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"Unlocking The Potential Of Normoblastemia In Critical Care: A Tertiary Hospital Prospective Experience"

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ABSTRACT:

Background: Normoblasts, integral to the process of erythropoiesis, are immature red blood cells characterized by the retention of a nucleus. These immature cells undergo several stages of development before maturing into functional erythrocytes. Normoblasts, typically confined to bone marrow during erythropoiesis, entering the bloodstream suggests an underlying disturbance. This deviation from the norm can be indicative of bone marrow stress or dysfunction, serving as a diagnostic marker for a spectrum of conditions.

Material and methods: A sample size of 50 adult patients admitted in the ICU for various causes were included in the study. The study was conducted for a period of 2 months.

Results: The common age group are between 20-24 year and males are the predominant population when compared to females. In the present study normoblasts were found in the peripheral blood of 6% of the critically ill patients.

Conclusion: Detecting normoblasts in the blood is an early occurrence preceding mortality. Therefore, incorporating normoblasts screening into diagnostic protocols may assist in promptly identifying individuals at an elevated risk.

Key words: Normoblast, critically ill patients, hypoxaemia.

INTRODUCTION:

Normoblastemia, a condition characterized by the presence of erythrocyte precursors in the blood, has gained attention in critical care settings due to its potential diagnostic implications[1]. Normoblasts, typically confined to bone marrow during erythropoiesis, entering the bloodstream suggests an underlying disturbance. This deviation from the norm can be indicative of bone marrow stress or dysfunction, serving as a diagnostic marker for a spectrum of conditions. Normoblasts contain residual ribosomes and mitochondria, which enable them to synthesize haem and maintain energy production for a short period after their release from

bone marrow. The presence of normoblasts in the peripheral blood of critically ill patients is a complex issue with several potential causes and consequences.

Assessing normoblastemia can influence decisions regarding blood transfusions in ICU patients. Tracking normoblastemia can aid in risk stratification and prognostication[2]. In healthy adults, normoblasts are typically absent in peripheral blood. Their existence in peripheral blood is interlinked with hypoxia or infections. proposed outcome would be improved patient care, prognosis, and diagnostic accuracy in critical care settings through normoblastemia research.

The aim of the present study is to assess the association between normoblast counts in peripheral blood and length of ICU stay, normoblast counts and mortality rates in critical care patients. Other objective included were evaluation of predictive accuracy of normoblast counts in identifying patients at risk of developing organ dysfunction and other ICU related complications and to explore the possible correlation between normoblast counts and the need of mechanical ventilation in critical care patients.

MATERIALS AND METHODS: The present study was conducted in a tertiary care teaching hospital for a period of two months (November 2023 to December 2023), after obtaining informed consent from the participants and approval fromthe institutional ethics committee.

Study design: Prospective observational study.

Inclusion criteria: Critically ill patients, not on ventilator, aged above 18 years admitted into medical ICU were included.

Exclusion criteria: Patients diagnosed with hematolymphoid malignancies, haemolytic anemias, patients admitted due to trauma or accident, post-surgical cases, patients aged less than 18 years were excluded from the study.

Sample size: 50.

Study Procedure: After obtaining informed consent, blood samples were collected in EDTA vacutainers from the patient who were fulfilling selection criteria. Blood samples were sent to laboratory for the preparation of peripheral blood smears. Examination of blood smears is done by two trained pathologist, who were blinded to all the clinical data. The data collected was tabulated using Microsoft excel 2020 software and presented in a form of percentages, scores and tables.

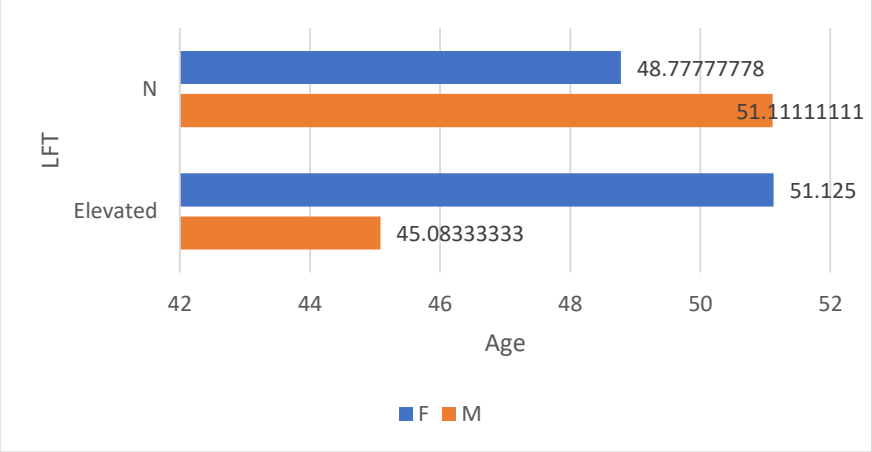
RESULTS: A total of 50 patients were included, with a male to female ratio of 1.5:1. Table 1 shows case distribution based on age and diagnosis.

Table 1: Age and diagnosis distribution of the cases included in the present study:

Diagnosis	21-30		31-40		41-50		51-60		61-70		71-80	
	M	F	M	F	M	F	M	F	M	F	M	F
Heart Failure/myocarditis	1		1	1				2		1		
Chronic Kidney Disease			1			1		3		3		
Chronic Liver Disease/Hepatitis/ portal hypertension			1		2		1				1	
Stroke/altered sensorium	1		1	1	1	1	1	1	1	2	1	1
Infection/sepsis					1	1		1	1	1		1
OP poisoning	1				2							
Others		3			1	3	3					
Total	**3**	**3**	**4**	**2**	**7**	**6**	**5**	**7**	**2**	**7**	**2**	**2**

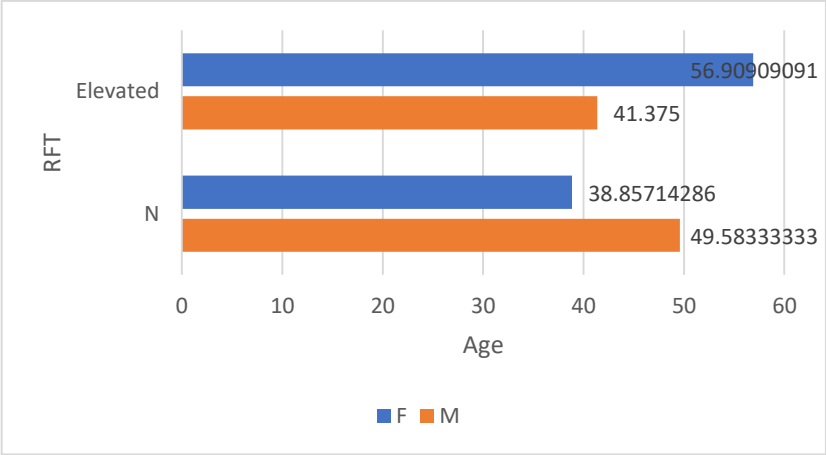
As depicted in the bar chart 2, elevated LFT is more commonly seen in females when compares to males. Elevated LFT is seen in the age group 42-52 years. The average age of women with elevated LFT is 48 years whereas the average age of men with elevated LFT is 46 years.

Chart 2: Bar diagram depicting distribution of cases based on liver function tests:



Distribution of age and gender with RFT is depicted in the bar chart 3. Elevated RFT is more commonly seen in females when compared to males. The average age of males having elevated RFT is 41 years and the average age of females having elevated RFT is 57 years.

Chart 3: Bar diagram depicting distribution of cases based on renal function tests:



In the present study 12% of the patients have normoblasts in their peripheral blood out of total 50 patients who have participated in the study. 88% of the patients do not have normoblasts in the peripheral blood. When patients were followed up, it was found that 66.67% (4 cases) of the patients whose peripheral blood showed normoblasts died due to multi-organ dysfunction.

DISCUSSION:

In a study conducted by Jose Glido de Moura Monteiro Junior [1] in 2015 it was shown that the presence of NRBC (nucleated red blood cells) has been linked to increased ICU mortality and in-hospital mortality rates. The correlation between NRBC count and mortality remained consistent across both coronary and non-coronary disease patients. The occurrence of NRBCs correlated with advanced age, prolonged ICU stay, elevated severity scores (SOFA and APACHE II), instances of sepsis, and cardiac etiology unrelated to coronary issues.According to the study conducted by Axel Stachon[2] the mortality rate among NRBC-positive patients significantly surpassed that of NRBC-negative patients. In relation to intensive care mortality, blood NRBCs demonstrated a sensitivity of 83.3% and a specificity of 78.9%. The research conducted by Axel Stachon [3] showed that the mortality rate among NRBC-positive patients exceeds that of NRBC-negative patients. Mortality escalates proportionally with the rise in NRBC concentration.Study conducted by J. Groen [4] concluded that Normoblasts are observed in peripheral blood, particularly in patients with heart failure who exhibit marked cyanosis or severe anaemia.In a study conducted by Benie T.

Constantino [5] showed that the normoblastosis in case of haemolytic anaemia of the newborn occurs due to the combination of marrow stress, the availability of extramedullary haematopoiesis and immature reticuloendothelial system.A study conducted by Tayyab Noor [6] concluded that Normoblasts become evident in peripheral blood only in instances of extreme anoxia, a condition typically associated with the most severe forms of heart failure.The research conducted by Sandra Kuert [7] showed that preliminary findings indicate that the partial pressure of oxygen (pO2) tends to be lower in NRBC-positive patients undergoing ICU treatment when juxtaposed with the pO2 levels of NRBC-negative patients.According to the study conducted by Steven W. Purtle [8], the likelihood of mortality within 90 days following hospital discharge exhibited a notable elevation in patients displaying a rising count of nucleated red blood cells (NRBCs).Research conducted by Katarzyna Pikora [9] concluded that in paediatric cases, nucleated red blood cell (NRBC) counts serve as valuable indicators of neonatal hypoxia, asphyxia occurrence, and subsequent neonatal mortality.Study conducted by Menk[10] showed that individuals experiencing moderate or severe ARDS exhibited markedly elevated nucleated red blood cell (NRBC) counts compared to those with mild ARDS.Present study revealed that 6% of the patients admitted in the ICU of the department of General medicine have normoblasts in their blood. This rate is less when compared to the study conducted by Stachon A et al [2] in the patients admitted in ICU. In most of the studies the concentration of normoblasts was assessed using a highly sensitive automated blood analyser. In the present study, normoblasts are detected through meticulous microscopic analysis of the stained blood smears.Our data substantiated the robust prognostic capability of normoblast detection in blood, particularly in relation to mortality. The overall in-hospital mortality was determined to be 24.49% which is less when compared with the mortality rate obtained by the Stachon et al[2,11,12].In the present study increased leucocyte count was correlated with normoblast concentration.

In another study conducted by Monteiro Junior et al [2] in the Pernambuco cardiac emergency unit 48.2% males and 51.8%females were having normoblasts in their blood. These rates are higher when compared with the present study. The overall mortality in the present study is found to be 24.49%. While the overall cardiovascular ICU mortality stood at 36.8%, and elevated NRBC levels exhibited a correlation with increased ICU mortality. After discharge from the ICU, hospital mortality was recorded at 18.8% contributing to an overall in-hospital all-cause mortality rate of 48.7%.In a study conducted by Noor et al [6] in different departments at national and medical centre,Lahore.62.5% of the patients were found to have normoblasts in their blood where as in the present study 6% of the patients have normoblasts in their peripheral blood. Mean value of normoblasts was found to be more in females when compared to males. Mortality in the patients with malignancy was 100% mirroring the findings of the present study.

In the present study normoblasts are found in the peripheral blood of 6% of the critically ill patients. The overall in hospital mortality in males is 16.33% and in females is 8.16%. The cause of death is different in all the patients most common being the cerebral causes. An indispensable aspect of laboratory haematology lies in the precision of normoblasts enumeration. This parameter should now be recognized as a powerful tool in guiding decisions related to diagnosis, prognosis, and treatment. The identification of normoblasts in peripheral blood serves as a noteworthy marker of disease severity, signalling an elevated risk of ICU mortality. Early assessment of normoblasts during the hospital stay, coupled with risk stratification of patients, holds promise in reducing mortality rates and enhancing disease prognosis[13].

CONCLUSION:

Detecting normoblasts in the blood is an early occurrence preceding mortality. Therefore, incorporating normoblasts screening into diagnostic protocols may assist in promptly identifying individuals at an elevated risk. Identifying normoblasts in the blood of patients in medical intensive care is linked to a substantial rise in in-hospital mortality. The prognostic importance of normoblasts remains significant independent of various laboratory and clinical risk parameters.

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