Original Article

Frequency of Different Perinatal Variables in Neonates with Different Reticulocyte Status During the Early Postnatal Period

Muhammad Rashid ul Hassan,[1] Mizna Arif,[2] Ammad Waheed Khan,[3] Zeekash ur Rehman Malik,[4] Muhammad Asif Ali,[5] Asad Nazir[6]

[1,2]Department of Pathology, King Edward Medical University, Lahore; [3,5]Department of Community Medicine, Shalamar Medical College, Lahore; [4,6]Department of Paeds Medicine, The Children's Hospital, Lahore

Abstract

Background: Reticulocyte is the young cell of the red blood cell and their estimation is very important to polarity marrow activity and erythropoiesis. During the early postnatal period, the transition from fetal to extrauterine life postnatal, physiologic changes occur and erythropoiesis is an essential part of the neonate oxygen delivery. Based on fact that reticulocytes reflect contemporary state of erythropoiesis, assessment of their numbers could prove effective in early detecting neonates with potential hematologic diseases and perinatal problems.

Objective: The objective of this study is to determine frequency of Different Perinatal Variables with Reticulocyte spectrum in neonate.

Method: This cross-sectional study was carried out on 160 neonates attending a tertiary health facility. Information obtained by using a structured questionnaire from medical records. Perinatal characteristics were investigated across reticulocyte status by applying chi-square tests, independent t-test, logistic regression, as well as the bivariate Pearson correlation.

Results: No association existed between reticulocyte status and type of delivery (p = 0.942) or SGA status (p = 0.884). Nevertheless, neonates within this cohort who had high reticulocyte count values when delivered had significantly lower APGAR scores of (p= 0.047). There was a near significant main effect for CPAP use in predicting high reticulocyte count (F [1:71] = 3.90; p = 0.069. Analyzed by logistic regression analysis, gestational age, SGA status, and mode of delivery could not be ranked as significant predictors of reticulocyte status since the values were found to be beyond the 0.05 level.

Conclusion: The results of this study underpin the importance of the studies carried out in order to determine the effectiveness of the reticulocyte counts as biomarkers in neonatal care.

Introduction

Reticulocyte is the young cell of the red blood cell and their estimation is very important to polarity marrow activity and erythropoiesis. The increase in their count is an index of the body's response to hypoxia,

anemia, or other hematologic stresses they are an important diagnostic indicator, especially in the newborn.[1] During the early postnatal period, the transition from fetal to extrauterine life postnatal, physiologic changes occur and erythropoiesis is an essential part of the neonate oxygen delivery.[2] Based on fact that reticulocytes reflect contemporary state of erythropoiesis, assessment of their numbers could prove effective in early detecting neonates with potential hematologic diseases and perinatal problems.[3]

Newborn prognosis differs count by several perinatal characteristics including gestational age, delivery mode, and SGA status. For example, preterm infants suffer from reversible anemia that lengthens erythropoiesis because of immaturity of the bone-marrow function, predisposing them to iron deficiency anemia in the early postnatal period.[4,5] Likewise, neonates with SGA status or prenatal hypoxia have increased reticulocyte count as an adaptation to the reprogramming strategies to combat intrauterine growth restrictiveness.[6] Based on past research the authors found that it would be important to utilize reticulocyte counts as a biomarker for these types of neonatal adaptations.[7]

Clinically, care strategies including CPAP (Continuous Positive Airway Pressure) are usually needed for treating RD in neonates. These interventions impact oxygenation and therefore indirectly controls erythropoietic activity by the generation of oscillations in oxygen need.[8] Explaining the correlation between oxygen dependency for neonates and the reticulocyte count is important to assess the level of preterm distress and differentiate optimal approaches.[9]

APGAR scores that evaluate the condition of a neonate that has just been born are on the list of perinatal indicators. Hypo APGAR scores are linked to emergent neonatal status and requirement for intervention care. Studies conducted have also shown that poor APGAR scores are indications of high reticulocyte counts which is as a result of hematological stress resulting from hypoxia associated with birth.[10] Nevertheless, the associations of these variables and the abilities of these variables to quantify neonatal morbidity and mortality have not really been investigated, especially in the context of Lower- and Middle-Income Countries like Pakistan.[11]

The importance of this study lies in establishing how reticulocyte count can serve as a predictive biomarker for neonatal outcomes. Understanding how a single reticulocyte reading determines future morbidity is crucial for early intervention strategies in neonatal care, potentially improving survival rates and reducing long-term complications in high-risk newborns. This research addresses a critical gap in neonatal hematologic assessment protocols.

Yet, reticulocyte count has been marginally applied in neonatal practice although it is a valuable instrument in clinical practice. This implies that the potential of using this parameter for day-to-day biomarkers in measuring neonatal health, especially with other perinatal factors should be studied further.[12] The purpose of this study is to identify perinatal characteristics that may correlate with reticulocyte count of newborns: factors are newborn's gestational age, APGAR scores, SGA status, mode of delivery, and requirement for CPAP. Thus, this work aims at adding evidence into context utilizing hematologic parameters enhancing neonatal healthcare.

Methods

This is a cross-sectional study done in a tertiary care facility in Pakistan over six months. Information was obtained from each patient's chart, then used in a retrospective analysis.

Sample size of 150 neonates using 95% confidence level, 8% margin of error with expected proportion having low reticulocyte count of 49.7%. A total of 160 patients were observed to manage the missing data. Inclusion Criteria of this study includes: both genders males and females, neonates of less than one week or 7 days of birth, neonates whether inpatient or outpatient whose care givers have granted permission, Neonates born preterm < 37 weeks on term between 37-42 weeks and post term after 42 weeks as per antenatal scan. The exclusion criteria of this study includes: births outside the hospital, presence of chromosomal anomalies, presence of congenital major malformations, and the presence of hemolytic diseases or feto-maternal transfusion syndrome. Data were collected using the following variables by a pre-defined proforma which include: Gestational Age (weeks), Small for Gestational Age (SGA) status (Yes/No), APGAR Score (1–10), CPAP / Bag and Mask Administration (Yes/No), Mode of Delivery (Vaginal / C-section) and Reticulocyte Count (% and High/Low classification). Data were analyzed by the Statistical Package for the Social Sciences (SPSS). The perinatal variables were described as percentages and means and standard deviations for continuous variables, and chi-squares were used to identify the relations between reticulocyte status (high/low) and discrete variables. A p value <0.05 was used for determining statistical significance.

Results

The descriptive statistics for the study sample showed the following: The average gestational age was 32.46 weeks (±5.29), with a range of 24–42 weeks. The average reticulocyte count was 5.009 (±1.63), ranging from 2.0 to 8.0. The average APGAR score was 7.43 (±1.15), with a range of 6 to 9. (Figure-1).
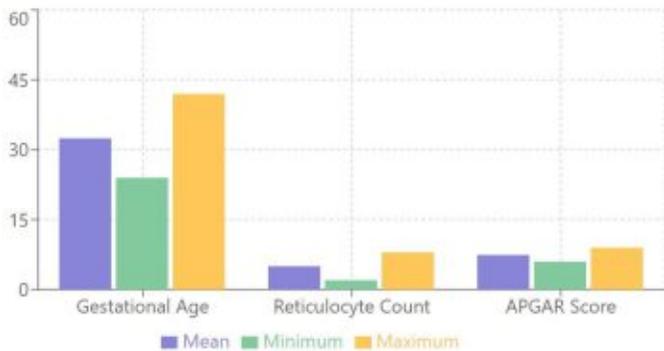

Figure 1: *The Descriptive Statistics Of Gestational Age, Reticulocyte Count And APGAR Score*

With respect to the mode of delivery-based reticulocyte count analysis, the findings indicated that 50 individuals with high reticulocyte counts were delivered vaginally and 32 by cesarean section, whereas 48 individuals with low reticulocyte counts were delivered vaginally and 30 by cesarean. A chi-square test indicated that there was no significant correlation between reticulocyte count and mode of delivery (p = 0.942).(Figure-2).

Figure 2: *Reticulocyte count analysis in relation to mode of delivery*

The chi-square test revealed no significant relationship between reticulocyte count and SGA status (p = 0.884) in neonates of Small for Gestational Age (SGA) status. 68 non-SGA infants and 14 SGA infants had high reticulocyte counts, while 64 non-SGA and 14 SGA infants had low reticulocyte counts (Table 3). Table 3: Reticu-

locyte Count and Small for Gestational Age (SGA)

Figure 3: *Reticulocyte Count and Small for Gestational Age (SGA)*

In the APGAR score analysis, neonates with high reticulocyte counts had a mean score of 7.26 (±1.15), while those with low reticulocyte counts had a mean score of 7.62 (±1.12). A t-test revealed a significant result (p = 0.047) with a small to medium effect size (Cohen's d = -0.316). Finally, a weak negative correlation was found between APGAR scores and reticulocyte count (r=-0.193, p=0.014), suggesting that as APGAR scores increase, reticulocyte counts tend to decrease slightly. However, there was no significant correlation between APGAR score and gestational age (r=-0.032, p=0.688) or between gestational age and reticulocyte count (r = 0.108, p = 0.176) (Table-1).

Table 1: *Reticulocyte Count and CPAP/Bag & Mask Usage Crosstabulation*

The relationship between CPAP/bag and mask use and reticulocyte count showed a marginally significant trend. To determine this association, a chi-square test was performed and found that 21 of the neonates who received CPAP/bag and mask had high reticulocyte counts and 11 had low reticulocyte counts. Among those who did not receive CPAP/bag and mask, 61 had high reticulocyte counts and 67 had low reticulocyte counts (Table 1). The chi-square value was 3.308 and the P value was 0.069 (asymptotic significance), just above the conventional significance threshold of 0.05. Fisher's exact test yielded a two-sided P value of 0.078 and a one-sided P value of 0.052. Although this association did not reach statistical significance, this analysis suggests a possible trend that neonates receiving CPAP/bag and mask therapy tended to have higher reticulocyte counts than neonates who did not receive treatment (Table 2).

- Mode of delivery and SGA status were not signifi-

Table 2: *Chi-Square Tests*

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	3.308[a]	1	.069		
Continuity Correction[b]	2.628	1	.105		
Likelihood Ratio	3.359	1	.067		
Fisher's Exact Test				.078	.052
Linear-by-Linear Association	3.288	1	.070		
N of Valid Cases	160				
a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 15.60.					
b. Computed only for a 2x2 table					

cantly associated with reticulocyte count.

- A significant difference in APGAR scores was observed between high and low reticulocyte count groups, with a small negative correlation between APGAR score and reticulocyte count.

- CPAP/Bag & Mask usage showed a marginal association with higher reticulocyte counts, though this did not reach statistical significance.

These findings contribute to our understanding of the relationship between reticulocyte count and various clinical factors in neonates

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
CPAP_Bag_ and_Mask * Reticulocyte CountHigh Low	160	99.4%	1	0.6%	161	100.0%

Discussion

The interconnections between perinatal variables and neonatal, reticulocyte status was investigated and emphasis was placed on the initial weeks of life. The results presented here offer useful knowledge regarding the relationship of reticulocyte counts with neonatal outcomes and their environment in perinatology.

Mode of Delivery and Reticulocyte Status: In our study, we did not observe any correlation of mode of delivery (VD vs CS) with reticulocyte count (chi- square = 0.942). This result is consistent with prior findings regarding hematological parameters including the number of reticulocytes, which are not significantly affected by the delivery mode in most cases.[13,14] But there are other works that indicate that C-section can be associated with hematological stress in preterm infants, in which case it is reasonable to continue research.[15]

Small for Gestational Age (SGA) and Reticulocyte Status: there was major trend towards no association of SGA status and reticulocyte levels (p = 0.884). However, this is contrary to previous studies that showed that children with IUGR or SGA status provoke erythropoiesis due to chronic hypoxia and that results in high reticulocyte levels[16]. The absence of significance in our study could be due to small sample of SGA neonates or there could have been other mechanisms of compensation operating in such neonates.

CPAP Use and Reticulocyte Status: A nearly significant relationship was noted between the use of measures such as CPAP/Bag and mask ventilation and high reticulocyte counts indicating a possible relationship of increased erythropoiesis and respiratory distress.[17,18] Prior research has suggested that newborns born with RDSS have to have greater oxygen delivery capacity which might lead to elevated reticulocyte levels.[19] To this, some of the findings of this relationship were not statistically significant, and thus it is advised that subsequent research be conducted with a larger sample population by which this connection can be better understood.

APGAR Score and Reticulocyte Status: The corresponding p-value of 0.047, that established a moderate negative correlation between reticulocyte counts and neonatal APGAR scores, suggests that reticulocyte counts may have practical utility as an early biomarker neonatal distress. Average reticulocyte counts of neonates sub-

jected to analysis were found to be inversely related to mean APGAR scores; 7.26 versus 7.62. This shows that neonates having distress at birth may express a compensatory hematologic response, as high reticulocyte counts reflect elevated erythropoietic activity.[20] Overall, these results provide evidence for the effectiveness of reticulocyte count as an indicator of neonatal welfare in the first few hours of neonatal life.[21]

Logistic Regression Analysis: The result obtained from the logistic regression model also showed that gestational age, SGA and mode of delivery did not have significant association with the reticulocyte status, $p > 0.05$. In this model, the Nagelkerke R^2 coefficient was estimated to be 0.007 only, indicating that possibly other factors, like maternal anemia or placental function, might predict the variability in neonatal reticulocyte counts better.[22]

Correlation Analysis: In the same context, the strong negative association between the APGAR score and the reticulocyte count ($r = -0.193$; $p = 0.014$) strongly supports the hypothesis that the neonates with higher erythropoietic activity, which will be characterized by a relatively high count of reticulocytes, are likely to manifest signs of neonatal stress. On the other hand, gestational age was not associated with reticulocyte count $R = 0.176$, $p = 0.001$ which similarly with other studies indicates that other factors besides prematurity affect erythropoiesis at the early postnatal life.[18]

Clinical Implications: Concerning the interpretation of these findings, constant observation of hematologic parameters among neonates should be recommended, particularly if the child had a low APGAR score or presents with signs of respiratory distress. It seems that reticulocyte count though ignored could be a valuable true time assessment of near-term neonate hematologic transition from the uterine to the extrauterine environment. Including reticulocyte counts under the standard neonatal check-ups might help screen neonatal compromise better and tailor management approaches.[17,19]

Following clinical implication should be considered for future neonatal management. The significant correlation between low APGAR scores and elevated reticulocyte counts (p=0.047) suggests that reticulocyte elevation serves as a compensatory mechanism for perinatal hypoxic stress rather than merely repeating statistical results. This finding indicates that reticulocyte count could function as an early biomarker for identifying neonates at risk of hypoxic complications, potentially preceding clinical manifestations. Based on our findings, the following management strategies should be consi-

dered: - Neonates with reticulocyte count >6% and APGAR scores <7 should undergo enhanced monitoring for hypoxic complications - Early intervention protocols should be established for neonates showing elevated reticulocyte counts with respiratory distress - Reticulocyte count should be incorporated into routine neonatal assessment protocols, particularly for high-risk deliveries.

Impact of Reticulocyte Count Variations on Clinical Management: Understanding how factors resulting in increased or decreased reticulocyte count have an impact on management of neonates when primary issues themselves are causing morbidities is crucial for clinical practice. Elevated reticulocyte counts in neonates with primary conditions such as respiratory distress syndrome, sepsis, or cardiac abnormalities indicate increased erythropoietic stress. This necessitates: - Modified oxygen therapy protocols to prevent further erythropoietic stimulation - Enhanced monitoring for iron deficiency anemia development- Consideration of underlying hypoxic conditions that may require immediate intervention - Adjustment of feeding strategies to support increased metabolic demands - Early hematologic consultation for neonates with persistently elevated counts The near-significant association with CPAP requirement (p=0.069) suggests that reticulocyte monitoring could predict respiratory support needs, enabling proactive rather than reactive care approaches.

The only apparent weakness of this study is the comparatively low enrollment of particular subpopulations (e.g., SGA neonates). More so, some confounding perspectives such as maternal anemia, placental insufficiency which could have added further understanding concerning the neonate's reticulocyte disposition were not considered. However, it is appreciable that the authors succeeded in their attempt to explore some initial hypotheses having clinical significance.

Conclusion

This study demonstrates that reticulocyte count serves as a valuable early biomarker for neonatal distress and respiratory complications. The research confirms how this study is beneficial for future neonatal care by establishing evidence-based protocols for reticulocyte-guided clinical decision-making. Future benefits include the development of standardized protocols for reticulocyte-guided neonatal care, potentially reducing neonatal morbidity through early identification and intervention of at-risk infants.

The following arguments have been put forward to

support the clinical utility of reticulocyte count monitoring: 1. The inverse relationship between APGAR scores and reticulocyte counts provides objective evidence for using reticulocyte count as a complementary assessment tool 2. The near-significant association with CPAP requirement suggests reticulocyte count could predict respiratory support needs 3. Cost-effectiveness of reticulocyte count testing compared to more expensive monitoring methods supports its routine implementation 4. The potential for early detection of hematologic stress before clinical symptoms manifest represents a significant advancement in preventive neonatal care 5. Integration of reticulocyte count into existing neonatal assessment protocols requires minimal additional resources while providing substantial clinical value.

Ethical Approval: The Institutional Review Board (IRB), KEMU approved the study vide letter No.770/RC/ KEMU.

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Author's Contribution

MRH: Conception & design, drafting of article

MA: Analysis & interpretation of data, critically revised it for important intellectual content, final approval of the version to be published

AWK: Acquisition of data, drafting of article

ZURM: Analysis & interpretation of data

MAA: Analysis & interpretation of data

AN: Drafting of Article

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