



Research Article

# Impact of Storage on Alteration in Biochemical and Hematological Characteristics in Locally Donated Blood from Lampung Province: Assessing Potential Risks for Recipients

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## ABSTRACT

The utilization of stored blood for transfusion purposes is a common practice in Blood Transfusion Units worldwide. However, the storage period can induce various cellular alterations, potentially comprising the quality and efficacy of blood transfusions. This study aims to investigate changes in biochemical and hematological parameters in blood donors during the storage period. This study was a prospective study involving the observation of 10 blood bags collected from local community donors in Lampung Province. The blood samples were stored in CPDA-1 anticoagulant bags at a controlled temperature of 2-6 ° C for 35 days. At regular intervals of 7 days, comprehensive assessments were performed, encompassing complete blood parameters, electrolyte concentration (Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>), and blood pH levels. After 35 days of storage, statistically significant alterations were observed. Notably, there was a significant increase in hematocrit levels ( $p=0.000$ ), mean corpuscular volume (MCV) ( $p=0.019$ ), lymphocyte counts ( $p=0.000$ ), and potassium concentrations ( $p=0.000$ ). Conversely, mean corpuscular hemoglobin concentration (MCHC) ( $p=0.025$ ), leukocyte counts ( $p=0.000$ ), neutrophil counts ( $p=0.000$ ), platelet counts ( $p=0.000$ ), sodium levels ( $p=0.000$ ), chloride levels ( $p=0.000$ ), and pH values ( $p=0.000$ ) were significantly declines. In conclusion, blood storage leads to notable alterations in biochemical and blood cell characteristics. Therefore, it is advisable to prioritize using fresh whole blood or blood stored for no more than seven days in transfusion practices to minimize the risk of post-transfusion reactions, especially in vulnerable recipients.

**Keywords:** Blood transfusion, biochemical changes, cellular changes, storage.

## INTRODUCTION

Blood transfusion services constitute a vital component of healthcare facilities, playing a crucial role in supplying blood for emergency care, surgical preparation, and the management of blood disorders (Wahidiyat & Adnani, 2017). Blood transfusion services in Indonesia are commonly



administered by Blood Transfusion Units (UTD) or Blood Banks. These services encompass three crucial aspects: the availability of blood supplies, the easy public access to blood products, and recipient safety. To streamline the management of blood availability and accessibility, UTDs store blood from donors in bags containing the CPDA-1 anticoagulant, maintaining it at a temperature of 2-6°C.

Stored blood undergoes a series of biochemical alteration (Yalcin et al., 2014), including changes in electrolyte levels (e.g., Na<sup>+</sup>, K<sup>+</sup>, and Cl<sup>-</sup>) (Cicha et al., 2000; Olivieri et al., 1993) and a decrease in blood pH levels (D'Alessandro et al., 2013). These changes could damage the cell membrane, resulting in alterations in cell shape, as manifested by changes in hematological parameters, such as the erythrocyte index value. Consequently, this condition shortens cell life and disrupts their biological function post-transfusion (Adams et al., 2015). Interestingly, donor characteristics such as genetics, lifestyle, and behavior also influence cell age, leading to variations in cell performance in donors from different populations after transfusion (Koch et al., 2019).

The reduction in cell age and disruptions in the biological function of cells following transfusion can significantly impact the effectiveness and attainment of desired clinical outcomes. Numerous studies have indicated that transfusions involving stored blood carry potential risks for recipients, especially those with severe medical conditions, such as acute myocardial infarction (Roback, 2011). Utilizing stored blood in transfusions may elevate the risk of adverse outcomes, including mortality, infections, kidney and lung impairment, thrombosis, swelling, as well as moderate to severe allergic reactions (Hod & Spitalnik, 2011; Sparrow, 2015; Spieth & Zhang, 2018).

Before a transfusion, blood transfusion units (UTDs) typically assess the compatibility of donors and recipients based on serological and immunological characteristics, as well as infectious diseases transmitted through transfusion. However, there has been a notable absence of assessments regarding the functional suitability of cells through the examination of biochemical and hematological parameters. Additionally, research on the biochemical and hematological changes in stored blood donated by local communities in Lampung Province remains relatively limited. This study aims to investigate the alterations in biochemical and hematological parameters during the storage period at UTDs for blood donors originating from the local communities in Lampung Province.

## **MATERIAL AND METHODS**

This study was a prospective study conducted at UTD Mesuji Health Service, UTD Pembina PMI Lampung Province, the Clinical Pathology Laboratory at Ragab Begawi Caram Regional Hospital in Mesuji Regency, and the regional health laboratory Lampung Province. This study conducted during May to June 2023 period.

This study involved the examination of blood samples obtained from local community donors in Lampung Province. The blood was stored in bags containing the anticoagulant CPDA-1 and maintained at a temperature between 2-6°C, mirroring the storage conditions for blood designated for transfusion. The study population consisted of all blood bags donated voluntarily at both the UTD Mesuji Health Service and UTD Pembina PMI Lampung Province during the period from May to June 2023. The sample size was determined using the Taro Yamane formula for a finite population, with a 5% margin of error, resulting in a total sample size of 10 blood bags from voluntary donors. The sampling technique employed was simple random sampling, with one blood bag selected as a sample from every five bags of donor blood.

Blood samples were subject to analysis for biochemical and haematological parameters both at the initiation of storage and subsequently at the end of each of the first, second, third, fourth, and fifth weeks. The biochemical parameters, included electrolyte levels (Na<sup>+</sup>, K<sup>+</sup>, and Cl<sup>-</sup>) and blood pH levels, which were assessed using a Caretium XI-921 instrument. On the other hand, haematological parameters encompassed erythrocyte count, leukocyte count, platelet count, haemoglobin (Hb) levels, haematocrit (Ht), erythrocyte index, leukocyte index, and platelet index were examined using a Sysmex XS-500i haematology analyser.

The data obtained from the examination of biochemical and haematological parameters have been analysed using the Repeated Measure ANOVA test or Friedman test with a confidence level of 95%. Subsequently, the Bonferroni or Wilcoxon test was employed to identify differences at each measurement time point. Data analysis was conducted using the SPSS Statistics 23.0 software program.

## RESULTS AND DISCUSSION

Several previous studies have documented various alterations that occur in blood stored for transfusion purposes (Abdalla et al., 2021; Cicha et al., 2000; D'Alessandro et al., 2013; Olivieri et al., 1993; Shirvastava & Dutta, 2020). The findings of our study are consistent with this research. In this investigation, changes in cell characteristics and biochemical properties were observed throughout the storage duration.

### The effect of storage on erythrocyte cells

This study indicates that storing whole blood for 35 days causes an increase in haematocrit levels. Conversely, the erythrocyte count tends to decrease, although not significantly. The study also shows that haemoglobin levels in stored blood did not experience significant changes. Furthermore, when examining erythrocyte indices, storage causes a significant increase in MCV, whereas MCHC shows a significant decrease. However, MCH does not exhibit a significant change during the storage period (Table 1).

**Table 1. Change in Hb, Ht, Erythrocyte Count and Erythrocyte Indices During Storage**

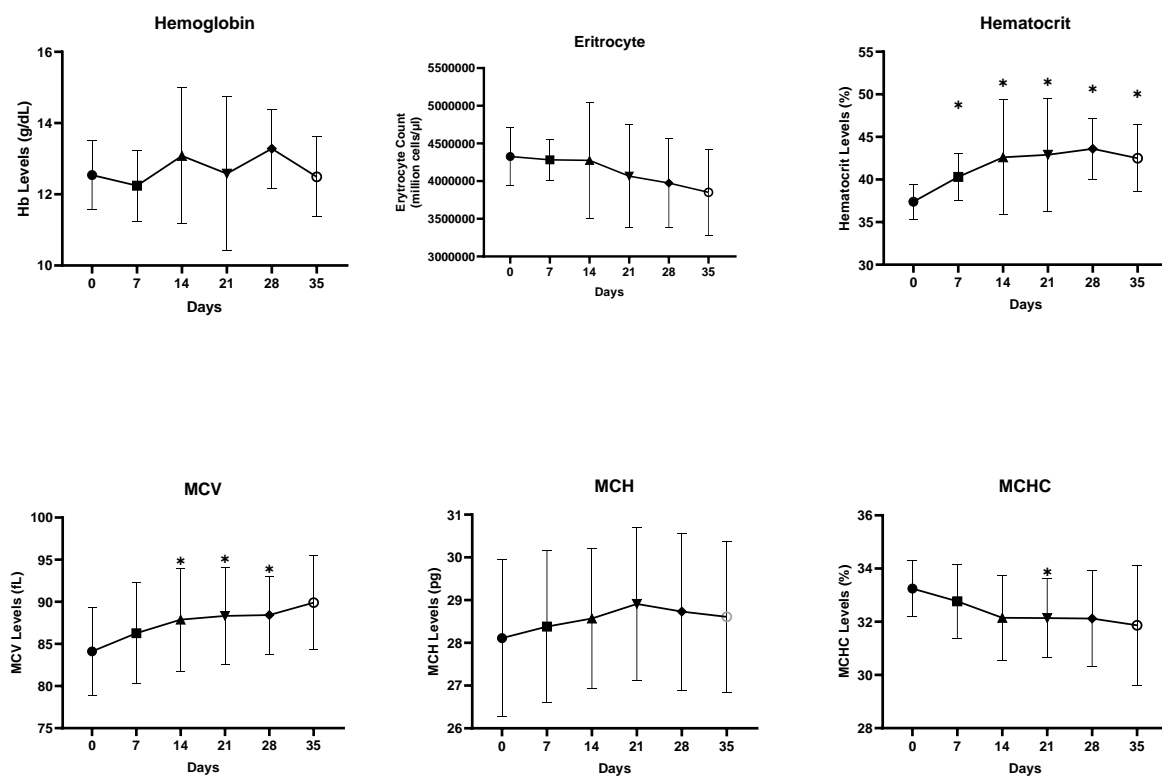
Parameter	n	Days						P
		0	7	14	21	28	35	
Hb (g/dL)	10	12,54±0,9	12,24±0,9	13,08±1,9	12,58±2,2	13,28±1,1	12,49±1,1	0,109
Eritrocytes (cells x10 <sup>6</sup> /μL)	10	4,33±0,4	4,28±0,3	4,27±0,8	4,06±0,7	3,98±0,6	3,85±0,6	0,270
Ht (%)	10	37,4±2,1	40,3±2,7	42,6±6,7	42,9±6,6	43,6±3,6	42,5±3,9	0,000*
MCV (fl)	10	84,12±5,3	86,28±5,9	87,88±6,1	88,32±5,7	88,43±4,6	89,91±5,5	0,019*
MCH (pg)	10	28,11±1,8	28,38±1,8	28,57±1,6	28,91±1,8	28,73±1,8	28,61±1,7	0,657
MCHC (g/dL)	10	33,25±1,1	32,77±1,4	32,15±1,6	32,14±1,5	32,12±1,8	31,87±2,3	0,025*

**Exp:\*** There is a significant difference in mean values based on the Repeated Measure Anova test or Friedmann test at  $\alpha=5\%$ .

Further test results revealed a significant increase in Ht levels starting from day 7 of storage, while MCV values exhibited a significant increase from day 14 onward. Although not statistically significant, there was a noticeable decreasing trend in the erythrocyte count beginning on day 14. Similar trends were observed in the MCHC values, which also showed a decreasing trend from day 14 onwards (Figure 1).

In this study, a noticeable trend of decreasing erythrocyte count was observed during storage period, although it was not statistically significant (Figure 1). These finding align with several previous study that also reported similar decreasing trend in erythrocyte count during storage (Batham & Nayak, 2018; García-Roa et al., 2017). Decrease in erythrocyte count indicates systemic

and biochemical changes in erythrocyte, resulting in a shortened cell lifespan. During storage, erythrocyte cells undergo an increase in lactic acid and a decrease in glycolysis, leading to reduce ATP levels (Mustafa et al., 2016). Insufficient ATP levels, disrupt ion pumps in cell membranes, disturbing cellular homeostasis and causing structural changes in erythrocyte cells. This condition leads to an increase in cell volume and a change in the shape of erythrocyte from biconcave to echinocyte, which are more susceptible to rupture (Mustafa et al., 2016; Orlov & Karkouti, 2015). These changes are corroborated by a significant increase in MCV and Ht values observed during storage (Table 1). An increase in MCV indicates an enlargement in cell volume, while an increase in Ht is known to be associated with alteration in cell morphology (Bosman et al., 2008). Interestingly, the significant increase in MCV began on day 14, indicating significant change in erythrocyte morphology on that day. These finding are supported by previous research conducted by Gupta et al. (2016), who observed a substantial increase in echinocyte forms in erythrocyte appearance after 14 days of storage (Gupta et al., 2016).



**Figure 1. Mean±SD erythrocyte cell parameters. \* indicates a significant difference compared to baseline (day 0) using the Bonferroni or Wilcoxon test at  $\alpha=5\%$ .**

Changes in the morphology of erythrocyte cells not only affect their age but also influence the effectiveness of transfusions. Erythrocytes with an echinocyte shape tend to promote clotting, potentially leading to blockages in microvascular blood vessels and causing tissue ischemia (Adams et al., 2015). Furthermore, this echinocyte form makes erythrocytes more susceptible to removal by macrophages following transfusion (Oyet et al., 2018). Additionally, the echinocyte shape reduces the elasticity of erythrocytes, impeding their ability to traverse narrow micro vessels. Consequently, oxygen-carrying erythrocytes may be unable to reach their intended target cells due to obstruction in the microvascular blood vessels (Yalcin et al., 2014).

**The effect of storage on leucocyte cells**

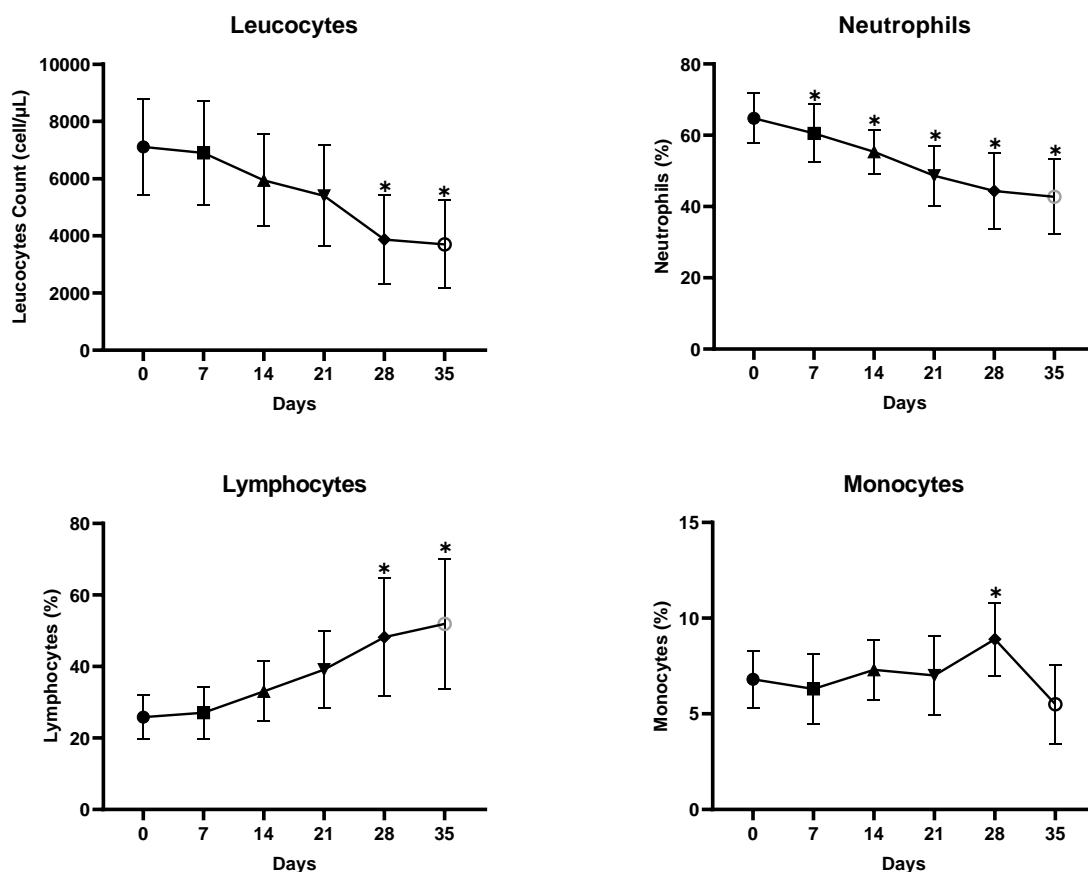
In this study, we found that storing whole blood caused a significant decrease in the number of leucocytes. Furthermore, during storage, the number of lymphocytes exhibited a significant increase, while the number of neutrophils exhibited a significant decrease (Table 2).

**Table 2. Change in Leucocyte Count and Differential Count During Storage**

Parameter	n	Days						p
		0	7	14	21	28	35	
Leucocytes (cells/ $\mu$ L)	10	7110 $\pm$ 1671	6895 $\pm$ 1808	5940 $\pm$ 1613	5400 $\pm$ 1766	3870 $\pm$ 1547	3700 $\pm$ 1536	0,000*
Neutrophils (%)	10	64,78 $\pm$ 7,1	60,54 $\pm$ 8,2	55,37 $\pm$ 6,2	48,62 $\pm$ 8,4	44,39 $\pm$ 10,7	42,74 $\pm$ 10,6	0,000*
Lymphocytes (%)	10	25,81 $\pm$ 6,1	27,08 $\pm$ 7,2	33,06 $\pm$ 8,4	39,14 $\pm$ 10,7	48,22 $\pm$ 16,6	51,91 $\pm$ 18,21	0,000*
Monocytes (%)	10	6,8 $\pm$ 1,5	6,3 $\pm$ 1,8	7,3 $\pm$ 1,6	7,0 $\pm$ 2,1	8,9 $\pm$ 1,9	5,5 $\pm$ 2,1	0,002*

**Exp:\*** There is a significant difference in mean values based on the Repeated Measure Anova test or Friedmann test

Further test results revealed a consistent decline in the number of leucocyte cells began from day 7, which continued steadily until day 35. Similar result were also found in neutrophil cells, which exhibited a significant decreasing trend beginning on day 7 of storage. In contrast, lymphocyte cell continued to increase throughout the storage period, with a significant increase observed on days 28 and 35. Furthermore, the number of monocytes showed a tendency to increase until day 28, but decreased again on day 35 (Figure 2).



**Figure 2. Mean $\pm$ SD leucocyte cells. \* indicates a significant difference compared to baseline (day 0) using the Bonferroni or Wilcoxon test at  $\alpha=5\%$ .**

This study also revealed a notable reduction in the number of leukocyte cells during blood storage, with the most significant decline observed on days 28 and 35. However, a downward trend in leukocyte cell count was evident on day 7, but not statistically significant (Table 2). These

findings suggest that alterations in leukocyte cells begin around the 7th day of storage, consistent with the significant decrease in neutrophil cells from day 7 to day 35. Similar findings have been reported in previous studies (Aninagyei et al., 2018; Jobes et al., 2011).

Several factors contribute to the decline in leukocyte cell count during storage. First, the decrease in ATP levels during storage leads to a loss of cell viability (Marabi et al., 2021). Second, microaggregate formation involving leukocytes, platelets, fibrin, cold globulin, and cellular debris occurs during storage (Ahmed & Orakah, 2021). The third factor involves the loss of cell characteristics as a result of cellular aging (Adias et al., 2012).

Interestingly, the research identified a noticeable trend of increasing lymphocyte counts. Similar findings are supported by prior studies conducted by Adias et al. (2012), Shirvasta & Dutta (2020), and Gupta et al. (2016), all of which observed a significant rise in lymphocyte percentages during storage. These results indicate that granulocytes are more susceptible to changes compared to mononuclear cells, specifically lymphocytes and monocytes, which exhibit greater stability throughout the storage period (Ahmed & Orakah, 2021).

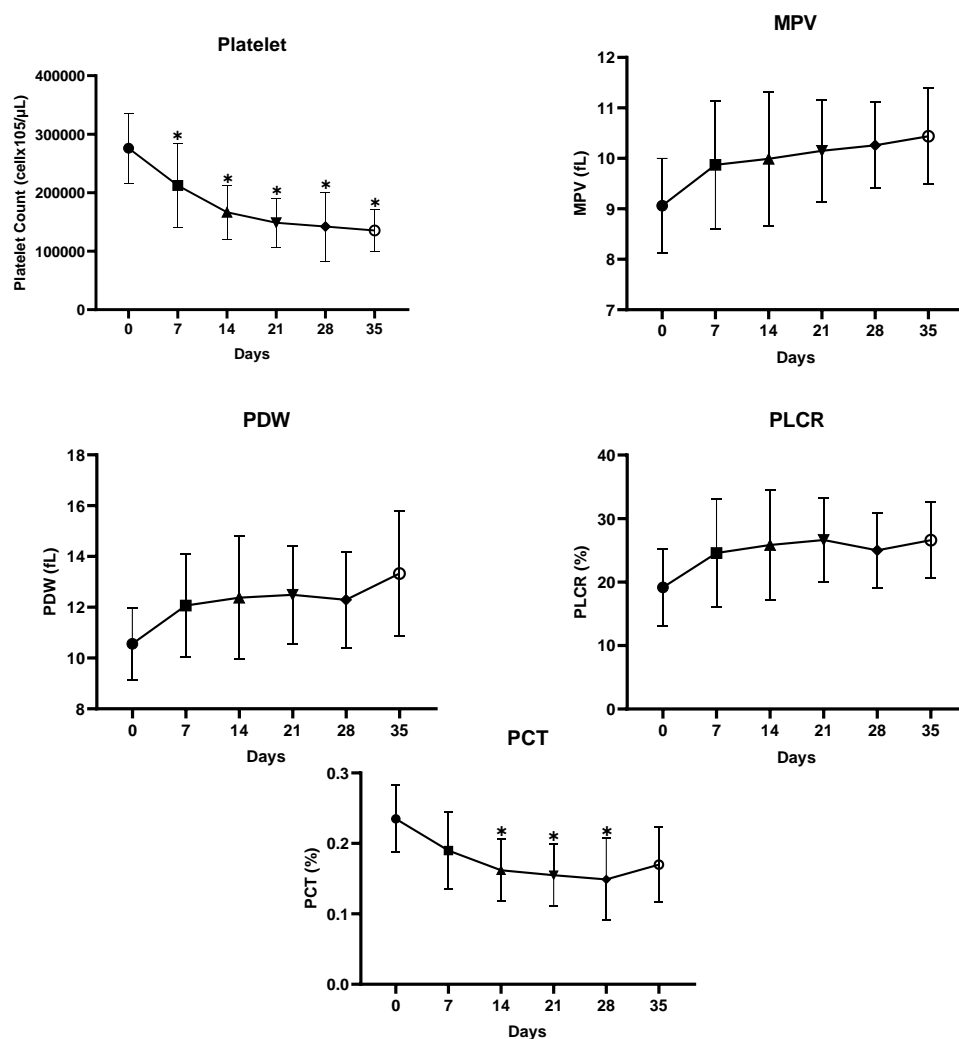
**The effect of storage on platelets**

Similar to leucocytes, the number of platelets in whole blood also decrease significantly during the storage period. This decline was accompanied by a trend toward increased values for MPV, PDW, and PLCR, although these changes were not statistically significant. In contrast, the PCT index showed a significant decrease throughout the storage period (Table 3). Further test result showed a significant decline in platelet count from day 7, which continued to decline significantly until day 35 (Figure 3).

**Table 3. Change in Platelet and Platelet Indices During Storage**

Parameter	n	Days						p
		0	7	14	21	28	35	
Platelet (x10 <sup>5</sup> /μL)	10	2,76±0,6	2,12±0,9	1,67±0,5	1,49±0,4	1,42±0,6	1,36±0,4	0,000*
MPV (fL)	10	9,06±0,9	9,87±1,3	9,99±1,3	10,15±1,0	10,26±0,8	10,44±0,9	0,084
PDW (fL)	10	10,56±1,4	12,07±2,0	12,38±2,4	12,49±1,9	12,29±1,8	13,33±2,4	0,108
PLCR (%)	10	19,16±6,0	24,58±8,5	25,83±8,6	26,63±6,6	25,00±5,9	26,60±5,9	0,151
PCT (%)	10	0,24±0,05	0,19±0,06	0,16±0,04	0,16±0,04	0,15±0,06	0,17±0,05	0,000*

**Exp:\*** There is a significant difference in mean values based on the Repeated Measure Anova test or Friedmann test at α=5%.



**Figure 3. Mean±SD platelet. \* indicates a significant difference compared to baseline (day 0) using the Bonferroni or Wilcoxon test at  $\alpha=5\%$ .**

Several previous studies have consistently reported a decline in platelet counts during storage (Adias et al., 2012; Ahmed & Orakah, 2021; Marabi et al., 2021). This reduction can be attributed to multiple factors. Firstly, diminishing cell viability due to decreased ATP levels during storage is a significant contributor (Marabi et al., 2021). The formation of microaggregates involving platelets during storage can also lead to decreased platelet counts (Ahmed & Orakah, 2021; Marabi et al., 2021). Moreover, the natural aging of cells results in the degradation of dead cells, further reducing platelet numbers (Ahmed & Orakah, 2021).

The decrease in platelet count during storage not only diminishes their effectiveness when transfused to patients but also increased risk of post-transfusion reactions. These reactions, such as sepsis, inflammation, or other immune system-related reactions, pose a significant threat to vulnerable patients, including those recovering from heart surgery or battling malignant diseases (Aubron et al., 2018).

### **The effect of storage on blood biochemical**

This study indicates that storing whole blood for 35 days can significantly impact the sodium, potassium, chloride, and blood pH levels. Specifically, sodium, chloride, and blood pH

levels showed significant decrease, while potassium showed a significant increase during storage period (Table 4).

**Table 4. Blood Biochemical Change During Storage**

Parameter	n	Days						p
		0	7	14	21	28	35	
Sodium (mEq/L)	10	149,3±1,2	147,9±2,1	146,4±3,9	148,8±12,6	139,8±6,2	138,5±13,7	0,001*
Potassium (mEq/L)	10	2,39±0,5	11,45±2,7	15,26±2,4	19,51±3,4	22,06±3,8	25,12±4,2	0,000*
Chloride (mEq/L)	10	84,50±1,8	82,50±1,3	79,60±1,8	77,50±1,9	77,20±3,8	75,30±4,2	0,000*
Blood pH	10	7,59±0,2	7,36±0,2	7,21±0,2	7,07±0,2	6,92±0,1	6,72±0,2	0,000*

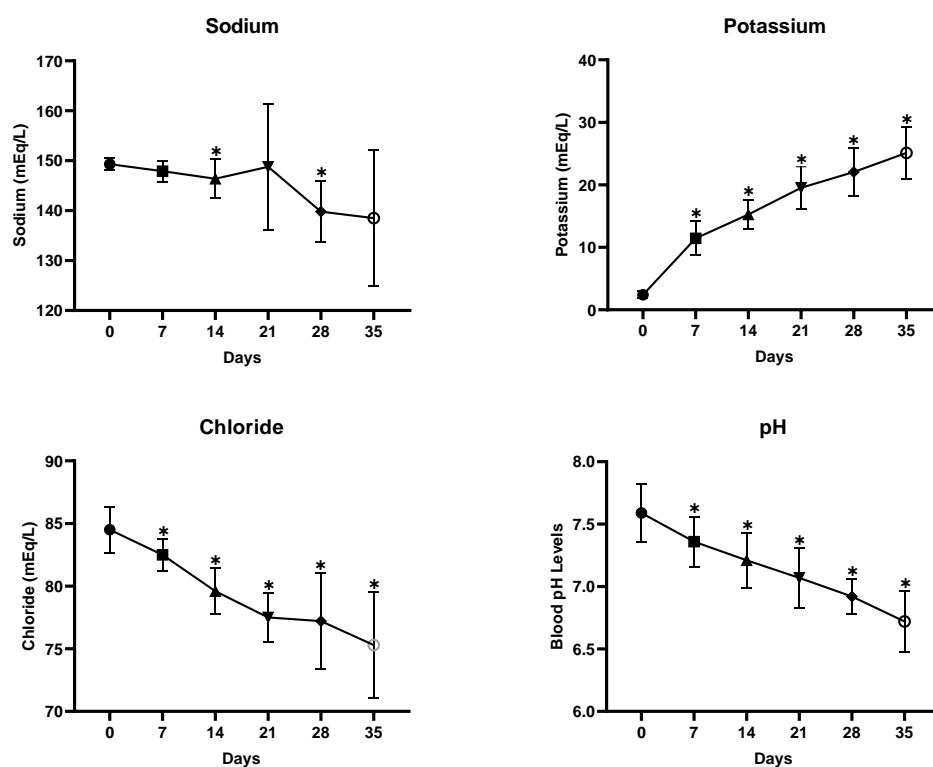
**Exp:\*** There is a significant difference in mean values based on the Repeated Measure Anova test or Friedmann test at  $\alpha=5\%$ .

Further test results revealed distinct trends in the levels of sodium, chloride, potassium, and blood pH during storage. Sodium levels showed a significant decline starting at day 14, continuing to decrease steadily until day 35. Similarly, chloride levels showed a significant decrease from day 7, with a continuous decline observed until day 35. In contrast, potassium levels followed an opposing trajectory, showing a significant increase from the 7th day of storage and continuing to increase significantly until the 35th day. Concurrently, blood pH underwent a significant decrease starting on the 7th day of storage, with the trend persisting until the 35th day (Figure 4).

In this study, a significant decrease in sodium levels was observed starting at day 14 of storage and continuing through day 35 (Figure 4). These findings align with previous study conducted on Packed Red Cells (PRC), which indicated that sodium levels in PRC stored for over 14 days were significantly lower compared to those stored for less than 14 days (Ashan et al., 2020). Similar outcomes have been reported in several studies involving diverse populations, including Indian, Portuguese, and Ghanaian subjects (Nogueira et al., 2015; Opoku-Okrah et al., 2015; Verma & Dahiya, 2015).

This study also revealed a significant increase in potassium levels, which began on day 7 and continued through day 35 of storage (Figure 4). These results are consistent with previous study conducted on both whole blood (Zetalini et al., 2019) and Packed Red Cells (PRC) (Asryani et al., 2018; Sutjiyanto et al., 2014). Moreover, studies conducted in various countries, including Portugal (Nogueira et al., 2015), Uganda (Oyet et al., 2018), and India (Verma & Dahiya, 2015), have reported similar findings.





**Figure 4. Mean±SD Electrolyte and pH. \* indicates a significant difference compared to baseline (day 0) using the Bonferroni or Wilcoxon test at  $\alpha=5\%$ .**

Changes in electrolyte levels in stored blood are closely linked to disruptions in the sodium/potassium pump that occur during storage. Throughout the storage process, there is a decrease in glycolysis, leading to a reduction in ATP production (Mustafa et al., 2016). The absence of ATP disrupts the functioning of the sodium/potassium pump in the cell membrane. Consequently, potassium ions exit the cell while sodium ions enter the cell through the semi-permeable membrane (Marabi et al., 2021). This process occurs continuously, gradually resulting in decreased sodium levels in the plasma and a significant increase in plasma potassium levels.

In this study, it was observed that on day 7, plasma potassium levels had increased significantly, reaching 11.45 mEq/L. This value is considerably higher when compared to the normal range for plasma potassium, which typically falls between 3.5 and 5.0 mEq/L. Such a substantial increase suggests that transfusions using whole blood stored for more than 7 days may pose potential risks to recipients, especially those with certain medical conditions, such as kidney and heart failure (Marabi et al., 2021). On the other hand, the storage of whole blood also resulted in a significant decrease in sodium levels. This decrease carries potential risks for the recipient, particularly in cases where recipients already have low sodium levels or are experiencing diarrhoea. Low sodium levels can make individuals more susceptible to oedema (Marabi et al., 2021).

In addition to the observed changes in blood cells and electrolytes, this study also demonstrates that the blood storage process leads to a decrease in blood pH. This decline begins at day 7 and steadily continues until day 35, with blood pH potentially dropping by as much as 0.87 points over this 35-day period. These findings align with previous study conducted in different countries and among diverse populations (Nogueira et al., 2015; Oyet et al., 2018; Verma & Dahiya, 2015). The decrease in pH during storage is primarily attributed to an increase in protons, which results from the accumulation of lactic acid within the blood bags (Oyet et al., 2018). Lactic acid is

the end product of the glycolysis process in erythrocytes. When the blood in the bag remains static, lactic acid production continues without the opportunity for breakdown. Consequently, as storage time increases, blood pH progressively decreases. The decrease in blood pH can cause cells membranes become more fragile and susceptible to lyse following transfusion.

## CONCLUSION AND SUGGESTION

Blood storage causes a significant decrease in sodium, chloride and blood pH levels, while potassium experiences a significant increase. Furthermore, blood storage also induces alterations in red blood cells, leukocytes, and platelets. In light of these findings, researchers suggest for the preference of fresh whole blood or blood stored for no more than 7 days when considering transfusions. This approach is recommended to minimize the occurrence of post-transfusion reactions, particularly in recipients who may be more vulnerable.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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