Original Research Article

STUDY OF HEMATOLOGICAL PARAMETERS AND ITS RATIOS IN EVALUATING THE SEVERITY OF PNEUMONIA IN CHILDREN OF RURAL BANGALORE

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A B S T R A C T

Background: According to WHO Pneumonia is the single largest infectious disease India accounting for 20% of those deaths and has higher burden of childhood pneumonia. Neutrophil to lymphocyte ratio (NLR) and Platelet lymphocytic ratio (PLR) reflect systemic inflammation. These ratios were used to evaluate the severity of infectious diseases. The objective is to hematological parameters and derived hematological ratios like neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) in children with pneumonia and to study the correlation of these ratios to severity of pneumonia in children.
Materials and Methods: Children fulfilling the eligibility criteria were included in the study after written informed consent. Required data were noted in proforma. Complete Blood Picture and other required investigations were done. Patients were classified as pneumonia or severe pneumonia as per WHO classification. Hematological parameters and ratios (NLR and PLR) were analyzed in children with pneumonia and severe pneumonia.
Results: In the study 74.8% had pneumonia and 25.2% had severe pneumonia. Mean Neutrophil to Lymphocyte Ratio among subjects with Pneumonia was 1.36 ± 0.54 and in subjects with severe pneumonia was 1.42 ± 0.33(p value 0.574). Mean Platelet to Lymphocyte ratio among subjects with pneumonia was 87.05 ± 29.33 and in subjects with severe pneumonia was 43.66 ± 19.76(p value <0.001). There was significant difference in in Neutrophil to Lymphocyte Ratio and Platelet to Lymphocyte ratio between two groups.
Conclusion: The combination of NLR and PLR has a higher value in evaluating the severity of children with pneumonia, which can be useful for treatment of the pneumonia.
Keywords: Neutrophil to lymphocyte ratio (NLR), Platelet to lymphocyte ratio (PLR), Pnuemonia.

INTRODUCTION

According to WHO Pneumonia is the single largest infectious disease India accounting for 20% of those deaths and has higher burden of childhood pneumonia than any other country.[1,2]
Typical clinical features may not be there in early stages of pneumonia. Lack of the typical clinical manifestations, along with improper use of empirical antibiotics can lead to gradual worsening to severe pneumonia.[1,2] Delay in the diagnosis and treatment of severe pneumonia in children is associated with high morbidity and mortality.[3]

Therefore, it is particularly important to identify severe pneumonia at an early stage and evaluate the prognosis in time, so as to formulate comprehensive and effective treatment plans to reduce the mortality of patients.[4] Neutrophil to lymphocyte ratio (NLR) is a blood routine index reflecting systemic inflammation. The neutrophil count (NEU) can reflect the inflammatory state of the body. The more severe the inflammatory reaction, the higher will be the neutrophil count (NEU) count.
The lymphocyte count (LYM) reflects the stress state of the body. The more severe the stress response, the lower the lymphocyte count (LYM) count will be.

Neutrophil to lymphocyte ratio (NLR) is easy to operate, low cost, and objective and has played an important role in the prognostic evaluation of tumor, diabetes, cardiovascular diseases, and respiratory diseases.[4]

Platelet lymphocytic ratio(PLR) can evaluate the severity of infectious diseases, as well as reflect or assess the degree of thrombosis and inflammatory response in the body.[5] Elevated Platelet lymphocytic ratio (PLR) on admission indicates increased risk of pneumonia progression.[6] These hematological parameters and ratios are well studied in sepsis.[7] However, studies on whether Neutrophil to lymphocyte ratio (NLR), Platelet lymphocytic ratio (PLR) can be used to determine the severity of pneumonia in children are relatively rare.

Hence, we aim to study the correlation of these hematological parameters and its ratios like neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) to severity of pneumonia in children.

The objective of the study was:
1. To study the hematological parameters and derived hematological ratios neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio in children with pneumonia (PLR)
2. To study the correlation of these hematological parameters and ratios like neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) to severity of pneumonia in children.

MATERIALS AND METHODS

Study Design: Prospective observational study.
Study Setting: Rural tertiary care hospital.
Study Period: 2 years.
Study Population: Children between the age group of 2 months to 5 years.
Inclusion Criteria
All patients aged 2 months to 5years admitted to hospital with clinical features of pneumonia defined as per WHO classification
Exclusion Criteria
1. Patients who are using Immunosuppressive drugs
2. patients with active Tuberculosis
3. Patients with hematological disorders and malignancy

Children between 2months to 5 years of age presented with symptoms and signs of pneumonia as per WHO were included in the study after obtaining valid consent from parents /Guardian. Demographic details, clinical history and examination findings were recorded in predetermined proforma and assessed for severity of pneumonia as per WHO/IMNCI Guidelines. Routine investigations like total count, differential count, platelet count, were done in all cases of pneumonia. Based on these NLR and PLR ratios were calculated and assessed for diagnostic value and severity. Any other investigation like CRP, Xray, Blood culture and Nasal swab/Throat were done wherever indicated. All the children were managed as per standard protocol.

Sample size: Sample size was estimated by using the sensitivity of NLR at 56.25%, in predicting the Prognosis of Children with Severe Pneumonia from the study by Xuejiao Qi et al. using the formula.

Statistical analysis: Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi- square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation.

Normality of the continuous data was tested by Kolmogorov– Smirnov test and the Shapiro–Wilk test. The independent t test was used as test of significance to identify the mean difference between two quantitative variables. Validity of Hematological parameters was plotted by ROC Curve sensitivity, specificity at best showing Cutoff. Graphical representation of data: MS Excel and MS word were used to obtain various types of graphs such as bar diagram, Pie diagram. p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

RESULTS

Demographic details: Total number of children enrolled in the study was 123.
Age Distribution in study population.
Total number of children of age 2months to 12months enrolled in the study were 25(20.3%) and 12months to 5year enrolled in the study were 98(79.7%).
Gender Distribution in study population
Total number of Male children enrolled in the study were 50(40.65%) and Female children enrolled in the study were 73(59.35%).
Severity of Pneumonia among children
In the study 74.8% had pneumonia and 25.2% had severe pneumonia.
Mean Age distribution of children with pneumonia and severe pneumonia.
Mean age of subjects with pneumonia was 27.45 ± 15.20 months and subjects with severe pneumonia was 33.35 ± 15.31 months. There was no significant difference in severity of pneumonia between two groups.
Gender distribution of children with pneumonia and severe pneumonia
Among subjects with pneumonia, 40.2% were males and 59.8% were females and among subjects with severe pneumonia, 41.9% were males and 58.1% were females. There was no significant difference in gender distribution between two groups.
Vital signs comparison between Pneumonia and Severe Pneumonia.

In the study there was a significant difference in mean SpO2, Respiratory rate and Heart rate between two groups. Mean SpO2 was low in severe pneumonia, RR was high in severe pneumonia and HR was high in severe pneumonia. There was no significant difference in Temperature between two groups.

Hematological parameters comparison between Pneumonia and Severe Pneumonia subjects.

Mean Total count among subjects with Pneumonia was 7562.99 ± 2074.25 and in subjects with severe pneumonia was 17072.06 ± 7222.56. There was significant difference in Total count between two groups.

Mean Absolute Neutrophil Count among subjects with Pneumonia was 4046.16 ± 1470.09 and in subjects with severe pneumonia was 9241.29 ± 4454.68. There was significant difference in Absolute Neutrophil Count between two groups.

Mean Absolute Lymphocyte count among subjects with Pneumonia was 3216.80 ± 1153.97 and in subjects with severe pneumonia was 6597.03 ± 2970.01. There was significant difference in Absolute Lymphocyte count between two groups.

Mean Neutrophil to Lymphocyte Ratio among subjects with Pneumonia was 1.36 ± 0.54 and in subjects with severe pneumonia was 1.42 ± 0.33. There was significant difference in Neutrophil to Lymphocyte Ratio between two groups.

Mean Platelet count among subjects with Pneumonia was 252179.35 ± 34162.61 and in subjects with severe pneumonia was 238506.45 ± 38074.62. There was significant difference in Platelet count between two groups. Mean Platelet to Lymphocyte ratio among subjects with Pneumonia was 87.05 ± 29.33 and in subjects with severe pneumonia was 43.66 ± 19.76. There was significant difference in Platelet to Lymphocyte ratio between two groups.

Severity of Pneumonia

Neutrophil to Lymphocyte Ratio
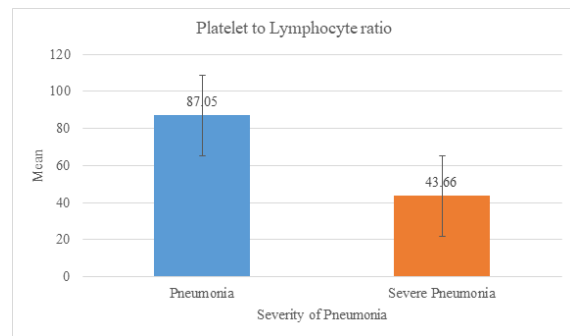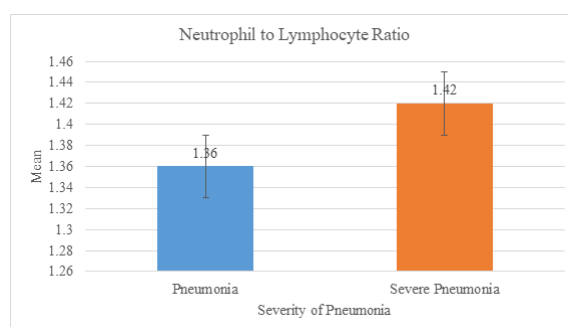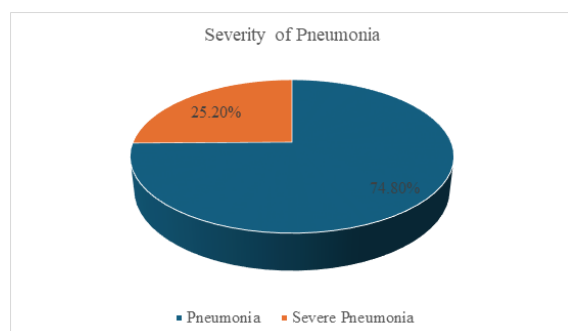
DISCUSSION

Pneumonia is the leading cause of death in children under 5 years old. Once an infection occurs in infants and young children, it can easily develop into bronchitis or bronchopneumonia, or even severe pneumonia, posing a serious threat to the health of infants and toddlers.[8] The main clinical difficulties are the differentiation from non-infectious diseases and the clarification of the pathogenic diagnosis of infants who have failed empirical treatment. While blood culture is only applicable to bacterial lung infections with bacteremia, and its clinical use is more limited, so it is clinically important to find some laboratory indicators for early diagnosis, disease assessment, and prognosis of pneumonia in children. The indicators currently included in the WHO guidelines for Pneumonia evaluation are neutrophil to- leucocyte- ratio (NLR), platelet lymphocyte ratio (PLR), CRP, and Procalcitonin, but the sensitivity and specificity of these indicators for clinical application are still unsatisfactory.[9] Cellular immune dysfunction and disorders are the most studied pathogenesis of pneumonia in addition to the direct pathogen invasion theory.[10] Leukocytes and their subtypes (monocytes, lymphocytes, and macrophages), as important immune cells involved in immune regulation, can cause changes in the level of relevant immune cells in the body when bacteria enter the body, and NLR, PLR and so on are important indicators reflecting the inflammatory response in the body obtained based on the level of immune cells.[11,12]

Hence A Prospective observational study was conducted among 123 children with pneumonia in the age group of 2 months to 5 years, at Rural tertiary care hospital. Study was carried out for a period of 2 years. Children on Immunosuppressive drugs, with active Tuberculosis and with hematological disorders and malignancy were excluded from the study. Patients will be classified as pneumonia or severe pneumonia as per WHO classification. Informed consent was obtained from parents and Institutional ethical clearance was obtained prior to the start of study. Hematological parameters and ratios (NLR and PLR) were analyzed in children with pneumonia and severe pneumonia.

In our study, NLR values are higher in severe pneumonia group, which is similar to findings in the study conducted by Güven D et al and Li L et al.

Severity of infections is characterized by increased systemic inflammation, which causes neutrophilia. Hence higher NLR values are seen in severe pneumonia.

Bacterial infections which are typically caused by extracellular pathogens, are primarily managed by innate immune system. Neutrophils act as the first line of defense, resulting in neutrophilia, leukocytosis and lymphocytopenia. Consequently, higher NLR values are observed in case of bacterial pneumonia. Viral infections, caused by intracellular pathogens, are primarily managed by adaptive immunity system, which involves lymphocytes more. As a result lymphocytosis occurs, leading to low NLR values in Viral pneumonia. Although the viral infection itself triggers lymphocyte response predominantly, the systemic inflammation especially higher Interleukin 6 paradoxically reduces the lymphocyte count resultant cellular immunity. Both these factors result in increase in NLR. Hence higher NLR predicts the severity of inflammation.

Neutrophils and lymphocytes were demonstrated to be shown to play critical roles in inflammatory conditions. It has been reported that the increase in neutrophils and again decrease in lymphocytes in pneumonia patients is associated with disease severity.[13] Elevated neutrophils and lymphocytes were associated with disease severity in our study.

NLR is a parameter determined by the ratio of neutrophils to lymphocytes. NLR is recognized to enhance inflammatory process and thought to be a forecaster of several inflammation process better than CRP.[14] In studies by O Kartal et.al and Bedas M et.al, NLR was reported to be an important marker, particularly for hospitalized children with Pneumonia.[15-17] Neutrophils and NLR values together were reported a stronger predictor of severity than pneumonia severity score and the tenacity of high levels of NLR with neutrophils count might be a crucial factor in the rapidly deteriorating of patient's poor outcome.[13,18,19] Continuous elevations in these variables might well indicate a severe and unmanaged immune reaction, causing the inability to fix the systemic inflammation process. Like these studies, in our study NLR and neutrophil count were found to be elevated in severe disease, significantly predicting disease severity. As our study did not have equal number of pneumonia and severe pneumonia cases and had both viral and bacterial pneumonia included, there was no statistically significant increase in NLR between the two groups. Platelets are essential inflammation cells that generate a big portion of cytokines and also can behave as acute phase reactants as well. Platelet counts were reported to be higher in children with pneumonia (20,21). We did find an association between platelet counts and Pneumonia severity.

In some studies PLR levels were found to be elevated in Pneumonia patients.[4,11,15,22] While PLR has been linked to disease severity in studies done by Wang J et.al. There was no significant relation to PLR and disease severity in studies done by Okartal.et.al. In study by Zheng HH et.al, children with bacterial infectious pneumonia had significantly lower PLR values than healthy children.[23] In our study PLR was found to be significantly lower in the Severe Pneumonia group compared to pneumonia group. Similarly study by Fan C et al., shows that Dynamic monitoring of platelet parameters in severe CAP children showed that PLT after 72 h of admission was significantly lower in the viral infection group than in the bacterial-involved infection group (including bacterial and viral-bacterial mixed infection). As Bacterial endotoxins like lipopolysaccharide can activate platelets and promote a prothrombin phenotype, while RNA viruses can enhance platelet adhesion to infected endothelial cells, interfere with the immune system, and decrease thrombopoietin production in the liver, leading to a decrease in circulating platelet count.[24] Our study primarily included higher number of Viral pneumonia cases, where we observe a predominance of lymphocytes. Consequently, the PLR was found to be low in severe pneumonia group.

WHAT THIS STUDY ADDS?

From the study findings it is recommended that hematological parameters such as Total count, Nuetrophil to lymphocyte ratio and Platelet to Lymphocyte ratio can be used to differentiate Severe Pneumonia and pneumonia among children in the age group 2 months to 5 years. In Health care facilities with inadequate infrastructure such as lack of X ray and other diagnostic facilities, these hematological parameters and ratios are helpful to provide adequate care at the earliest and hence reducing morbidity and mortality.

Limitations

1. Sample size of Pneumonia and Severe Pneumonia children were not equal. Hence can be a potential bias in findings.
2. VIRAL and BACTERIAL Pneumonia were not differentiated, and both were taken.
3. Other hematological parameters such as CRP were not included in the study.
4. The findings were not compared with Gold standard investigations such as X Ray.

CONCLUSION

The study concluded that hematological parameters such as Total count, Absolute Neutrophil Count, Absolute Lymphocyte count, Platelet count and derived hematological ratios neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio are significantly affected with respect to severity of Pneumonia.

The combination of NLR and PLR has a higher value in evaluating the severity of children with pneumonia, which can be useful for treatment of pneumonia.

NLR and PLR biomarkers are simple useful tests which can be done at all levels of health care which can be helpful to provide adequate care at the earliest

in children with pneumonia, hence reducing morbidity and mortality.

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