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The systemic immune-inflammation index and neutrophil-lymphocyte ratio in pediatric burned patients – a pilot study

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ABSTRACT

Introduction: The aim was to assess the usefulness of blood analytical markers such as systemic immune-inflammation index (SII) and neutrophil-lymphocyte ratio (NLR) in pediatric burned patients.
Material and methods: The study group included 73 children (23 girls and 50 boys; mean age: 3.83; SD: 4.77; min–max: 0–17 years old) hospitalized due to burns. A retrospective analysis of selected complete blood cell count parameters (leucocytes; platelets – PLT; SII; NLR) collected on the day of injury and selected parameters of burns (extent, depth of the injury, duration of hospitalization, type of treatment) was performed.
Results: Children with burns that exceeded 10% total body surface area had higher levels of leucocytes than children with less extensive burns ($p = 0.023$). The PLT count on the day of injury was higher in children with burn wounds that required surgical treatment ($p = 0.021$). The analysis of groups of children that differed in the values of NLR revealed that children with NLR over 3 were hospitalized longer (on average 3.5 days) than children whose NLR was lower than 3 ($p = 0.048$). It was found that children with SII over 250 were hospitalized longer than children with SII less than 250 ($p = 0.019$). There were no differences in the type of treatment ($p = 0.21$), but children with SII over 250 had more often full thickness burns ($p = 0.036$). Children under 2 years old with SII over 200 more often required surgical treatment than children with SII less than 200 ($p = 0.005$). Children under 2 years old with SII over 200 more often had full thickness burn wounds than children with SII less than 200 ($p = 0.045$). Children under 2 years old with NLR over 2 had more extensive burn wounds ($p = 0.049$) than children with NLR under 2.
Conclusions: The systemic immune-inflammation index and NLR can be useful in assessment of pediatric patients with burns. Further studies on larger groups including children with major burns are necessary.

KEY WORDS:
children, burn injury, neutrophil-lymphocyte ratio (NLR), systemic immune-inflammation index (SII).

INTRODUCTION

Burns are considered as an environmental emergency [1]. Children are a very vulnerable group due to their thin and delicate skin. The most common type of burn injury in the pediatric population is scalds [1]. The wound that results from a burn initiates an inflammation-driven process [2]. The progression of inflammation can lead to evolution of an initial partial-thickness thermal burn wound to a full-thickness injury [2]. The immune response after burn injury results is very complex [3]. It depends on many factors such as the host response, erythrocyte aggregation, and tissue ischemia [2]. It has been suggested that neutrophil dysfunction plays a key role in the development of burn injury [3].

New attention have been paid to the inexpensive and readily available markers assessed using measures obtained on routine blood testing such as the systemic immune-inflammation index (SII) and neutrophil-lymphocyte ratio (NLR).

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The systemic immune-inflammation index is defined as SII = platelets (PLT) × neutrophils/lymphocytes counted based on peripheral lymphocyte, neutrophil and platelet counts [4, 5]. It is considered a good index that reflects the local immune response and systemic inflammation [4]. The neutrophil-lymphocyte ratio defined as NLR = neutrophil/lymphocyte counted based on peripheral lymphocyte and neutrophil counts is considered an inflammatory marker [6].

There are no studies on the value of these markers in children with burns.

The aim of the study was to assess the usefulness of blood analytical markers, composed of the combination of systemic inflammation parameters such as SII and NLR, in providing useful information regarding the prognosis and care of burned patients.

MATERIALS AND METHODS

The study group comprised 73 children (23 girls and 50 boys; mean age: 3.83; SD: 4.77; min–max: 0–17 years old) hospitalized due to burns. A retrospective analysis of selected complete blood cell count parameters (white blood cell count – WBC; PLT; SII; NLR) collected on the day of injury used as biomarkers of inflammation and selected parameters of burns (extent and depth of the injury, duration of hospitalization, type of treatment) was performed.

The blood samples were collected on the day of injury. The doctor provided information about the area of burned skin (expressed as % of total body surface area – % TBSA), depth of the injury, type of treatment (surgical or conservative), and length of the hospitalization (days). The area of burned skin (expressed as % TBSA) was counted using the Lund-Bowder chart for children under 16 years old and with the rule of nines for children over 16 years old. Depth of burn was classified clinically into 4 degrees and children were divided into two groups: partial thickness burns (grades 1 and 2) and full thickness burns (grades 3 and 4).

Inclusion criteria were:

- hospitalization due to a burn,
- agreement of caregivers and patients over 16 years old to participate in the study,
- patient age under 18 years old.

Exclusion criteria: disagreement of caregiver/patient to participate in the study.

Statistical analysis of the obtained data was performed using Excel and Statistica v. 12. The study was accepted by the Bioethical Committee of Wroclaw Medical University (KB 109/2014).

RESULTS

The study group comprised 73 children – 23 girls and 50 boys (mean age – M: 3.83; median – Me: 1; standard deviation – SD: 4.77; min–max: 0–17 years old) hospitalized due to burns. The extent of burns in selected cases did not exceed 20% of TBSA (M: 7.51% TBSA; Me: 8; SD: 3.98); approximately 35.8% of children had full-thickness burns. The duration of hospitalization varied from 1 to 47 days (M: 8.59; Me: 6; SD: 2). For each case SII (M: 777.22; Me: 730.85; SD: 508.77) and NLR (M: 2.16; Me: 2.37; SD: 1.86) were calculated. Moreover, the analyzed BCC parameters included WBC (M: 14.01; Me: 1.1; SD: 4) and PLT (M: 379.72; Me: 365; SD: 72).

The results indicate that there was no relationship between mean values of NLR and SII and selected parameters of burns, which is presented in Table 1. Children with burns that exceed 10% TBSA had higher levels of leucocytes than children with less extensive burns ($p = 0.023$). The PLT count on the day of injury was higher in children with burn wounds that required surgical treatment ($p = 0.021$).

Moreover, to analyze the groups of children that differed with respect to the values of NLR, three types of analysis were performed. The analysis of groups of children that differed with respect to the values of NLR revealed that children with NLR over 3 were hospitalized longer (on average 3.5 days) than children whose NLR was lower than 3 ($p = 0.048$). The lowest p-values were obtained in the group of children with NLR over and lower than 3, but there were no statistically significant differences in the type of required treatment ($p = 0.126$), extent of burn wound ($p = 0.273$) and depth of injury ($p = 0.129$).

The analysis of groups of children that differed with respect to the values of SII the groups of children that differed with respect to the values of SII four types of analysis were performed. It was found that children with SII over 250 were hospitalized longer than children with SII less than 250 ($p = 0.019$). There were no differences in the type of treatment ($p = 0.21$), but children with SII over 250 had more often full thickness burns ($p = 0.036$).

Surprisingly, children under 2 years old with SII over 200 more often required surgical treatment than children with SII less than 200 ($p = 0.005$). Moreover, the group of children under 2 years old with SII over 200 more often had full thickness burn wounds than children with SII less than 200 ($p = 0.045$). There were no statistically significant differences in duration of hospitalization ($p = 0.12$) and the extent of burn wound ($p = 0.082$). Moreover, in this age group children with NLR over 2 had more extensive burn wounds ($p = 0.049$) than children with NLR under 2.

DISCUSSION

Recently, increasing attention has been paid to peripheral blood inflammatory markers and their usefulness in establishing prognosis in different diseases, such as cervical cancer, colorectal cancer, psychiatric disorders, and

TABLE 1. The results of the statistical analysis of blood cell parameters and burns

Parameters		WBC			PLT			NLR			SII		
		Mean ±SD	Median (min–max)	*p*-value	Mean ±SD	Median (min–max)	*p*-value	Mean ±SD	Median (min–max)	*p*-value	Mean ±SD	Median (min–max)	*p*-value
Depth of injury	Partial thickness	14.21 ±6.00	13.30 (5.89–34.9)	0.445	366.19 ±118.34	353 (136–667)	0.117	2.14 ±1.94	1.55 (0.26–9.16)	0.349	739.85 ±645.44	566.43 (57.09–3198.57	0.398
	Full thickness	13.99 ±6.14	11.84 (5.1–32.3)		407.01 ±136.75	369.5 (257–778)		1.98 ±1.34	1.50 (0.32–4.29)		779.64 ±556.73	571.89 (117.73–2134.71)	
Extension of burn wound	< 10% TBSA	13.23 ±4.84	13 (5.1–32.3)	0.023*	382.99 ±114.27	353 (229–679)	0.410	2.06 ±1.85	1.51 (0.32–9.16)	0.434	752.22 ±643.81	548.08 (99.37–3198.57)	0.484
	≥ 10% TBSA	16.58 ±8.02	13.22 (8.7–34.9)		374.89 ±155.63	366 (136–778)		2.14 ±1.46	1.82 (0.25–3.47)		759.23 ±530.53	679.00 (57.09–1289.01)	
Type of treatment	Surgical	13.09 ±6.18	11.33 (5.1–32.3)	0.227	430.73 ±143.27	384.5 (257–778)	0.021*	2.09 ±1.40	1.50 (0.32–4.29)	0.427	857.69 ±590.42	722.19 (117.73–2134.71)	0.274
	Conservative	14.31 ±5.83	13.3 (5.89–34.9)		363.03 ±109.88	351 (136–667)		2.19 ±2.00	1.55 (0.26–9.17)		750.88 ±657.52	566.43 (57.09–3198.57)	
Length of hospitalization	≤ 7 days	13.93 ±5.45	13.2 (6.5–34.9)	0.439	376.14 ±111.24	353 (185–667)	0.378	2.29 ±2.00	1.55 (0.26–9.16)	0.239	805.49 ±721.21	566.43 (57.09–3198.57)	0.319
	> 7 days	14.15 ±6.65	11.72 (5.1–32.3)		385.47 ±135.52	367.5 (136–778)		1.96 ±1.23	1.50 (0.32–4.29)		731.78 ±489.45	599.66 (117.73–2134.71)	

**Statistical significance*

infections [4, 6–9]. Neutrophil-lymphocyte ratio and SII were shown to be prognostic markers for malignancies and inflammatory conditions [4, 6–9].

Inflammation is very important for burn wound healing [9]. The burn-induced inflammatory process is very complex. The balance between all inflammatory mediators can be analytically reflected by the blood levels of PLT and leukocytes, especially neutrophils and lymphocytes [8]. Neutrophils and monocytes play a crucial role in the initial inflammatory phase [10]. Due to localized vasodilation and fluid extravasation they migrate to the site of injury and initiate an immune response [10]. The inflammatory phase plays a crucial role in infection prevention, necrotic tissue degradation and activation of signals important for wound repair and healing [10].

The novelty of the study is the fact that there are no studies about the peripheral blood inflammatory markers such as SII and NLR in burned children. The main limitation of the study is the relatively small group of patients. Moreover, the children included in the study group were hospitalized in the Department of Pediatric Surgery, which means that children with major burns who had indications for admission to the Burn Centre were not included in the study group.

Temiz *et al.* found that high levels of NLR are a risk factor affecting the mortality in patients with burns [11]. In their study the NLR in patients who died was higher than in the patients who survived (12.96 ±9.70 vs. 6.34 ±12.13; $p < 0.001$) [11]. However, it must be noted that children who were included in the analysis were not hospitalized due to major burns and all of them survived. The calculated levels of NLR were lower than in the study of Temiz *et al.*

Moreover, it is confirmed that burns that exceed 20% TBSA result in acute systemic responses that probably can be more reflected in the calculated parameters [11]. It can be assumed that NLR and SII can provide more useful information in patients with major burns than in minor burns.

Nie *et al.* tested whether there are differences in blood parameters and liver enzyme levels between burned and traumatically injured children [12]. They analyzed routine blood parameters (WBC and PLT) and found that WBC concentration in burned children was significantly higher than that in traumatically injured children ($p < 0.05$) [12]. Moreover, the mean PLT concentration in burned children was significantly higher than that in traumatically injured children ($p = 0.001$) [12].

Mulder *et al.* claim that in the first three weeks after burn injury increased numbers of immature neutrophils are present in peripheral blood, but total lymphocyte numbers did not increase [13]. According to Sen *et al.* WBC counts are initially elevated after burn injury but decrease over the first 4 days [14]. Osuka *et al.* stated that early thrombopenia and lymphopenia were independent risk factors for 60-day mortality after burns, but neu-

trophil count was not a risk factor [15]. Laggner *et al*. also found that absolute leukocyte and neutrophil numbers were strongly increased in adult patients with burn wounds covering over 10% TBSA [16].

CONCLUSIONS

The systemic immune-inflammation index and NLR can be useful in assessment of pediatric patients with burns. However, it must be underlined that blood cell count parameters still have value, with particular relevance in the group of younger children. Further studies on larger groups including children with major burns are necessary to provide more knowledge about the relationship with NLR and SII and the future prognosis in pediatric patients with burns.

DISCLOSURE

The authors declare no conflict of interest.

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