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Original Research Article

# Correlation of Neutrophil-Lymphocyte Ratio, Monocyte-Lymphocyte Ratio, and Platelet-Lymphocyte Ratio with Stunting in Children

**Gwyneth Trixie Stanpo[1*], Paulus Budiono Notopuro[2,4*], Nur Aisiyah Widjaja[3,4]**

[1]*Faculty of Medicine, Universitas Airlangga, Indonesia*
[2]*Department of Clinical Pathology, Faculty of Medicine, Universitas Airlangga, Indonesia*
[3]*Departement of Child Health, Faculty of Medicine, Universitas Airlangga, Indonesia*
[4]*Dr. Soetomo General Hospital, Indonesia*

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**Abstract**

**Background**: Globally, stunting affected approximately 148 million children under five in 2022. Chronic infection contributes to stunting through immune hyperactivation and excessive cytokine release. Since anthropometric assessments are prone to errors and may not accurately reflect the underlying inflammatory status, common systemic inflammatory markers, such as the Neutrophil-Lymphocyte Ratio (NLR), Monocyte-Lymphocyte Ratio (MLR), and Platelet-Lymphocyte Ratio (PLR), can serve as alternatives. These markers are simple, affordable, and accessible in every health center.

**Objective**: To analyze the correlation of NLR, MLR, and PLR with stunting.

**Methods**: A cross-sectional study involving pediatric patients aged 1-5 years from the Nutrition and Metabolic Outpatient Clinic of Dr. Soetomo Regional Hospital in Surabaya from 2022 to 2023. Forty-one samples met the inclusion and exclusion criteria. Data on NLR, PLR, MLR, and other hematological variables were obtained from the patients' hematology profiles. Group differences, correlations, and diagnostic performance were analyzed using Kruskal–Wallis, Spearman, and ROC methods, respectively.

**Results**: Forty-one subjects were obtained and divided into three groups: 21 (51.2%) normal, 10 (24.4%) stunted, and 10 (24.4%) severely stunted. RBC and lymphocytes significantly increased in normal patients, whereas neutrophils, platelets, NLR, MLR, and PLR significantly increased in severely stunted patients. NLR, MLR, and PLR differed significantly between normal and stunted children (p =<0.001; p =0.002; and p =<0.001, respectively) and showed positive correlations between the NLR (p =<0.001; r =0.687), MLR (p =<0.001; r =0.558), and PLR (p =<0.001; r =0.784) with stunting. At cutoff values of 0.844 (NLR), 88.527 (PLR), and 0.174 (MLR), their AUCs were 0.90, 0.95, and 0.82, with sensitivities of 75%, 80%, and 60%, respectively.

**Conclusion**: NLR, MLR, and PLR significantly differ among normal, stunted, and severely stunted children, showing positive associations with stunting. These markers, particularly PLR, may serve as a practical screening tool, warranting further validation through larger studies.

**Keywords**: *Stunting; Neutrophils; Monocytes; Platelets; Lymphocytes; Biomarker; Child health.*
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## INTRODUCTION

In 2022, approximately 148 million children under five were stunted globally.[1] Among the Southeast Asian subregion, Indonesia, the Philippines, and Timor-Leste are countries with the highest prevalence of stunting.[2] In Indonesia, about 21.6% children under five years old were suffering from stunting.[3] This number is still considered high, as it falls within the 20%–30% range.[4]

Although the prevalence of stunting has declined, efforts to address this issue are not equally attained across regions.[5] In East Java, the prevalence of stunting reaches 19.2%. This reveals a notable disparity compared to East Nusa Tenggara, where the prevalence reaches 35.2%.[3]

Stunting affects children both in the short and long term. Stunting is linked to developmental delay in children.[6] These children are also more likely to experience insulin resistance, increasing their risk of suffering non-communicable diseases such as hypertension, diabetes, and dyslipidemia.[7] The stunting condition also affects the anti-bacterial function of the immune system. In response to the bacterial antigen, stunted children produce higher pro-inflammatory cytokines compared to non-stunted children.[8] In the long term, a weakened immune system increases the mortality risk of children under 5 years old who are stunted.[9] Chronic infection plays a crucial role in the incidence of stunting. This condition causes hyperactivation of the body's immune system, resulting in the excessive release of cytokines and inflammatory substances, which leads to soft tissue impairment and immune imbalance.[10]

The inaccuracy of anthropometric measurements due to insufficient understanding and skill remains a common occurrence, resulting in unreliable stunting diagnosis.[11] Thus, the use of NLR, PLR, and MLR can be an alternative. NLR, PLR, and MLR are common systemic inflammatory biomarkers that are simple, affordable, efficient, and accessible in every health centre.[12,13] An increase in neutrophil count suggests the presence of inflammation, whereas a decrease in lymphocyte count indicates stress and poor nutritional status.[14] Platelets secrete pro-inflammatory mediators, such as cytokines and chemokines, which can exacerbate inflammation.[15] These parameters have been proven to be used as a prognostic factor in various pathological conditions, from cancer[16–18], cardiovascular disease[19], rheumatoid arthritis[20], to psychological disorders.[21]

Within the context of nutrition-related conditions, numerous studies have demonstrated a relationship between those parameters and adults' nutritional status.[22,23] Studies on pediatric samples are still limited to two studies, which were conducted on term AGA neonates in Turkey[24] and hospitalized children in Switzerland.[25] There hasn't been any accessible literature regarding the association of MLR with pediatric nutrition status. These gaps underscore the need for additional research on inflammatory biomarkers, particularly in relation to stunting. Hence, this research aims to analyze the correlation of NLR, MLR, and PLR with stunting.

## MATERIALS AND METHODS

The authors designed a cross-sectional study involving pediatric patients aged 1-5 years from the Nutrition and Metabolic Outpatient Clinic of Dr. Soetomo Regional Hospital in Surabaya, conducted between 2022 and 2023. This study included 41 samples that met the inclusion and exclusion criteria. The following groups were excluded from the study: children with congenital disorders such as Down syndrome, achondroplasia, and cerebral palsy; oncologic conditions; HIV; SLE; chronic kidney failure; hypothyroidism; cholestasis; and other liver disorders. Data on patients' medical conditions and hematological profiles were obtained from the patients' medical records in compliance with approved ethical standards. As a cross-sectional study utilizing past medical records, written informed consent was not feasible.

Data were processed using IBM SPSS Statistics 27. The qualitative variables were presented as frequencies (percentages), while the quantitative variables were presented as medians (interquartile ranges) since they were not normally distributed, as assessed using the Shapiro-Wilk test. In this study, stunting variables were considered ordinal variables and divided into three groups, which are severely stunted (Z-score <-3 SD), stunted (Z-score -3 SD to <-2 SD), and normal (Z-score -2 SD to +3 SD). Data regarding body length/weight in the medical records were measured using the SECA infantometer 416/SECA stadiometer 213. Hematological parameters in this study were obtained from routine laboratory examinations performed during the patients' initial hospital visit and measured using the Sysmex XN 3000 flow cytometry method.

The neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. The platelet-to-lymphocyte ratio (PLR) was calculated by dividing the platelet count by the lymphocyte count. The monocyte-to-lymphocyte ratio (MLR) was calculated by dividing the monocyte count by the lymphocyte count. A comparison of the hematological profile among the normal, stunted, and severely stunted groups was performed using the Kruskal-Wallis test. To examine the relationship of NLR, MLR, and PLR with stunting, the Spearman correlation test was used. In addition, the predictability of NLR, MLR, and PLR in diagnosing stunting was assessed using receiver operating characteristic (ROC) curve analysis. Ethical permission was taken from the Ethics Committee of Dr. Soetomo General Hospital, Surabaya, Indonesia (No. 3072/121/4/VII/2024).

## RESULTS

A total of 41 subjects, consisting of 19 (46.3%) males and 22 (53.7%) females, were obtained in this study. Most of the subjects within this study were under 2 years old, as shown in **Table 1**. The most common diagnosis that the subjects have is tuberculosis of lung, confirmed histologically. Further information regarding the subjects' medical diagnoses was summarized in **Table 2**.

The hematological profile of the subjects is given in **Table 3**. Since the data were not normally distributed, they are presented as median (IQR). RBC and

*Corresponding author:
E-mail:
*paulusbudiono@yahoo.com*
(Paulus Budiono Notopuro)
*gwyneth.trixie.anpo-2022@fk.unair.ac.id*
(Gwyneth Trixie Stanpo)

**Table 1.** Subjects' characteristics based on gender and age

| Subjects' Characteristics | Total (n = 41) | Normal (n = 21) | Stunting (n = 20) |
|---|---|---|---|
| *Gender* | | | |
| Male | 19 (46.3%) | 9 (42.9%) | 10 (50.0%) |
| Female | 22 (53.7%) | 12 (57.1%) | 10 (50.0%) |
| *Age (years)* | | | |
| <2 | 23 (56.1%) | 13 (61.9%) | 10 (50.0%) |
| 2 - <4 | 14 (34.1%) | 7 (33.3%) | 7 (35.0%) |
| 4 – 5 | 4 (9.8%) | 1 (4.8%) | 3 (15.0%) |

**Table 2.** Subjects' nutrition status and medical diagnosis

| Subject's Characteristics | | Result |
|---|---|---|
| *Nutritional Status (HAZ)* | | |
| - | Normal | 21 (51.2%) |
| - | Stunted | 10 (24.4%) |
| - | Severely stunted | 10 (24.4%) |
| *Medical Diagnosis* | | |
| - | Acute nasopharyngitis [common cold] | 2 (4.9%) |
| - | Allergy, unspecified | 1 (2.4%) |
| - | Anemia, unspecified | 2 (4.9%) |
| - | Asthma, unspecified | 2 (4.9%) |
| - | Blount Disease | 1 (2.4%) |
| - | Bronchopneumonia | 1 (2.4%) |
| - | Constipation | 1 (2.4%) |
| - | Cough, unspecified | 1 (2.4%) |
| - | Diarrhea | 4 (9.8%) |
| - | Epilepsy, unspecified | 2 (4.9%) |
| - | Fever | 1 (2.4%) |
| - | Flat foot [pes planus] (acquired) | 2 (4.9%) |
| - | Iron deficiency anemia, unspecified | 5 (12.2%) |
| - | Lower limb pain | 1 (2.4%) |
| - | Lymphadenopathy multiple | 1 (2.4%) |
| - | Other disorders of bone development and growth | 1 (2.4%) |
| - | Other nonspecific lymphadenitis | 1 (2.4%) |
| - | Pneumonia | 2 (4.9%) |
| - | Resp tb unspecified without mention of bacteria or histology confirmation | 1 (2.4%) |
| - | Tuberculosis of lung, confirmed histologically | 7 (17.1%) |
| - | Tuberculous peripheral lymphadenopathy | 1 (2.4%) |
| - | Urinary tract infection, site not specified | 1 (2.4%) |

HAZ: Height for Age Z-score

lymphocytes were significantly higher in normal patients. Neutrophil, platelet, NLR, MLR, and PLR were notably elevated in severely stunted patients.

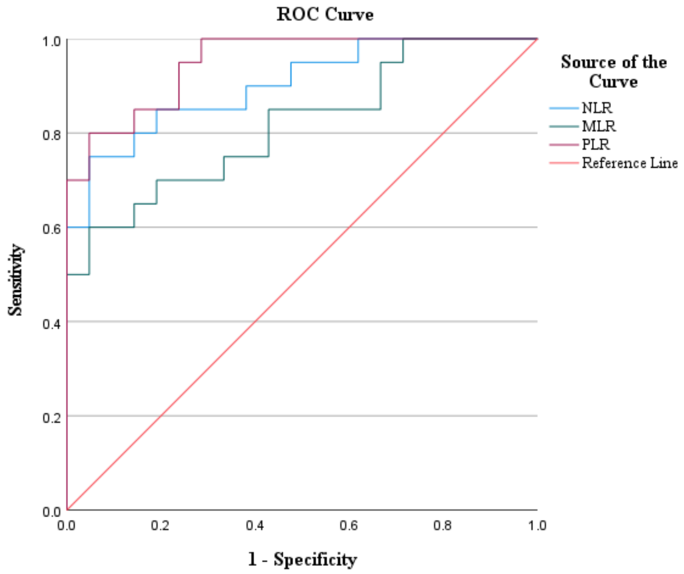
The ROC curve was plotted to find the specificity and sensitivity of NLR, PLR, and MLR in predicting stunting (**Figure 1** All three variables showed significant predictive ability in predicting stunting, as shown in **Table 4**. The cut-off value of NLR at 0.844 had a sensitivity of 75% and a specificity of 95.2%. The cut-off value of PLR at 88.572 had a sensitivity of 80% and a specificity of 95.2%. The cut-off value of MLR at 0.174 had a sensitivity of 60% and a specificity of 95.2%.

NLR, MLR, and PLR correlated directly with stunting, as shown in **Table 5**. PLR exhibited a strong positive correlation with stunting (r=0.784, p<0.001), followed by NLR with a strong correlation (r=0.687, p<0.001). Meanwhile, MLR demonstrated a moderate positive correlation (r=0.558, p<0.001).

**Table 3.** Hematological profile of normal, stunted, and severely stunted patients

| Parameter | Normal | Stunted | Severely stunted | p-value |
|---|---|---|---|---|
| Hgb (g/dL) | 11.8 (10.8-12.3) | 11.6 (10.2-12.2) | 10.9 (10.7-11.4) | 0.359 |
| RBC | 5.04 (4.53-5.25) | 4.39 (4.09-4.66) | 4.52 (4.04-4.77) | 0.005* |
| Hematocrit (%) | 34.8 (33.5-37.4) | 35.0 (30.5-37,4) | 33.3 (32.6-34.4) | 0.226 |
| MCV (fL) | 70.8 (67.4-78.1) | 77.9 (70.9-83.7) | 73.9 (71.1-80.9) | 0.168 |
| WBC ($10^3$/µL) | 10.3 (8.06-12.3) | 9.61 (7.68-13.0) | 10.4 (7.15-11.9) | 0.894 |
| Neutrophil ($10^3$/µL) | 3.21 (2.16-3.84) | 3.93 (3.15-7.91) | 4.36 (3.54-5.74) | 0.020* |
| Monocyte ($10^3$/µL) | 0.72 (0.54-0.93) | 0.78 (0.59-1.23) | 1.02 (0.51-1.28) | 0.334 |
| Platelet ($10^3$/µL) | 330 (295-429) | 476 (319-515) | 477 (344-524) | 0.031* |
| Lymphocyte ($10^3$/µL) | 5.68 (4.77-7.29) | 4.23 (2.75-5.52) | 3.67 (1.96-5.21) | 0.010* |
| NLR | 0.57 (0.42-0.71) | 0.97 (0.71-1.67) | 1.39 (0.88-1.89) | <0.001* |
| MLR | 0.13 (0.10-0.14) | 0.16 (0.13-0.34) | 0.25 (0.14-0.36) | 0.002* |
| PLR | 62.3 (54.2-71.3) | 96.0 (74.9-127) | 132.4 (102-154) | <0.001* |

Hgb: Hemoglobin; RBC: Red Blood Cell; MCV: Mean Corpuscular Volume; WBC: White Blood Count; NLR: Neutrophil-Lymphocyte Ratio; MLR: Monocyte-Lymphocyte Ratio; PLR: Platelet-Lymphocyte Ratio; *p<0.05 was considered statistically significant; Differences among groups were analyzed using the Kruskal–Wallis test




ROC: Receiver Operating Characteristic

**Figure 1.** Ability of NLR, PLR, and MLR to predict stunting based on ROC curve

**Table 4.** ROC analysis of NLR, PLR, and MLR on stunting in children

| Variable | AUC | p-value | 95% CI | Cut-off | Youden's Index |
|---|---|---|---|---|---|
| NLR | 0.902 | <0.001* | 0.810-0.995 | 0.844 | 0.702 |
| PLR | 0.950 | <0.001* | 0.892-1.000 | 88.527 | 0.752 |
| MLR | 0.817 | 0.001* | 0.686-0.947 | 0.174 | 0.552 |

AUC: Area Under the Curve; CI: Confidence Interval; *p<0.05 was considered statistically significant

## DISCUSSION

Stunting is described as low height-for-age due to prolonged undernutrition, generally associated with financial difficulty, maternal malnutrition and health vulnerabilities, repeated illness, and/or improper feeding and care in early life[2]. In this study, the majority of medical diagnoses among the patients were related to infectious diseases, particularly tuberculosis. Stunted children are prone to having high symptomatic and asymptomatic pathogen carriers[26], thus making them more susceptible to infection. Being one of the common causes of secondary immunodeficiency, poor nutritional status can impair the innate and adaptive immune system by weakening or inhibiting the mycobactericidal response, cellular immunity, and the release of cytokines such as TNF-α, IFN-γ, and IL-12.[27]

A study consisting of severe acute malnutrition children in India[28] obtained similar results that RBC

**Table 5.** Correlation of NLR, MLR, and PLR with stunting

| Variable | Spearman rho correlation | |
|---|---|---|
| | r | p-value |
| NLR | 0.687 | <0.001* |
| MLR | 0.558 | <0.001* |
| PLR | 0.784 | <0.001* |

*p<0.05 was considered statistically significant and lymphocyte were significantly higher in normal patients than stunting patients. Low RBC is probably due to the tendency of stunted children to experience deficiencies in macronutrients and micronutrients.[29] At the same time, a sufficient amount of iron and vitamins is necessary to sustain the normal hematopoiesis process.[30] Malnutrition leads to thymic atrophy, resulting in a reduction in lymphocyte production.[31] These findings align and reinforce the role of nutrient deficiency in impaired hematopoiesis and immune function.

Elevated hematological variables, including neutrophils, platelets, NLR, MLR, and PLR, were observed in severely stunted children. Similar patterns were found in studies conducted in India[28] and Eastern Democratic Republic of the Congo[32], which found higher neutrophil counts in children with severe acute malnutrition. Another study from India[33] also found that malnourished children had a higher average platelet count. Likewise, higher NLR and PLR have been documented in children[25] and neonates[24] who are at risk of malnutrition compared to those who are not. Higher levels of TNF-α in stunted children[34] elevate blood neutrophil levels[35] and induce platelet hyperactivation.[36] The observed trend of higher neutrophil and platelet count, followed by lower lymphocyte count, contributes to the finding of increased NLR, MLR, and PLR in severely stunted children. Based on the ROC analysis, NLR, MLR, and PLR can be promising tools for predicting stunting in children. To the best of the writer's knowledge, there have not been any available studies that report the accurate cut-off value of NLR, MLR, and PLR for stunting prediction. Among those three variables, PLR is most likely to be the best variable for stunting screening, as it has the highest sensitivity and specificity among them.

Our study showed a positive correlation between NLR, MLR, and PLR with stunting. Previous research showed similar results regarding the NLR and PLR variables. Similar trends have been reported in research in Switzerland, involving a population of hospitalized children[25], where higher NLR and PLR were significantly associated with higher PYMS scores, indicating a greater risk of malnutrition. In contrast, a negative correlation between malnutrition with NLR and PLR in term AGA neonates was reported in Turkey.[24] In the geriatric population, a significant association was also found between nutritional status and NLR, both in outpatients[23] and in hospitalized patients.[37] Based on the accessible literature, there have been no studies examining the relationship between MLR values and stunting in children. However, some studies have shown an increase in monocytes[38] and a decrease in lymphocytes[28] in stunted children. Furthermore, a notable negative relationship between TNF-α and CRP with HAZ (Height-for-Age Z score) was reported in nutritionally stunted Egyptian children.[39] An increase in TNF-α contributes to an increase in neutrophils[19] and platelets, as well as a decrease in the number of lymphocytes. An increase in CRP contributes to an increase in monocyte count.[40] Together, these findings reinforce the role of chronic inflammation in the pathophysiology of stunting and highlight the importance of further mechanistic and longitudinal studies.

There are a few limitations in this study. Being a cross-sectional study, there may be a bias due to the lack of prospective follow-up of the research subjects. This study is based on medical records; thus, there are limitations in excluding sample data. Moreover, the parameters in this study were not measured directly from the patients, resulting in differences in the timing of data collection among samples. Therefore, prospective studies with direct laboratory measurements are needed to validate the cutoff values.

## CONCLUSION

There is a significant difference in NLR, MLR, and PLR between normal, stunted, and severely stunted children. This study suggests that NLR, MLR, and PLR positively correlate with stunting in children. Based on their predictive ability, NLR, PLR, and MLR can potentially be screening tools for stunting. The parameters in this study were not measured directly from the patients, resulting in differences in the timing of data collection among the samples. Future retrospective studies with direct laboratory measurements are recommended to validate the use of NLR, MLR, and PLR as practical screening tools for early detection of stunting.

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