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The Systemic Immune-Inflammation Index (SII) and Neutrophil-Lymphocyte Ratio (NLR) are related to hospitalisation time in paediatric burn patients

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A – Study Design, **B** – Data Collection, **C** – Statistical Analysis, **D** – Data Interpretation, **E** – Manuscript Preparation, **F** – Literature Search, **G** – Funds Collection

Summary **Background.** The Systemic Immune-Inflammation Index (SII) and Neutrophil-Lymphocyte Ratio (NLR) are new markers of the immune response. There are few studies about the usefulness of these markers in the paediatric population with burns.
Objectives. The aim of the study was to reveal the differences in the Systemic Immune-Inflammation Index (SII) and Neutrophil-Lymphocyte Ratio (NLR) in paediatric patients treated due to thermal burn.
Material and methods. The study group consisted of 61 children (19 girls, 42 boys; mean age: 3.76; SD 4.79; min–max: 2 months – 17 years of age) treated due to thermal burn in the Paediatric Surgery Department. Analysis of chosen complete blood cell count parameters (leucocytes – WBC; platelets – PLT; Systemic Immune-Inflammation Index – SII; Neutrophil-Lymphocyte Ratio – NLR) collected on the day of injury was used as biomarkers of inflammation in patients with and without wound cooling after injury.
Results. Children with burns < 5 years of age who had higher PLT values on the day of admission (the day of injury) more frequently required surgical treatment (p = 0,027). Children with more extensive burn wounds (exceeding 10% TBSA) had higher WBC values on the day of the injury (p = 0.034). Higher NLR and SII values were related to longer hospitalisation (p < 0.05).
Conclusions. The SII and NLR seem to be promising prognostic markers in children with burns. Further studies on larger groups are necessary to reveal the relationship of the new inflammatory markers with other aspects of burn injury in the paediatric population.
Key words: first aid, burns, child, wounds and injuries.

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Background

Thermal burns, such as scalds, are the most common type of burns in the paediatric population. The first aid given to children after this type of injury includes wound cooling. Literature provides information about the significance of burn wound cooling [1–3]. The Systemic Immune-Inflammation Index (SII) and Neutrophil-Lymphocyte Ratio (NLR) are new markers of the immune response. There are few studies about the usefulness of these markers in the paediatric population with burns.

Objectives

The objective of the study was to assess the usefulness of NLR and SII markers in paediatric patients with burns, as well as to substantiate the pathogenetic significance of the application of cooling in the treatment of burn wounds in children and to reveal the differences between the SII and NLR in paediatric patients treated due to thermal burn with and without cooling of the wound after injury.

Material and methods

A total of 61 children treated due to thermal burn in the Paediatric Surgery Department participated in the study (19 girls, 42 boys; mean age: 3.76; SD 4.79; min–max: 2 months – 17 years of age).

Inclusion criteria: (a) admission to hospital due to thermal burn; (b) no concomitant diseases; (c) the consent of caregivers and patients over 16 years of age to participate in the study; (d) under 18 years of age.

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

Blood samples were collected on the day of injury. Complete blood cell count parameters were analysed. The SII and NLR were calculated (SII = platelets × neutrophils/lymphocytes counted based on peripheral lymphocyte, neutrophil and platelet counts; NLR = neutrophil/lymphocyte counted based on peripheral neutrophil and lymphocyte counts).

The extension of the burn wound was expressed as a percentage of total body surface area (% TBSA). The Lund-Bowder chart was used to calculate the burn surface for children under 16 years of age, and the rule of nines was used for children over 16 years of age. The caregivers were asked if the burn wound was cooled after injury or not. The correctness of burn wound cooling was assessed in each case individually.

Excel was used to perform statistical analysis. The chi-square test was used for categorical variables, and a *t*-Test was used for continuous variables (non-categorical). The study obtained a positive opinion from the Bioethical Committee (KB 109/2014).

Results

All the patients included in the study group were hospitalised in the Paediatric Surgery Department due to a burn injury that occurred on the day of admission. The children did not present any accompanying pathology. Most children (62.3%)

Table 1. Basic statistics of tested parameters and the results of the comparison between patients less than 5 years of age and those over 5 years of age

	All patients (n = 61)					Children ≤ 5 years of age (n = 50)					Children > 5 years of age (n = 11)					
	Mean	SD	Median	Min	Max	Mean	SD	Median	Min	Max	Mean	SD	Median	Min	Max	p
WBC	14.17	6.17	13.04	5.10	34.90	14.92	6.37	13.40	5.89	34.90	10.76	3.52	10.80	5.10	17.32	**0.004**
PLT	380.84	126.88	363.00	136.00	778.00	389.47	134.57	364.00	136.00	778.00	362.55	115.96	349.00	254.00	667.00	0.297
NLR	2.05	1.76	1.45	0.26	9.16	1.61	1.18	1.21	0.26	5.40	4.11	2.41	3.84	0.69	9.16	**0.004**
SII	737.25	605.89	548.08	57.10	3198.57	670.69	593.51	462.00	57.10	3198.57	1389.17	778.68	1252.08	268.68	3198.57	**0.005**

WBC – leucocytes, PLT – platelets, SII – Systemic Immune-Inflammation Index, NLR – Neutrophil-Lymphocyte Ratio.

suffered from partial-thickness burn injuries (I and II degrees). 37.7% of the patients had full-thickness burns (III and IV degrees). The surface of the burn did not exceed 15% of the total body surface area (mean: 7.31; SD: 4.01; min–max: 1–15; median: 8). The duration of hospitalisation lasted from 1 to 47 days (mean: 9.25; SD: 8.05; median: 7; min–max: 1–47).

17 patients required surgical treatment. 19.6% of children with thermal burns did not receive appropriate burn wound cooling (defined in the guidelines). The group of children who received wound cooling as first aid (51 children) and the group of children who did not receive wound cooling (10 children) did not differ in age (mean age: 3.19 vs 6.67; $p = 0.07$; $p > 0.05$) or the extent of burn wound (8.27 vs 14.2% TBSA; $p = 0.09$; $p > 0.05$). The gender differences between these groups were insignificant (27.5% vs 50%; $p = 0.53$; $p > 0.05$). Children who received appropriate burn wound cooling less frequently required surgical treatment (21.6% vs 60%; $p = 0.013$).

The basic statistics of the tested parameters are presented in Table 1. As there were features of the ratio between neutrophils and lymphocytes in children depending on age, the children were divided into two age groups (up to 5 years of age and older).

The basic statistics of tested parameters and the results of the comparison between patients less than 5 years of age and those over 5 years of age are presented in Table 2. Significant differences were found between the WBC, NLR and SII values ($p < 0.05$).

In the study group, 50 children were under 5 years of age (14 girls, 36 boys; mean age: 1.6; median: 1; SD 1.195; min–max: 0.16–5 years of age). The surface of the burn wound differed from 1% to 15% TBSA (mean: 7.52% TBSA; median: 7.5; SD: 4.06). 33 children (66%) had partial-thickness burns (I and II degrees), and 17 children had full-thickness burns (III and IV degrees). 11 children (22%) required surgical treatment. The duration of hospitalisation ranged from 1 to 30 days (mean: 8.12; mean: 7; SD: 5.61).

No differences were found when analysing the basic parameters in children with and without burn wound cooling under 5 years of age. The basic statistics of tested parameters and the results of the comparison between patients under 5 years of age are presented in Table 2. Due to the small number of patients > 5 years of age, performing valuable statistical comparison in this age group was not possible.

Burned children < 5 years of age who had higher PLT values on the day of admission (the day of injury) more frequently required surgical treatment ($p = 0.027$). Children with more extensive burn wounds (exceeding 10% TBSA) had higher WBC values on the day of injury ($p = 0.034$). Higher NLR and SII values were related to longer hospitalisation ($p < 0.05$).

Discussion

According to Lord et al., the high concentrations of proinflammatory cytokines after a burn injury increase the activity of neutrophils, causing them to migrate across the damaged endothelium [4]. The aim of wound cooling is to avoid secondary burn progression. Laggner et al. revealed that leukocyte and neutrophil counts in patients with burns were significantly increased on the day of admission [5]. According to the results of their study, the level of lymphocytes decreases in the first 7 days post injury, and the serum levels of neutrophil elastase is elevated in patients with 3rd degree burn injuries [5].

Studies on adult patients with burns demonstrate that the Neutrophil to Lymphocyte Ratio (NLR) has a prognostic value in burned patients [6, 7]. Hu et al. revealed that an NLR above 14 was associated with decreased survival in patients with extensive burns [6]. Qiu et al. underlined the role of NLR as a marker of inflammation and suggested that 3rd-day NLR is associated with an increased risk of death in severely burned patients [7].

Table 2. Basic statistics of tested parameters and the results of the comparison among children < 5 years of age																				
	WBC					PLT					NLR					SII				
	Mean	SD	Median	Min–Max	*p*	Mean	SD	Median	Min–Max	*p*	Mean	SD	Median	Min–Max	*p*	Mean	SD	Median	Min–Max	*p*
First aid																				
Without burn wound cooling	13.16	5	11.33	9.5–24.2	0.22	377.33	69.37	355	305–512	0.411	1.89	0.99	1.95	0.59–3.5	0.25	670.96	316.24	671.41	299.75–1193.5	0.297
With burn wound cooling	15.16	25.87	21.1	0.2–778		385.9	134.87	364	136–778		1.55	1.18	1.03	0.26–5.4		583.31	461.7	433.03	57.1–2134.71	
Treatment																				
Surgical	15.52	6.54	12.84	9.7–32.3	0.372	474.75	161.52	413	281–778	**0.027**	1.46	1.14	1.06	0.32–4.29	0.338	668.5	552.76	430.84	117.73–2134.71	0.309
Non-surgical	14.75	6.32	13.6	5.89–34.9		359.52	104.85	353	136–579		1.63	1.16	1.43	0.26–5.4		572.77	410.76	462.52	57.1–1971	
Hospitalisation duration																				
≤ 4 days	13.93	14.7	4.07	6.5–20.59	0.182	411.19	417	97.31	236–579	0.129	1.17	0.89	0.88	0.26–3.13	**0.022**	449.63	323.86	299.34	99.37–1118.61	**0.031**
> 4 days	15.43	13	7.23	5.89–34.9		371.31	351	140.44	136–778		1.81	1.45	1.23	0.31–5.4		668.11	576.88	491.16	57.1–2134.71	
Burn wound depth																				
Partial thickeness	14.39	13.5	6.44	5.89–34.9	0.212	363.82	355	108.15	136–579	0.081	1.63	1.43	1.18	0.26–5.4	0.387	577.72	462.52	421.02	57.1–1971	0.372
Full thickeness	15.94	13	6.11	9.75–32.3		425.72	373	153.53	261–778		1.53	1.01	1.13	0.32–4.29		625.09	394.94	493.8	117.73–2134.71	
Burn surface																				
< 10 % TBSA	13.59	13.07	4.85	5.89–26.36	**0.034**	382.84	358	107.92	229–678	0.444	1.55	0.97	1.2	0.32–5.4	0.346	579.78	426.1	463.64	99.37–2134.71	0.358
≥ 10 % TBSA	18.34	17.25	8.26	7.5–34.9		390.08	370.5	171.09	0–778		1.7	1.4	1.05	0.26–3.47		629.96	520.15	401.4	2–1289.01	
Albumin infusion																				
Yes	13.61	14.93	2.81	9.7–16.2	0.287	303.33	318	28.87	263–329	**0.009**	2.64	2.8	0.99	1.35–3.77	0.125	780.8	921.2	249.07	430.84–990.36	0.189
No	15	13.3	6.53	0.29–34.9		390.07	369	130.95	0.01–778		1.53	1.01	1.14	0.12–5.4		581.9	435.22	454.81	0.19–2134.71	

Moreover Fuss et al. claimed that NLR also has a prognostic value in patients with burn injuries for the diagnosis of sepsis and bacteraemia [8]. The authors underlined the fact that this ratio is easy to implement in clinical practice and is also cost effective [8], as NLR is calculated with the use of available biomarkers (neutrophil count and lymphocyte count) [8]. Surprisingly, Kim et al. found that a preoperative NLR value is a risk factor for acute kidney injury after burn surgery [9]. The study by Angulo et al. described the evolution pattern of NLR in adult burn patients [10]. They found that NLR decreased after admission in all patients but was higher in non-survivors [10]. They described a significant correlation between NLR on admission and burn extension and severity [10].

There are few studies on NLR and SII conducted on paediatric patients with burns. The results of the study by Gunduz et al. also confirmed the value of NLR in paediatric patients [11]. The results of their study indicated a positive relationship between NLR and length of hospital stay [11]. However, the study group consisted of 39 paediatric scald burn patients, and the authors did not distinguish the age groups in their analysis [11].

According to the results of a study on children by Thakkar et al., an abnormal lymphocyte percentage 72 hours or more after burn injury was an independent predictor of infection [12]. Moreover, it was associated with a significant increase in infection and length of stay [12].

The results of the study indicate that surgical treatment was more often performed in patients that did not receive appropriate wound cooling after injury. The role of wound cooling in the prognosis of patients with burns is well established [13–16]. The authors compared the burn wound cooling methods [2, 3, 17]. Unfortunately, compliance with the Burns First Aid Guidelines, rules of wound cooling and initial management of a burn wound is suboptimal [18, 19]. Kilshaw et al. suggested that burn first aid could be improved with easy access to the Internet and smart device apps with information online [20].

Limitations of the study

The limitation of the performed study was the small number of patients included in the study group. All the children were hospitalised in the Department of Paediatric Surgery and suffered from mild and average burns. There were no fatal cases included in the study group. In Poland, most children with severe burns are hospitalised in burn centres.

Conclusions

Appropriate wound cooling plays a crucial role in the reduction of indications for surgical treatment. Thus, the education of parents and medical personnel who have first contact with children after burns about the importance of correct first aid seems crucial to minimise the impact of the injury on the children's thin skin.

The SII and NLR seem to be promising prognostic markers in children with burns. Further studies on larger groups are necessary to reveal the relationship of the new inflammatory markers with other aspects of burn injury in the paediatric population.

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