Clinical utility of Immature granulocyte percentage and NLR in Critical care unit patients in a tertiary care hospital

Hari Krishnan¹, Yogalakshmi E²*, Vimal Chander³, Muthuvel E⁴

¹II MBBS Student, Saveetha Medical College, Thandalam, Chennai -602105.
²Tutor, Department of Pathology, Saveetha Medical College, Thandalam, Chennai -602105
³Associate Professor, Department of Pathology, Saveetha Medical College, Thandalam, Chennai -602105.
⁴Professor, Department of Pathology, Saveetha Medical College, Thandalam, Chennai -602105

*Corresponding author: kiruba.yoga@gmail.com, Mobile: 9884055930 (Yogalakshmi)

ABSTRACT:

Immature granulocytes such as myelocytes, promyelocytes, and metamyelocytes are the precursors of WBC. These cells increased during bacterial infection in bloodstream, bone marrow activity, or in sepsis. Neutrophils, monocytes, and lymphocytes play crucial role in systemic inflammatory response to severe infection. Neutrophilia and lymphocytopenia are physiological response of innate immunity system to systemic inflammation, injury and stress. This study is aimed to evaluate the significance of Immature granulocyte percentage and NLR among the ICU patients when compared to the NON-ICU patients. The study included 174 patients of non critical admitted in ward and 20 patients admitted in critical ICU care. The statistical analysis is done for the haematological parameters among the ICU and NON-ICU patients by using Independent samples t-test. The mean value of Immature granulocyte percentage, NLR, WBC count and ANC among the ICU patients is high, showing the statistical significance of p<0.05, when compared to NON-ICU patients. Hence IG%, NLR along with routine WBC count and ANC are effective markers in predicting the severity of infection in critical ill patients and need for the earlier intervention

KEYWORDS: Immature granulocyte percentage, NLR, WBC count

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INTRODUCTION:

Granulocytes are the types of white blood cells which are neutrophil, eosinophil, basophil. They are called so as it contains cytoplasmic granules. Immature granulocytes are the precursor of WBCs which are myelocytes, promyelocytes, and metamyelocytes. Immature granulocytes elevated in peripheral blood circulation during conditions such as bone marrow activity, inflammation, bacterial infection in bloodstream and in sepsis, septicemia.

Leukocytosis, neutrophilia, and increasing bands in peripheral blood (indicating left shift in differentiation) are classical hallmarks of infection. Nowadays, differential count of WBC can be automated in modern cell counting machines. This allows simple fast and inexpensive quantification of IG count and percentage as marker of bone marrow activity without need of taking extra blood samples. IG percentages are studied as predictor of neonatal sepsis and bloodstream infection. Increase in IG percentage helps to predict infection superior to C reactive protein level.[1]

IG count and percentage and differential WBC count etc used for parameters to predict positive blood culture. Early detection of bacteremia facilitates timely initiation of antimicrobial therapy, reduces morbidity and mortality. [2] Left shift of WBC is defined as an elevated neutrophil band count (or)an elevated immature/total granulocyte ratio (I/T).In neonatal sepsis cases ,it is difficult to determine reference ranges for IGs in infants because there cells undergo rapid fluctuation during first 5 days of postnatal life.[3] Sepsis is a very serious condition in which severe cases result in shock, disabilities, organ failure, or even death. Presence of bacteria or their toxic products in circulation called sepsis and result in manifestations.[4] Neutrophils eradicate the microbes invading the body by the process of phagocytosis. In severe sepsis, phagocytosis gets affected. A compensatory increase of immature neutrophils in circulation is a criterion to define the systemic inflammatory response syndrome (SIRS) and sepsis. In non sepsis cases, reduced functional response of immature neutrophils observed.[5]

AIM:
To study the utility of immature granulocytes percentage and neutrophil lymphocyte ratio as a predictor in assessing the severity of illness in critical care unit patients.

MATERIALS AND METHODS
This is a retrospective study conducted in Saveetha Medical College and Hospital hospital during the period of December 2019. This study included 174 patients admitted in the ward (Non-ICU) for various illnesses as a control group and 20 cases admitted in the ICU for suspected sepsis. Neonates and pregnant woman were excluded from the study. Complete blood examination were analysed using Sysmex automated haematology analyser XN-1000 .The Haematological parameters such as Total leukocyte count, Absolute Neutrophils count, Absolute Lymphocytes count and immature granulocyte counts were observed and
neutrophils lymphocyte ratio was calculated. These parameters of the Non-ICU cases were compared with the ICU cases. Statistical analysis was done by using SPSS statistical package version 21. Ethical committee approval was obtained with no: SMC/IEC/2019/01/ on Jan. 2020.

RESULTS

The study included 174 NON-ICU cases and 20 ICU cases. Among the ICU patients common age was observed between 51-60yrs and among the Non ICU patients common age was observed between 40-60 yrs showed in Table.1

<table>
<thead>
<tr>
<th>AGE</th>
<th>ICU</th>
<th>NON ICU</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-10</td>
<td>-</td>
<td>6</td>
</tr>
<tr>
<td>11-20</td>
<td>-</td>
<td>23</td>
</tr>
<tr>
<td>21-30</td>
<td>2</td>
<td>22</td>
</tr>
<tr>
<td>31-40</td>
<td>3</td>
<td>21</td>
</tr>
<tr>
<td>41-50</td>
<td>1</td>
<td>44</td>
</tr>
<tr>
<td>51-60</td>
<td>6</td>
<td>37</td>
</tr>
<tr>
<td>61-70</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>71-80</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>81-90</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>TOTAL</td>
<td>20</td>
<td>174</td>
</tr>
</tbody>
</table>

Male to Female ratio among the ICU Patients was 3:1 and among the NON-ICU patients were 0.6:1 shown in Table.2.
Table 2: SEX Distribution between ICU and NON ICU patients

<table>
<thead>
<tr>
<th>SEX</th>
<th>ICU</th>
<th>NON ICU</th>
</tr>
</thead>
<tbody>
<tr>
<td>MALE</td>
<td>15</td>
<td>70</td>
</tr>
<tr>
<td>FEMALE</td>
<td>5</td>
<td>104</td>
</tr>
<tr>
<td>TOTAL</td>
<td>20</td>
<td>174</td>
</tr>
</tbody>
</table>

Table 3: Comparison of Haematological parameters between ICU and NON-ICU patients

<table>
<thead>
<tr>
<th>HAEMATOLOGICAL PARAMETERS</th>
<th>ICU (Mean+/−SD) n=174</th>
<th>NON-ICU (Mean+/−SD) n=20</th>
<th>pVALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLC</td>
<td>15913+/−7903</td>
<td>9062+/−4424</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ANC</td>
<td>1478+/−6740</td>
<td>6214+/−4022</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ALC</td>
<td>1685+/−2188</td>
<td>2084+/−1097</td>
<td>0.177</td>
</tr>
<tr>
<td>IG %</td>
<td>1.5+/−1.7</td>
<td>0.7+/−1.5</td>
<td>0.047</td>
</tr>
<tr>
<td>NLR</td>
<td>13.6+/−8.9</td>
<td>3.9+/−4.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 3 showed the Comparison of haematological parameters among the ICU patients and NON-ICU patients. The mean Total count, ANC, IG% and NLR were higher among the ICU patients when compared to the NON-ICU patients. The statistical analysis done by using unpaired T test showed the significant p value <.05.
Fig 1. Box plot distribution of NLR values between ICU and NON-ICU Cases

Limitation of this study - This study was done in a limited sample size.

DISCUSSION:

Immature granulocytes—the precursor cells of WBC are increased in blood circulation during bacterial infections and in sepsis cases. In this study, in this study among the ICU patients the common age group observed is between 51 to 60 yrs and Male to female ratio is about 3:1. The statistical analysis is done among the ICU and NON-ICU patients by using Independent samples t-test. The mean value of Immature granulocyte percentage, NLR, WBC count and ANC among the ICU patients is high, showing the statistical significance of p<0.05, when compared to NON-ICU patients. The mean and SD among the ICU is 13.6 +/-8.9 when compared to the NON-ICU patients mean and SD is 3.9 +/-4.8 which is significantly high.

According to Zahorec R study on NLR,

Neutrophils, monocytes, lymphocytes play crucial roles in systemic inflammatory response to severe infection. Lymphocytopenia and neutrophilia are the physiological response of the innate immune system to systemic inflammation, injury and stress. Lymphocytopenia is due to margination, redistribution of lymphocytes within the lymphatic system and marked accelerated apoptosis. Neutrophilia is due to demargination of neutrophils, delayed apoptosis and stimulation of stem cells growing factors.[6]

Danielle Benedict Sacdalan study shows,

NLR - neutrophil lymphocyte ratio. Systemic inflammation is associated with prognosis in solid tumors. NLR is a marker for general immune response to various stress stimuli. Elevated NLR and T Cells (peripheral blood regulators) are highlighting the importance of inflammation in the prognosis of cancer patients.[7] cancers like prostatic, lung, and primary liver cancer etc.

Complete Blood Count study by Joshua David Farkas,
Physiological stress generally increases neutrophil number and decreases. Number of lymphocytes. NLR is not an indication solely of inflammation but it may be increased by any source of physiological stress (hypovolemic shock). NLR increases rapidly following acute physiological stress. May be useful in sorting out patients with severe systemic illness than the acute ill patients.[8]

According to Yılmaz Unal M.D et al study, Immature granulocytes % is a new inflammation marker and more effective marker in predicting the severity of infection than the traditional markers such as the WBC count, CRP, and NLR. This is due to technological advantages in automated hematological analyzers.[9]

Jae-Sang Park et al, study shows, elevated IG% implies enhancement of bone marrow activity to fight sources of infections before leukocytosis occurred. It has been found to be a good indicator of blood stream infection and neonatal sepsis. Although the early phase of acute appendicitis cannot induce systemic inflammatory responses, it may induce proliferation of IG before leukocytosis occurred. IG% may be beneficial for detecting appendicitis in addition to classic inflammatory markers including WBC count, a left shift in neutrophil and CRP at no additional cost.[10]

Thomas Daix MD et al research shows, clinical severity was associated with higher percentage of IGs and deeper T cell lymphocytopenia. Increased IG% was related to occurrence of new organ failures, and especially with T cell lymphocytopenia associated with early and late death. With IG% severity of patients sepsis status identified and treated as early as possible.[11]

According to Lanlan Zeng, Shuhui Wang, et al study, CONS has emerged as an important pathogen of hospital infection and most common bacteria that cause blood culture contamination. IG is a new detection index for diagnosis of infectious diseases. IG does not exist in peripheral blood of healthy people. However severe clinical conditions such as sepsis and septicemia can consume large numbers of peripheral blood granulocytes and body compensates by releasing IGs from bone marrow to peripheral blood circulation. Peripheral blood NLR as an indicator reflecting the body's systemic inflammatory response and immune status. It is proven that its accuracy in predicting the outcome of patients with major cardiac events, ischemic stroke, cancers, sepsis and infectious pathologies.[12]

Eduarda et al in a study, neutrophil lymphocyte ratio, band neutrophil count, total leucocyte were evaluated for sepsis prediction. Among these, best performance was observed for Band neutrophil followed by NLR.[13]

CONCLUSION-

The mean value of Immature granulocyte percentage, NLR, WBC count and ANC among the ICU patients is high, showing the statistical significance of p<0.05, when compared to NON-ICU patients. Hence IG%, NLR along with routine WBC count and ANC are effective markers in predicting the severity of infection in critical ill patients.

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Conflict of Interest-Nil.

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[12] Evaluation of time to positivity of blood culture combined with immature Granulocytes, Neutrophil-to-Lymphocyte ratio and CRP in identifying blood stream coagulase - negative Staphylococci infection in Pediatric patients - Lanlan Zeng, Shuhui Wang, Minchuncin, Yaxing Chen, Qiulian Deng, Huamin Zhung, Xiaoshan Guan, Shuwen Yao, Haiying Liu (2020)