm/term babies the values for babies off oxygen may be used.

**May use 8.5g/dl depending on clinical situation.

CPAP: Continuous positive airway pressure HFNC: high flow nasal cannula

Table 2.7: Local (Kenyan) guidelines on RBC transfusion in neonates (57)

Postnatal Age	**Suggested transfusion Threshold Hb(g/dl)**		
	Ventilated On	Oxygen/CPAP	Off Oxygen
First 24 hrs	<12	<12	<10
≤ Week 1(days 1-7)	<12	<10	<10
Week 2 (days 8-14)	<10	<9.5	<7.5-8.5 depending onclinical situation
≥Week 3 (day 15 onwards)	<8.5		

The Swiss Society of Neonatology currently recommends haemoglobin transfusion thresholds consistent with the restrictive strategy of the ETTNO trial (39), as shown in table 2.8 belo

Table 2.8: RBC transfusion threshold for neonates without acute blood loss (39)

Day of life	**Critical health state[1] Hb (g/dl)**	**Non-critical health state[2] Hb (g/dl)**
0-7	11.3	9.3
8-21	10.0	8.0
>21	9.0	7.0

2.3.2 Available guidelines on platelet transfusion in neonates

There is no agreement on indications and platelet count cutoffs for platelet transfusions in neonates, with documented cutoffs ranging from 10 to 150×10^9/litre (6, 55,40,56). Table 2.9 shows some international guidelines on platelet transfusion cutoffs available online, while table 2.10 shows local (Kenyan) guidelines.

Table 2.9: Some international guidelines and Platelet count cutoff for platelet transfusions

	British Committee for Standards in Haematology,2016 (55)	Australian National Blood Authority, 2016 (40)	Canadian Blood Services, 2017 (56)
Prophylactic in stable infant	25 X 10^9/L	10–20 X 10^9/L	20 X 10^9/L
Bleeding or invasive procedure	50 X 10^9/L	50 X 10^9/L	50 X 10^9/L

Table 2.10: Kenyan guidelines on platelet transfusion (57)

Platelet Count	**Indication for transfusion**
Platelets <20 x 10 ^9/L	Absence of bleeding
Platelets <50 x 10 ^9/L	Bleeding, current coagulopathy, planned surgery or exchange transfusion
Platelets <100 x 10 ^9/L	Major bleeding, major surgery

2.3.3 Available guidelines on plasma transfusion in neonates

Based on the scarce evidence available, indications for FFP transfusion are as shown in table 2.11

Table 2.11: Indications for FFP transfusion in neonates (1)

1. PT and aPTT > 1.5x normal value for age and bleeding or about to undergo a major surgery.
2. Congenital clotting factors defiencies and specific factor unavailable.
3. Disseminated intravascular coagulation (DIC)

4. Emergency reversal of warfarin effects.

The local (Kenyan) guidelines (57) recommend FFP following conditions:

- Correction of coagulation abnormalities with bleeding e.g Hemophilias and coagulation factor deficiencies.
- Massive transfusion.
- Bleeding due to warfarin therapy refractory to vitamin K.

The dose is 10-20ml/kg of group specific plasma transfused over 2-4hrs.

The amount of FFP to be given should be pegged on normalization of PT and aPTT.

STUDY JUSTIFICATION

Blood transfusion is a commonly used supportive therapy in neonatal units worldwide. However, while this therapy may be life-saving, several adverse effects have been reported following neonatal transfusions (14, 15). Moreover, blood products are expensive and a limited resource and judicious use is essential.

A few recent clinical trials comparing the risks and benefits of liberal versus restrictive/conservative transfusion strategies, seem to favour restrictive criteria (15-17). It is important that the existing evidence is translated into practice in the neonatal population. This

will help in reducing unnecessary transfusions and associated risks, potentially leading to better short- and long-term outcomes.

There is currently no data on blood transfusion practices in the newborn unit of Kenyatta National Hospital. This study therefore sought to provide insight on the current neonatal blood and blood components transfusion practices in the KNH NBU.

STUDY QUESTIONS

1. What is the prevalence of blood and blood components transfusion among neonates admitted to the New Born Unit of Kenyatta National Hospital?
2. What are the pretransfusion haematological parameters of neonates receiving blood and blood components transfusions in the New Born Unit of Kenyatta National Hospital?
3. What are the transfusion practices of blood and various blood components among clinicians in the New Born Unit of Kenyatta National Hospital?

STUDY OBJECTIVES

Broad objective

To determine the prevalence, pretransfusion haematological parameters and transfusion practices of blood and various blood components in the New Born Unit of Kenyatta National Hospital.

Specific objectives

1. To estimate the prevalence of blood and blood components transfusion among neonates admitted in the New Born Unit of Kenyatta National Hospital.
2. To determine the pretransfusion haematological parameters of neonates receiving blood and blood components transfusions in the New Born Unit of Kenyatta National Hospital.
3. To describe the transfusion practices of blood and various blood components among clinicians in the New Born Unit of Kenyatta National Hospital.

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study design

This was a hospital-based descriptive cross-sectional study. The study involved:

- A retrospecitive review of medical records of eligible neonates admitted over a period of three months (January to March, 2023) to determine the proportion of neonates who receive any blood or blood component transfusion during their period of stay in hospital until discharge, death or until day 28 of life (period prevalence).
- A survey of the clinicians working in the new born unit during the study period to establish the blood and blood components transfusion practices. Topics covered in the questionnaire addressed transfusion thresholds or indications for various blood components, duration and volumes of transfusion, and opinions about selected blood transfusion practices or services in the KNH and/ or KNH NBU.

3.2 Study site

The study was conducted in the Newbrn Unit (NBU) of Kenyatta National Hospital (KNH). KNH is a tertiary referral hospital in Nairobi, which also serves as the teaching hospital for the University of Nairobi (UoN), College of Health Sciences. The KNH NBU is a level 3 newborn unit located in the first floor of the hospital. It has a bed capacity of 100 and admits on average 200 babies per month. Due to the inevitable long-stay of preterm neonates, the NBU is most often at more than 100% occupancy with about two or three neonates sharing an incubator or a cot. The KNH NBU admits both in-born neonates as well as neonates referred from other hospitals across the country. On admission to the KNH NBU blood samples are taken from all neonates for routine investigations which include C-reactive protein, full haemogram and blood culture. Blood and blood components used in the NBU are obtained from the KNH blood transfusion unit (BTU) which also serves the rest of the hospital. The 2018 Kenyan Ministry of Health Neonatal guidelines has a section on blood and blood components transfusion in neonates. However, these guidelines have not been formally adopted in the KNH NBU. The decision on the need to transfuse any neonate is based on the assessment by any of the clinicians in the unit who include; neonatologists, fellows in neonatal medicine, paediatric residents, high

diploma clinical officers doing their clinical rotation in the NBU and, occasionally, there may be one or two medical officers deployed in the NBU.

3.3 Study population

Inclusion criteria

- Neonates admitted to the NBU of KNH over the months of January, February and March, 2023.

Exclusion criteria

- All well babies accommodated in the NBU awaiting maternal stabilization.
- All critically ill neonates who die within 24 hours of admisssion.
- All preterm/LBW infants admitted aged > 28 days.

The healthcare providers' cross-sectional survey targeted all clinicians working in the NBU during the study period.

3.4 Sample size calculation

The sample size was calculated using the formula for single proportions. This was based on the primary objective of determining the prevalence of any transfusion during the during the patient's hospital stay until discharge, death or day 28 of life.

$$n = \frac{z^2\, pq}{d^2}$$

Where

n = required minimum sample size

Z = the *z*-score or critical value of desired level of confidence, which at 95% confidence level is 1.96

p= estimated prevalence of an indicator, which in this study will be 30.8%, the prevalence of neonatal transfusion in a Nigerian neonatal unit by Ayede *et al.* (27).

q= 1-p

d = Desired margin of error = 5%

$$n = \frac{1.96 \times 1.96 \times 0.308 \times 0.692}{0.05 \times 0.05}$$

=327

Based on the above assumptions a minimum sample size of **327 Neonates** was required.

3.5 Sampling techniques

Medical records of eligible neonates admitted over a period of 3 months (January to March 2023) were consecutive sampled until the desired sample size was achieved.

3.6 Study period

Data collection ran for a period of one month, that is, May 2023.

3.7 Variables

3.7.1 Dependent variable

- Any blood or blood component transfusion during the patient's hospital stay until discharge, death or day 28 of life.

A transfusion in this study was defined as the transfer of blood or a blood component from a donor into the bloodstream of another (in this study a neonate) through a vein. In determining the period prevalence of blood transfusion, only one transfusion event was counted for any particular study participant even if multiple transfusions may have occurred during their hospital stay.

3.7.2 Independent variable

Neonatal demographic and clinical characteristics

- Gender.
- Birth weight.
- Gestational age at delivery.
- Mode of delivery.
- Whether the neonate was out-born or in-born.
- Singleton/multiple gestation.
- Hb level, platelet count (and aPPT, PT and/or international normalized ratio (INR) if done) at admission.

Additional information obtained for neonates who received a blood transfusion included:

- Age at the time of first transfusion
- Oxygen requirement at time of first transfusion
- Ventilatory support at the time of first transfusion
- Type of Blood component transfused
- If RBC, type of blood transfusion: exchange vs top-up.
- Volume of blood product transfused (total and in mls/kg).
- Monitoring during transfusion.
- Pre-transfusion haemoglobin, platelet count and INR, PT and/or aPPT.

3.8 Pre-testing of the survey questionnaire

The survey questionnaire was pre-tested with five (5) paediatric residents who had already completed their clinical rotation in the NBU. The PI took note of all the concerns/ issues raised by the testers and the survey tool was improved to address those problems.

3.9 Data collection procedure

The study involved retrospective review of prospectively collected data of eligible neonates admitted to the NBU of KNH over a period of three months (January to March, 2023). The data was extracted from the Electronic Health Records (EHR) system, CIN (Clinical

information Network) and collaborated with the patients' physical medical records as well as records from the KNH Blood Transfusion Unit (BTU). A special code was assigned to each data abstraction form for each study participant.

To answer the third study question on assessing blood transfusion practices in the NBU of KNH, a cross-sectional survey of all clinicians working in the unit during the period of study was conducted using anonymous self-administered pre-tested questionnaires. The questionnaire comprised fifteen questions; five as open-ended questions, nine in multiple choices format and one question as a Likert scale. The principal investigator (PI) informed each clinicians about the survey and requested their participation. The PI distributed the questionnaires to the clinicians in the unit and agreed with each clinician on when to receive back the filled questionnaires. Each questionnaire was coded and no identifier information was required. For the clinicians who could not be reached physically, an anonymous survey was generated on Google Forms and sent to each of them via electronic mail.

3.10 Materials

-Data abstraction form

-A healthcare providers' survey tool/questionnaire

3.11 Training procedure

All data was collected by the principal investigator and a research assistant, a registered clinical officer who previously worked in the NBU. Prior to commencement of data collection, the PI trained the research assistant on how to appropriately fill the data abstraction tool.

3.12 Ethical consideration

Approval to carry out this study was sought from the KNH/UoN Ethics and Research Committee (KNH-UoN ERC) and the KNH administration. Letter of protocol approval was obtained prior to the commencement of the study. The study involved review of patients' medical records only and no direct interview or examination of patients. A request for waiver

of individual patients' consent was sought from the KNH-UoN ERC. To ensure confidentiality, the extracted data was stripped of all patient identifiers such as the names and assigned unique codes.

For the healthcare providers' survey, vervbal informed consent was sought from each healthcare provider prior to participation. All questionnaires were coded and no identifier information was required. To ensure anonymity, participants' were not be required to sign the consent form and waiver of written documentation of consent was sought from KNH-UoN ERC. The survey tool that was filled electronically was anonymous.

3.13 Data management

Data collected was coded and transferred into Microsoft Excel worksheet, cleaned and verified and subsequently exported to SPSS 21.0. for analysis. Descriptive statistics for categorical variables were summarized using counts and proportions and, for continuous variables using measures of central tendency (medians and means) and dispersion (standard deviation, range and interquartile). Data was presented using tables, pie charts and bar graphs as appropriate.

3.14 Study limitation and how to minimize them

This was a single-centre study hence study findings may not be generalizable to other newborn units in other hospitals. However, the findings of this research will provide empirical data which can be utilized as a baseline for a larger multi-centre study. Being a retrospective study, there was the limitation of missing data due to incomplete medical records. To minimize this, every effort was made to collaborate information from all patients' documents including electronic medical records, clinicians' notes, nurses' records, monitoring and treatment charts as well as laboratory records and blood transfusion request cards. All data that was conflicting, missing, ambiguous or unknown was handled uniformly.

3.15 Study results dissemination plan

The findings of this study will be communicated via an in-person presentation to the healthcare providers in the KNH NBU. Printed and digital copies of the research findings will also be submitted to the UoN library and digital repository respectively. A manuscript of this study will be submitted to a peer-reviewed journal for publishing.

3.16 Study time frame

TASK	2022							2023							
	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug
1. Proposal development and writing															
2. Proposal Submission/ ethical approval															
3. Data collection															
4. Data analysis															
5. Thesis writing															
6. Preparation of reports and publication															

4. RESULTS

4.1 Clinical Characteristics of the study population

A total of 330 medical records of eligible neonates admitted over the months of January to March, 2023 were reviewed. Table 1 shows the clinical characteristics of the study population. Males accounted for slightly over half of the participants (52.4%). The vast majority of the participants were inborn (83.3%), and were delivered via caesarean section (68.2%). Over 90% of the study participants were admitted on the first day of life. Term and late preterms accounted for 42% and 36% of the participants respectively. Forty five percent (45%) of the participants had a normal birthweight (>2500g), followed by those with LBW (1500-2499g), 33%.

Table 4.1: Clinical characteristics of the study population

Variable	Transfused n=36 (10.9%)	Not transfused n=294 (89.1)	Overall n= 330 (100)
Gender			
Males	17 (47.2)	156 (53.1)	173 (52.4)
Females	19(52.8)	138 (46.9)	157 (47.6)
Gestational age			
<28 weeks	2 (5.6)	10 (3.4)	12(3.6)
28- <32 weeks	13(36.0)	46(15.6)	59(17.9)
32- <37 weeks	10(27.8)	109(37.1)	119(36.1)
≥37 weeks	11 (30.6)	129 (43.9)	140 (42.4)
Birth weight			
<1000g	5 (13.9)	16 (5.4)	21(6.4)
1001-1499g	7(19.5)	45 (15.3)	52(15.8)
1500-2499g	12(33.3)	97(33.0)	109(33.0)
>2500g	12(33.3)	136(46.3)	148(44.8)
Postnatal Age at admission			
1 day	24 (66.7)	275 (93.5)	299(90.6)
2-7 days	7(19.4%)	14 (4.8)	21(6.4)
8-14 days	3 (8.3)	4(1.4)	7(2. 1)
15-21 days	1 (2.8)	0	1(0.3)
22-28 days	1(2.8)	1(0.3)	2(0.6)
Place of birth			
Inborn	23(63.9)	252(85.7)	275(83.3)
Out born	13(36.1)	42(14.3)	55(16.7)
Mode of delivery			
Vaginal delivery	14(38.9)	91(31.0)	105 (31.8)
Caesarean section	22(61.1)	203(69.0)	225(68.2)

4.2 Prevalence of blood and blood components transfusion

Thirty six (36) out of the 330 neonates whose medical records were reviwed received at least one blood component transfusion during their hospital stay, that is; until discharge, death or day 28 of life, giving an overall transfusion rate of 10.9% (95% CI 7.6-14.3). More than one type of blood component was needed in 16 (44.4%) neonates. As shown in table 1, females accounted for more than half (52.8%) of the neonates transfused and the majority of them were inborn (23; 63.9%). Most neonates (34/36; 94.4%) were singleton and over half (22/36; 61.1%) had been delivered via caesarean section. Two thirds of the neonates had low birth weight (<2500g), and were preterm (< 37 weeks gestation). All neonates who had a request for blood transfusion made, received blood transfusion.

The median age at the time of first blood transfusion was 9 days (range 1-21), with most neonates, 58.3% (21/36) receiving the blood transfusion in the second postnatal week (Figure 4.1).

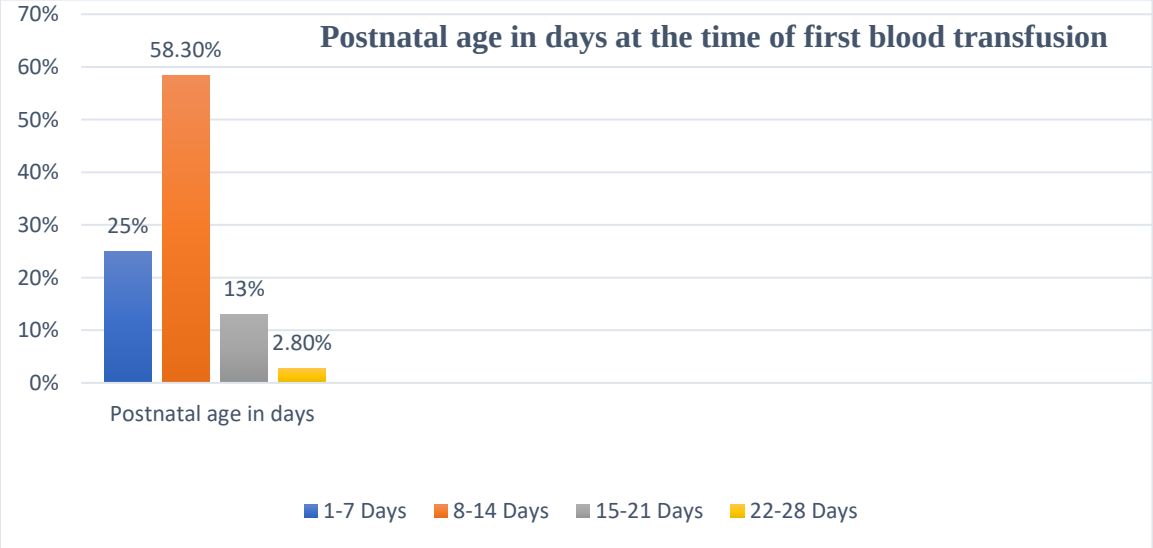

Figure 4.1: Postnatal age in days at the time of first blood transfusion

Figure 4.2 shows the frequency of transfusion of various blood components. The most commonly used blood component was packed RBC accounting for 66.7% (24/36) of all transfusions followed by platelet concentrates at 27.8% (10/36), while fresh frozen plasma accounted for only 5.5% (2/36) of transfusions. Whole blood was not used during the study period and none of the babies required exchange transfusion.

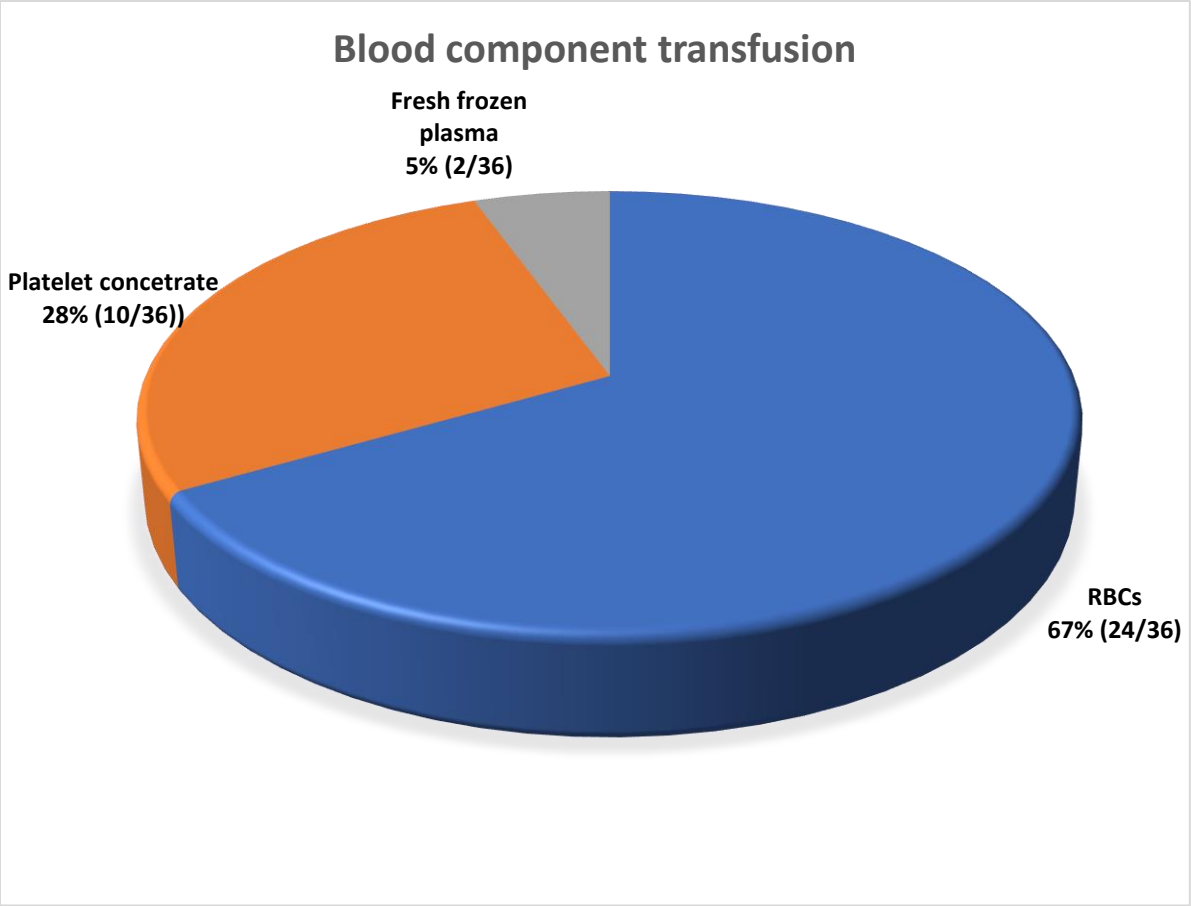

Figure 4.2: Frequency of blood components transfused

4.3 Pretransfusion haematological parameters

Table 4.2 shows the mean Hb levels pre-RBC transfusion based on the postnatal age and the type of respiratory support. The majority of neonates, 87.5% (21/24) were on some form of respiratory support at the time of PRBC transfusion. The overall mean Hb cut off at the time of transfusion was 10.8g/dl (range 6.2-17.7), and was highest in neonates who were

transfused in the 2nd postnatal week (11.3g/dl; range 6.2-15.4) and those on oxygen via nasal prongs (13.4g/dl; range 12.2-15.4) compared to those transfused in the 1st or 3rd postnatal week and those on mechanical ventilation, NCPAP or not on any respiratory support, respectively.

Table 4.2: Hb levels Pre- RBC transfusion based on postnatal age and respiratory support

		Haemoglobin level (g/dl)				
Postnatal age	Number (%) n=24	Overall Mean (range)	On room air Mean (range)	On O2 via nasal prongs Mean (range)	On NCPAP Mean (range)	On mechanical ventilation Mean (range)
1-7 days	6 (25.0)	10.1 (7.4-17.7)	0	0	12.8 (7.9-17.7)	8.8(7.4-9.7)
8-14 days	14 (58.3)	**11.3 (6.2-15.4)**	11.6(9.2-14)	13.8(12.2-15.4)	9.7(9.4-9.9)	9.9(6.2-13)
≥15 days	4 (16.7)	11.1 (9.2-13.0)	9.2	13	0	9.3
Overall	24 (100)	10.8 (6.2-17.7)	10.4(9.2-14	**13.4 (12.2-15.4)**	11.3(7.9-17.7)	9.3(6.2-13)

Overall, 3 (12.5%) neonates received RBC transfusions based on a clinical finding of pallor despite normal Hb levels; one, a neonate on NCPAP on day 4 of life with a pretransfusion Hb of 17.7g/dl, and two, in the 2nd week of life both on oxygen via nasal prongs with a pretransfusion Hb of 14.6g/dl and 15.4g/dl. Four (16.7%) neonates on mechanical ventilation received RBC transfusion based on pretransfusion Hb obtained from the arterial blood gas (ABG). Their mean pretransfusion ABG Hb level was 11g/dl (range 6.2-10.5) while the mean pretransfusion laboratory Hb was 14.7g/dl (range 13.2-15.6). The mean difference between the laboratory and ABG Hb levels was 6.5 $\pm$ 2.8 g/dl (95% CI 3.8 – 9.2).

All the neonates who received platelet transfusion had either confirmed (70%), or suspected (30%) neonatal sepsis and the median platelet count at the time of transfusion was 14 $x10^9$/l (range 3-32). None of the patients had obvious signs of hemorrhage.

Only 2 (5.6%) of the transfused neonates received fresh frozen plasma, and both neonates had active bleeding with deranged coagulation profile. One of the neonates had an INR of 3.95 and the other had an INR of >10 on days 8 and 6 of life respectively.

4.4 Blood components prescribing and monitoring practices

Only 27.8% (10/36) of the neonates transfused had the blood component transfusion prescription written on the treatment sheet or fluid charts, with the need or request for blood transfusion noted only in the patients' notes in the files and/ or the blood transfusion request cards. In addition, only slightly over half (55.6%; 20/36) of the neonates had some documentation of monitoring of vital signs during the blood transfusion. Overall, 16.7% (6/36) of the neonates received furosemide during blood component transfusion. Table 4.3 shows some of the blood components prescribing and monitoring practices noted in the study.

Table 3.4 Some Blood components prescribing and monitoring practices

Blood component	Number n=36	Volume prescribed Mean (range)	Duration of infusion Median (range)	Furosemide Prescribed n=6	Vital signs monitored n=20
PRBC	24	17(10-24.3)	2½ hrs(1¾-6hrs)	3 (12.5)	13 (54)
Platelets	10	17(13-25)	1½ hrs (½- 2¼)	2 (20)	5(50)
FFP	2	12.5 (10-15)	1½ hrs(1-2 hrs)	1(50)	2 (100)

The mean prescribed volume of PRBCs and platelets was 17mls/kg while that of FFP was 12.5mls/kg. The median duration of infusion was 2½ hours for PRBCs and 1½ hours for both platelets and FFP.

4.5 Survey results

To further understand the blood and blood component transfusion practices, a cross-sectional survey was conducted among the clinicians. Questionnaires were distributed to 20 clinicians working in the KNH NBU during the study period comprising of 4 neonatologists, 1 consultant pediatrician, 5 neonatal fellows, and 10 pediatric residents. A total of 19 filled questionnaires were returned yielding an overall response rate of 95%. Overall, only 31.6% (6/19) of the respondents reported that they were aware of some local guidelines on blood and blood components transfusion in neonates. Of these only 2 respondents reported that they often made reference to these guidelines in their practice.

Table 3.3 shows the references that the respondents reported to use when making a decision to transfuse RBCs. Over half of the respondents (57.9%) reported that they used some standard practice guidelines, most from other countries. An equal number of respondents (4/19; 21%) reported that they consulted a colleague prior to making the decision or used personal clinical judgement.

Table 3.3: References cited by respondents in determining need for RBCs in neonates.

Reference	Number (%)
Standard practice guidelines	11 (57.9%)
Personal clinical judgement	4(21%)
Consult colleague(s)	4 (21%)
Guidelines in the UpToDate electronic clinical resource tool	2(10.5%)
Text books	2(10.5%)
Neonatal guide phone application	1 (5.3%)

Note: Some respondents gave more than one response

Three out of the eleven (27.2%) respondents who reported the use of standard practice guidelines in determining their decision to transfuse RBCs cited the United Kingdom guidelines, while two respondents each cited the MOH-Kenya guidelines-2022, Canadian Pediatrics Society guidelines and the Neonatal Guide by the Cape Town Neonatal Consultancy. Two respondents however, failed to specify the standard guidelines they used. Figure 2 shows the commonly referenced standard practice guidelines for RBC transfusion in neonates.

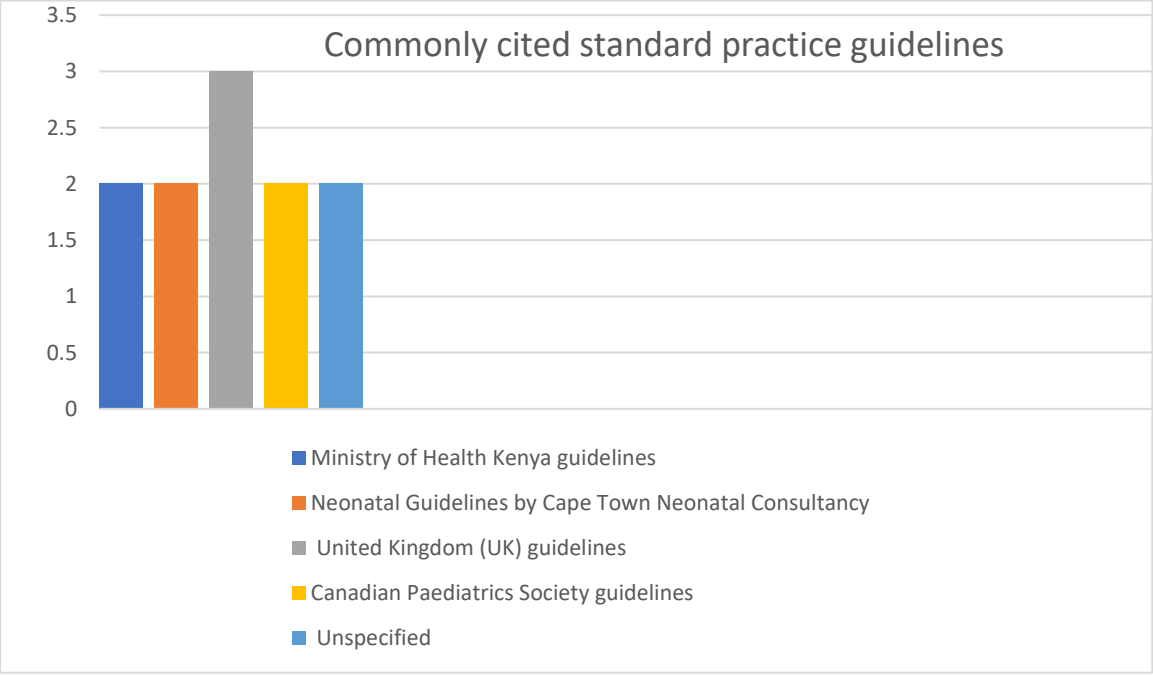

Figure 4. 1: Commonly referenced standard practice guidelines

Table 3.4 show platelet transfusion thresholds for various clinical case scenarios as reported by clinicians. Platelet count cut off below 20×10^9 /L was reported by half of clinicians in non-bleeding neonates, threshold below 50 $x10^9$ was reported by 47.4% of clinicians for bleeding neonates while 52.9% reported a threshold below 100 x 10^9/L for neonates before a surgical procedure.

Table 3.4: Platelet transfusion thresholds for various case scenarios as reported by clinicians

Case scenario	**Platelets Count** < 20x 10^9/L	<25x10^9/L	<30x10^9/L	<50X 10^9/L	<100x x10^9/L	<150x10^9/L
Stable non-bleeding neonate	**9** **50%**	3 16.7%	5 27.8%	1 5.6%	0	0
Bleeding neonate	1 5.3%	0	4 21.1%	**9** **47.4%**	3 15.8%	2 10.5%
Neonate pre-surgery	0	0	1 5.9%	7 41.2%	**9** **52.9%**	0

All clinicians reported that they would transfuse FFP to neonates with coagulopathy with active bleeding. Other indications reported for FFP transfusion included; disseminated intravascular coagulopathy, 89.5% (17/19), coagulopathy without active bleeding, 47.4% (9/19); and thrombocytopenia, 5.3% (1/19).

Two thirds (66.7%) of the clinicians 'routinely' prescribed RBC at 20mls/kg, over half (52.9%) prescribed FFP 15mls/kg while about 40% prescribed platelet at 20mls/kg. Table 3.5 shows the volumes of various blood components as prescribed by clinicians.

Table 3.5: Volumes of various blood components as prescribed by clinicians

Blood components	10ml/kg	15mls/kg	20mls/kg
Red blood cells	5 27.8%	2 11.1%	**12** **66.7%**
Platelets	5 27.8%	6 33.3%	**7** **38.9%**
Plasma	3 17.6%	**9** **52.9%**	4 23.5%

The duration of transfusion ranged from 2- 4 hours for RBCS, and 30 minutes to 4 hours for both platelet and FFP. Parenteral furosemide was 'usually' prescribed with PRBCS, platelets and FFP transfusions by 57.9%, 44.4%, and 38.9% of clinicians, respectively.

Table 3.6 shows clinician's rating of various blood transfusion services and practices in the KNH NBU. 'Use of family/replacement donors compared to voluntary non-remunerated blood donors' was reported as 'acceptable' or 'good' by 73.6% of clinicians while 'timeliness in the issuance of blood and blood products requested from BTU to the KNH NBU' was reported as 'poor' by 58% of clinicians. 'Uniformity in blood and blood components prescribing practices in the KNH NBU was reported as 'acceptable', 'good' or 'very good' by the majority of clinicians, (14/19; 79.4%), while 'monitoring of neonates during blood and blood components transfusion' was reported as 'good' or ' acceptable by more than half of the clinicians (11/19; 57.9%).

Table 3.6: Clinicians' rating of selected blood transfusion services and practices in the KNH/NBU

	Very poor	Poor	Acceptable	Good	Very good
a) Use of family/replacement donors compared to voluntary non-remunerated blood donors	2 10.5%	3 15.9%	**7** **36.8%**	**7** **36.8**%	0
b) Timeliness in the issuance of blood and blood products requested from BTU to the KNH NBU	2 10.5%	**11** **57.9%**	3 15.8%	2 10.5%	1 5.3%
c) The communication and working relationship between the NBU and BTU staff	0	**8** **44.4%**	6 33.3%	2 11.1%	2 11.1%
d) Agreement between clinicians in NBU and BTU staff on the indications/need for various blood products requested	1 5.3%	**6** **31.6%**	**6** **31.6%**	5 26.3%	1 5.3%
e) Uniformity in blood and blood components prescribing practices in the KNH NBU	1 5.3%	4 21.1%	**10** **52.6%**	3 15.8%	1 5.3%
f) Monitoring of neonates during blood and blood components transfusion	2 10.5%	6 31.6%	4 21.1%	**7** **36.8%**	0

DISCUSSION

The principal goal of this study was to provide baseline data concerning blood and blood components transfusion practices in the newborn unit of Kenyatta National Hospital. The strength of this study was that it involved a retrospective review of prospectively collected data of 330 neonates admitted over a three-months period, as well as a cross-sectional survey of 95% the clinicians working in the unit at the time. The results therefore reflect a clear picture of the practice in the unit at the time.

In this study, the prevalence of blood components transfusion was 10.9%. This was similar to the rates of 11.0% and 11.7% reported by Ochoga MO *et al* and Joel-Medewase VI *et al,* respectively, both from Nigeria (26, 59). Almost 70% (69.4%; 25/36) of the neonates who were transfused were preterm (< 37 weeks gestation), and two thirds (24/36;66.7%) had low birth weight <2500g). Blood and blood components usage has been shown to be inversely proportional to the postconceptional age and weight of the neonates.

PRBCs were the most commonly transfused blood components accounting for 68% of all transfusions, followed by platelets at 27.8%. This finding was consistent with other studies (26,29). However, a study by Kuer *et al* in India reported a predominance of platelet transfusions and attributed this to high rates of neonatal sepsis (24). Similarly in our study, all

the neonates who received platelet transfusion had thrombocytopenia associated with either confirmed or suspected neonatal sepsis, and almost all neonates who required more than one type of blood component had sepsis.

The overall mean pretransfusion Hb level in this study was 10.8/dl, with a higher mean cut off of 13.4g/dl unexpectedly reported among neonates who were on oxygen via nasal prongs, compared to those on NCPAP or mechanical ventilation, 11.3g/dl and 9.3g/dl respectively. These findings were in contrast to most standard practice guidelines as well as the recently published ETTNO and TOP RCTs in which the recommended pretransfusion Hb cut offs vary with the level of respiratory support with critically ill neonates on mechanical ventilation receiving transfusion at higher Hb cut off (16,17,40,55,56). The possible reasons for these unexpected findings are threefold. Firstly, although few patients who were on oxygen via nasal prongs received blood transfusion, the decision to transfuse in 40% of them was based on a clinical finding of pallor despite normal Hb levels. While, pallor is a commonly recognized sign of anaemia, it may also be associated with nohematologic conditions such respiratory failure, poor tissue perfusion/shock, or hypoglycaemia (57). Secondly, the much lower levels of Hb at transfusion in neonates on mechanical ventilation may be attributed to the fact that in 40% of them, the decision to transfuse PRBCs was based on pretransfusion Hb levels obtained from the arterial blood gas which was much lower than the Hb from the laboratory sample with a mean difference between the laboratory and ABG Hb levels of 6.5 + 2.8 g/dl (95% CI 3.8 – 9.2). Thirdly, and probably most importantly, the unexpected results may be due to the lack of standardization of RBC prescribing practices in the unit with a wide range of references used by the clinicians, as was demonstrated in the survey.

The median platelet count at the time of transfusion in this study was 14 x109/l (range 3-32), and although most patients had platelet counts < $30x10^9$/l, none of them had obvious signs of hemorrhage. In addition, half of the surveyed clinicians reported that they would consider platelet transfusion in stable non-bleeding neonates if the platelets counts were <20 × 10^9/litre. These findings were consistent with a study by Stanworth et al. (45) who reported that although one third of neonates enrolled in their study developed thrombocytopenia of <20 $x10^9$ platelets per L, 91% did not develop major hemorrhage, and that the nadir platelet count was similar for neonates who had severe, small, or no hemorrhage. There is currently no convincing evidence that low platelet count causes bleeding, or whether infusion of platelets prevents bleeding (46). Recent RCTs show that a lower platelet transfusion cut-off of 20 to 25 × 10^9/litre is beneficial for preterm infants, with lower rates of mortality and major bleeds reported compared to higher platelet transfusion cut off (47- 49).

Fresh frozen plasma was transfused in two (5.6%) neonates in this study, and both had deranged coagulation profile and active bleeding. This rate was slightly lower than the 9.4% reported by Joel-Medewase et al. (26). Studies have shown that coagulation profiles in neonates are poor predictors of clinical hemorrhage, and that abnormal coagulation test findings without symptoms or a risk of hemorrhagic complication do not warrant the transfusion of FFP (51,31). In addition, FFP transfusion has no role in treatment of thrombocytopenia in neonates. However, in this study 47.4% of clinicians reported that they would transfuse FFP to neonates with coagulopathy without active bleeding, and 5.3% would transfuse neonates with thrombocytopenia

The mean volume of PRBCs transfused in this study was 16.9mls/kg (range 10 to 24.3 ml/kg) and the duration of infusion ranged from 1hour and 45 minutes to 6 hours. Two thirds

(66.7%) of the clinicians reported that they 'routinely' prescribe RBC at 20mls/kg. While packed RBCs transfusion volume in neonates is typically between 10 to 20 ml/kg, given at an infusion rate of 5- 6 ml/hr (40, 41), most preterm neonates have been found to tolerate 20 ml/kg well, with a greater increase in Hb and fewer exposures to donors (42). It is also recommended that PRBCs should not to be at room temperature (20–24 °C) for longer than 4 hours and, thus, need to be transfused within that time (1). The mean volume of platelet and FFP transfused was 17.2ml/kg (range 13 to 25 ml/kg), and 17.5ml/kg (range 10 to 15ml/kg), respectively. In addition, the infusion duration ranged from 30mins to 2hrs 15 mins for the platelet, and 1 to 2 hours for FFP. Neonatal platelets are typically administered at volumes of 10-20 ml/kg, and the recommended volume of FFP in neonatal transfusion is 10-20mls with both blood components infused at a rate of 10-20 ml/kg/ hr (31,54).

In the survey of clinicians working in the KNH NBU, 68.4% (13/19) reported that they were not aware of any local guidelines on blood and blood components transfusion in neonates. This is despite the fact that there is a Ministry of Health, Kenya guideline on the appropriate use of blood, blood components and products that was launched in the year 2022 and has a section on neonatal blood and blood components transfusion (59). The possible reason for this is that these guidelines may not have not been disseminated widely to the clinicians. In the rating of selected services and practices on blood and blood components transfusion in KNH and/or NBU, 'Use of family/replacement donors compared to voluntary non-remunerated blood donors' was reported as 'acceptable' or 'good' by 73.6% of clinicians.

Interestingly, although only slightly over half (55.6%; 20/36) of the neonates had their vital signs monitored during blood transfusion, 'monitoring of neonates during blood and blood components transfusion' was reported as 'good' or 'acceptable' by 57.9% of clinicians in the

survey. In addition, despite the differences noted among clinicians in Hb thresholds for RBC transfusion, the wide range of references reported to be used in decisions-making, and the fact that only 27.8% (10/36) of the neonates had the blood component transfusion prescription written on the treatment sheets or fluid charts, 'uniformity in blood and blood components prescribing practices in the KNH NBU' was reported as 'acceptable', good or 'very good' by the majority of the clinicians (79.4%; 11/19). These contradictory findings may be due to the fact that no prior audit of blood and blood component transfusion practices had been conducted in the unit and therefore the overall assumption may have been that the practice was within acceptable standards.

CONCLUSION

The prevalence of blood components use in the KNH NBU was 10.9% with PRBC being the most commonly transfused blood component. There was a wide variation in Hb thresholds for PRBC transfusion among clinicians and suboptimal monitoring of neonates during transfusion of all types of blood components. The transfusion thresholds for platelets and FFP were however in accordance with the current available evidence and recommendations.

RECOMMENDATIONS

There is an urgent need to address the identified gaps by implementing quality improvement activities on blood and blood components transfusion practices in the KNH NBU. Adoption and adherence to one clinical practice guideline, such as the Ministry of Health-Kenya 2022 guidelines for appropriate use of blood, blood components and blood products will help standardize the blood transfusion practice in the unit, and ensure rational and judicious use of these resources. A similar study in other wards in the KNH is recommended in order to identify and address any gaps. A larger multi-center study will provide more information on

the extent to which healthcare facilities are adhering to the recommended national guidelines, and potentially inform a change in dissemination strategies.

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BUDGET AND BUDGET JUSTIFICATION

	Research Stage	Item	Cost (Ksh)	Total cost (Ksh)
1	Proposal development	Internet bundles Printing draft proposal Pre-testing questionnaire	5,000 10,000 3,000	18,000
2	Data collection	Training research assistant Research assistant's allowance	4,000 36,000	40,000
3	Data analysis	Statistician's allowance Internet bundles	25,000 5,000	30,000
4	Results presentation	Printing and binding final book	13,000	13,000
	GRAND TOTAL			101,000

Source of funding: Principal investigator's own resources.

APPENDICES

APPENDIX 1: DATA ABSTRACTION TOOL

Study number _____

Investigator's initials _____ Date of data collection _____

A) Mother's demographic and clinical characteristics

1. Age in years _____
2. Parity _____
3. Was the pregnancy ☐ Singleton OR ☐ Multiple gestation
4. Is there maternal history of any of the following illnessses? Tick where applicable.

   ☐ HTN ☐ DM ☐ APH ☐ ITP ☐ Others, specifiy_____

5. Is there history of blood transfusion during birth hospitalization?

   ☐ Yes ☐ No

   If yes, what blood product was transfused?

   ☐ Whole blood ☐ PRBC ☐ Platelets ☐ FFP

B) Infant's demographic and clinical characteristics

5. Gender ☐ Male ☐ Female
6. Date of birth (dd/mm/yy) _____
7. Date of admission _____
8. Birth weight in grams_____
9. Clinical gestational age at birth _____weeks.
10. Apgar score at 5 minutes _____
11. Mode of delivery

    ☐ SVD ☐ CS ☐ Breech

12. Place of birth KNH ☐ Referral ☐

13. Diagnoses at admission _____

_____

_____

14. Haemoglobin level at admission_____g/dl

15. Platelet count at admission _____

16. INR at admission _____

C) Has the infant received any blood transfusion?

☐ Yes ☐ No

If yes,

17. What was the age in days at 1st transfusion? _____

18. What was the weight in grams at 1st transfusion? _____

19. What blood product was transfused?

☐ Whole blood ☐ PRBC ☐ Platelets ☐ FFPs

20. If whole blood or PRBCs, what type of transfusion was it?

☐ Excahnge transfusion ☐ Top-up transfusion

20. What is the infant's blood group?_____

21. What was the age of blood/ blood component transfused?_____

22. What volume of blood product was transfused? in _____mls

_____mls/kg

23. Over what duration was the blood product administered? _____

24. What was the patient's respiratory support at the time of blood transfusion?

☐ Off Oxygen or resp. support ☐ On Oxygen or CPAP ☐ Ventilated

25. Any additional diagnosis at the time of 1st transfusion?

☐ Yes ☐ No

If yes, specify_____

_____

24. What were the pretransfusion a) Haemoglobin level _____

b) Platelet count _____

c) INR_____

25. What were the indications for blood transfusion as documented in the blood request form? _____

_____

26. What volume of blood/ blood component was requested for as documented in the blood request form?_____

APPENDIX 2: QUESTIONNAIRE/ SURVEY TOOL

Serial No._____

BLOOD AND BLOOD COMPONENTS TRANSFUSION PRACTICES IN KNH NBU

Objective: To determine the transfusion practices of blood and various blood components in the Newborn Unit of Kenyatta National Hospital.

1. Designation	○ Paediatric resident ○ Neonatologist ○ HND RCO	○ Neonatology fellow ○ Medical officer

2. Have you prescribed/recommended any blood or blood components transfusion since you began working in the KNH newborn unit?

○ Yes ○ No

3. Are you aware of any local/ Kenyan guidelines on neonatal blood and blood components transfusion?

○ Yes ○ No

If Yes, please specify which one (s) :_____

4. If yes, to number 3 above, do you routinely refer to these guidelines when prescribing blood and blood components to neonates?

○ Yes ○ No

5. What is/are your reference (s) when determining the need for red blood cell transfusion in neonates?

○ Text book (please specify which one) _____

○ Standard Practice Guidelines (please specify which one) _____

_____

○ Consult a colleague

○ Other (please specify) _____

6. What factors, in addition to haemoglobin/ haematocrit level influence your decision to transfuse red blood cells in neonates? (tick all applicable)

○ Pallor ○ Gestational age ○ Weight gain/loss

○ Postnatal age ○ Respiratory support

○ Others, please specify _____

7. At what infusion rate (in mls/kg/hr) or over what duration (hours or minutes) do you transfuse the following blood products?

   a) Red blood cells_____

   b) Platelets _____

   c) Plasma _____

8. What volume of the following blood products do you routinely prescribe? Please tick where applicable or specify in writing.

	10ml/kg	15mls/kg	20mls/kg	Other (Please specify in writing)
Red blood cells				
Platelets				
Plasma				

9. Do you usually give furosemide (Lasix) with:

   a) Red blood cell transfusion? O Yes O No

   b) Platelet transfusion? O Yes O No

   c) Plasma transfusion ? O Yes O No

10. In which of the following clinical settings/scenarios in the neonate would you consider transfusion of fresh frozen plasma (FFP)? Please tick all applicable.

O Abnormal coagulation profile with bleeding

O Thrombocytopenia

O Abnormal coagulation profile without bleeding

O Partial exchange transfusion for hyperviscosity

11. What threshold for platelet transfusion would you consider in the following case scenarios? (Please tick where applicable)

Case scenario	**Platelets Count**					
	< 20x 10^9/L	<25x10^9/L	<30x10^9/L	<50X 10^9/L	<100x x10^9/L	<150x10^9/L
Stable non-bleeding neonate						
Bleeding neonate						
Neonate pre-surgery						

12. How would you rate the following blood transfusion services or practices in the KNH? (please tick where applicable)

	Very good	Good	Acceptable	Poor	Very poor
g) Use of family/replacement donors compared to voluntary non-remunerated blood donors					
h) Timeliness in the issuance of blood and blood products requested from BTU to the KNH NBU					
i) The communication and working relationship between the NBU and BTU staff					
j) Agreement between clinicians in NBU and BTU staff on the indications/need for various blood products requested					
k) Uniformity in blood and blood components prescribing practices in the KNH NBU					
l) Monitoring of neonates during blood and blood components transfusion					

THANK YOU FOR YOUR PARTICIPATION.

APPENDIX 3: HEALTHCARE PROVIDERS' INFORMATION AND CONSENT FORM

Blood and blood components transfusion practices in the newborn unit, Kenyatta National Hospital.

Principal Investigator: Dr. Serah Kajuju Ngugi

Supervisors: Dr. Jalemba Aluvaala- University of Nairobi

Dr. Wairimu Kimani- Kenyatta National Hospital

Investigator Note: Thank you for agreeing to read this form. It offers information about this study which will help you decide if you will take part in this study or not.

Introduction: Blood transfusion is a commonly used supportive therapy in neonatal units worldwide. There is however currently no consensus on neonatal transfusion thresholds for various blood components. As a result, there is a wide variation in blood transfusion practices among countries, neonatal units and clinicians. There is paucity of data on blood transfusion practices in neonatal units in Kenya. This study therefore seeks to carry out a cross-sectional survey to determine the blood transfusion practices among clinicians in the newborn unit of Kenyatta National Hospital.

What will happen if you decide to participate in this study?

If you agree to participate in this study, I will give you a questionnaire to fill comprising 13 questions; 8 in multiple choices format, 4 as open-ended questions, and 1 question as a Likert scale. The questionnaire will take you between 10-15 minutes to fill and covers blood transfusion practices of blood and various blood components.

Are there any risks associated with this study?

There are no foreseeable risks associated with this study. The information you give will be held in strict confidence and only used for the purpose of the study. No identifying information e.g. Names or signatures will be used. We will instead use code numbers to identify you.

W**hat are the benefits of participating in this study?**

The information you provide will help us to better understand the transfusion practices of blood and various blood components in the NBU of KNH and, potentially inform the development of local guidelines to standardize the practice.

What are your other choices?

Your decision to participate in this study is voluntary. You are free to decline participation in the study and you can withdraw from the study at any point.

Problems or questions*:* If you have any questions about the study or about the use of the results you can contact the principle investigator: Dr. Serah Ngugi, on 0721-298698

If you have any questions on your rights as a research participant you can contact Kenyatta National Hospital/University of Nairobi Ethics and Research Committee (KNH-UoN ERC) by email uonknh-erc@uonbi.ac.ke or on 02 2726300 Ext 44102

By agreeing to fill this questionnaire is an indication that you understand the conditions of this study and that you verbally consent to participate in it.

Investigator's signature: _____

Date: _____

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Ref: KNH-ERC/A/137

29th March, 2023

Dr. Serah Kajuju Ngugi
Reg.No.H120/41438/2021
Fellow in Neonatal Medicine
Dept. of Paediatrics & Child Health
Faculty of Health Sciences
University of Nairobi

KENYATTA NATIONAL HOSPITAL APPROVED 29 MAR 2023 KNH/UoN-ERC P.O. Box 20723 - 00202 NAIROBI

Dear Dr. Ngugi,

RESEARCH PROPOSAL: BLOOD AND BLOOD COMPONENTS TRANSFUSION PRACTICES IN THE NEWBORN UNIT, KENYATTA NATIONAL HOSPITAL (P8/01/2023)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P8/01/2023.** The approval period is 29th March 2023 – 28th March 2024.

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to KNH-UoN ERC.

Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://research-portal.nacosti.go.ke and also obtain other clearances needed.

Yours sincerely,

DR. BEATRICE K.M. AMUGUNE
SECRETARY, KNH-UoN ERC

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