"AN ANALYSIS OF BLOOD TRANSFUSION PRACTICE AT THE KENYATTA NATIONAL HOSPITAL INTENSIVE CARE UNIT."

A DISSERTATION SUBMITTED IN PART FULFILMENT OF THE REQUIREMENT FOR THE AWARD OF THE DEGREE OF MASTER OF MEDICINE IN ANAESTHESIA AT THE UNIVERSITY OF NAIROBI.

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1.1 TITLE

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1.2 DECLARATION

This thesis work is my original work and to my knowledge has not been presented for a degree in any other university.

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GOD BLESS YOU ALL!

1.4 DEDICATION

'The great and glorious masterpiece of man is to know how to live to purpose'. ***Michel de Montaigne.***

This work is dedicated to my loving parents. Damian and Josephine Mutiso. and my dear husband. James Mbithi. for their constant presence. encouragement and prayers in all the phases of my life. May the good Lord bless you abundantly.

'If we do not plant knowledge when young. it will not give us shade when we are old'. ***Lord Chesterfield.***

1.5 TABLE OF CONTENTS

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1.7 ABBREVIATIONS:

KNH: - Kenyatta National Hospital

ICU: - Intensive Care Unit

0_2 - Oxygen

2. 3 DPG: - 2. 3 diphosphoglycerate

RBC: - Red Blood Cell

PO_2:- Partial Pressure of Oxygen.

D.IC:- Disseminated Intravascular Coagulopathy

F.F.P:- Fresh Frozen Plasma

EPO: - erythropoietin

Hb: - Haemoglobin

APACHE: - Acute Physiology & Chronic Health Evaluation.

SOFA: - Sequential Organ Failure Assessment Score

UON: - University of Nairobi

E.R:- Extraction Ratio

Ig A: - Immunoglobulin A

C.O:- Cardiac Output.

C.I:- Cardiac Index

S.V.R:- Systemic Vascular Resistance.

CvO_2 - Venous oxygen content

C.P.D.A:- Citrate Phosphate Dextrose –Acetate.

Ca O_2 :- Arterial Oxygen Content.

W.H.O:- World Health Organization.

1.8 ABSTRACT

Blood transfusion in the critically ill is a subject that has been under focus in many parts of the world in order to establish safe and proper transfusion practices. This study was thus undertaken so as to determine the transfusion practices at the Kenyatta National Hospital Intensive Care Unit, and in so doing, to be able to highlight some recommendations on safe transfusion practice.

The study design was a prospective, observational, descriptive study. It was carried out from December 2007 to March 2008. A total of 64 patients were analysed, among them 40 males and 24 females, as long as they required transfusion at some point while at the ICU. The patients' ages ranged from 1 to 90 years with a mean of 33.39 years. Among these, 10 were children aged 12 years and below.

The study established a blood transfusion rate of 21.26%, out of the total number of ICU inpatient admissions that were 301 during the study period. The commonest indication for transfusion was anaemia without any signs of active bleeding with 22 males (55%), and 13 females (54.2%). In the patients assessed, seventeen (42.5%) of the males were being given a haematinic, while for the females, six (25%) of them received a haematinic during the study period. The respiratory and the neurological systems were the most common primary admission categories (36 and 35 patients, i.e. 56.25% and 54.7%) respectively, while most of the admission types were emergency with 45 patients (70.3%).

Twenty nine patients (45.3%) were transfused one unit of whole blood. while twenty five (39.1%) received two units of whole blood. Out of all the patients transfused. seven (10.9%) got a transfusion reaction. with the majority. five patients (7.8%) being a transient febrile reaction.

The mean haemoglobin level at admission was 9.97grams/decilitre for all the patients. The mean pre-transfusion haemoglobin level was 7.08grams/decilitre with a minimum of 3.0 and a maximum of 10.0 grams/decilitre. while the mean post-transfusion haemoglobin level was 9.72 grams/decilitre. with a minimum of 5.90 and a maximum of 14.90 grams/decilitre. The mean duration of stay in the critical care unit before the patients got their first transfusion was 8.23 days.

Statistical analysis revealed a positive correlation between the pre-transfusion and the post-transfusion haemoglobin level. with a Spearman Rank Correlation $R=0.624$: $p<0.05$ (0.000). There was also a positive correlation between the amount of blood transfused and the presence of a transfusion reaction. [Mann Whitney U test $Z=2.033$: $P<0.05$ (0.042)].

Blood transfusion should therefore be used sparingly, bearing in mind the potential risks and poor outcomes in critically ill patients.

2.0 INTRODUCTION & LITERATURE REVIEW

2.1 History

Samuel Pepys recorded the first blood transfusion in his celebrated diary (2). On November 14, 1666, Pepys wrote that Richard Lower of the royal society made the first direct blood transfusion from the artery of one dog to the vein of another. Mr Lower used quills to convey the blood (3).

This feat was dependent upon the discovery made by William Harvey earlier that century of the course of blood in the circulation. Harvey announced his discovery to the college of physicians in 1616 and published his treatise on it, entitled ' Exercitato anatomica de motu cordis et sanguinis in animalibus', in 1628

Haemoglobin

This is the protein molecule in red blood cells which carries oxygen from the lungs to the tissues and returns carbon dioxide to the lungs. It consists of 6 % heme and 94 % globin. Each globin chain enfolds a single heme moiety, consisting of a protoporphyrin-IX ring complexed with a single iron atom in the ferrous (Fe^{2-}) state, positioned in a manner for reversible binding of oxygen. Each heme moiety can bind a single oxygen molecule; every molecule of haemoglobin can thus transport up to four oxygen molecules. The haemoglobin level is expressed as the amount of haemoglobin in grams per decilitre of whole blood.

Measurement of haemoglobin

Several methods exist. Currently, this is done by automated machines designed to perform several different tests on blood.

Within the machine, the red blood cells are broken down to get the haemoglobin into a solution. The free haemoglobin is exposed to chemical containing cyanide which binds tightly with the haemoglobin molecule to form cyan-met haemoglobin. By shining a light through the solution and measuring how much light is absorbed (specifically at a wavelength of 540 nanometres), the amount of haemoglobin can be determined.

Normal haemoglobin values

These values have been taken from the World Health Organisation (W.H.O) guidelines (4). These are also the same values used as the reference ranges at the Kenyatta National Hospital:-

Age/gender	Normal haemoglobin range (g/dl)	Anaemic if Hb range less than: (g/dl)*
Birth (full-term)	13.5-18.5	13.5 (Hct 34.5)
Children: 2-6 months	9.5-13.5	9.5 (Hct 28.5)
Children: 6 months-6 years	11.0-14.0	11.0 (Hct 33.0)
Children: 6-12 years	11.5-15.5	11.5 (Hct 34.5)
Adult males	13.0-17.0	13.0 (Hct 39.0)
Adult females: non-pregnant	12.0-15.0	12.0 (Hct 36.0)
Adult females: pregnant		
First trimester: 0-12 weeks	11.0-14.0	11.0 (Hct 33.0)
Second trimester: 13-28 weeks	10.5-14.0	10.5 (Hct 31.5)
Third trimester: 29 weeks-term	11.0-14.0	11.0 (Hct 33.0)

* These values simply define anaemia. They are often used as thresholds for investigation and treatment, but are *not* indications for transfusion.

These values may vary slightly between laboratories.Abnormally high haemoglobin levels may be found in patients from high altitudes, smokers, those with dehydration, lung disease, some kinds of tumours, in polycythemia rubra Vera and with abuse of the drug erythropoietin (epogen) by athletes for blood doping purposes.

2.2 CAUSES OF ANAEMIA IN CRITICAL CARE PATIENTS

Anaemia can be due to various factors related to blood loss, reduced erythropoiesis or increased red blood cell destruction.

Blood loss:-

This is as it occurs in trauma or surgical patients (5). There may also be losses due to invasive procedures such as catheter or drain insertion. or with tracheostomy which is particularly common in the ICU patients. There may also be occult blood loss from the gastro-intestinal tract (6). Repeated blood sampling is another cause. Von Ahsen et al in 1999 found an average of 41 millilitres of blood in the A.B.C study (Anaemia and Blood transfusion in the Critically ill patients) (1).

Reduced erythropoiesis:-

It can be the result of nutritional or haematological factors. The pro-inflammatory cytokines such as tumour necrosis factor (T.N.F). interferon gamma and transforming growth factor beta all reduce the production of erythropoietin (7. 8. and 9).

Increased red blood cell destruction:-

This results from haemolysis. The red blood cell lifespan can be reduced by critical illness. especially due to an alteration in the red blood cell structure (10. 11).

Other factors:-

During the first 3 days of ICU stay. there is usually a drop of Hb level by about 1 gm/ dl/ day (32). After the third day in the I.C.U. there is a less marked fall in the haemoglobin level. which is related to the disease severity and is assessed by the APACHE 2 and SOFA scores.

This is more marked in septic patients, thus supporting the role of pro-inflammatory cytokines in the pathogenesis of anaemia in the critically ill. Nguyen et al (31) studied the time course of Hb levels in 91 non-bleeding ICU patients and they found that the Hb concentration fell by 0.52+0.69 gm/ dl/ day. For the 33 patients who stayed in the ICU longer than 3 days, the fall was more marked in the first three days than later on during their ICU stay (0.66+0.84 gm/ dl/ day, versus 0.12+0.29 gm/ dl/ day).

2.3 THE TYPE OF PATIENTS THAT REQUIRE BLOOD TRANSFUSION IN THE I.C.U

More surgical than medical ICU patients are transfused .Groeger et al in the U.S.A got a transfusion rate of 27% in the surgical ICU and 16% in the medical ICU (12) .Duration of stay is also important. Corwin et al found that 85% of patients staying more than 1 week in ICU received transfusion (13).

The type of hospital into which the patient is admitted is also important. The transfusion rates were 44% in university hospitals, 40 % in regional hospitals and 35%in community hospitals according to ABC (Anaemia and Blood transfusion in the critically ill) study (1).This is despite the fact that the average transfusion trigger was the same at 8.4 gm/dl across all the hospital types.

The disease severity also matters according to the SOFA score. In the same ABC study (1), the mean SOFA score was 5.4 in the academic hospitals, 5.1 in the regional hospitals and 4.5 in the community hospitals ($p<0.001$). This could be attributed to the fact that sicker patients were admitted to the teaching hospitals.

The age is also an important determinant. In the ABC study(1), the transfusion rates were: 30% for patients less 30 years, 40 % for patients between 50-60 years and 54% for patients older than 80 years ($p<0.001$).Older patients also have more severe disease as indicated by SOFA and APACHE II scores. They also have longer ICU stays (6days versus 3 days for the younger patients) (1).

In the ABC study (1), the overall mortality was 13.5%, but 18.5% for transfused patients compared to 10.1% for those who were not transfused. The Hebert trial (14) suggests that apart from patients with acute coronary syndromes, patients tolerate much lower Hb levels than previously thought, and the well accepted transfusion trigger of 10 gm/dl can be acceptably lowered in many patients.

Using the Hb value as a transfusion trigger requires definition of the 'optimal' haemoglobin, which is subjective measure and varies according to multiple factors; for example, the optimal haemoglobin may be different for surgical and non surgical patients, for children and the elderly, for a patient with chronic anaemia, coronary artery disease or compromised cardiac contractility.

Other factors including the severity of the disease process as well as the underlying cause of the anaemia will also determine the optimal Hb of any individual patient. The optimal Hb is, in fact, a balance between the benefits of maximum Hb levels and potential adverse effects of blood transfusion and a raised haematocrit.

The critical Hb is perhaps more easily defined than the optimal Hb, being the Hb level below which the oxygen delivery is compromised and regional ischaemia may occur leading ultimately to organ dysfunction and failure.

2.4 TRANSFUSION AND OUTCOME

The possible relationship between blood transfusion and poor outcome has led several centres to review their transfusion practices .There are two main reasons to give a blood transfusion in a critically ill patient.

1. **To increase tissue oxygenation**: The Hb level is, with cardiac output and the $Pa0_2$ an essential determinant of oxygen transport. Nevertheless, increased Hb levels via transfusion will not necessarily increase tissue oxygenation. By increasing the number of red blood cells, the blood viscosity increases which in turn can lower cardiac output and hence limit oxygen delivery (15, 16).

   Also, blood transfusions rarely increase oxygen uptake except under extreme condition where oxygen uptake is directly dependent on oxygen delivery, essentially in circulatory shock associated with hyperlactatemia (17, 18, and 19) or in severe anaemia with Hb levels less than 6 gm/dl.

   Hebert and chin-yee (20) identified 14 studies in which the impact of blood transfusion on oxygen kinetics was assessed, and only 5 reported an increase in oxygen consumption following transfusion.

   Good tolerance to anaemia is due to increases in cardiac index (CI) and oxygen extraction ratio (O_2ER) which maintain oxygen consumption (VO_2).However, even though a high cardiac index in an anaemic patient may appear to be adequate, if analysed in isolation the cardiac response may still be inadequate for the degree of anaemia.

The CI: O_2ER ratio can help to assess the adequacy of the cardiac index during anaemia in critically ill patients with a low CI: O_2ER ratio suggesting an inadequate cardiac index response to anaemia (21).

2. **To avoid myocardial ischemia**: During anaemia the high cardiac output (due to low viscosity and adrenergic stimulation) augments myocardial oxygen demands and patients with acute myocardial instability tolerate anaemia poorly. A large retrospective study of 78.974 ICU patients aged more than 65 years with acute myocardial infarction had reduced mortality with transfusion for haematocrit less than 33% (22).

2.5 OXYGEN DELIVERY AND OXYGEN CONSUMPTION

This is a function of arterial oxygen content [CaO_2] and cardiac output .CaO_2 is in turn a function of Hb level. Hb saturation (SaO_2) and O_2 dissolved in plasma (PaO_2).

CaO_2 is expressed as the number of ml of oxygen contained in 100ml of blood and is calculated as follows:--

$$CaO2 = [Hb \times 1.34 \times SaO2] + [0.003 \times PaO2]$$

The rate of oxygen delivery [DO_2] to the tissues is dependent on the product of cardiac output [co] and the arterial oxygen content of blood. Oxygen delivery to the tissues is calculated as follows:-

Oxygen delivery = cardiac output x $CaO_{2\,[arterial}$ oxygen content].

These simple calculations highlight the inadequacy of previous transfusion practices that considered Hb concentration without reference to cardiac output or Hb saturation.

Oxygen consumption

This is the product of cardiac output and the difference between arterial oxygen content and the venous [CVO_2]:-

Oxygen consumption = CO x [CaO_2 – $CV0_2$]

Where, CO= cardiac output.

CaO_2 = arterial oxygen content.

CvO2= venous oxygen content.

Factors that increase oxygen extraction include sepsis, hyperthermia and any other state of high metabolic activity, such as hyperthyroidism (21).

2.6 OXYGEN EXTRACTION RATIOS AND MIXED VENOUS OXYGEN SATURATION

The ER [extraction ratio] defines what fraction of total oxygen delivered is consumed or extracted by tissues, as follows:

ER = oxygen consumption / oxygen delivery

ER = [CO x CaO_2 – CVO_2] / [CO*CaO_2]

= [CaO2-CvO2] / CaO2

The mixed venous oxygen saturation reflects the oxygen consumption of many vascular beds, with some tissues (muscle, skin, viscera) extracting less oxygen and others (brain, heart) extracting proportionally more. Organs with the greatest extraction ratios will have the least oxygen reserve. Because the heart has the highest extraction ratio, it is the organ at greatest risk under conditions of normovolemic anaemia (24).

2.7 ANAEMIA AND THE METABOLIC REGULATION OF OXYGEN DELIVERY IN CRITICAL ILLNESS

The ability to tolerate low Hb levels, even in critically illness, is explained by the circulation's efficient compensation to anaemia (25). Tissue oxygenation requires that oxygen supply be 'matched' with oxygen needs, and supply can be understood by review of the oxygen delivery equation, as shown above.

Blood flow in response to a falling Hb concentration is regulated at three levels of circulation (25):-

I. central (by increasing the cardiac output)
II. regional (this is by redistribution of blood flow between organs)
III. microregional (this is by redistribution of blood flow within the organ)

In critical illness, limitations to tissue oxygenation affect all three levels of circulation. Oxygen delivery is first redistributed to the heart and brain because the ability to increase oxygen extraction is limited. This is from 'non vital' organs such as the splanchnic circulation. In addition, central and micro-regional circulations also adapt in anaemia by an increase in cardiac output and by microcirculatory changes that promote more oxygen extraction (23).

2.8 COMPENSATORY MECHANISMS DURING ANAEMIA:-

When anaemia develops but blood volume is maintained (isovolemic haemodilution), four compensatory mechanisms serve to maintain oxygen delivery:

1. Increase in cardiac output.
2. A redistribution of blood flow to organs with greater oxygen requirement.
3. Increase in the extraction ratios of some vascular beds.
4. Alteration of oxygen – Hb binding to allow the Hb to deliver oxygen at lower oxygen tensions.

2.8.1. INCREASED CARDIAC OUTPUT

This is due to an increase stroke volume brought about by decrease in systemic vascular resistance (SVR).

There are 2 main determinants of SVR: - (26)

- Vascular tone and
- Viscosity of blood.

As the haematocrit decreases, the reduction in blood viscosity reduces the systemic vascular resistance and blood flow to the tissues. Because oxygen transport peaks at hematocrits of 30% oxygen delivery may remain constant between the haematocrits of 45 to 30% (26). The exact Hb value at which cardiac output rises varies among individuals and is influenced by age and whether the anaemia is acute or develops slowly (27).

2.8.2. REDISTRIBUTION OF CARDIAC OUTPUT

Blood flow to the tissues increases. but this is not equal. Organs with higher extraction ratios (brains and heart) receive disproportionately more of the increase in blood flow than organs which lower extraction ratios (muscle. skin. viscera).

Coronary blood flow may increase by 400 – 600%. Because the heart under basal conditions already has a high extraction ratio. (between 50 – 70% vs. 30% in most tissues). and the primary compensation for anaemia involves cardiac work (increase cardiac output). the heart must rely upon redistribution of blood flow to increase oxygen supply (28).

2.8.3. INCREASED OXYGEN EXTRACTION

This is thought to play an important adaptive role when the normovolemic haematocrit drops below 25%. Increased oxygen extraction in multiple tissue beds leads to an increase in mixed venous oxygen saturation. Some organs (brain. heart) already have a limited capacity to increase oxygen delivery by this mechanism (24).

2.8.4. CHANGES IN OXYGEN – HAEMOGLOBIN AFFINITY

The affinity of Hb for oxygen is described by the sigmoid shaped oxygen – Hb dissociation curve. The curve relates the partial pressure of oxygen in the blood to the % saturations of the Hb molecule with oxygen. The partial pressure of oxygen at which the Hb molecule is 50% saturated with oxygen and 50% unsaturated is termed the P_{50}. The P_{50} in adult Hb at 37° C and a pH of 7.4 is 27 mmHg.

When the curve is shifted to the left. as with hypothermia or alkalosis. the P_{50} is lowered (29). With a lower P_{50}. the Hb has more affinity and requires lower partial pressures to release oxygen to the tissues i.e. the Hb molecule does not release 50% of its oxygen until an ambient PO2 of less than 27mmHg is reached. This may impair tissue oxygenation.

By contrast. right shifting the oxygen – Hb curve. as occurs with hyperthermia or acidosis. results in an increase in P_{50}. decreases Hb affinity for the oxygen molecule. and release of oxygen to tissues at higher partial pressures of oxygen.

When anaemia develops slowly. the affinity of Hb for oxygen may be decreased. i.e. the curve is right shifted. as a result of the accumulation in red blood cells of 2. 3 – diphosphoglycerate (29). Synthesis of supranormal levels of 2. 3 DPG begins at an Hb of 9 gm/dl. At Hb levels of 6.5. the curve is shifted more prominently. All stored red blood cells become depleted of 2. 3 DPG. Temperature reductions and storage related pH decreases also reduce the P_{50} of stored blood.

These changes are however quickly reversed in vivo but the re-synthesis of 2. 3 DPG by the red blood cells may require 12-24 hours or longer (28).

ISOVOLEMIC ANAEMIA VERSUS ACUTE BLOOD LOSS:-

Although the same compensatory mechanisms are operative in acute and chronic anaemia. they have different degrees of importance and occur at different levels of Hb. With acute blood loss, hypovolemia induces stimulation of the adrenergic nervous system, leading to vasoconstriction and an increased heart rate. Increased cardiac output does not contribute.

In chronically anaemic patients, cardiac output may not change until the Hb decreases to approx 7 -8 gm/dl (30). In these patients, the accumulation of 2, 3 DPG in the red blood cells, thereby increasing the P_{50} of Hb, is the important first mechanism for compensation.

CONDITIONS THAT MAY DECREASE TOLERANCE FOR ANAEMIA AND INFLUENCE THE RED BLOOD CELL TRANSFUSION THRESHOLD.

There are various conditions which would reduce the ability of the red blood cell to tolerate anaemia and thus influence the decision by the clinician on the threshold for transfusion.

Increased oxygen demand, as would occur with hyperthermia, hyperthyroidism or in pregnancy, leads to an imbalance in the demand-supply relationship in such patients who also have a reduced haemoglobin level. Oxygen delivery to the tissues is thus reduced. Anaemia is poorly tolerated in such patients and the transfusion threshold is therefore lowered. This also applies to patients with impaired oxygenation, such as patients with pulmonary disease or in increased altitudes (31).

Patients with a limited ability to increase cardiac output also tolerate anaemia poorly and will blood transfusion at much higher haemoglobin levels. Such patients include those with coronary artery disease, myocardial dysfunction (infarction or cardiomyopathy) or patients on beta- adrenergic blockade. During anaemia, the increased cardiac output (due to reduced viscosity and adrenergic stimulation) augments myocardial oxygen demands, and hence the reduced threshold for transfusion (22).

There is also decreased tolerance for anaemia in patients who have inability to redistribute cardiac output. This includes patients with decreased systemic vascular resistance states, such as in patients with sepsis and post-cardiopulmonary bypass. This also applies to patients with occlusive vascular disease, cerebral or coronary (32).

A left shifting of the oxygen-haemoglobin dissociation curve, such as occurs with alkalosis and hypothermia, leads to a lowering of the p50. With this, the Hb molecule has more affinity and requires lower partial pressures to release oxygen to the tissues, i.e., the Hb molecule does not release 50% of its oxygen until an ambient PO_2 less than 27 mmHg is reached. This may impair tissue oxygenation (29).

The presence of abnormal haemoglobin in the circulation also influences the transfusion threshold (33). The presence of stored red blood cells is associated with reduced levels of 2, 3 DPG, leading to right shifting of the oxygen- haemoglobin dissociation curve and impairment of tissue oxygenation. Acute anaemia is also associated with limited 2, 3 DPG compensation (28).

2.9.0 RISKS OF BLOOD PRODUCTS ADMINISTRATION

2.9.1. RISKS ASSOCIATED WITH TRANSFUSION OF RED BLOOD CELLS:-

i) **Citrate intoxication;**

The citrate in the CPDA anticoagulant solution prevents coagulation of stored blood by chelating ionized calcium, leading to signs of hypocalcaemia, hypotension, narrow pulse pressure, elevated ventricular end- diastolic pressure and increased central venous pressure.

ii) **Acid base balance;**

When CPD (citrate phosphate – dextrose) solution is added to a unit of freshly drawn blood. pH decreases to 7.0 – 7.1 (34). Further decrease in pH will occur during storage as a consequence of ongoing metabolism of glucose to lactate. The appropriate course of management is to base bicarbonate therapy on blood gas analysis.

iii) **Decrease in 2.3 DPG:-**

Storage of blood (red blood cells) is associated with a progressive decrease in intracellular ATP and 2. 3 DPG. This leads to a left shift of oxygen – Hb curve. with less efficient oxygen delivery. - After transfusion. 2. 3 DPG levels return towards normal over 12 – 24 hours (35).

iv) **Hyperkalemia:** –

During storage. K^+ moves out of red blood cells in part to maintain electrochemical neutrality as H^- ions generated during storage redistribute. Hazards exist if large volumes of stored blood are administered rapidly. The hyperkalemia is aggravated by hypovolemia. hypothermia and acidosis. (24).

v) **Volume overload**:-

Occurs when blood or fluid is transfused too rapidly for compensatory fluid redistribution to take place.

vi) **Hypothermia**:-

Packed red blood cells are stored between 1-6°c and hypothermia may result from rapid transfusion of large amounts of cold blood. The administration of 1 unit of packed red blood cells at 4°c will reduce the core temperature of a 70 kg patient by 0.25°c.Transfusions administered rapidly or with substantial volume should be warmed to prevent hypothermia. With decrease body temperature cardiac output decreases. perfusion is impaired (due to vasoconstriction and left shifting of the O2 – Hb dissociation curve). and metabolic acidosis may develop (24. 36).

vii) **Micro aggregate delivery**:-

Stored blood contains micro aggregates (24). Platelet aggregates form during day 2- 5 of storage and after 10 days. larger aggregates composed of fibrin. degenerated white cells and platelets appear (34). Micro aggregates of red blood cells also develop. Micro aggregates have been implicated in the pathogenesis of pulmonary insufficiency and development of ARDS. which often follows large – volume transfusions (defined as more than 10 – 12 units in 24 hrs) (24).

viii) **Dilutional coagulopathy**:-

Administration of large volumes of fluid deficient in or devoid of platelets and clotting factors predictably leads to the development of a coagulopathy as a consequence of dilution.

Patients receiving large- volume isovolemic transfusions suggest that clinically significant dilution of fibrinogen, factor 11, V and VIII, and platelets will occur after volume exchanges of 140%, 200 – 230% and 230% (i.e. 1.4.2 and 2.3 blood volumes) respectively (37).

2.9.2 IMMUNOLOGICALLY MEDIATED TRANSFUSION REACTIONS:-

Reactions to transfused blood products can occur as result of the presence of constitutive antibodies (e.g. anti- A, anti – B): antibodies formed as a result of prior exposure to donor red blood cells, white blood cells, platelets and / or proteins: or as a consequence of the effects of transfused white blood cells.

A). REACTIONS TO RED BLOOD CELL ANTIGENS

I) Immediate haemolytic Transfusion reaction

The most feared of the immune reactions is the immediate haemolytic transfusion reaction against foreign red blood cells. Haemolysis of donor red blood cells often leads to acute renal failure, disseminated intravascular coagulopathy (DIC) and death.

The antibodies that fix complement and commonly produce immediate intravascular haemolysis include; anti-A, anti-B, anti-Kell, anti- Kidd, anti-Lewis and anti – Duffy. Incidence is 1 per 6000 – 7000 units transfused (38).

When incompatible blood is administered, antibodies and complement in recipient plasma attack the corresponding antigens on donor red blood cells. Haemolysis ensues. The haemolytic reaction may take place in the intravascular space or in the endoplasmic reticulum. The antigen – antibody complexes activates Hageman factor (factor XII) which in turn acts on the kinin system to produce bradykinin. This increases capillary permeability and dilates arterioles, both of which contribute to hypotension.

Activation of complement system leads to release of histamine and serotonin from mast cells, resulting in bronchospasm. 30 – 50% of patients develop DIC (38).

Renal damage occurs for several reasons:-

- Blood flow to the kidneys is reduced due to systemic hypotension and renal vasoconstriction.
- Free Hb and red blood cells stroma (not Hb) may precipitate in the renal tubules, causing mechanical obstruction and nephrotoxicity (34, 38).
- Antigen – antibodies complexes may be deposited in the glomeruli.
- If the patient develops DIC, fibrin thrombi will also be deposited in the renal vasculature, further compromising perfusion.

With renal failure, oliguria develops. If a reaction is suspected, the transfusion should be stopped, and the identity of the patient and the labelling of blood rechecked.

ii) Delayed Haemolytic Transfusion reactions:-

These reactions occur when the donor red blood cells bear an antigen to which the recipient has previously been exposed, either by transfusion or by pregnancy. Over time, the recipients' antibodies are too low to be detected by compatibility testing. When transfused again, the recipient undergoes an anamnestic response and produces more antibodies which eventually lyse the foreign red blood cells. Haemolysis is seen 1 -2 weeks after transfusion. Reactions may be undetected or the patient may have low grade fever, increased bilirubin with or without mild jaundice, or an unexplained decrease in the Hb level. It is confirmed by a positive direct antiglobulin test (Coombs test).

B) TRANSFUSION REACTION TO DONOR PROTEINS

Allergic reactions to proteins in donor plasma cause urticarial reactions in 0.2 – 2% of all transfusions (24). It occurs in patients with hereditary immunoglobulin A deficiency that have been sensitized by previous transfusions or pregnancy. Treatment involves stopping the transfusion and administration of methyl prednisolone and epinephrine. Washed red blood cells, frozen deglycerolized red blood cells, or red blood cells from IgA- deficient donors should be used for such patients (38).

C) WHITE BLOOD CELLS RELATED TRANSFUSION REACTIONS

i) Febrile reactions:-

Patients who receive multiple transfusions of packed red blood cells or platelets often develop antibodies to the human leukocyte antigens (HLAs) on the leukocytes in these products. During future red blood cell transfusions. febrile reactions may occur as a result of antibody attack on donor leukocytes.

This occurs in about 1% of all red blood cell transfusions (38). Commercially available leukodepletion filters may be used to prevent febrile. nonhaemolytic transfusion reactions.

ii)Graft – versus- Host Disease (GVHD)

Packed red blood cell and platelet concentrates both contain a significant number of viable donor lymphocytes. When transfused ('transplanted') into immuno-compromised patients. the donor lymphocytes may become engrafted. proliferate and establish an immune response against the recipient. In essence. the engrafted lymphocytes reject the host. It typically progresses rapidly to pancytopenia. and the fatality rate is very high (39).

iii) Transfusion – Related Acute Lung Injury (TRALI)

It is a rare reaction (about 1 per 10.000 transfusions) that occurs as a consequence of the deposition of white blood cells – antibody aggregates in the pulmonary vasculature (40). It occurs when agents present in the plasma phase of donor blood activate leucocytes in the host. (41). The agents are often antileucocytes antibodies formed as a result of previous transfusion or pregnancy or through cytokines and biological active lipids.

IV) Immunomodulation.

Alteration of immune function has been associated with allogeneic transfusion (42, 43). There is increased incidence of postoperative infections, earlier occurrence of cancer and more rapidly progression of AIDS / HIV (44). Transfused white blood cells are thought to the mediators. This has led to the development of application of techniques for leukocyte depletion of donor blood products (45).

D) **Infectious risks associated with blood product administration.**

The potentially transmissible diseases / agents include:-

Viruses – Hepatitis A, B, C, D, E and G. (46, 47)

- Human T-cell lymphotrophic viruses (HTLV – 1 and 2).
- HIV 1 and 2
- CMV
- EBV

Prions - Jacob – Creutzfeldt bacteria

Parasites - Malaria, Chaga's disease

-Syphillis.

Bacterial contamination:-

-Red blood cells – Yersinia enterocolitica

- Platelets – staphylococcus aureus, Klebsiella pneumonia, Serratia marcescens, Staphylococcus epidermidis.

2.10 STUDIES ON THE CURRENT PRACTICE:-

Jean Louis Vincent (Belgium) et al have studied the occurrence of anaemia as a component critical illness (1). By the time of discharge, the Hb level of the patients is 10-11 gm/dl. More than 35% of patients were transfused with Hb trigger of 8.5 gm/dl. The predictor of blood transfusion was the length of ICU stay. Within 48hrs, 58 % of the patients were transfused whereas within 1 week 73% of the patients were transfused. In the study, the indications for the transfusions included emergency operations, trauma and elective surgery, inadequate Hb without evidence of bleeding and in patients with medical diseases.

Mitchell levy et al (Rhode Island, USA) were involved in the CRIT trial (13). They used a pre-transfusion Hb level of 8gm/dl and a higher transfusion trigger in cardiovascular disease of 10gm/dl. They concluded that exposure to blood transfusion seems to increase the length of ICU stay.

Hebert et al in Canada (14) found that patients who died in ICU had low Hb levels and were transfused more frequently. Higher Hb values in anaemic patients with cardiovascular disease were also associated with better outcome, measured as survival.

2.11 STUDIES ON PROPOSED CARE:-

Paul Hebert et al (Canada) have recommended that blood should not be transfused in ICU, patients (without heart disease and with APACHE II scores less than 20) until the Hb level is less than 7 gm/dl(20).

2.12 STUDIES ON THE PROBLEMS OF BLOOD TRANSFUSIONS:

William Sibbard et al in Canada (1993) found that the use of blood transfusion to increase the Hb concentration in septic ICU patients improved calculated oxygen delivery but reduced the intramucosal oxygenation (measured by gastro-intestinal tonometry),when blood was stored for 12-15 days(22).

The disadvantages of old blood include:-

1. 2. 3 diphosphoglycerate (DPG) depletion.
2. Altered red blood cell endothelial interactions.
3. Altered red blood cell/Nitric oxide (NO) homeostasis.

2.13 STUDIES ON THE WAY FORWARD

Howard Corwin et al (New Hampshire) have tried to look for alternatives to blood transfusion to increase the Hb in critically ill patients (due to shortages of blood in the blood banks and the side effects of using stored blood). They have recommended the use of erythropoietin (EPO) on patients in ICU from day three. In their study, blood transfusions were reduced by almost 50% in the EPO group. The total number of units transfused in the EPO group was 166 and total units in the placebo group was 305 (11).

STUDY RATIONALE /JUSTIFICATION

There are many reasons for the observed variability around blood transfusion practices in the ICU. There is clearly clinical uncertainty about the optimal Hb level – the concentration of Hb that, after good volume resuscitation, maximises tissue oxygenation and facilities survival.

Clinicians believe that improving tissue oxygen availability is an important component of their care for ICU patients However: clinical studies suggest that the frequency of blood transfusions used in ICU in the past may not be necessary to optimise patient survival in the future (13). Indeed, there is evidence that excessive use of blood transfusions may be harmful (26).

Because there is some concern over the use of blood transfusion as a means to improve tissue oxygenation, and there is clearly concern about supply when blood transfusions are appropriate, other strategies such as EPO (erythropoietin) may become an option.

What is certain is that blood transfusion to improve tissue oxygenation in the ICU patients is undergoing intense re-examination both at the bench and the bedside.

This is clearly a 'story in progress', with studies being planned and under way to identify how best to use blood, blood products, blood substitutes and synthetic EPO in the ICU.

3.2 HYPOTHESIS:-

Whole blood is transfused arbitrarily in the KNH ICU patients rather than because of a physiologic need for blood.

AIMS AND OBJECTIVES

3.3 MAIN OBJECTIVE

To study the pattern of blood transfusion practices at the Kenyatta National Hospital intensive care unit.

3.4 SPECIFIC OBJECTIVES

1. To determine the pre-transfusion haemoglobin levels (transfusion trigger) and the rate of blood transfusion in the KNH ICU.
2. To profile patients transfused in KNH. ICU. in relation to: age. gender. diagnosis. duration of stay. and other reasons for transfusion.
3. To identify the types of transfusion reactions encountered in the KNH ICU.
4. To make recommendations on safe blood transfusion practices for the hospital.

4. 0 STUDY METHODOLOGY

4.1. STUDY DESIGN : Prospective. observational. descriptive study.

4.2. STUDY SITE : The study was conducted at the intensive care unit of the Kenyatta National Hospital. Kenya.

4.3. STUDY DURATION : This study was conducted over a period of 4 months (December 2007 to March 2008).

4.4. STUDY POPULATION: All patients that required blood transfusion while at the ICU.Both genders. male and female.

4.5 INCLUSION CRITERIA

1. All patients admitted to ICU who required blood transfusion during their stay in the ICU. These included:-

- Patients who had an acute blood loss in the ICU.
- Patients who had coronary artery disease. or any of the other forms of myocardial dysfunction.
- Patients with diminished haemoglobin physiological reserves.
- Patients with non-acute bleeding.

4.6 EXCLUSION CRITERIA

1. Any patient who was unwilling to participate or failed to give consent for any reason.
2. Patients who stayed on beyond the period of study.
3. Jehovah's Witnesses patients.
4. Patients who were known sicklers. or had congenital cyanotic heart diseases.
5. Patients who came into the unit while already being transfused.

5.0 DATA COLLECTION AND ANALYSIS

5.1 SAMPLE SIZE ESTIMATION

Previous studies on the rate of blood transfusion elsewhere have shown a transfusion rate of 16 % (5. 13).

Using the one sample situation as shown by the statistical manual of WHO. the sample size formula for estimating a single rate is given by:-

$$n = r/ e^2$$

Where, n= sample size

r=rate established elsewhere

e=estimated error rate.

Confidence level=90%.

Therefore. $n=\frac{16/100}{0.05*0/05}$=64 patients.

5.2 SAMPLING TECHNIQUE AND PATIENT RECRUITMENT

Patients were recruited into the study sequentially as long as they satisfied the inclusion criteria. Patients were followed up in the ICU from the pre-transfusion period to the time after transfusion when any transfusion reactions encountered were being noted. As shown above, patients who came into the unit while already being transfused were excluded from the study.

Eligible patients, or their relatives in cases whereby the patients were comatose, were then taken through consent explanation. The purpose of the study was explained to the patient or their next of kin, where the patient was unable to give consent. Written informed consent was then sought, and only patients with consent were included. It was, however, clarified that refusal to consent would not result in discrimination of medical care to the patient.

Demographic data was collected on admission into ICU. A data capture form or questionnaire (see appendix), was used to collect data from both patients and their files, and from the primary clinicians in the ICU.

5.3 MATERIALS AND METHODS

For each of the recruited subjects. a history was obtained and details of the patients' demographics. age. gender. diagnosis and duration of stay in the ICU noted. either from the patient or from the medical records of the patient. In this respect. direct questions were sometimes needed to obtain the information. The patients' haemoglobin level before a transfusion was also noted. This was from the routine morning Hb levels done in the ICU laboratory. and from the routine Hb levels done on admission of ICU patients.

The admission type of the patient was noted. the primary admission category. the number of units transfused and the indication for transfusion (appendix 3). Any transfusion reactions encountered was also noted.

A) PATIENTS DIAGNOSIS

This was obtained from the patients' files or from the primary clinician in the ICU. This included a description of what the patient was suffering from. and it was noted in the data capture form.

B) PATIENTS HAEMOGLOBIN LEVELS

This was sought from the patients' files. This was either from the routine daily Hb levels done in the ICU or from the full haemogram levels done routinely in the ICU twice weekly. The figure was given a numerical value with one decimal place.

The patients haemoglobin levels at admission were noted: then the level before being transfused and also the level one day after being transfused.

C) INDICATION FOR TRANSFUSION

This entailed noting the reason for transfusion. This was obtained either from the patients file or by asking the primary ICU clinician. The indication was then noted from four possible options namely, anaemia without any obvious bleeding, post-operative patient, acute blood loss or obstetric haemorrhage.

D) DURATION OF STAY IN THE ICU

This was sought from the patients file or from other relevant patient records within the ICU. This was then recorded as a numerical integer value.

E) HAEMATINICS

Information was sought either from the patients file or from the primary ICU physician as to whether the patient was on haematinics or not. This was then recorded as either yes or no.

F) PRIMARY ADMISSION CATEGORY

This involved finding out which body system was primarily involved as the patient was being admitted into the ICU. The categories included: cardiovascular, respiratory, trauma, gastro-intestinal, hepato-biliary or neurological. For some patients, it was possible to have more than one system involved. Data was entered as either yes or no for each system.

G) ADMISSION TYPE

This referred either to the urgency of the patients admission (either emergency or elective) or to the broad class of ailment (trauma, medical or surgical). To each of these categories, it was entered as either yes or no in the data capture form.

H) AMOUNT OF BLOOD TRANSFUSED

This information was sought from the patients file and then recorded numerically as amount in millilitres of blood. One unit of whole blood contains 450 millilitres of whole blood and 63 millilitres of the anticoagulant citrate phosphate dextrose-acetate (CPD-A); the CPD-A is made up of 206 grams of anhydrous citric acid, 1.66 grams of anhydrous sodium citrate, 140 milligrams of hydrous monobasic sodium phosphate, 1.83 grams of anhydrous dextrose, 17.3 milligrams of adenine and a sterile pyrogenic fluid path.

I) TYPE OF TRANSFUSION REACTION

Patients were observed during and after transfusion for any reaction, and this was sought either from the medical records or from the primary ICU physician. This was then entered as either yes or no. For those who had a transfusion reaction, a descriptive account of the transfusion reaction was written.

J) RATE OF BLOOD TRANSFUSION

This was calculated by dividing the number of patients in the study population (64), by the total number of in- patient admissions during the same study period, from December 2007 to March 2008. This data was obtained from the Kenyatta National Hospital medical records department.

5.4 DATA ANALYSIS

Descriptive and analytical statistics were done for both continuous and categorical data. Measures of central tendency and dispersion were used for continuous data, together with proportions and frequencies. Data was analyzed using the SPSS software version 12.0.1. Data was coded and entered. Data was cleaned by running frequencies and all errors in data were corrected, where categorical data was used.

Chi-squares tests and Fischer's exact test were used to determine significant differences between males and female on all key variables. Mann Whitney u-test was used to determine significance between transfusion reaction and amount of blood transfused.

Scatter plots were used to explore if there was any correlation between the duration of stay and the post-transfusion haemoglobin level; the age and the post-transfusion haemoglobin level; the age and pre-transfusion haemoglobin level; the pre-transfusion and the post transfusion haemoglobin level; the duration of stay in the ICU and age; the duration of stay in the ICU and the post transfusion haemoglobin level.

Spearman's rank correlation was used to determine correlation between pre-transfusion and post transfusion haemoglobin levels. Significance level were set at $\alpha=0.05$.

6.1 ETHICAL CONSIDERATIONS

1. The study did not entail any invasive procedures on the patient.
2. Data collected was based on the routine ICU information as per the KNH ICU protocol.
3. No change of treatment or management was effected if no consent was given.
4. Confidentiality of information was maintained at all times.
5. Study was only carried out after approval by the KNH Ethical Research Committee (ERC).
6. The study was only carried out on patients from whom an informed consent was obtained. either from the patient or from their next of kin.
7. Refusal of consent did not lead to discrimination in care.

7.1 RESULTS

A total of sixty four patients. both male and female, were recruited into the study. All patients were critical care patients who had been transfused at some point during their stay at the critical care unit. The results are summarized in tables. in mean (SD).

TABLE 1: SUMMARY OF CLINICAL AND DEMOGRAPHIC CHARACTERISTICS OF PATIENTS INCLUDED IN THE STUDY.

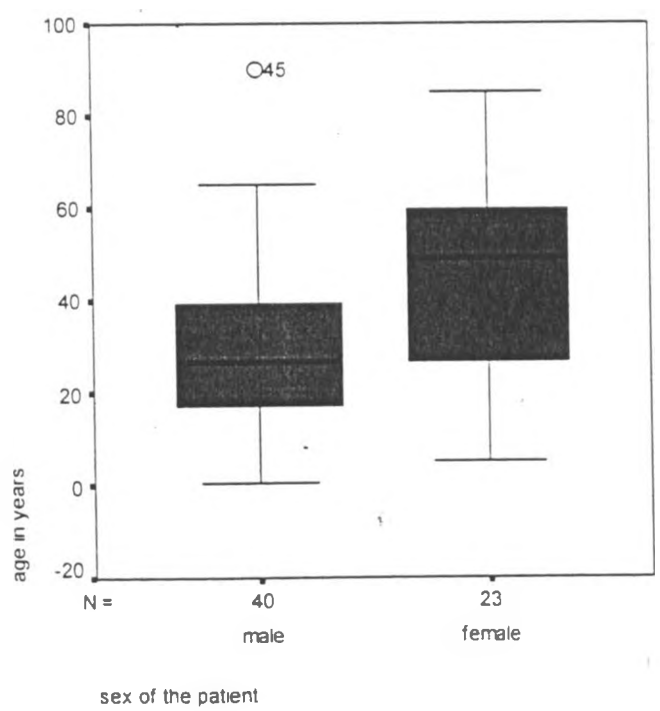
Variable	Sex		Statistical test
	Male	Female	
Age group			
0-12 years	8(20%)	2 (8.7%)	
13-25 years	10 (25%)	3 (13.0%)	
26-38 years	11 (27.5%)	6 (26.1%)	
39–	11 (27.5%)	12 (52.2%)	
Indications for transfusion	22(55.0%)	13 (54.2%)	
Anaemia	7 (17.5%)	3(12.5%)	
Acute blood loss	N/A	2 (8.3%)	
Obstetric haemorrhage	11 (27.5%)	6(25%)	
Post operative			
Haematinics			χ^2= 1.995: 1df:
Being given	17 (42.5%)	6 (25%)	P>0.05 (0.158)
Not being given	23 (57.5%)	18(75%)	

There were more males than females in all the age groups except in those aged more than 39 years. The most common indication for transfusion in both males and females was anaemia, followed by transfusion in post-operative patients.

There was found to be no statistical difference between the two sexes in receiving a haematinic. This was tested using the chi square test. [$p>0.05$ (0.158)].

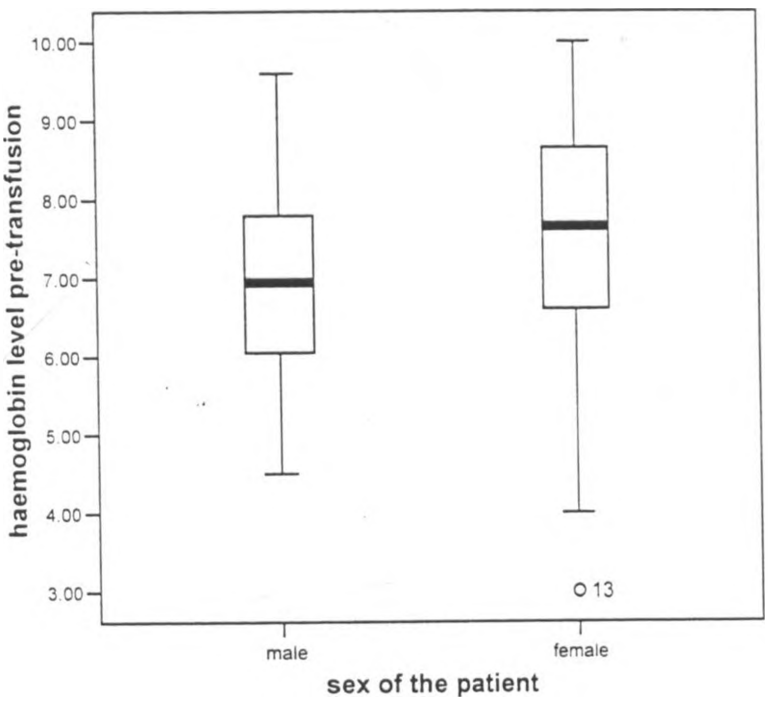
Of the patients studied, forty (62.5%) were male and twenty four (37.5%) were female. The patients' ages ranged from one to ninety years with a mean of 33.39 years, with no significant variation between the two sexes. The mean age for males in the study was lower than that in females, as shown in the box plot above.

FIGURE 1. BOX PLOT SHOWING AGE DISTRIBUTION OF PATIENTS INCLUDED IN THE STUDY.



The pre-transfusion haemoglobin level ranged between 3 to 10 grams/ decilitre, with a mean of 7.08grams/ decilitre. The most common value was 6.4 grams/ decilitre in five (7.8%) of the patients. The mean pre-transfusion haemoglobin level was lower in males than in females.

FIGURE 2. BOX PLOT SHOWING THE DISTRIBUTION OF STUDY PATIENTS BY THE PRE-TRANSFUSION HAEMOGLOBIN LEVELS.



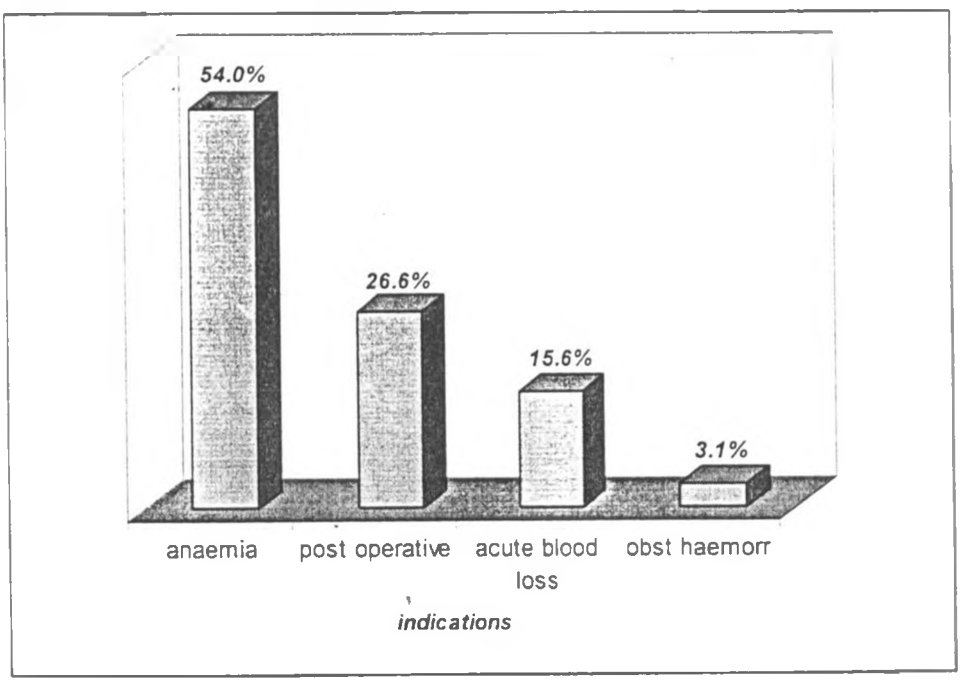
The mean level of haemoglobin at admission was 9.97 grams/ decilitre, ranging from 3 to 18 grams/ decilitre. The mean level in males was higher at 10.34 grams/ decilitre while that for females was 9.35 grams/ decilitre.

The post- transfusion haemoglobin level ranged from 5.9 to 14.9 grams/ decilitre with a mean of 9.71 grams/ decilitre. However, there was no statistically significant difference in the mean levels between males and females (9.72 and 9.70 grams/ decilitre respectively).

In the study population, haematinics were given to 42.5% (17) of the male patients and to 25% (six) of the females. Overall, 23 (35.9%) of the total study population received a haematinic.

The most common indication for transfusion was anaemia without any active bleeding in 54% of the patients, followed by transfusion given to post-operative patients (26.6%). Two female patients (3.1%) were transfused due to obstetric haemorrhage.

FIGURE 3. BAR CHART SHOWING THE DISTRIBUTION OF PATIENTS BY THE INDICATION FOR TRANSFUSION.



Transfusion reactions were encountered in 7 (10.9%) of the patients. the most common reaction being a transient febrile reaction. The other two patients got an allergic skin reaction/urticaria (1 patient) while the other one had fluid overload with a raised central venous pressure.

The mean duration of stay in the critical care unit for the study period was 8.23 days, with a range from 1 to 48 days. The most frequent value for the duration of stay was 2 days, with a median value of 3 days.

TABLE 2.SUMMARY OF THE PRIMARY ADMISSION CATEGORY AND THE ADMISSION TYPE OF THE STUDY POPULATION.

SUMMARY OF THE PRIMARY ADMISSION CATEGORIES

Variable	**Sex**		**Statistical test**
	Male	**Female**	
Cardiovascular system			χ^2= 8.195: 1df:
Yes	12 (30%)	16 (66.7%)	P<0.05 (0.004)
No	28 (70%)	8 (33.3%)	
Respiratory system			χ^2= 0.610: 1df:
Yes	24 (60%)	12 (50%)	P>0.05 (0.435)
No	16 (40%)	12 (50%)	
Trauma			χ^2= 16.213: 1df:
Yes	19 (47.5%)	0(0%)	P<0.05 (0.000)
No	21 (52.5%)	24 (100%)	
Gastro intestinal system	2 (5%)	1 (4.2%)	Fischer's Exact χ^2= 0.023: 1df:
Yes	38 (95%)	23 (95.8%)	P>0.05 (0.879)
No			
Neurological system			χ^2= 2.627: 1df:
Yes	25 (62.5%)	10 (41.7%)	P>0.05 (0.105)
No	15 (37.5%)	14 (58.3%)	
Renal system			Fischer's Exact
Yes	3 (7.5%)	6 (25%)	χ^2= 3.801: 1df:
No	37 (92.5%)	18 (75%)	P>0.05 (0.051)
Endocrine system			Fischer's Exact
Yes	3 (7.5%)	3 (12.5%)	χ^2= 0.441: 1df:
No	37 (92.5%)	21 (87.5%)	P>0.05 (0.506)

Obstetric system			Fischer's Exact
Yes	0 (0%)	4 (16.7%)	χ^2= 7.111: 1df:
No	40 (100%)	20 (83.3%)	P<0.05 (0.008)

SUMMARY OF THE ADMISSION TYPES IN THE STUDY POPULATION

Elective			
Yes	10 (25%)	9 (37.5%)	χ^2= 1.123: 1df:
No	30 (75%)	10 (62.5%)	P>0.05 (0.289)
Emergency admission			χ^2= 1.123: 1df:
Yes	30 (75%)	15 (62.5%)	P>0.05 (0.289)
No	10 (25%)	9 (37.5%)	
Trauma type of admission	17 (42.5%)	0(0%)	χ^2= 13.89: 1df:
Yes	23 (57.5%)	24 (100%)	P<0.05 (0.000)
No			
Medical type of admission	9 (22.5%)	13 (54.2%)	χ^2= 6.67: 1df:
Yes	31 (77.5%)	11 (45.8%)	P<0.05 (0.010)
No			
Surgical			χ^2= 6.67: 1df:
Yes	30 (75%)	11 (45.8%)	P<0.05 (0.019)
No	10 (25%)	13 (54.2%)	

Most patients admitted had the respiratory system as the primary admission category (56.3%), followed by the neurological system (54.7%). Twenty eight (43.8%) of the patients had the cardiovascular system involved. A patient could have more than one primary admission category.

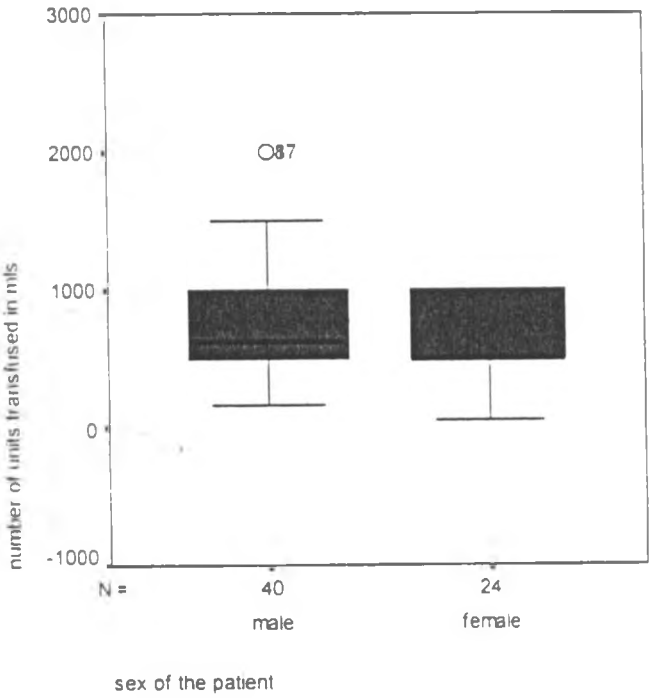
In the cardiovascular system, there were significantly more female admissions than males [$p < 0.05$ (0.004)]. There was no difference in gender for patients admitted with respiratory disease, the gastrointestinal system, the neurological system, the renal system and the endocrine system. All the trauma patients admitted during this study period were males.

There were statistically significant more female medical admissions [$p < 0.05$ (0.010)], and more male surgical admissions [$p< 0.05$ (0.019)]. There was no statistically significant difference between males and females for the emergency admissions [$p> 0.05$ (0.289)].

Forty five (70.3%) of the patients were admitted as an emergency as opposed to 19 (29.7%) of the patients who were admitted electively. Twenty two (34.4%) of the patients were medical ICU patients while 41 (64.1%) were surgical patients. The trauma cases admitted during the study period were 17(26.6%)

Most of the patients. 29 (45.3%) were transfused one unit of whole blood. 25 of them (39.1%) were transfused two units of whole blood. The amount of blood transfused in the study population ranged from 60 to 2000 millilitres with a mean value of 736.71 millilitres of whole blood.

FIGURE 4. BOX PLOT SHOWING THE DISTRIBUTION OF THE AMOUNT OF BLOOD TRANSFUSED IN THE STUDY POPULATION.



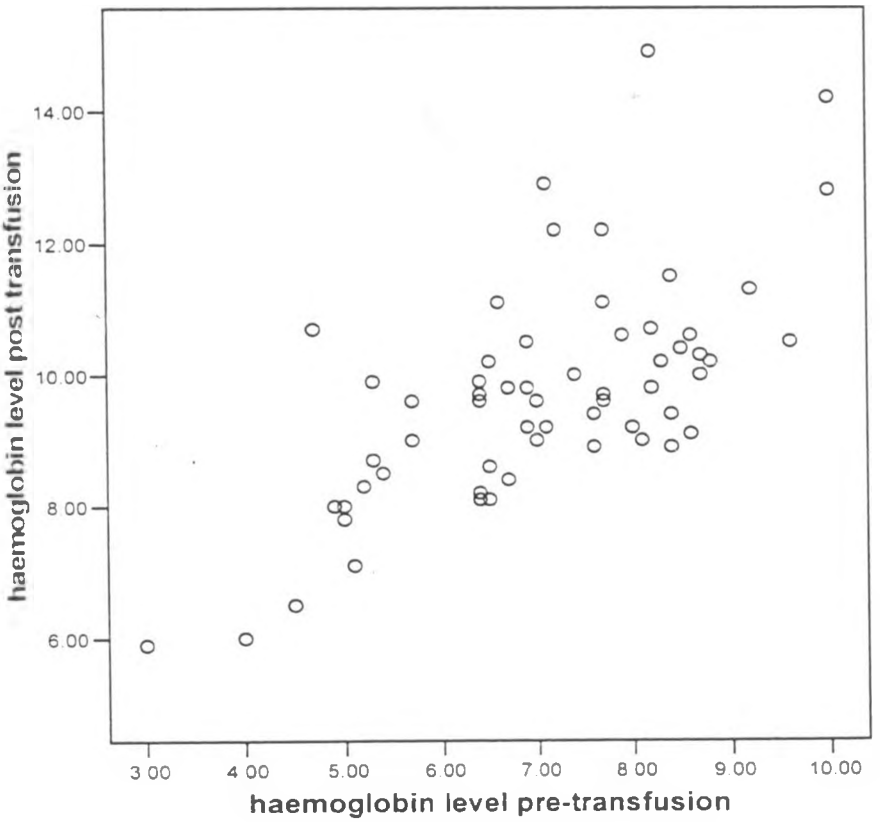
There was found to be a significant correlation between the amount of blood transfused and the presence of a transfusion reaction. Mann Whitney U-Test Z= -2.033: P<0.05 (0.042)

TABLE 3: CORRELATION BETWEEN THE AMOUNT OF BLOOD TRANSFUSED AND THE PRESENCE OF A TRANSFUSION REACTION

presence of transfusion reaction	Mean	N	Std. Deviation	Median	Minimum	Maximum
Yes	1071.4286	7	534.52248	1000.0000	500.00	2000.00
No	695.6140	57	331.47408	500.0000	60.00	2000.00
Total	736.7187	64	372.63138	500.0000	60.00	2000.00

There was found to be a positive linear correlation between the pre-transfusion and the post transfusion haemoglobin levels.

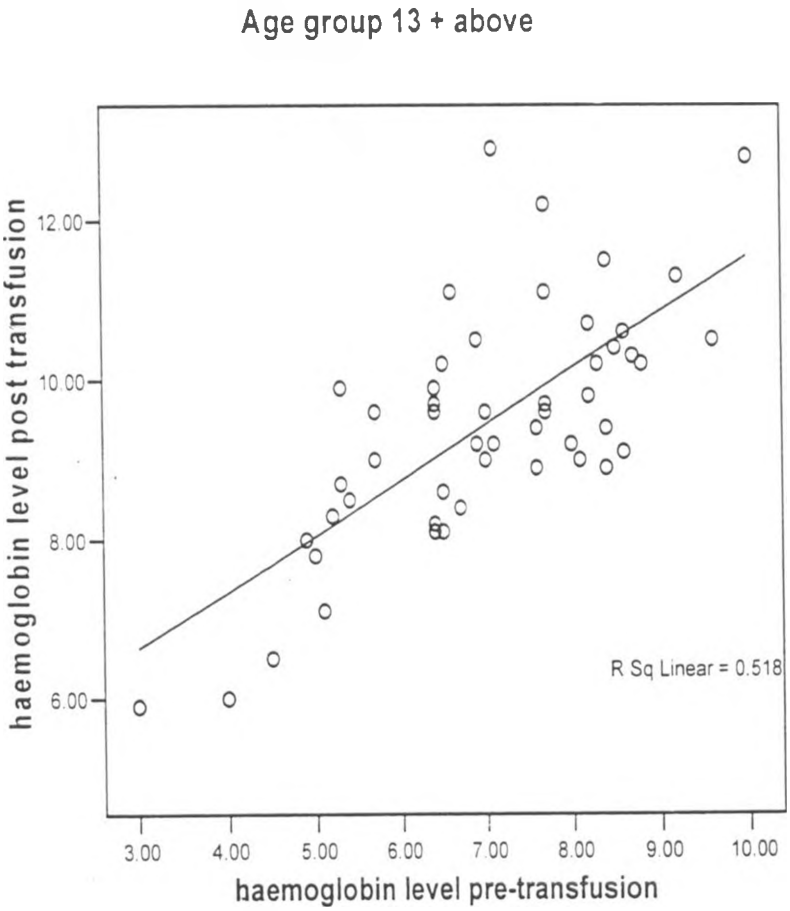
FIGURE 5. SCATTER DIAGRAM SHOWING CORRELATION BETWEEN THE PRE-TRANSFUSION AND THE POST-TRANSFUSION HAEMOGLOBIN LEVEL. FOR ALL THE PATIENTS



This linear correlation was then further tested using the Spearman Rank Correlation and found that there was a statistically significant correlation between the pre- transfusion and the post transfusion haemoglobin levels , R= 0.624; $p < 0.05$ (0.000).

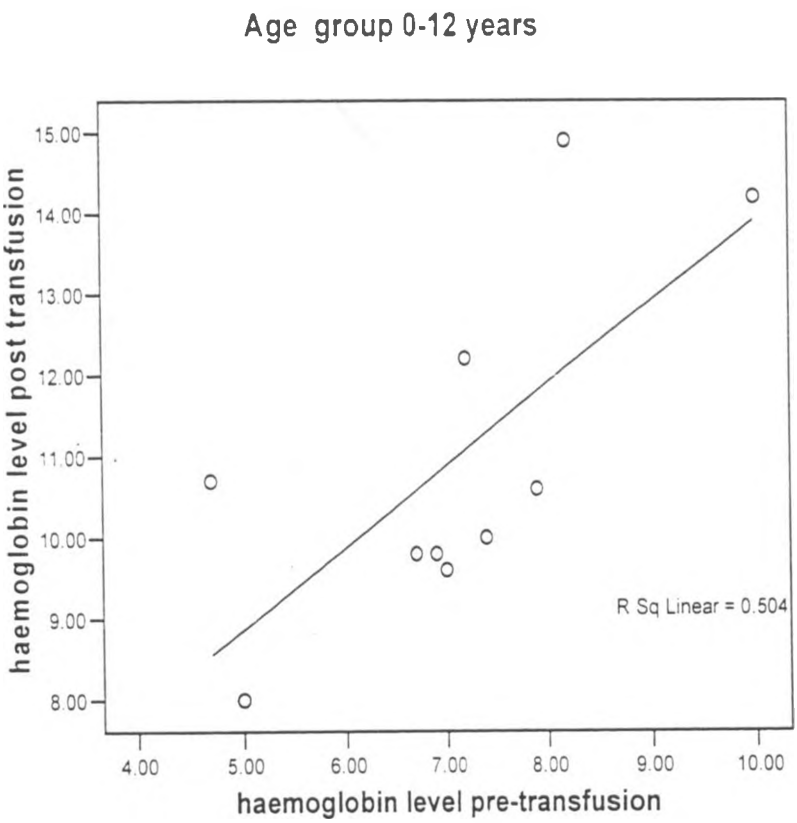
This correlation was further tested for patients aged 13 years and above and there was still found to be a positive correlation. This was tested using the Spearman Rank correlation coefficient $R=0.668(p<0.01)$.

FIGURE 6. SCATTER DIAGRAM SHOWING CORRELATION BETWEEN THE PRE-TRANSFUSION AND THE POST-TRANSFUSION HAEMOGLOBIN LEVELS FOR PATIENTS AGED 13 YEARS AND ABOVE.



The correlation between the pre-transfusion and the post-transfusion haemoglobin level was found to be not significant for patients aged 0 to 12 years, and this could be attributed to the small sample size of 10 patients. The Spearman Rank correlation coefficient $R=0.632(p>0.05)$. This is as shown in the scatter diagram below.

FIGURE 7. SCATTER DIAGRAM SHOWING CORRELATION BETWEEN THE PRE- AND POST-TRANSFUSION HAEMOGLOBIN LEVELS FOR PATIENTS AGED 0 TO 12 YEARS.



For this age group of 0 to 12 years, the percentage volume of blood transfused as compared to their total expected blood volume was sought and results presented in the table below.

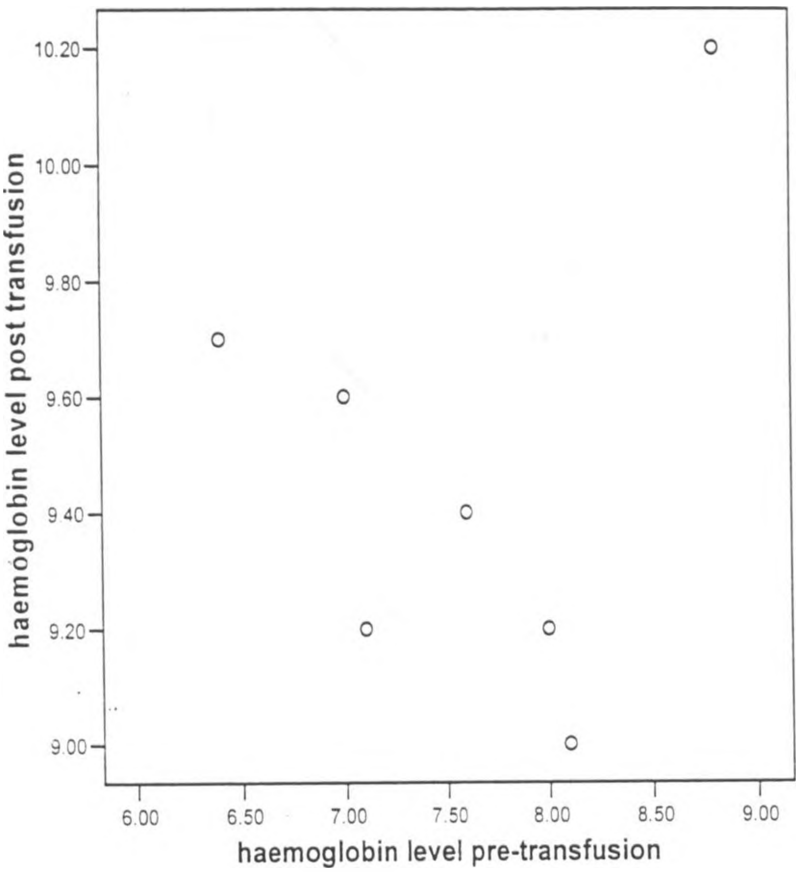
TABLE 4. DISTRIBUTION OF THE PERCENTAGE VOLUME OF BLOOD TRANSFUSED FOR PATIENTS AGED 0 TO 12 YEARS.

Age in years	Percentage volume of blood transfused
1	22.5%
1	25.0%
1	20.0%
5	27.78%
5	34.72%
5	34.72%
5	27.78%
8	52.08%
10	22.32%
10	22.32%

There was an outlier in the above results. This was a child of 8 years who was transfused 52.08% of his blood volume. He was a neurological patient with acute blood loss. The rest of the paediatric patients were transfused between 20.0 to 34.72%.

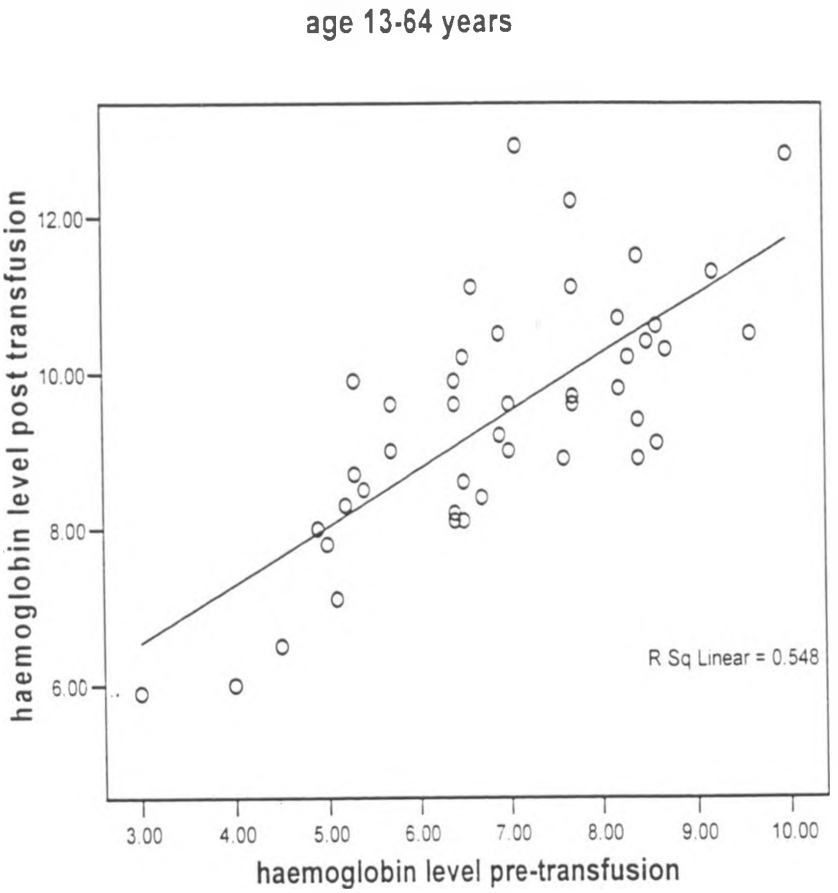
For the elderly patients aged 65 years and above, there was no pattern and this could be attributed to the small sample size, n=7. This is as shown in the scatter diagram below.

FIGURE 8. SCATTER DIAGRAM SHOWING THE CORRELATION BETWEEN THE PRE- AND POST-TRANSFUSION HAEMOGLOBIN LEVELS FOR PATIENTS AGED 65 YEARS AND ABOVE.



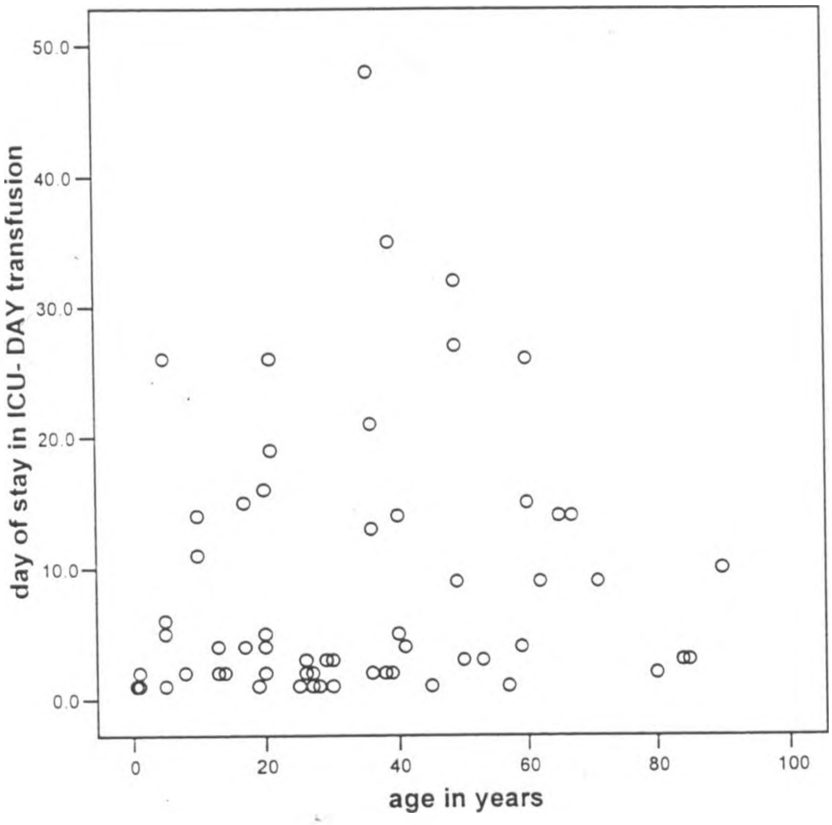
There was a positive correlation between the pre-transfusion and the post-transfusion haemoglobin level for patients aged 13 to 64 years. with a Spearman Rank correlation coefficient $R=0.716(p<0.01)$. This is as shown in the scatter diagram below.

FIGURE 9. SCATTER DIAGRAM SHOWING THE CORRELATION BETWEEN THE PRE- AND THE POSTTRANSFUSION HAEMOGLOBIN LEVEL FOR PATIENTS AGED 13 TO 64 YEARS.



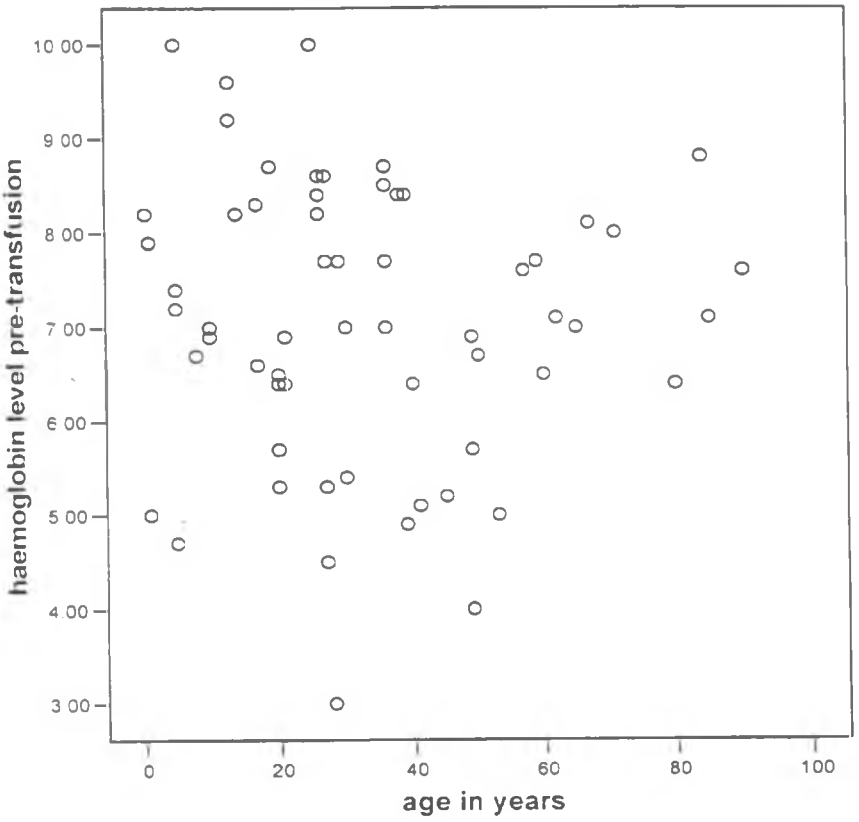
From the scatter diagram shown below, there was found to be no correlation between the duration of stay in ICU and the patients' ages in years.

FIGURE 10. SCATTER DIAGRAM SHOWING CORRELATION BETWEEN AGE IN YEARS AND THE DURATION OF STAY IN THE ICU.



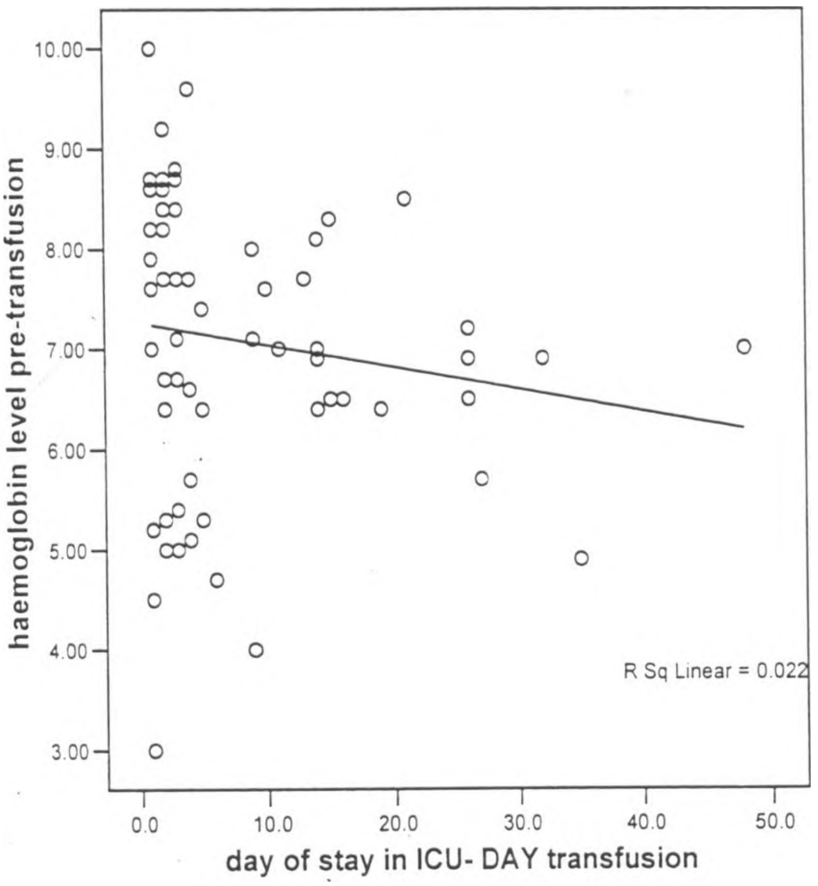
Among the study population, there was found to be no correlation between the patients' age in years and the pre- transfusion haemoglobin level, as shown in the scatter diagram below.

FIGURE 11. SCATTER DIAGRAM SHOWING CORRELATION BETWEEN THE AGE IN YEARS AND THE PRE-TRANSFUSION HAEMOGLOBIN LEVEL



Statistical analysis also revealed no significant correlation between the duration of stay before the first transfusion and the pre-transfusion haemoglobin level. This is as shown in the scatter diagram below.

FIGURE 12. SCATTER DIAGRAM SHOWING CORRELATION BETWEEN THE DURATION OF STAY BEFORE THE FIRST TRANSFUSION AND THE PRE-TRANSFUSION HAEMOGLOBIN LEVEL.



7.2 DISCUSSION

Anaemia is a common problem among critically ill patients, so much so that the majority of I.C.U patients will need a blood transfusion at some point during their I.C.U stay (1). However, the decision to transfuse or not is not always clearly defined and in recent years this issue has seen some considerable debate and controversy. The traditional transfusion 'trigger' of 10gm/decilitre is no longer considered optimal with transfusions now being given at much lower Hb levels of 8 gm/dl(1).

This study has shown the pattern of blood transfusion at the KNH ICU. The transfusion trigger (pre-transfusion haemoglobin level) was 7.07 grams/ decilitre with a standard deviation of 1.48 grams/ decilitre. This means that blood is transfused at much lower haemoglobin levels as opposed to other centres that are now adopting transfusion trigger values of 8 gm/dl (1). In the anaemia and blood transfusion study in the critically ill (ABC) study, the transfusion trigger was 8.4 gm/dl ($p<0.0001$) (1).In the CRIT trial done in the USA in 2004(14), the mean pre-transfusion haemoglobin level was 8.6 +/- 1.7 gm/dl.

There was also found to be a rate of 21.26% of blood transfusion among the critically ill patients at the KNH ICU during the study period. This compares with a rate of 25% by Hebert et al (14) in their study of 5298 patients in Canada. Recently in the SOAP (Sepsis Occurrence in Acutely ill Patients) study (33), carried out between May and June 2002, 3147 patients in 198 ICUs were studied and it was found that 33% of the patients received a transfusion during their ICU stay.

Age also tends to have an effect on the blood transfusion practice in the ICU. In this study, 23(35.9%) of the patients were aged 25 years and below, 17 (26.6%) were aged between 26 to 40 years, and 23 (35.9%) were aged 40 years and above. In the ABC study (1), 54% of the patients were aged more than 80 years ($p<0.0001$). Therefore, more elderly patients were transfused. This can be explained by the fact that older patients tend to have higher SOFA and APACHE 2 scores, and thus they have more associated co-morbidities (25, 32).

The haemoglobin level at admission was a mean of 9.97 gm/dl with a standard deviation of 3.26 gm/dl. The haemoglobin level then decreased during the ICU stay, dropping to a pre-transfusion level of 7.08 gm/dl. This compares with the CRIT trial of the USA (14), whereby the mean haemoglobin level at admission was 11.0 +/- 2.4 gm/dl. This decreased through the duration of stay, dropping to a mean pre-transfusion haemoglobin level of 8.6 +/- 1.7 gm/dl. There may be losses due to invasive procedures such as catheter or drain insertion, or with tracheostomy which is particularly common in the ICU patients. There may also be occult blood loss from the gastro-intestinal tract (6). Repeated blood sampling is another cause. Von Ahsen et al in 1999 found an average of 41 millilitres of blood in the A.B.C study (Anaemia and Blood transfusion in the critically ill patients) (1).

In this study, 54% of the patients were transfused due to anaemia without any signs of active bleeding and 26.6% of them were post-operative patients. In the ABC study (1), 54% of the patients were also transfused because of inadequate haemoglobin concentration without any active signs of bleeding.

In a multi-centre cohort study done by Hebert et al in 1999 (25), the most frequent reasons for administering blood were acute bleeding (35%) and augmentation of oxygen delivery (25%).

The mean time to the first ICU transfusion in the study was 8.23 days. The mode value was 2 days, with a median of 3 days. In the CRIT trial (14), the mean time to the first transfusion was 2.3 +/- 3.7 days. In both studies, the number of transfusions was associated with a longer ICU stay. Corwin et al (13) found that 85% of patients who stayed for more than one week in the ICU received a transfusion during their ICU stay. Therefore, the longer the duration of stay in the ICU, the more likely the chances are of receiving a transfusion.

During the study period, the emergency admissions comprised of 30 (75%) males and 15(62.5%) females, and overall, 45 (70.3%) of the patients were emergency admissions. This is much higher as compared to the value of 57% for emergency admissions who were transfused in the ABC study (1). The trauma patients who were transfused during the study period were 17 (26.6%), all males, while in the ABC study they were 47% trauma admissions. Elective admissions in this study were 19 (29.7%) whereas in the ABC study they were 42%.

In the study, 7 (10.9%) of the patients got a transfusion reaction, the most common reaction being a transient febrile reaction in 5 (7.8%) of the study population. Four out of the five patients had received more than five hundred millilitres. Transient febrile reactions usually occur in patients who receive multiple transfusions and then develop antibodies to the human leukocyte antigen (HLA) on the leukocytes in these products.

During future transfusions, the febrile reactions may occur due to antibody attack on the donor leukocytes in about 1% of the population (38). To counter this, commercially available leukodepletion filters may be used to prevent non-haemolytic febrile reactions.

It is therefore important that all patient characteristics be put into consideration before a critical care patient is transfused. The benefits and the risks of transfusing these patients need to be weighed before such a decision is arrived at.

Recent advances in this area of blood transfusion in the critically ill patients such as using a much lower transfusion trigger and use of blood substitutes such as erythropoietin need to be explored and incorporated as in other critical care units.

The methods used in this study were selected because they are simple, reproducible, non-invasive and they provide a good assessment of patient characteristics and the blood transfusion practices.

7.3 STUDY LIMITATIONS

Despite the study having been successfully carried out, there were some problems and limitations encountered during the study period.

Firstly, there were periods when there was lack of blood from the blood transfusion unit and therefore patients would have to be transfused much later than when prescribed by the ICU clinician.

It was also difficult to obtain patients weights, especially for the adults, because most of the patients were critically ill and moribund and therefore they could not stand on the weighing machines. The weight would have helped in calculating the percentage volume of blood transfused as compared to the patients total blood volume.

The system of record keeping was also a challenge because some pages from the patients' record would be missing and one would have to look elsewhere for the information. One would therefore spend more time in so doing.

All in all, the study was able to answer the research questions and the conclusions related with the study objectives.

7.4 CONCLUSIONS

1. The rate of blood transfusion in the KNH ICU during the study period was 21.26%.
2. The mean transfusion trigger (pre-transfusion haemoglobin level) was 7.08 grams/ decilitre. with a statistically significant linear correlation between the pre- transfusion and the post transfusion haemoglobin levels.
3. The mean baseline haemoglobin level at admission was 9.97 grams/ decilitre.
4. The most common indication for transfusion was anaemia without any signs of active bleeding.
5. The average duration in the critical care unit before the first transfusion was 8.23 days.
6. The respiratory and the neurological systems were most commonly affected in the critical care patients who were transfused.
7. More surgical than medical patients required to be transfused. and most patients were emergency admissions as opposed to being electively admitted.
8. Most patients were transfused one unit of whole blood. with a statistically significant correlation between the amount of blood transfused and the presence of a transfusion reaction.

7.5 RECOMMENDATIONS

1. Considering the 10.9% of patients who got a transfusion reaction in this study, it is prudent to transfuse patients with a physiologic need rather than based on the haemoglobin level alone so as to reduce the frequency of unnecessary transfusions.

2. Critical care clinicians and policy makers need to review the transfusion trigger and formulate guidelines on the use of other blood alternatives, such as the use of erythropoietin, blood products and blood substitutes.

3. A long term prospective study on the associated morbidity and mortality associated with blood transfusions needs to be carried out.

4. An assessment of the incidence of anaemia in our critical care patients needs to be carried out and outcomes assessed in relation to causation and associated morbidity.

5. A review of the amount and type of blood transfused to critical care patients will be required, so that patients are transfused with specific blood components and with the least amounts possible.

8.0 APPENDICES

8.1APPENDIX 1

DEFINITION OF TERMS RELATING TO BLOOD TRANSFUSION IN THE ICU.

Apheresis: – The process of removing a specific component from blood and returning the remaining to the donor in order to collect more of one particular part of the blood than could be separated from a unit of whole blood. It is also called hemapheresis or pheresis.

Blood bank: – A place where blood is collected from donors, typed, separated into components, stored and prepared for transfusion to recipient. It may be a separate free – standing facility or part of a large laboratory in a hospital.

Blood transfusion: - The transfer of blood or blood components from one person (the donor) into the blood stream of another person (the recipient). This may be done as life saving manoeuvre to replace blood or blood products lost through bleeding.

Autologous blood transfusion: - Transfusion of patients own blood. Safest method, but requires planning and not all patients are eligible.

Directed donor blood: – allows the patients to receive blood from known donors.

Exchange transfusion: - slow removal of a person's blood and its replacement with an equal amount of a donor's blood (e.g. as is done in the treatment of neonatal jaundice).

Volunteer donor blood: - Usually most readily available and when properly tested has a low incidence of adverse effects.

APPENDIX 2

CONSENT EXPLANATION

My name is Emma Mutio, a postgraduate in anaesthesia at the University of Nairobi (UON). Part of my study requires me to do a study thesis based on clinical research as I am now doing.

My study is based on determining the blood transfusion practices among the critically ill patients in the KNH ICU.

This is important in order to avoid unnecessary blood transfusion together with its associated risks wherever possible. To do this, I shall obtain sequential records of patients' haemoglobin levels before transfusion and assess the indications of the same, and in this way come up with recommendations for managing anaemic patients who are critically ill.

Therefore I shall need your consent as the patient/ parent / guardian in order to be included in the study. This is a voluntary exercise and no victimization will occur on basis of refusal to be part of the study. One can also withdraw from the study at any point in time.

Any information obtained in the course of the study is beneficial to the management of the patient shall be released to the clinician directly managing the patients.

All information will also be treated with utmost confidentiality.

My contacts:

Emma Mutio

P.O. Box 1170-00200

NAIROBI.

TEL: 0722-984035.

020-2060748

PATIENT CONSENT

I..... of ..... Or I next of kin to ..... of ..... hereby give consent to participate in the study to determine the blood transfusion practice in the KNH ICU.

I have been informed that the techniques and inventions used in the study are safe and will not compromise the patient in any way.

I have the freedom to decline to participate in the study at ant time.

Signed:..... .....

Date:.....

I confirm that I have explained to the patient / Guardian the nature of the study.

Signed:.....

Date:.....

KIBALI CHA MGONJWA

Mimi..... kutoka ..... ama mimi jamaa wa karibu wa ..... kutoka ..... nimekubali kushiriki katika utafiti wa kubainisha namna ya utumizi wa damu katika matibabu ya wagonjwa mahututi.

Ninaelewa ya kwamba uchunguzi utafanyika bila madhara yoyote kwa mgonjwa.

Nina uhuru wa kujiuzulu kutoka kwa utafiti huu wakati wowote ule.

Sahihi.....

Tarehe.....

Ninathibitisha ya kwamba nimemuelezea mgonjwa kwa ukamilifu kuhusu huu utafiti

Sahihi.....

Tarehe.....

8.3 APPENDIX 3: DATA CAPTURE FORM

BLOOD TRANSFUSION PRACTICE AT THE KNH ICU.

Study number:_____

Name of patient (Initials) _____

Sex: Male = 1. Female = 2 _____

Age (years):_____

Diagnosis: _____

Haemoglobin level at admission_____

Haemoglobin level pre-transfusion _____

Post transfusion Haemoglobin level_____

Indication for transfusion:_____

Duration of stay in ICU: _____

Haematinics: 1 = being given 2= Not being given _____ _____

Primary admission category: Cardiovascular. Respiratory. Trauma.

Gastro-intestinal. Hepatobiliary. Neurological. Others. _____

Admission type: Elective. Emergency. Trauma. Medical. Surgical_____

Number of units transfused _____

Type of transfusion reaction encountered _____

APPENDIX 4: HAEMOGLOBIN ESTIMATION METHOD

This was done by automated machines designed to perform several different tests on blood. The measurements were done at the KNH ICU laboratory.

Within the machine, the red blood cells are broken down to get the haemoglobin into a solution. The free haemoglobin is exposed to chemical containing cyanide which binds tightly with the haemoglobin molecule to form cyan-met haemoglobin. By shining a light through the solution and measuring how much light is absorbed (specifically at a wavelength of 540 nanometres), the amount of haemoglobin can be determined.

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5th December 2007

Dr. Emma Mutio
Dept. of Surgery
School of Medicine
University of Nairobi

Dear Dr. Mutio

RESEARCH PROPOSAL. "AN ANALYSIS OF BLOOD TRANSFUSION PRACTICE AT THE KENYATTA N.HOSPITAL INTENSIVE CARE UNIT" (P258/09/2007)

This is to inform you that the Kenyatta National Hospital Ethics and Research Committee has reviewed and approved your revised research proposal for the period 5th December 2007 – 4th December 2008.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimen must also be obtained from KNH-ERC for each batch.

On behalf of the Committee, I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study

This information will form part of database that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

PROF C. KIGONDU
AG. SECRETARY, KNH-ERC

c.c. Prof. K.M. Bhatt, Chairperson, KNH-ERC
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