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Significance of inflammatory markers in children's infectious diseases

Znaczenie wskaźników stanu zapalnego w chorobach infekcyjnych u dzieci

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Abstract

Aim of the study: The aim of the study was to assess the clinical utility of inflammatory markers for differentiating the aetiology of diseases associated with fever in children. **Material and methods:** A retrospective analysis was performed on the medical records of 1,454 children (658 girls and 796 boys) hospitalised at a paediatric department in 2016–2017 for diseases associated with fever. The analysis was performed on the whole study group, which was divided into the following age groups: children in their 1st year of life (n = 422; 29.1%), children between their 2nd and 6th year of life (n = 870; 59.8%) and children from their 7th year onwards (n = 162; 11.1%). The following inflammatory markers were analysed: white blood cell count, C-reactive protein level, procalcitonin level, erythrocyte sedimentation rate and neutrophil-to-lymphocyte ratio. **Results:** C-reactive protein, erythrocyte sedimentation rate and neutrophil-to-lymphocyte ratio turned out to be useful in the identification of aetiology of upper and lower respiratory tract infections in all children ($p < 0.05$). Higher inflammatory marker values were observed in compound infections as opposed to single conditions ($p < 0.05$). C-reactive protein and erythrocyte sedimentation rate were proven to be useful in identifying the aetiology of acute gastroenteritis. A detailed analysis was performed on the group of children in their 1st year of life. It revealed that inflammatory markers were higher for urinary tract infections than for lower respiratory tract infections and gastroenteritis ($p < 0.05$). **Conclusions:** Inflammatory markers may be helpful for determining the aetiology of infectious diseases associated with fever in children. However, therapeutic decisions should always be taken based on the complete clinical picture.

Keywords: inflammatory markers, pneumonia, acute gastroenteritis, urinary tract infection, children

Streszczenie

Cel: Celem pracy była ocena przydatności klinicznej wskaźników stanu zapalnego w różnicowaniu etiologii chorób przebiegających z gorączką u dzieci. **Materiał i metody:** Analizie retrospektywnej poddano dokumentację medyczną 1454 dzieci (658 dziewczynek i 796 chłopców) hospitalizowanych na oddziale pediatrycznym w latach 2016–2017 z powodu chorób przebiegających z gorączką. Analizę przeprowadzono w całej badanej grupie, z podziałem na następujące grupy wiekowe: dzieci w 1. roku życia (n = 422; 29,1%), dzieci między 2. a 6. rokiem życia włącznie (n = 870; 59,8%) oraz dzieci od 7. roku życia (n = 162; 11,1%). Przeanalizowano wartości parametrów stanu zapalnego: liczbę leukocytów, stężenia białka C-reaktywnego, prokalcytoniny, odczyn Biernackiego oraz wskaźnik NLR (stosunek bezwzględnej liczby neutrofilów do bezwzględnej liczby limfocytów). **Wyniki:** W różnicowaniu etiologii zakażeń górnych i dolnych dróg oddechowych u wszystkich dzieci przydatne okazały się stężenie białka C-reaktywnego, odczyn Biernackiego oraz wskaźnik NLR ($p < 0,05$). Wyższe wartości wskaźników stanu zapalnego odnotowano w przypadku infekcji złożonych w porównaniu z pojedynczymi jednostkami chorobowymi ($p < 0,05$). Wykazano przydatność stężenia białka C-reaktywnego i odczynu Biernackiego w różnicowaniu etiologii ostrego nieżytu żołądkowo-jelitowego. Analizy szczegółowej dokonano w grupie dzieci w 1. roku życia, wykazując wyższe wartości wskaźników stanu zapalnego w przypadku zakażeń układu moczowego w porównaniu z zakażeniami dolnych dróg oddechowych oraz nieżytem żołądkowo-jelitowym ($p < 0,05$). **Wnioski:** Wskaźniki stanu zapalnego mogą być pomocne w różnicowaniu etiologii chorób infekcyjnych przebiegających z gorączką u dzieci. Jednak podejmując decyzje terapeutyczne i lecznicze, należy zawsze brać pod uwagę całość obrazu klinicznego.

Słowa kluczowe: wskaźniki stanu zapalnego, zapalenie płuc, ostry nieżyt żołądkowo-jelitowy, zakażenie układu moczowego, dzieci

INTRODUCTION

Fever, defined as body temperature exceeding 38°C, is one of the main reasons for parents to report with their children to the emergency department or a doctor's office[1]. Fever is a non-specific sign of a number of infections, particularly in the paediatric population. Fever may accompany both serious bacterial diseases and self-limiting viral infections. Due to the different management and treatment of these infections, it is important to be able to diagnose the aetiology of the infection quickly and easily. However, physical examination is often insufficient for differentiating between diseases associated with fever in children[2]. Sensitive and specific laboratory markers of infection may be helpful to this end[3].

The first inflammatory markers to be used to detect a bacterial infection associated with fever of unknown origin in children were white blood cell (WBC) count and absolute neutrophil count (ANC)[4]. Later on, C-reactive protein (CRP) and procalcitonin (PCT) tests appeared[3,5,6]. C-reactive protein is an acute-phase protein produced in the liver in response to proinflammatory cytokines. The CRP level rises very quickly in response to inflammation and drops equally quickly as the disease subsides. For this reason, it may be used to monitor the infection[7]. Procalcitonin, a calcitonin precursor, is also released in response to inflammation, but faster than CRP[2,8]; in addition, it reaches much higher levels in bacterial infections than viral infections, thus allowing one to differentiate between these two aetiologies[8].

Another marker which may be helpful in the identification of a bacterial infection is neutrophil-to-lymphocyte ratio (NLR)[9,10]. The advantages of NLR include low cost and ease of calculation only based on a complete blood count.

Another frequently used inflammatory marker is the highly non-specific erythrocyte sedimentation rate (ESR)[11]. It is a marker of not only infection, but also of various systemic or neoplastic diseases. An increased level of fibrinogen that occurs in diseases associated with fever accelerates the ESR[11,12].

Many studies have been conducted in order to develop a method of distinguishing severe bacterial infections from self-limiting viral infections using inflammatory markers[1,3,13–15]. However, the marker values were not compared between different conditions.

The aim of this study was to assess the clinical utility of inflammatory markers for differential diagnosis of diseases associated with fever in children depending on their aetiology.

MATERIAL AND METHODS

In this retrospective study, medical records were analysed of 1,454 children (658 girls and 796 boys) hospitalised in 2016–2017 at the Department of Paediatrics, Paediatric Nephrology and Allergology of the Military Institute of Medicine in Warsaw, Poland, due to diseases associated with fever. The following conditions were identified: upper respiratory tract infection (URTI), lower respiratory tract infection (LRTI) (divided into pneumonia and bronchitis), urinary tract infection (UTI), acute gastroenteritis (GE; divided into viral and bacterial GE), meningitis, sepsis and compound infection (CI; coexistence of at least two infections in the systems mentioned above).

The analysis was performed on the whole study group, which was divided into the following age groups: children in their 1st year of life (n = 422; 29.1%), children between their 2nd and 6th year of life (n = 870; 59.8%) and children from their 7th year onwards (n = 162; 11.1%). The following inflammatory markers were analysed in every group: WBC, CRP, PCT, ESR and NLR.

Measures of central tendency and their spread as well as statistical distribution were determined for the analysed variables. The non-parametric Mann–Whitney U test was used to compare variables whose distribution was significantly different from the Gaussian distribution. Every time, the probability value of $p < 0.05$ was considered statistically significant. Statistica 13.3 and Microsoft Excel were used for analysis.

RESULTS

Group profile

In the studied population, the most commonly diagnosed condition was LRTI (n = 792; 54.47%). The next were: GE (n = 285; 19.6%), URTI (n = 174; 11.97%), UTI (n = 120; 8.25%), CI (n = 68; 4.68%), meningitis (n = 11; 0.76%) and sepsis (n = 4; 0.28%). These results are presented in Tab. 1.

Children in their 1st year of life

Among children in their 1st year of life the most commonly diagnosed condition was LRTI (n = 270; 63.98%), followed by: GE (n = 54; 12.8%), UTI (n = 54; 12.8%) and CI (n = 22; 5.21%). In this age group, URTI (n = 19; 4.5%) and meningitis (n = 3; 0.71%) were relatively uncommon.

Children from 2nd to 6th year of life

Children from their 2nd to 6th year of life accounted for the largest proportion of the study group. The most common

Diagnosis	1st year	2nd–6th year	From 7th year onwards	All children
LRTI	270	446	76	792
URTI	19	128	27	174
CI	22	38	8	68
GE	54	198	33	285
Sepsis	0	4	0	4
Meningitis	3	5	3	11
UTI	54	51	15	120
Total	**422**	**870**	**162**	**1,454**

LRTI – lower respiratory tract infection; **URTI** – upper respiratory tract infection; **CI** – compound infection; **GE** – gastroenteritis; **UTI** – urinary tract infection.

Tab. 1. Number of cases of different conditions by age group

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	WBC			CRP			PCT			ESR			NLR		
	Lower quartile	Median	Upper quartile	Lower quartile	Median	Upper quartile	Lower quartile	Median	Upper quartile	Lower quartile	Median	Upper quartile	Lower quartile	Median	Upper quartile
LRTI	8.840	12.150	16.210	0.200	0.700	2.100	0.110	0.230	0.825	10.000	16.000	30.000	0.504	1.217	2.644
URTI	8.703	11.995	17.125	0.200	1.800	4.825	0.160	0.320	0.838	9.750	21.500	41.000	1.054	1.885	3.732
CI	11.148	15.165	20.225	1.050	3.900	8.400	0.340	0.935	2.510	21.000	38.000	53.250	0.866	1.656	2.838
GE	7.705	10.570	14.605	0.100	0.400	1.300	0.173	0.200	0.323	6.000	11.000	18.750	0.931	2.207	4.661
Sepsis	23.825	26.370	27.930	9.100	17.700	25.675	5.925	8.750	11.145	36.500	61.000	67.500	4.028	5.506	7.619
Meningitis	12.965	18.510	21.885	0.500	1.400	5.600	0.080	0.280	0.410	9.250	13.000	27.750	3.016	6.344	12.649
UTI	9.998	13.475	17.373	0.100	1.300	4.700	0.395	0.810	1.478	9.750	19.000	45.000	0.637	1.132	1.915

WBC – white blood cells; **CRP** – C-reactive protein; **PCT** – procalcitonin; **ESR** – erythrocyte sedimentation rate; **NLR** – neutrophil-to-lymphocyte ratio; **LRTI** – lower respiratory tract infection; **URTI** – upper respiratory tract infection; **CI** – compound infection; **GE** – gastroenteritis; **UTI** – urinary tract infection.

Tab. 2. Inflammatory marker values for different conditions in all children

diagnosis among them was LRTI (n = 446; 51.26%). These children also had a relatively high rate of GE (n = 198; 22.76%) and URTI (n = 128; 14.71%). The conditions which were less commonly diagnosed in this group included: UTI (n = 51; 5.86%), CI (n = 38; 4.37%) and meningitis (n = 5; 0.58%). Cases of sepsis were observed only in this age group (n = 4; 0.46%).

Children from 7th year of life onwards

In the oldest children, the diagnosis data were the following: LRTI (n = 76; 46.91%), GE (n = 33; 20.37%), URTI (n = 27; 1.23%), UTI (n = 15; 9.26%), CI (n = 8; 4.94%) and meningitis (n = 3; 1.85%).

Inflammatory marker values for different conditions are presented in Tab. 2 (for all children) and 3 (per age group).

Differential diagnosis of medical conditions based on inflammatory markers

All children

The utility of inflammatory markers was also analysed with regard to differentiating between medical conditions.

		WBC			CRP			PCT			ESR			NLR		
		Lower quartile	Median	Upper quartile	Lower quartile	Median	Upper quartile	Lower quartile	Median	Upper quartile	Lower quartile	Median	Upper quartile	Lower quartile	Median	Upper quartile
LRTI	**1st year**	10.100	12.630	16.060	0.100	0.300	1.200	0.095	0.240	0.700	7.000	11.000	21.000	0.251	0.430	0.919
	2nd–6th year	8.870	11.895	15.855	0.300	1.000	2.700	0.138	0.320	0.938	12.000	19.000	35.000	0.915	1.702	3.375
	From 7th year	7.290	10.280	14.720	0.200	0.900	2.775	0.098	0.120	0.163	10.000	17.000	29.500	1.585	2.830	5.450
URTI	**1st year**	7.620	14.870	18.245	0.100	0.300	1.800	0.310	0.320	0.650	8.500	11.000	27.750	0.418	0.645	1.539
	2nd–6th year	9.303	12.100	16.420	0.425	2.250	5.150	0.185	0.420	0.943	11.000	25.000	43.000	1.149	2.000	3.957
	From 7th year	7.993	8.940	13.975	0.100	1.600	3.000	0.070	0.130	0.250	4.000	10.500	28.000	1.548	2.416	4.897
CI	**1st year**	11.010	15.560	19.880	0.500	2.600	5.600	0.255	0.330	0.508	12.000	33.000	59.000	0.349	0.689	1.536
	2nd–6th year	11.930	15.445	20.980	2.100	5.600	10.875	0.440	1.050	2.775	32.500	42.500	58.250	1.501	2.230	2.981
	From 7th year	6.308	11.120	15.975	0.800	3.750	6.700	0.140	0.140	0.140	20.500	28.000	31.000	1.809	3.173	6.149
GE	**1st year**	8.850	10.920	13.900	0.100	0.200	0.500	0.175	0.180	0.190	5.000	9.000	18.750	0.368	0.673	1.385
	2nd–6th year	7.565	10.690	14.920	0.100	0.400	1.400	0.185	0.225	0.533	6.000	11.000	21.000	1.072	2.394	4.613
	From 7th year	6.730	9.470	14.770	0.100	0.900	1.700	0.130	0.180	0.340	3.750	8.000	12.500	3.863	5.778	15.103
Sepsis	**1st year**	23.825	26.370	27.930	9.100	17.700	25.675	5.925	8.750	11.145	36.500	61.000	67.500	4.028	5.506	7.619
	2nd–6th year	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data
	From 7th year	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data
Meningitis	**1st year**	13.865	18.990	19.635	0.750	1.400	1.850	0.148	0.215	0.283	4.750	6.500	8.250	1.151	2.120	2.523
	2nd–6th year	18.510	23.490	25.790	0.500	6.800	8.500	0.280	0.410	0.590	15.000	32.000	44.000	4.516	8.364	11.329
	From 7th year	9.075	10.120	12.965	0.650	0.800	2.600	0.078	0.115	0.153	9.000	9.000	11.000	10.824	15.305	20.004
UTI	**1st year**	11.668	14.600	20.048	0.100	0.900	4.825	0.260	0.710	0.930	11.000	28.500	44.000	0.404	0.963	1.360
	2nd–6th year	9.805	12.920	15.530	0.100	2.000	5.700	0.530	1.440	2.720	10.000	17.000	49.500	0.783	1.096	2.135
	From 7th year	8.005	10.270	11.840	0.125	0.700	2.275	1.840	3.580	5.320	9.000	13.000	31.000	1.610	2.260	3.661

WBC – white blood cells; **CRP** – C-reactive protein; **PCT** – procalcitonin; **ESR** – erythrocyte sedimentation rate; **NLR** – neutrophil-to-lymphocyte ratio; **LRTI** – lower respiratory tract infection; **URTI** – upper respiratory tract infection; **CI** – compound infection; **GE** – gastroenteritis; **UTI** – urinary tract infection.

Tab. 3. Inflammatory marker values for different conditions by age group

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LRTI vs. URTI		
	Z	*p*
WBC	–0.520187	0.602934
CRP	–4.99247	0.000001
PCT	–0.755124	0.450175
ESR	–2.97958	0.002887
NLR	–5.55664	0.000000

LRTI – lower respiratory tract infection; **URTI** – upper respiratory tract infection; **WBC** – white blood cells; **CRP** – C-reactive protein; **PCT** – procalcitonin; **ESR** – erythrocyte sedimentation rate; **NLR** – neutrophil-to-lymphocyte ratio.

Tab. 4. Markers used to differentiate between LRTI and URTI

CRP, ESR and NRL turned out to be useful in the differentiation between URTIs and LRTIs. The values are higher in URTIs (Tab. 4).

Inflammatory markers were also found to be higher in CIs than in single conditions. Detailed analysis is provided in Tab. 5.

For differential diagnosis between pneumonia and bronchitis a statistically significant difference was found for CRP and ESR. Higher levels were found for pneumonia (Tab. 6).

As for the aetiology of GE, CRP and ESR were found to be higher in bacterial infections. No marker was statistically significant for rotavirus vs. adenovirus infections (Tab. 7).

Analysis of children in their 1st year of life

Due to the lack of characteristic signs of infection in children below 12 months of age, this group was subjected to detailed analysis.

All inflammatory markers were found to be higher in UTIs as opposed to LRTIs. These differences were statistically significant (Tab. 8).

The comparison of inflammatory markers in UTI and acute GE also revealed higher values for UTI. The following markers were found to be statistically significant: WBC, CRP, PCT and ESR (Tab. 8).

The only marker which made it possible to differentiate between URTI and LRTI in children below 12 months of age was NLR, indicating a larger proportion of neutrophils in URTIs. The results are presented in Tab. 8.

Pneumonia vs. bronchitis		
	Z	*p*
WBC	0.077769	1.763789
CRP	4.057060	0.000050
PCT	1.367007	0.171624
ESR	4.066869	0.000048
NLR	0.156040	0.876001

WBC – white blood cells; **CRP** – C-reactive protein; **PCT** – procalcitonin; **ESR** – erythrocyte sedimentation rate; **NLR** – neutrophil-to-lymphocyte ratio.

Tab. 6. Inflammatory markers used to differentiate between pneumonia and bronchitis

DISCUSSION

In 1993, Baraff et al. presented an algorithm for the management of children with fever of unknown source which would make it possible to detect bacterial infection, and thus use the right kind of treatment. This algorithm primarily used WBC, ANC and urinalysis[4]. Further studies have also been conducted on new markers which were supposed to differentiate between bacterial and viral infections. Relatively inexpensive and easily available parameters such as NLR[9,10] and ESR[16,17], and more expensive and less easily available markers such as lipopolysaccharide-binding protein (LBP), fibrinogen, interleukins-6 and -8 and interleukin-1 receptor antagonist were investigated[1,18,19]. In the present study, simple, largely relatively inexpensive and easily available parameters were used: WBC, CRP, ESR, PCT and NLR.

These markers were investigated with regard to their ability to differentiate between URTIs and LRTIs. It was found that CRP and ESR might be helpful in this respect since they reach much higher values in URTIs regardless of the age group. In URTIs NLR is also higher, which indicates the presence of a higher proportion of neutrophils in peripheral blood. In the study group, lower levels of inflammatory markers in children with pneumonia as opposed to those with URTI may be associated with the predominance of viral pneumonia. To date, in the literature, inflammatory markers were used mainly for identifying the aetiology of respiratory tract infections. Hoshina et al. demonstrated that PCT is the most useful parameter for differentiating between bacterial and viral pneumonia, while

	LRTI vs. CI		URTI vs. CI		GE vs. CI		UTI vs. CI	
	Z	*p*	*Z*	*p*	*Z*	*p*	*Z*	*p*
WBC	–4.53293	0.000006	–3.33001	0.000869	–5.53950	0.000000	–2.07952	0.037571
CRP	–6.90565	0.000000	–3.27474	0.001058	–7.69317	0.000000	–3.68348	0.000230
PCT	–3.20193	0.001365	–2.45870	0.013945	–3.13454	0.001721	–0.134060	0.893355
ESR	–6.19424	0.000000	–3.71859	0.000200	–8.00277	0.000000	–3.25562	0.001132
NLR	–2.22317	0.026205	1.154269	0.248391	1.591689	0.111456	–2.47294	0.013401

LRTI – lower respiratory tract infection; **CI** – compound infection; **URTI** – upper respiratory tract infection; **GE** – gastroenteritis; **UTI** – urinary tract infection; **WBC** – white blood cells; **CRP** – C-reactive protein; **PCT** – procalcitonin; **ESR** – erythrocyte sedimentation rate; **NLR** – neutrophil-to-lymphocyte ratio.

Tab. 5. Inflammatory markers used to differentiate between a CI and single medical conditions

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	Rotaviruses vs. *Salmonella*		Rotaviruses vs. adenoviruses	
	Z	***p***	***Z***	***p***
WBC	0.369875	0.711476	0.00	1.000000
CRP	–4.01337	0.000060	1.287031	0.198085
ESR	–3.26823	0.001082	–0.179115	0.857848
NLR	0.260727	0.794303	–1.48555	0.137400

WBC – white blood cells; **CRP** – C-reactive protein; **ESR** – erythrocyte sedimentation rate; **NLR** – neutrophil-to-lymphocyte ratio.

Tab. 7. Inflammatory markers used for differentiating the aetiology of GE

ANC is the most useful marker for determining the aetiology of bronchitis[20]. Gauchan et al. reported that CRP level may be used for identifying the aetiology of pneumonia[10]. Flood et al. obtained similar results in their meta-analysis[21]. However, none of the studies mentioned above used inflammatory markers for identifying the level of respiratory tract infection (URTI vs. LRTI).

The comparison between test results in children with a single condition (URTI, LRTI, UTI or GE) and those with a minimum of two conditions diagnosed revealed that inflammatory markers reach much higher levels in CIs. Therefore, if inflammatory marker levels are very high, more than one source of infection should be suspected.

In order to facilitate the decision on using an antibiotic for acute LRTI in children, a chest radiograph is often taken[22]. However, at least due to the radiological protection recommended in children, it seems important to identify laboratory inflammatory markers which would make it possible to differentiate between pneumonia and bronchitis, and thus choose the right kind of treatment[23,24]. According to the results obtained by the present authors, CRP and ESR may be useful in this respect: they are higher in pneumonia, and therefore, they may be an indication of the severity of the disease (Tab. 6). Similar results were obtained by Hopstaken et al., proving that increased CRP (>20 mg/L) and ESR values are predictors of pneumonia in acute LRTI[17,18]. These authors also found that CRP in this case is characterised by higher diagnostic sensitivity than physical examination, WBC or ESR[17].

	LRTI vs. UTI		UTI vs. GE		LRTI vs. URTI	
	Z	***p***	***Z***	***p***	***Z***	***p***
WBC	–3.36148	0.000775	4.006187	0.000062	–0.961146	0.336479
CRP	–3.67038	0.000242	3.441106	0.000579	–0.496306	0.619679
PCT	–2.00783	0.044662	2.154137	0.031230	–0.920264	0.357435
ESR	–3.86916	0.000109	3.462714	0.000535	–0.513482	0.607614
NLR	–3.88023	0.000104	0.946247	0.344024	–2.226380	0.025989

LRTI – lower respiratory tract infection; **UTI** – urinary tract infection; **GE** – gastroenteritis; **URTI** – upper respiratory tract infection; **WBC** – white blood cells; **CRP** – C-reactive protein; **PCT** – procalcitonin; **ESR** – erythrocyte sedimentation rate; **NLR** – neutrophil-to-lymphocyte ratio.

Tab. 8. Inflammatory markers used for differential diagnosis of medical conditions in children in their 1st year of life

Antibiotics are too frequently administered for gastrointestinal tract infections compared to recommendations. For this reason, it is important to try to differentiate between a bacterial and viral source of infection. Unfortunately, microbiological testing results are usually not available until after 48–72 hours; therefore, it is important to make use of inflammatory markers[25]. The observation from the present study shows that CRP and ESR may be used to distinguish a viral infection from that caused by *Salmonella* spp., since they reach higher levels in the latter. However, no parameter seems to be useful in differentiating between infections caused by different types of viruses. Martínez et al. obtained similar results; in their study, elevated CRP values in cases of bacterial GE were also accompanied by increased PCT values[26]. Korczowski and Szybist also demonstrated that even though CRP may be used to differentiate the aetiology of GE, it is PCT that is characterised by a higher sensitivity and specificity for this purpose[25].

In children below 12 months of age, differentiating between medical conditions is particularly difficult; for this reason, the scope of analysis in this age group was extended. Vomiting is common in UTIs in such children, while the observation of signs of dysuria is difficult. Therefore, the results obtained in order to differentiate between UTIs and GE are important. They reveal that all markers (WBC, CRP, PCT and ESR) reach higher levels in UTIs and exceed the upper limit of normal much more frequently than in GE. The comparison between results for UTI and those for LRTI shows a similar tendency: again, inflammatory marker levels are higher in UTI. In addition, the investigation of NLR shows that neutrophilia is statistically more common in UTIs. A number of studies show that the most common cause of fever of unknown origin in infants (particularly below 3 months of age) is UTI[16,27,28]. Therefore, this diagnosis always needs to be taken into account in a febrile child with increased inflammatory markers, even when atypical symptoms are present (such as vomiting, for example).

The present retrospective study has certain limitations. One of them is the disproportion between the number of subjects in different groups of conditions. It also needs to be emphasised that the study group was composed of hospital patients, which may have resulted in a relatively large number of children treated for pneumonia. Therefore, further, prospective research on a larger group of children is needed for any definitive conclusions to be possible. Due to the fact the study group included only single cases of severe infections, a comparison between meningitis and sepsis was practically impossible, whereas such findings would have been interesting. Nevertheless, the ultimate decision on the choice of treatment and the use of antibiotic therapy should be taken on a case-by-case basis, taking into account the whole clinical picture and not just the results of additional tests. Inflammatory marker values should only serve as additional guidance. Moreover, one cannot rely on a single instance of testing: repeating the tests may be necessary in order to be able to observe any trend in the results.

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In addition, the paediatric population is characterised by a large variability of reference ranges depending on the age. NLR may be particularly unreliable due to the different neutrophil and lymphocyte counts in peripheral blood in different age groups.

CONCLUSIONS

1. Inflammatory markers may be helpful for differentiating the aetiology of infectious diseases associated with fever in children.
2. The determination of a number of markers provides more information and has a much higher diagnostic value than the analysis of a single parameter.
3. When making specific diagnostic and therapeutic decisions one should always take into account the complete clinical picture.

Conflict of interest

The authors do not report any financial or personal affiliations to persons or organisations that could adversely affect the content of or claim to have rights to this publication.

References

1. Hsiao AL, Baker MD: Fever in the new millennium: a review of recent studies of markers of serious bacterial infection in febrile children. Curr Opin Pediatr 2005; 17: 56–61.
2. Olaciregui I, Hernández U, Muñoz JA et al.: Markers that predict serious bacterial infection in infants under 3 months of age presenting with fever of unknown origin. Arch Dis Child 2009; 94: 501–505.
3. Andreola B, Bressan S, Callegaro S et al.: Procalcitonin and C-reactive protein as diagnostic markers of severe bacterial infections in febrile infants and children in the emergency department. Pediatr Infect Dis J 2007; 26: 672–677.
4. Baraff LJ, Bass JW, Fleisher GR et al.: Practice guideline for the management of infants and children 0 to 36 months of age with fever without source. Ann Emerg Med 1993; 22: 1198–1210.
5. Bonsu BK, Chb M, Harper MB: Identifying febrile young infants with bacteremia: is the peripheral white blood cell count an accurate screen? Ann Emerg Med 2003; 42: 216–225.
6. Galetto-Lacour A, Zamora SA, Gervaix A: Bedside procalcitonin and C-reactive protein tests in children with fever without localizing signs of infection seen in a referral center. Pediatrics 2003; 112: 1054–1060.
7. Du Clos TW: Function of C-reactive protein. Ann Med 2000; 32: 274–278.
8. Gendrel D, Bohuon C: Procalcitonin as a marker of bacterial infection. Pediatr Infect Dis J 2000; 19: 679–687.
9. Holub M, Beran O, Kaspříková N et al.: Neutrophil to lymphocyte count ratio as a biomarker of bacterial infections. Cent Eur J Med 2012; 7: 258–261.
10. Gauchan E, Adhikari S: C-reactive protein versus neutrophil/lymphocyte ratio in differentiating bacterial and non-bacterial pneumonia in children. J Nepal Health Res Counc 2016; 14: 154–158.
11. Ramsay ES, Lerman MA: How to use the erythrocyte sedimentation rate in paediatrics. Arch Dis Child Educ Pract Ed 2015; 100: 30–36.
12. Sox HC Jr., Liang MH: The erythrocyte sedimentation rate. Guidelines for rational use. Ann Intern Med 1986; 104: 515–523.
13. Chiu IM, Huang YH, Su CM et al.: C-reactive protein concentration can help to identify bacteremia in children visiting the emergency department: a single medical center experience. Pediatr Emerg Care 2018. DOI: 10.1097/PEC.0000000000001453.
14. Markic J, Kovacevic T, Krzelj V et al.: Lab-score is a valuable predictor of serious bacterial infection in infants admitted to hospital. Wien Klin Wochenschr 2015; 127: 942–947.
15. Manzano S, Bailey B, Gervaix A et al.: Markers for bacterial infection in children with fever without source. Arch Dis Child 2011; 96: 440–446.
16. Cuello García CA, Tamez Gómez L, Valdez Ceballos J: [Total white blood cell count, erythrosedimentation rate and C-reactive protein for the detection of serious bacterial infections in 0- to 90-day-old infants with fever without a source]. An Pediatr (Barc) 2008; 68: 103–109.
17. Hopstaken RM, Muris JW, Knottnerus JA et al.: Contributions of symptoms, signs, erythrocyte sedimentation rate, and C-reactive protein to a diagnosis of pneumonia in acute lower respiratory tract infection. Br J Gen Pract 2003; 53: 358–364.
18. Hopstaken RM, Cals JW, Dinant GJ: Accuracy of lipopolysaccharide-binding protein (LBP) and fibrinogen compared to C-reactive protein (CRP) in differentiating pneumonia from acute bronchitis in primary care. Prim Care Respir J 2009; 18: 227–230.
19. Lacour AG, Gervaix A, Zamora SA et al.: Procalcitonin, IL-6, IL-8, IL-1 receptor antagonist and C-reactive protein as identificators of serious bacterial infections in children with fever without localising signs. Eur J Pediatr 2001; 160: 95–100.
20. Hoshina T, Nanishi E, Kanno S et al.: The utility of biomarkers in differentiating bacterial from nonbacterial lower respiratory tract infection in hospitalized children: difference of the diagnostic performance between acute pneumonia and bronchitis. J Infect Chemother 2014; 20: 616–620.
21. Flood RG, Badik J, Aronoff SC: The utility of serum C-reactive protein in differentiating bacterial from nonbacterial pneumonia in children: a meta-analysis of 1230 children. Pediatr Infect Dis J 2008; 27: 95–99.
22. Correia MA, Mello MJ, Petribú NC et al.: Agreement on radiological diagnosis of acute lower respiratory tract infection in children. J Trop Pediatr 2011; 57: 204–207.
23. Turczyńska A, Kułak P, Gościk E et al.: Radiation protection from the point of view of patients of the Radiology Department at the University Clinical Hospital in Białystok. Piel Zdr Publ 2016; 6: 29–38.
24. Pruszyński B (ed.): Radiologia. Diagnostyka obrazowa. Wydawnictwo Lekarskie PZWL, Warszawa 2000.
25. Korczowski B, Szybist W: Serum procalcitonin and C-reactive protein in children with diarrhoea of various aetiologies. Acta Peaediatr 2004; 93: 169–173.
26. Martínez L AB, Marañón P R, Cobo E PV et al.: [Use of procalcitonin as diagnostic marker in acute gastroenteritis]. Rev Chil Pediatr 2014; 85: 157–163.
27. Bachur RG, Harper MB: Predictive model for serious bacterial infections among infants younger than 3 months of age. Pediatrics 2001; 108: 311–316.
28. Gajdos V, Foix L'Hélias L, Mollet-Boudjemline A et al.: [Factors predicting serious bacterial infections in febrile infants less than three months old: multivariate analysis]. Arch Pediatr 2005; 12: 397–403.

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