# IMPACT OF STORED RED BLOOD CELLS ON HAEMATOLOGICAL AND BIOCHEMICAL PARAMETERS IN CRITICALLY ILL PATIENTS IN A TERTIARY CARE HOSPITAL

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## ABSTRACT

## INTRODUCTION

The RBC transfusion rate in critically ill patients is reported between 20-40% in ICU. In-vitro storage of RBCs in a liquid medium at low temperature slows down their metabolism leading to accumulation of metabolic waste and cellular debris in the supernatant. Also, RBCs undergo

structural, functional, biochemical, biomechanical and immunological changes known as '*storage lesions'* which tend to increase with storage time.

**AIM** To determine the effectiveness of stored RBC utilization in critically ill patients admitted to ICU.

## OBJECTIVES

1. To compare transfusion of stored RBCs (≤ 7 days versus ≥ 21 days)
2. To evaluate the hematological & biochemical parameters in critically ill patients

## MATERIALS AND METHODS

A prospective observational cohort study from March 2020 to September 2021 in 195 ICU patients was done. It included patients in the age group of 20-80 years admitted to ICU & received packed red cell transfusions.

The patients were evaluated for severity of disease assessed by Acute Physiology And Chronic Health Evaluation II (APACHE II). Group 1 included 92 patients who received fresh RBCs (≤ 7 days) and group 2 included 103 patients who received old RBCs (≥ 21 days).

Samples were collected before and after 24 hours of transfusion. Parameters like Hb, Hct, K+, Na+ & pH were noted both pre and post transfusion.

## RESULTS

The majority of study population were males (51.80%) and females (48.2%). The most common indication for PRBC transfusion was pre-operative procedure (58.46%) & only 41.54% due to low Hb.

The overall mean rise in Hb in group 1 was 3.052g/dl and in group 2 was 2.736 g/dl respectively. Similarly, the overall mean rise in Hct in group 1 was 9.404% and in group 2 was 8.112%. Therefore, mean rise in Hb & Hct after transfusion in both the groups were statistically significant ($p=0.0022$ for mean rise in Hb, $p=0.0001$ for mean rise in Hct).

In about 5 patients of group 2 who were massively transfused with a mean of 6.6 PRBC units / patient, resulted in a mean increase in K+ level by 1.07mmol/L and the rise was statistically significant (p value<0.0001 ). As the patients' condition improved at the time of discharge, the APACHE II score in both the groups decreased from the time of ICU admission meaning that the patients' outcome improved & were statistically significant ($p<0.0001$).

## CONCLUSION

Transfusion of fresh PRBCs (≤ 7 days old) can be limited to patients undergoing cardiac surgeries, acute upper gastrointestinal bleed & acute renal failure patients.

**Keywords** : RBC (Red Blood Cell), ICU(Intensive Unit Care), APACHE II (Acute Physiology And Chronic Health Evaluation II), Hb (Hemoglobin), Hct (Hematocrit)

## **INTRODUCTION** :

Red Blood Cell (RBC) transfusion is one of the most important and common therapeutic intervention among patients in Intensive Care Unit ICU[1].Although they are lifesaving, they have come under immense scrutiny over the last few decades[2]. Anaemia is common in 90% of critically ill patients by day 3 of their ICU stay[3]. The RBC transfusion rate in critically ill patients is reported between 20-40% in ICU[3].

RBC transfusion is mainly indicated for improvement of oxygen-carrying capacity of blood to tissues. Stored blood may be transfused upto 42 days depending upon the anticoagulant used for storage. However, the regulatory requirements for this limit are based only on the percentage RBC survival 24 hours after transfusion as ≥ 75% and not on oxygen delivery capacities or clinical endpoints[4].

*In vitro* storage of RBCs in a liquid medium at low temperature slows down their metabolism leading to accumulation of metabolic waste and cellular debris in the supernatant. Also, RBCs undergo structural, functional, biochemical, biomechanical, immunological changes known as "**storage lesions**" which tend to increase with storage time.

The most sentinel event during RBC storage is rapid fall in 2,3-diphosphoglycerate (DPG) levels which is a allosteric modifier of hemoglobin that helps in release of oxygen at end organ. These levels are not undetected by 14 days of storage of the RBCs. Other changes include hemolysis, decreased adenosine triphosphate (ATP), pH, increased potassium and RBCs are transformed into echinospherocytes characterized by increased fragility and loss of deformability[4].

During packed red cell storage (PRBC), bioactive substances are progressively released into the supernatant that have the potential to prime neutrophils and mononuclear cells to synthesize cytokines and interleukins (ILs) like IL-1b, IL-6, Tumor Necrosis Factor – alpha (TNF-α) and RANTES which have a variety of inflammatory and immunomodulatory effects (transfusion-related immunomodulation [TRIM] effects *in vivo*[5]. RBCs prone to increased oxidative injury undergo protein and lipid peroxidation with release of lysophospholipids, which may cause transfusion-associated acute lung injury (ALI)[5].

Based on "first in, first out" policy, blood banks deliver oldest available RBC units when transfusion is requested to reduce wastage[6]. This lead to inevitable adverse effects like immunomodulation and alterations in the physiology of vascular perfusion. These effects can manifest themselves, especially in the vulnerable critically ill patients owing to their already altered homeostasis and altered immunological status [7]. Thereby, making structural changes to transfusion policy to deliver only fresh RBCs to critically ill patients would have far-reaching logistics. Hence, a stratified approach to RBC transfusion must be justified.

**AIM** :

To determine effectiveness of stored RBC utilization on critically ill patients admitted to ICU

**OBJECTIVES:**

To determine the influence of transfusion of stored RBCs (≤ 7days versus ≥ 21days) on certain haematological and biochemical parameters in the critically ill patients

**MATERIALS AND METHODS**

A prospective observational cohort study was done from March 2020 to September 2021 in 195 ICU patients after getting approval from Ethical and Research Committee of VMKV Medical College and Hospital. It included patients in the age group of 20-80 years admitted to ICU & received packed red cell transfusions. Our study excluded patients on chemotherapy, patients with length of ICU stay < 2 days and length of hospital stay < 1 week, terminally ill patients with brain stem dysfunction, burns patients, Chronic Kidney Disease (CKD) patients, patients with hepatic failure with elevated liver transaminases.

The patients were evaluated for severity of disease assessed by Acute Physiology And Chronic Health Evaluation II (APACHE II). Group 1 included 92 patients who received fresh RBCs (≤ 7 days) and group 2 included 103 patients who received old RBCs (≥ 21 days). Samples were collected before and after 24 hours of transfusion. Parameters like Hb, Hct, K+, Na+ & pH (obtained from MINDRAY BC-5000 Hematology Analyzer & RAPIDLab 348 EX Blood Gas Analyzer) were noted both pre and post transfusion.

Patients were followed up during their stay in ICU until they were stepped down to a ward. Statistical analysis was done using SPSS software version 19.

**RESULTS :**

The majority of study population were males (51.80%) and females (48.2%). The most common indication for PRBC transfusion was pre-operative procedure (58.46%) & only 41.54% due to low Hb. Most of the patients in group 1 received 4 units of PRBCs and 2 units of PRBCs in group 2 respectively.

The overall mean rise in Hb in group 1 was 3.052g/dl and in group 2 was 2.736 g/dl respectively as shown in figure 1. Similarly, the overall mean rise in Hct in group 1 was 9.404% and in group 2 was 8.112% as shown in figure 2. Therefore, mean rise in Hb & Hct after transfusion in both

the groups were statistically significant (p=0.0022 for mean rise in Hb, p=0.0001 for mean rise in Hct).

In group 1, there was a strong positive correlation between the number of PRBCs transfused & mean rise in Hb & Hct; r=0.943 for mean Hb rise, r=0.874 for mean Hct rise, p value statistically significant (p<0.0001 ) .

Similarly, in group 2 r=0.899 for mean Hb rise, r=0.814 for mean Hct rise, p value was statistically significant (p<0.0001). There were no significant changes in the concentration of Na+, K+ & pH after transfusion of PRBCs in both the groups.

In about 5 patients of group 2 who were massively transfused with a mean of 6.6 PRBC units / patient, resulted in a mean increase in K+ level by 1.07mmol/L and the rise was statistically significant (p value<0.0001 ) as shown in table 1. As the patients' condition improved at the time of discharge, the APACHE II score in both the groups decreased from the time of ICU admission meaning that the patients' outcome improved & were statistically significant (p<0.0001).

**Figure 1 : Distribution of mean rise in hemoglobin in patients who received < 7 days old PRBCs (group 1) and > 21 days old PRBCs (group 2)**

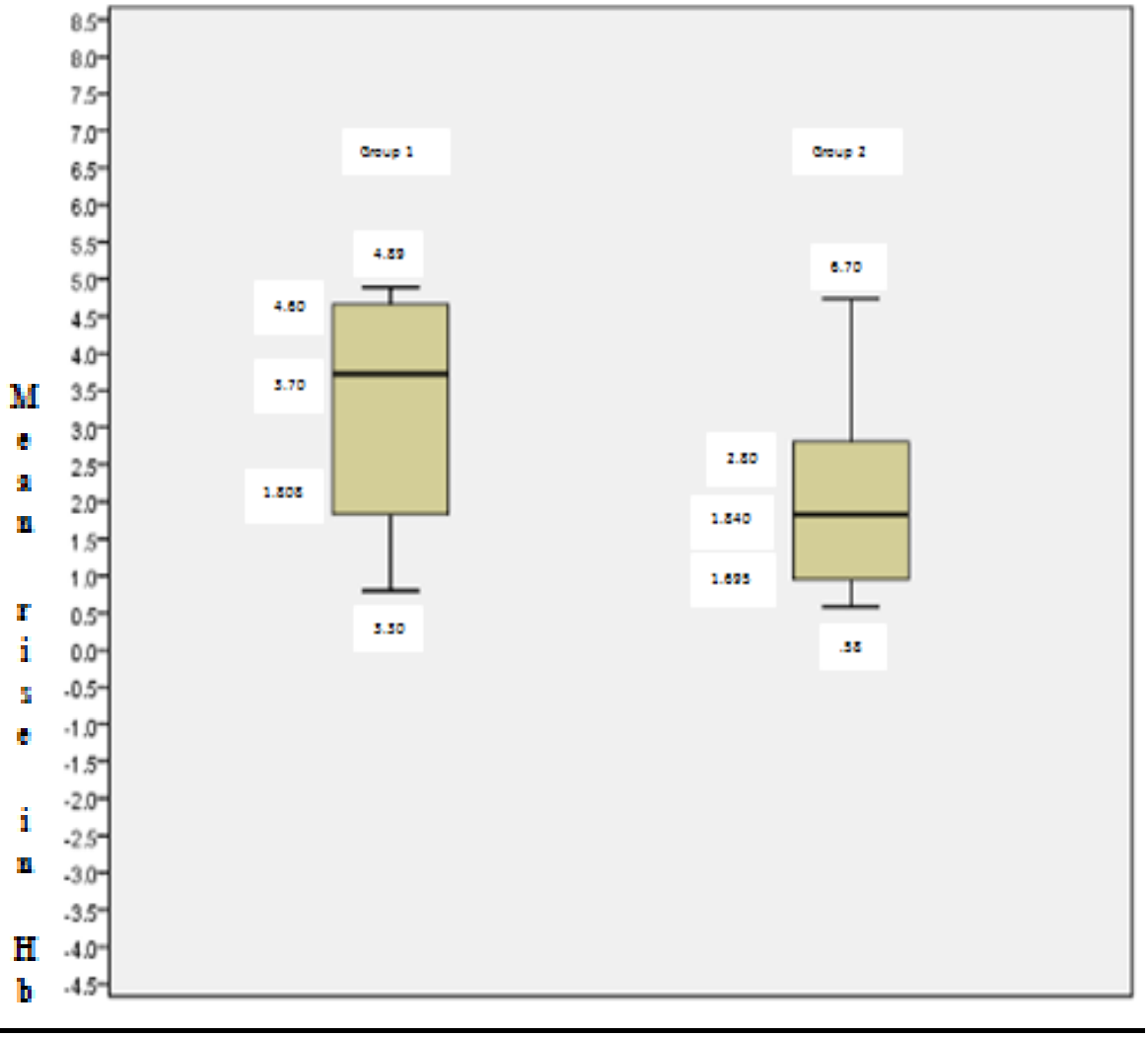


**Figure 2 : Distribution of mean rise in hematocrit in patients who received < 7 days old PRBCs (group 1) and > 21 days old PRBCs (group 2)**

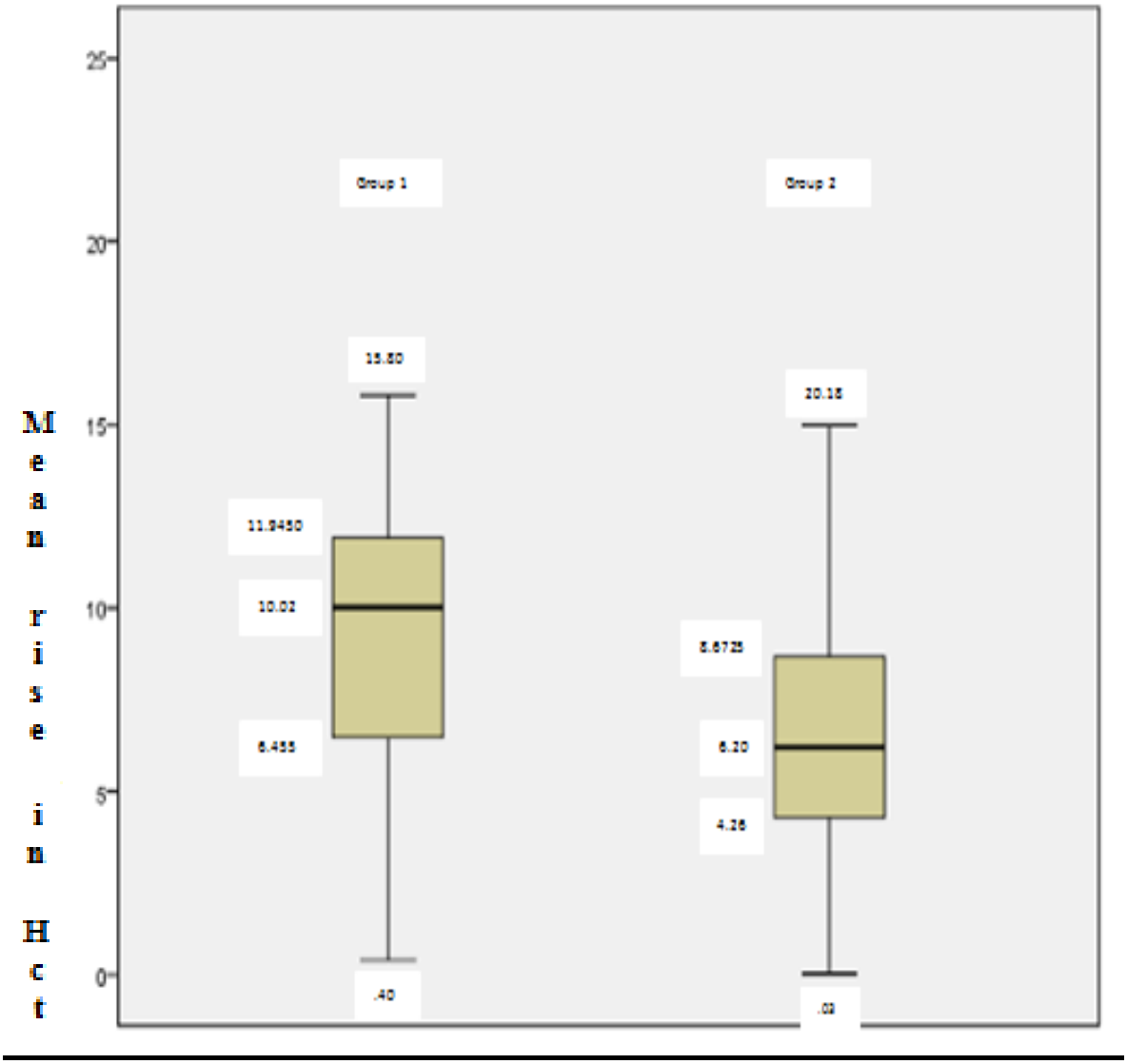


**Table 1 : Distribution of increased potassium levels in multi-transfused individuals (≥ 6 PRBC units/patient) with age of RBCs > 21 days old**

| **HYPERKALEMIA** | **NO. OF PATIENTS** | **INCREASE IN K+ (mmol/L)** | **NO. OF RBC UNITS** | **MEAN AGE OF RBCs (days)** |
|---|---|---|---|---|
| **Mild 5.5-6.5 K+ (mmol/L)** | 5 | + 0.72<br>+ 0.97<br>+ 1.02<br>+ 1.04<br>+ 1.59 | 7,6,6,7,7 | 29 |

## DISCUSSION

In the developing countries, anemia is a crucial problem that is very common yet the most forsaken matter. Worldwide, India is one of the countries with the highest prevalence of anemia. Approximately, 50% of the Indian population are anemic. Hence, anemia in the critically ill patients is an important issue. Many landmark studies have computed the prevalence of anemia and the impact of packed red cells transfusion in the critically ill patients.

Our prospective observational cohort study was done to determine the influence of transfusion of stored RBCs (≤ 7days versus ≥ 21days) on certain haematological and biochemical parameters in the critically ill patients which was the primary outcome. The most common indication for transfusion of packed red cell concentrates among the present study subjects was prior to the surgeries i.e. 58.46% and 41.54% due to low hemoglobin and medical co-morbidities. This was in concordance with Vincent *et al* (2002) where 65.2% of transfusions were prior to surgeries, 25% due to medical reasons and 9.9% in trauma cases [8].

In this study, the mean and standard deviation of APACHE II score at the time of admission among the study population who received < 7 days old packed red cells was 18.01 ± 5.98 and those who received > 21 days old packed red cells was 20.36 ± 6.72 which was statistically significant (p = 0.011). This was similar to a study by Phuping Akavipat *et al* [9], where the mean APACHE II score in ICU patients was 16.67 ± 5.99.

Among the study population, the severity of anemia based on their hemoglobin levels prior to the packed red cell transfusion were found to be moderate in 62.05 % followed by mild in 25.13 %. Also in our study, the mean hemoglobin level among the study subjects at the time of admission to ICU was 8.27±1.28 which was comparable to other studies – 8.3 ± 1.2, 8.2 ± 1.4 [10],[11]. In this study, the comparison of certain hematological parameters before and after transfusion of packed red cell concentrates in both the groups showed a statistically significant increase as shown in table 2

**TABLE 2** : Comparison of Hb levels before and after packed red cell transfusion

| **AUTHOR** | **NO. OF UNITS TRANSFUSED** | **MEAN±SD PRE-TRANSFUSION Hb(g/dl)** | **MEAN±SD POST-TRANSFUSION Hb(g/dl)** | **MEAN INCREMENT IN Hb LEVELS POST TRANSFUSION** |
|---|---|---|---|---|
| Wright et al[10] | 3 (1-4) units | 8.3±**1.2** | 11.2±**1.4** | 2.9±**1.24** |
| Sakr et al[11] | 1 unit | 7.1±**1.4** | 8.2±**1.2** | 1.1±**0.65** |
| Elizalde et al[13] | 2 units | 7.6 | 9.88 | 2.24±**0.68** |
| Salhan et al[14] | 2 units | 7.2±**1.5** | 8.6±**1.8** | 2.09±**1.5** |
| PRESENT STUDY | 4 (1-6) units | 8.04±**0.99** | 11.8±**0.90** | 3.81±0.11 |

Also, in this study, the mean hematocrit rise after 1,2,3,4, ≥ 5 units of PRBC transfusion was 3.23, 6.12, 8.68, 11.51 and 17.48 respectively in the group who received < 7 days old PRBCS. The mean hematocrit rise after 1,2,3,4, ≥ 5 units of PRBC transfusion was 3.18, 5.86, 8.52, 10.95 and 12.62 respectively in the group who received > 21 days old PRBCS. This was similar to a study by Pieracci *et al* [12] where there was significant increment in hematocrit level after transfusion of < 14 days old PRBCs as compared to ≥ 21 days old PRBCs (5.6% vs 3.5%, respectively; $p$ =0.005).

It is evident from our study, that there was a mild rise in potassium levels in 5 patients (2.56%) following administration of RBCs > 21 days old and is dependent upon the mean age of RBCs i.e 29

days and also on the number of PRBCs (≥ 6 units / patient ) transfused. This was comparable to a study by Radovan Uvizl *et al* [15] where rise in potassium levels were noted in 74% of patients (a mean of 8.47 RBC units / patient, mean storage time of 16.32 days) as shown in table 3.

**TABLE 3**: Comparison of changes in biochemical parameters *in vivo* after administration of stored RBCs

| **AUTHOR** | **MEAN AGE OF RBCs (in days)** | **BIOCHEMICAL PARAMETERS** | **PRE-TRANSFUSION (Mean ± SD)** | | | **POST-TRANSFUSION (Mean ± SD)** | | | **P value** |
|---|---|---|---|---|---|---|---|---|---|
| Radovan Uvizl *et al* [15] | 16.32 | Na+<br>K+<br>pH | 137**±5.5** | 4.31**±0.79** | 7.31**±0.12** | 139**±5.6** | 4.85**±0.82** | 7.3**±0.11** | 0.01<br><0.0001<br>0.429 |
| PRESENT STUDY | 29 | Na+<br>K+<br>pH | 133.49±4.16 | 4.55± 0.84 | 7.35± 0.09 | 133.63± 1.97 | 4.81± 0.62 | 7.36± 0.03 | 0.761<br>0.623<br>0.293 |

In this study, APACHE II Score was the secondary outcome of the patients. APACHE II Score is a scoring tool to predict mortality risk among the critically ill ICU patients. But in our study it was used to assist the clinical decision making and study the patient outcome at the time of discharge. It was observed that the patient outcome improved at the time of discharge i.e. mean and standard deviation of 9.62 ± 2.33 in patients who received < 7 days old PRBCs and a mean and standard deviation of 10.67 ± 4.96 in patients who received > 21 days old PRBCs. This was comparable to a study by Vincent JL *et al* [16].

However , our study includes a few limitations like small sample size . Also, APACHE II scoring tool was used to predict the mortality of the patients, it was dependent on patient's co-morbidities. Another limitation of this scoring tool was that the physiological variables in this tool were influenced by the ongoing treatment and therefore, time bias was present. It was also seen that the massively transfused patients received concomitant blood products like FFP and PLTs to avoid dilutional coagulopathy which does not fit in the inclusion criteria of our study.

## CONCLUSION :

Transfusion of fresh PRBCs (≤ 7 days old) can be limited to patients undergoing cardiac surgeries, acute upper gastrointestinal bleed & acute renal failure patients.

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## CONFLICT OF INTERESTS :

There are no conflicts of interest.

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