Evaluation of the Neutrophil-lymphocyte ratio in the prediction of systemic infection in normal newborns in Lubumbashi: Cross-sectional study.

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Abstract

Background and Purpose: Despite progress in the surveillance of newborns in hospitals around the world in general and the country in particular, systemic infection remains a major concern. The purpose of this study to assess the ability of neutrophil-lymphocyte ratio (NLR) to predict systemic infection in newborns in clinics in Lubumbashi.

Methods: Cross-sectional and analytical study that included 430 normal newborns in 25 medical facilities in the city of Lubumbashi, chosen in a simple random manner during the period from November 2015 to December 2017. The clinical and biological characteristics of newborns were studied.

Results: out of 430 children who performed a complete blood count, 106 had an NLR> 3, a frequency of systemic infection of 24.7%. The mean values of neutrophils, lymphocytes, esosinophils, basophils monocytes were significantly higher in patients with an NLR> 3. Mean RNL values were 2.5 ± 1.2, it was 1.9 ± 0.6 in children with NLR≤3, and 4.3 ± 1.2 in those with RNL> 3. The area under the curve (AUC) for NLR, Neutrophil, Lymphocyte and Platelet were 0.887, respectively; 0.738, 0.639 and 0.552. NLR is more sensitive and specific in predicting systemic infection compared to neutrophil, lymphocyte and platelet count.

Conclusion: The results show that NLR is an effective indicator in the diagnosis of systemic infection than neutrophil, lymphocyte and platelet count.

Background

Systemic infection is a generalized disease that progresses rapidly and can lead to high mortality [1, 2]. This infection sets in from a progression of various pathogenic microorganisms that enter the bloodstream, reproduce and then release toxins and metabolites [2]. The toxins and metabolites released induce a systemic inflammatory response [3]. Currently, sepsis and bacteremia are collectively referred to as systemic infection [3]. In recent years, due to the irrational use of drugs (antibiotics, hormones, immunosuppressants, etc.), chemotherapy and organ transplantation, the incidence of systemic infections has increased [2, 4]. From various invasion pathways of pathogenic microorganisms, patients are witnessed a complex development of systemic infections due to their virulence. Depending on the patient's immune defense, the infection can progress rapidly to complication or death [5]. Early assessment of systemic infections is very important for clinicians as it enables rapid decision-making to finally reduce mortality [6]. The level of white blood cells, neutrophils, lymphocytes, CRP and the neutrophil-to-lymphocyte ratio are common indices used to diagnose a systemic infection [6]. In recent years, the role of the Neutrophil-to-Lymphocyte Ratio has been confirmed in the diagnosis of systemic infections, but they have not been widely used due to controversies [7].

During inflammation, bacteria invade the body, release chemokines in vivo, including the release of cytokines, and then stimulate chemotaxis by producing and releasing large numbers of neutrophils in the bone marrow. This results in elevated local and systemic neutrophilia. Throughout the reaction, the

patient's immune system function is diminished, a number of T cells are apoptotic, apoptotic cells inhibit a large number of activated T cells, and the proliferative activity of T cells decreases [8–10]. Peripheral lymphocytes decrease, platelets and neutrophils increase. Therefore, the neutrophil-lymphocyte ratio will also increase. This is why the neutrophil-lymphocyte ratio is often used as a biomarker of systemic inflammatory disease [9–13]. The purpose of this study to assess the ability of neutrophil-lymphocyte ratio (NLR) to predict systemic infection in newborns in clinics in Lubumbashi.

Population And Methods

An analytical cross-sectional study was carried out in 25 medical facilities in the city of Lubumbashi, chosen in a simple random manner during the period from November 2015 to December 2017. The study population was made up of all babies born in maternity hospitals in all of the medical training courses selected. The eligibility criteria for the study were, babies born eutrophic at term, without any complications in the facilities selected during the study period and whose parents had consented to participate in the study. Simple probability and random sampling with a sample step of 3 was used to collect the data for this study. The sample size was calculated from Fisher's formula: n ≥ (Z ^ 2 x (p) (1-p)) / d ^ 2 where n = Sample size, z = 1, 96 (confidence coefficient), p = previous prevalence, d = 0.05 (margin of error or range of imprecision reflecting the degree of absolute precision desired). Because of the probable non-responding subjects, 10% of the number calculated at the height should be added. We estimated the frequency of systemic infection to be 50% in infants, as prescribed in the literature, in the absence of such a documented prevalence in the country. The sample size thus calculated was n≥ (1.96) 2x0.5x0.5 / (0.05) 2 = 384. By including the 10% of non-respondents, we had obtained 422 babies to include. Thus, the distribution of the babies retained was made according to the active file of each Medical Training given the quotas of babies born by selected Medical Training. Data were collected using a structured survey form. Respondents were admitted consecutively by interview of mothers conducted by the principal investigator and her team. Those who had consented were informed of the purpose of the study and the reasons for which they were approached. An information sheet with detailed explanations was read for them.

The following definitions were used in this work: systemic infection, newborn with a Neutrophil-to-lymphocyte ratio > 3 if it is NLR ≤ 3, the newborn has no infection. Bacterial infection, newborn baby with a WBC Zscore or neutrophil <-2DS.

Statistical analyzes

Analyzes were performed on SPSS 21.0. Descriptive statistics consisted of calculating the mean and standard deviation for quantitative data and proportions for categorical data. Pearson's chi-square test or Fisher's exact test was used to compare the proportions, on the other hand Student's t test compared the means. The prediction of RNL in systemic infection was made using the ROC curves and calculating the area under the curve (AUC). The p value <0.05 was considered to be the threshold of statistical significance.

Ethical considerations

The study respected the rules of anonymity, confidentiality, justice and the charity of newborns. Beforehand, the protocol for this study was submitted and approved by the Lubumbashi ethics committee under Approval No. UNILU/CEM/070/2017.

Results

Of 430 children who performed a complete blood count, 106 had an NLR > 3, for a frequency of systemic infection of 24.7%.

General characteristics of the study population

The sex ratio of the children used was 1H / 1F, no gender predominance. The mean values of neutrophils, lymphocytes, eosinophils, basophils monocytes were significantly higher in patients with an NLR > 3. Mean NLR values were 2.5 ± 1.2, it was 1.9 ± 0.6 in children with NLR ≤ 3, and 4.3 ± 1.2 in those with NLR > 3. For the other variables, the differences were not statistically significant (Table 1).

Table 1
General characteristics of the study population according to the category of NLR

Variable	Over all n = 430	NL R ≤ 3 n = 324	NLR > 3 n = 106	p
Gender				0.437
Male	228(53.0)	173(53.4)	55(51.9)	
Female	202(47.0)	151(46.6)	51(48.1)	
Birth weight (g)	3167.1 ± 430.6	3165.4 ± 436.2	3172.1 ± 414.9	0.891
Hight (cm)	48.6 ± 2.6	48.6 ± 2.6	48.8 ± 2.4	0.603
Cranial perimeter (cm)	34.8 ± 1.4	34.8 ± 1.4	34.7 ± 1.4	0.439
Thoracic perimeter (cm)	33.5 ± 1.4	33.5 ± 1.3	33.5 ± 1.7	0.941
Gestational age (SA)	38.6 ± 1.6	38.6 ± 1.6	38.4 ± 1.7	0.366
White globule 10^9LH	17.7 ± 5.4	17.0 ± 5.1	19.6 ± 5.9	**< 0.001**
Neutrophil 10^9LH	11.1 ± 4.2	9.9 ± 3.4	14.5 ± 4.5	**< 0.001**
Lymphocyte 10^9LH	4.9 ± 1.8	5.4 ± 1.8	3.5 ± 1.1	**< 0.001**
Eosinophil	530.1 ± 162.9	510.8 ± 153.8	588.9 ± 176.1	**< 0.001**
Basophil	132.5 ± 40.7	127.7 ± 38.4	147.2 ± 44.0	**< 0.001**
Monocyte	883.5 ± 271.5	851.4 ± 256.3	981.6 ± 293.6	**< 0.001**
RNL	2.5 ± 1.2	1.9 ± 0.6	4.3 ± 1.2	**< 0.001**
HB, g/dl	17.9 ± 2.4	18.0 ± 2.3	17.7 ± 2.6	0.260
RBC 10^{12}LH	6.1 ± 3.3	6.1 ± 3.8	5.8 ± 0.9	0.367
TCMH, pg	30.9 ± 2.8	31.0 ± 2.9	30.8 ± 2.7	0.398
CCMH, g/dl	31.9 ± 1.8	31.8 ± 1.8	32.1 ± 1.6	0.114
VGM, fl	96.6 ± 8.7	96.9 ± 9.1	95.7 ± 7.2	0.220
PLT 10^9LH	237.1 ± 88.1	233.2 ± 85.3	248.8 ± 95.7	0.114

Prediction of NLR in systemic infection

The ROC curves of NLR, Neutrophil, Lymphocyte and Platelet in the prediction of systemic infection are by Figs. 1 and 2 and the values interpreting the curves are summarized in Table 2. The area under the curve

(AUC) for the NLR, Neutrophil, Lymphocyte and Platelet were 0.887, respectively; 0.738, 0.639 and 0.552. NLR is more sensitive and specific in predicting systemic infection compared to neutrophil, lymphocyte and platelet count.

Table 2
Prediction of biomarkers in the diagnosis of systemic infection

Marqueurs	AUC	SD	p	95% CI	Se	Sp
NLR	0.887	0.036	< 0.001	0.816–0.959	0.976	0.898
Neutrophil ($x10^9$/l)	0.738	0.039	< 0.001	0.662–0.814	0.982	0.885
Lymphocyte ($x10^9$/l)	0.639	0.038	0.001	0.565–0.713	0.891	0.781
Platelet ($x10^6$/l)	0.552	0.041	0.216	0.470–0.633	0.565	0.491

Discussion

Systemic infection is a medical emergency requiring early diagnosis and prompt management for the clinician. Delayed treatment increases the mortality rate [10, 14]. We conducted a cross-sectional study in 430 apparently healthy newborns in 24 hospitals in the city of Lubumbashi. The objective of this study was to assess the diagnostic performance of NLR in predicting systemic infection. The salient results showed that NLR better predicted systemic infection, relative to neutrophil, lymphocyte and platelet count.

The mean NLR values of patients with systemic infection were 4.3 ± 1.2, which is significantly higher than patients without systemic infection (1.9 ± 0.6). Our data are consistent with observations in the literature, including the work of Terradas et al. [15] and Zahorec [8]. It is generally believed that NLR > 3.0 could symbolize positive blood culture results.

The critical value of NLR for the diagnosis of systemic infection was set at 3.0, its sensitivity 97.6% and its specificity 89.8%. Additionally, NLR is a good indicator of systemic infection with a subsurface curve of 0.885 (95% CI: 0.816–0.959). It is therefore necessary in poorly equipped settings where blood culture is not feasible, to be satisfied with NLR to enable a systemic infection to be diagnosed earlier.

Neutrophil count predicted systemic infection less, but more better than lymphocyte and platelet count. The sensitivity and specificity of neurophil count in predicting systemic infection was 98.2% and 88.5% and its area under the ROC curve was 0.738 (95% CI: 0.662–0.814). Our results relate to the literature, including the results of Charles et al [16], Brodska et al. [17] and Clec'h et al. [18], but unlike those of Dandona et al. [19], who believes that there is no significant difference in the prediction of systemic infection between NLR and neutrophil count. For Dandona et al, RNL is more related to the neutrophil level. An elevation in neutrophils should be linearly related to an elevation in NLR because they are closely related. This elevation of neutrophils often observed in systemic infection is due to chemotaxis due to the presence of bacteria in the body during the release of endotoxin as a pro-inflammatory cytokine [20]. On

the other hand, Surbatovic et al. had neutrophil and lymphocyte count predicted systemic infection better compared to NLR [21]. The observed difference could be due to the divergence in methods and sample size between the two studies.

There were some limitations to this research. First of all, this is a cross-sectional study, the outcome of which was affected by other factors. We cannot know if other primary diseases, such as neutropenia, would influence the NLR value. Second, the rapid change in the condition of the newborn after birth can cause the NLR to change rapidly, which also affects the accuracy of statistical data.

Conclusion

The results of this study show that NLR is an effective indicator in the diagnosis of systemic infection. It could be used as a tool in systemic infection in settings where blood culture is difficult to obtain because its sensitivity and specificity is greater.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the ethics committee of the University of Lubumbashi (UNILU/CEM/070/2017). The study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Written informed consent was requested from the parents or guardian at the beginning of the study. The informed consents included that data from the participants can be published in scientific journals in an anonymized format in which individual responses never are made visible or possible to identify.

Consent for publication

This is not an experimental study but a transversal study and hence, no separate consent for publication is needed.

Availability of data and materials

The data the study is based on contains personal and intimate information that according to initial agreements with the participants from the start of the study cannot be transferred to third parties or outside the borders of Lubumbashi. Theoretically some subsets of data could on reasonable request be delivered but unfortunately, in most cases it probably would be evaluated as not possible along with this. The datasets used and analyzed during the current study are available from the corresponding author on reasonable request: nkodilaaliocha@gmail.com

Competing interests

The authors declare no conflict of interest.

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Authors' contribution

Amir Yuma N'simbo Assumani and Aliocha Natuhoyila Nkodila initiated the study; Jean Lambert Ehungu Gini participated in the study design; Amir Yuma N'simbo Assumani, Aliocha Natuhoyila Nkodila, Oscar Numbi Luboya and Stanislas Okitosho Wembonyama wrote the manuscript; Gray Kateng A Wakamb, Gauthier Kasansaika Mutoba supervised data collection; Kasim N'simbo Sangwa, Maguy Omoy Ngongo and Aliocha Natuhoyila Nkodila validated and analyzed the data; Aliocha Natuhoyila Nkodila interpreted the data; all authors made intellectual contributions to the draft manuscript and approved the final manuscript for submission.

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Figures

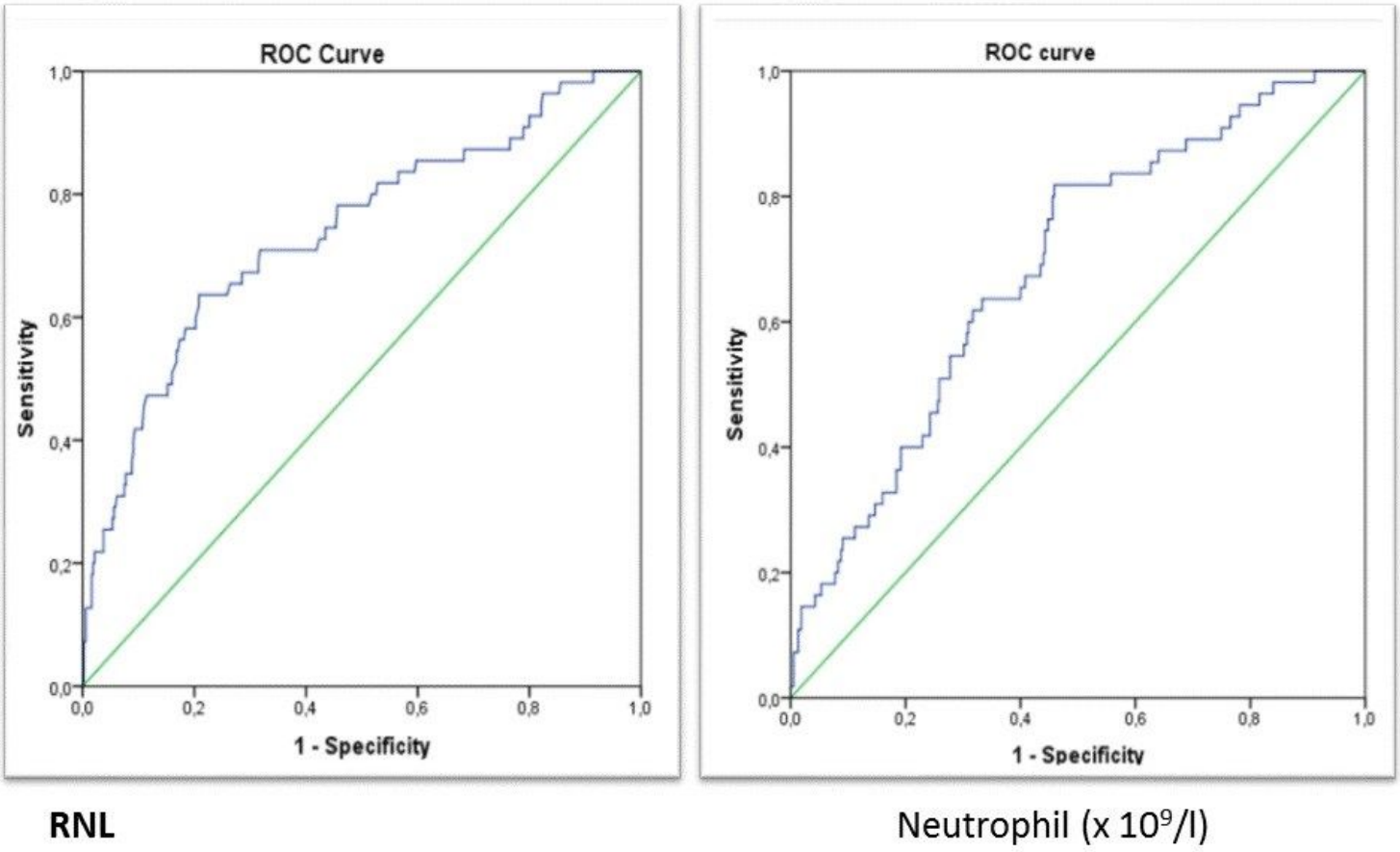
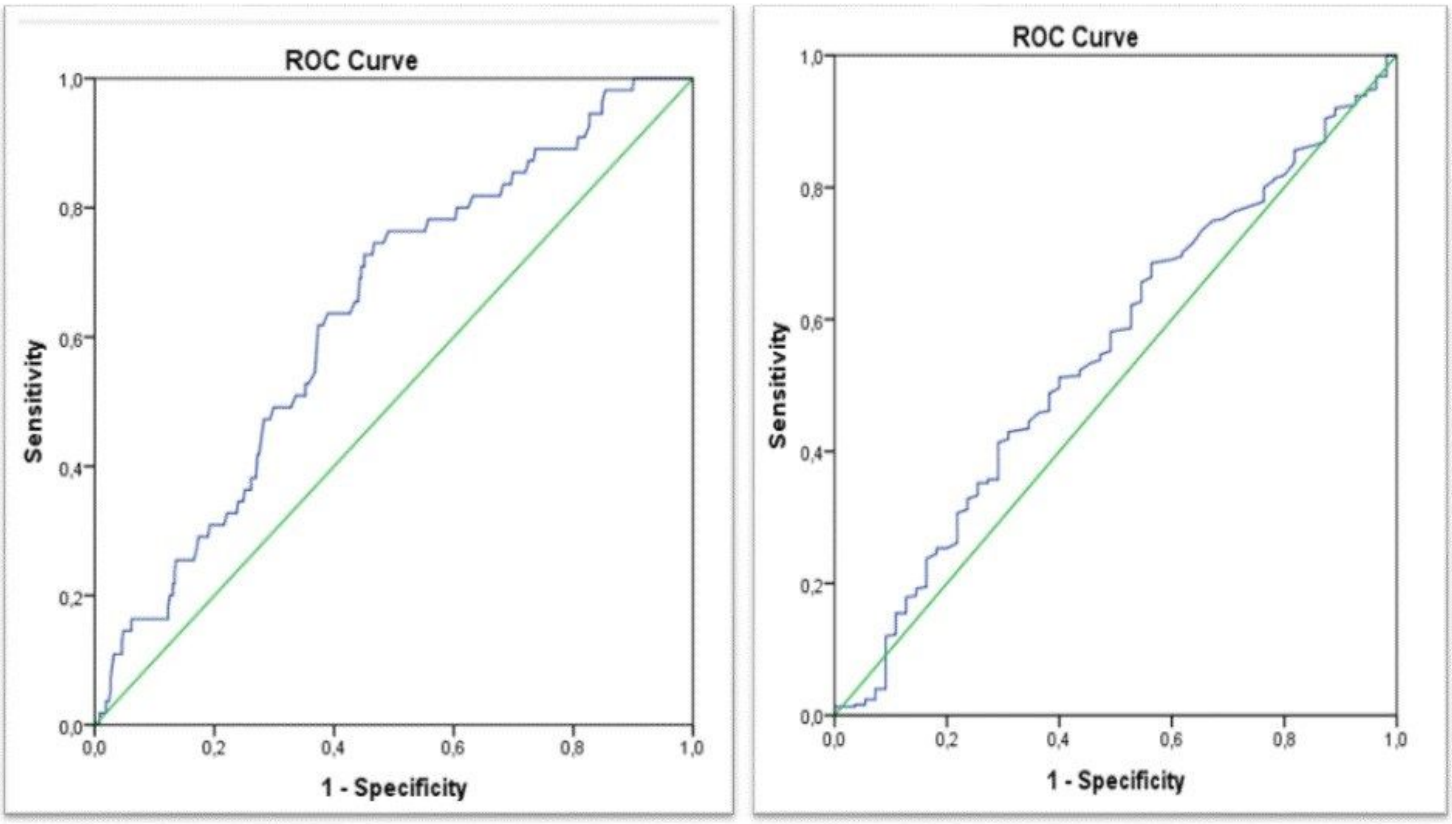


Figure 1

ROC curves predicting systemic RNL and neutrophil infection.



Lymphocyte (x10^9 /l)

PLT (x10^6 /l)

Figure 2

ROC curves for predicting systemic lymphocyte and platelet infection.