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Analysis of neutrophil to lymphocyte ratio, platelet to lymphocyte ratio and mean platelet volume to platelet count ratio in children with acute stage of immunoglobulin A vasculitis and assessment of their suitability for predicting the course of the disease

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Abstract

Immunoglobulin A vasculitis (IgAV) is the most common systemic vasculitis in developmental age. The disease is most often characterized by a self-limiting course and good prognosis, but sometimes serious complications, like gastrointestinal bleeding or glomerulonephritis, may develop. The neutrophil to lymphocyte (NLR) and the platelet to lymphocyte (PLR) ratios are indicators related to clinical outcome in various inflammatory diseases. The mean platelet volume to platelet count ratio (MPR) has not been evaluated in patients with IgAV. The aim of this study was to analyze the values of the NLR, PLR and MPR in patients with an acute stage of IgAV compared to healthy children and to assess their suitability for predicting the severity of the disease. All children with IgAV hospitalized in our institution between 2012 and 2017 were reviewed retrospectively. The selected laboratory data were recorded before starting the treatment; these results allowed for NLR, PLR, and MPR calculation. The study involved 71 IgAV children. 57.7% of patients revealed signs of systemic involvement (including GT bleeding and/or glomerulonephritis) and 42.3% were nonsystemic (presenting skin and joint symptoms). 83% of patients were classified as mild and 17% as severe course of the disease. The NLR and the PLR were significantly higher in all IgAV children and in the systemic involvement group in comparison with non-systemic. The MPR was significantly lower in all IgAV group with the exception of children without systemic involvement. The NLR is a more valuable indicator than the PLR to identify patients at higher risk of systemic involvement in the course of IgAV. Clinical usefulness of the MPR requires further research.

Keywords Henoch-Schonlein Purpura · IgAV · NLR · PLR · MPR · Children

Introduction

Immunoglobulin A vasculitis (IgAV), formerly known as Henoch-Schonlein Purpura, is the most common vasculitis in childhood. It is a leukocytoclastic vasculitis with IgA1-dominant immune deposits, affecting the small vessels of the skin, gastrointestinal tract, kidney and frequently causes arthritis [1]. The disease is most often characterized by a mild, self-limiting course and good prognosis, but in some cases, serious complications may develop. Symptoms from the gastrointestinal tract (GT) concern 50–70% of patients [2]; most often, these are abdominal pains and latent bleeding from GT. Haematemesis, melaena and severe complications such as intussusception or GT perforation are less frequent. According to various sources, renal involvement occurs in 40–50% of cases,

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usually haematuria and/or proteinuria appear within 4–6 weeks from the beginning of the disease. The risk of developing chronic renal failure in the pediatric population does not exceed 7% [3]. Considering the possibility of serious complications in the course of IgAV, research is needed to identify patients at higher risk of developing severe extracutaneous symptoms. Inexpensive and easily available laboratory parameters that can be used to assess the severity of systemic inflammation include the following ratios: neutrophils/lymphocytes (NLR) and platelets/lymphocytes (PLR). The shifts in the percentage formula of white blood cells (neutrophilia and lymphopenia) are the physiological response of the immune system to the ongoing inflammatory process, injury or stress [4], and NLR and PLR reflect these changes. Until now, their relationship with the severity of the disease and/or prognosis in patients with autoimmune diseases, malignancies, cardiovascular and respiratory diseases, and in the pediatric population also in allergic diseases such as bronchial asthma or atopic dermatitis were studied [5–11]. Few studies indicate significant differences in NLR and PLR values in IgAV patients compared to healthy subjects. Elevated NLR and PLR, as well as low MPV (mean platelet volume), appear to be indicators related to GT bleeding in the course of IgAV [12–14]. The MPV/PLT ratio (MPR), considered a marker for platelet activation and inflammation, has not been evaluated in patients with IgAV. The aim of this study was to analyze the values of NLR, PLR, and MPR in patients with acute stage of IgAV compared to healthy children and to assess their suitability for predicting the severity of the disease.

Materials and methods

The study included 71 children with IgAV hospitalized in the Pediatric Department of the Clinical Hospital No. 1 in Zabrze in 2012–2017. Diagnosis of the disease was based on the EULAR/PRINTO/PRES criteria [15], which as a prerequisite for the diagnosis mention a detectable, non-thrombocytopenic purpura or ecchymosis located mainly on the lower limbs along with meeting at least one of the other criteria (diffuse abdominal colicky pain; arthritis/arthralgias; renal involvement—hematuria/proteinuria; biopsy showing IgA deposition). The clinical scoring scale (Table 1) from Muslu et al. and De Matia et al. modified by Fessatou S et al., which is the sum of points depending on the severity of joint, renal and gastrointestinal symptoms, was used to assess the disease severity (mild ≤ 4 points, severe > 4) [16–18]. Gastrointestinal bleeding was defined as haematemesis, melaena, hematochezia, and positive fecal occult blood test (FOBT). Renal involvement was defined as hematuria (> 5 RBC in the field of vision), macroscopic hematuria or proteinuria (> 300 mg/24 h).

43 healthy children were included in the control group, selected in terms of age and gender (Table 2). Children from the control group attended the outpatient pediatric clinic for non-immunological, non-inflammatory health problems and needed venous puncture. A blood sample for laboratory tests was collected at the time of the patient's admission to the hospital (before the start of treatment) and tested in the central laboratory within the first hour after collection. Standard tubes with ethylenediaminetetraacetic acid (EDTA) were used. The following laboratory data were recorded:

Table 1 The clinical scoring system in patients with IgAV [16–18]

Arthritis score	
0	No symptom
1	Artralgia and/or slight swelling (normal walk)
2	Artralgia and/or moderate swelling (difficult to walk)
3	Artralgia and/or severe swelling (refuse to walk)
Abdominal score	
0	No symptom
1	Mild abdominal pain and/or occult blood in stool (+)
2	Moderate abdominal pain (transient complaints brought to medical attention) and/or occult blood in stool (++/+++)
3	Severe abdominal pain and/or melena and/or hematemesis and/or intussusception and/or surgical consultation required
Renal score	
0	No proteinuria and/or 3–5 RBC/HPF
1	Proteinuria 30 mg/dl and/or microalbuminuria and/or 10–15 RBC/HPF
2	Proteinuria 30–150 mg/dl and/or > 50 RBC/HPF
3	Proteinuria 150 mg/dl and/or macroscopic haematuria

RBC red blood cells, *HPF* high-power field

Table 2 Demographic, clinical and selected laboratory characteristic of study and control groups

Parameter	IgAV group ($n=71$)	Control group ($n=43$)
Median age (years) (Q_{25}–Q_{75})	6 (5–9)	8 (5–13)
Gender M/F	32/39	20/23
BMI (kg/m^2)	16.17 (14.53–19.25)	16.81 (15.2–18.7)
Laboratory data (median)		
IgA (g/l)	1.81 (1.5–2.27)*	1.37 (0.8–1.87)
IgG (g/l)	9.43 (7.97–11.67)	10.25 (8.58–10.96)
IgM (g/l)	0.895 (0.74–1.19)	0.98 (0.78–1.22)
IgE (IU/ml)	74 (14.26–204.65)	55.69 (20.96–116.19)
C3 (g/l)	1.25 (1.13–1.39)	Not studied
C4 (g/l)	0.25 (0.21–0.295)	Not studied
Median duration of symptoms on admission (days) (Q_{25}–Q_{75})	3 (2–6)	
Month of diagnosis		
Spring	20 (28%)	
Summer	12 (17%)	
Autumn	22 (31%)	
Winter	17 (24%)	
Trigger		
Respiratory tract infection	35 (49%)	
Gastrointestinal infection	5 (7%)	
Unknown	31 (44%)	
Symptoms and signs		
Purpura (P)	71 (100%)	
Arthritis/ arthralgia (A)	43 (60.6%)	
Gastointestinal tract involvment (GI)	46 (64.8%)	
Abdominal pain	40 (56%)	
Gastointestinal bleeding (GB)	41 (57.7%)	
Melena/ hematochezia	8 (11%)	
Positive FOBT	33 (80%)	
Kidneys involvemnt (KI)	16 (22.5%)	
Proteinuria (> 300 mg/24 h)	2 (2.8%)	
Hematuria (> 5 RBC wpw)	5 (7%)	
Proteinuria and hematuria	9 (12.7%)	
Other		
Scrotum involvment (epididymitis, oedema)	2 (2.8%)	
Headache	1 (1.4%)	
Severity score		
Mild (≤ 4 points)	59 (83%)	
Severe (> 4 points)	12 (17%)	
Systemic involvment		
Yes: GB + KI	41 (57.7%)	
No: P + A	30 (42.3%)	

*IgA concentration in whole IgAV group vs control group: $p<0.0001$

hemoglobin level (Hgb), white blood cell count (WBC), neutrophil and lymphocyte count, platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), C-reactive protein (CRP) and immunoglobulins level. The haemogram-derived parameters were determined using an automatic hematology analyzer and the total and differential leukocyte counts in blood were measured using an automated blood cell counter. For all tested parameters, the norms for age were included. NLR was calculated by dividing the neutrophil count by the lymphocyte count, PLR was calculated by dividing the platelets count by the lymphocyte count and MPR was calculated by dividing the MPV by the

platelets count. The present study was approved by the Ethics Committee of the Medical University of Silesia in Katowice on 01.07.2014 (KNW/0022/KB1/66/14; KNW/0022/KB1/66/III/14/16/17) and written informed consent was obtained from children's parents.

Statistical evaluation

Statistical calculations were made using the MedCalc ver. 18.2.1 (Ostend, Belgium). For all parameters, the normality of distribution was determined by the Shapiro–Wilk test. Summary statistics were expressed as medians and 25–75th percentiles (Q_{25}–Q_{75}). Comparative analysis of groups was performed using the non-parametric test (Mann–Whitney *U* test). Logistic regression analysis and receiver operating characteristic (ROC) curves were performed to determine possible factors associated with systemic involvement in IgAV. $p < 0.05$ was considered significant.

Results

The children from the study and control groups did not differ significantly in terms of age, sex, and BMI. Demographic and clinical characteristics of both groups are presented in Table 2.

Characteristic of IgAV patients

Patients were included after a median duration of symptoms of 3 days. In 49% of patients, IgAV was triggered by the infection mostly of the respiratory tract. The occurrence of petechial purpura in some children was preceded by arthritis ($n = 7$, 9.9%) or abdominal discomfort ($n = 6$, 8.5%). In four children, GT obstruction, appendicitis, and intussusception were initially suspected. The majority of patients presented symptoms from GT (64.8%) and joints (60.6%), and 22.5% of children showed signs of glomerulonephritis. 4 subgroups were distinguished within the study group depending on the severity of the disease and the presence of systemic involvement. According to the disease severity scale, 83% of patients ($n = 59$) were classified as mild (1) and 17% ($n = 12$) as severe (2). 57.7% ($n = 41$) of patients revealed signs of systemic involvement (3), including GT bleeding and/or glomerulonephritis, and 42.3% ($n = 30$) were non-systemic (4) presenting skin and joint symptoms. No isolated renal involvement was observed in any of the patients studied.

The comparison of selected parameters in all separate subgroups and in the control group is presented in Table 3.

IgAV patients in comparison with the control group

Children with IgAV had significantly higher values of WBC, neutrophils, PLT, NLR, CRP compared to the control group, regardless of the severity (for WBC, neutrophils, CRP all IgAV children vs control, mild vs control, severe vs control: $p < 0.0001$; for NLR all IgAV children vs control, mild vs control, severe vs control: $p < 0.002$; for PLT all IgAV children vs control, mild vs control, severe vs control: $p < 0.01$). Similar differences in the parameters assessed were observed in children with systemic involvement (systemic involvement vs control for WBC, neutrophils, CRP, NLR: $p < 0.0001$, for PLT: $p < 0.001$). In the group without systemic involvement, in addition to higher WBC, neutrophils and CRP (vs control $p < 0.002$) a significantly higher lymphocyte count was found. The lymphocyte count in the whole IgAV group was higher than the control ($p = 0.05$), but this difference probably resulted from higher lymphocyte values in the group with mild and no systemic involvement (vs control $p < 0.05$; $p < 0.01$ respectively). In all groups of IgAV children with the exception of children without systemic involvement, the MPR was statistically significantly lower than that in the control group (all IgAV children vs control: $p = 0.005$, mild vs control: $p = 0.01$, severe vs control: $p = 0.04$, systemic involvement vs control: $p = 0.002$). There was no significant statistical difference in the value of Hgb, MPV, PDW, and PLR between these groups and the control group.

The severe-course group in comparison with the mild-course group

In the group of patients with severe IgAV, statistically significant higher values of WBC and neutrophils were found in comparison to the mild group ($p = 0.034$; $p = 0.021$, respectively).

The systemic-involvement group in comparison with the without-systemic-involvement group

In the group of patients with systemic involvement, statistically significantly higher values of WBC, neutrophils, NLR and PLR were found ($p = 0.02$, $p < 0.001$, $p < 0.001$, $p < 0.003$, respectively) in comparison to patients without organ involvement.

The logistic regression analysis for possible risk factors of systemic involvement and the receiver operating characteristic (ROC) curves

The logistic regression analysis of WBC, neutrophils, NLR and PLR to identify the predictive factors for systemic

Table 3 Comparison of selected laboratory parameters between patients with mild and severe course of the disease, between patients with and without systemic involvement and in comparison with control group

Parameter	IgAV	Control group
Hgb (g/dL)		12.94 (12.13–13.7)
All IgAV group ($n=71$)	12.8 (12.4–13.7)	
Severe course ($n=12$)	12.9 (12.35–14.3)	
Mild course ($n=59$)	12.8 (12.4–13.7)	
Systemic involvment ($n=41$)	13.1 (9.6–16)	
Without systemic involvment ($n=30$)	12.67 (11.5–15.2)	
PLT ($\times 10^3$/uL)		303 (243–332)
All IgAV group ($n=71$)	355 (289–400)*	
Severe course ($n=12$)	372.5 (311–411.5)*	
Mild course ($n=59$)	352 (289–399)*	
Systemic involvment ($n=41$)	369 (317–416)*	
Without systemic involvment ($n=30$)	325.5 (281–388)	
MPV (fL)		8.32 (7.68–9.5)
All IgAV group ($n=71$)	8.35 (7.55–9.3)	
Severe course ($n=12$)	8 (7.43–9.3)	
Mild course ($n=59$)	8.4 (7.55–9.3)	
Systemic involvment ($n=41$)	8.2 (6.4–10.8)	
Without systemic involvment ($n=30$)	8.5 (7.1–10.3)	
PDW (fL)		12.25 (10.6-13.58)
All IgAV group ($n=71$)	11 (9.79–13.6)	
Severe course ($n=12$)	11.9 (10.3–13.7)	
Mild course ($n=59$)	11 (9.7–13.4)	
Systemic involvment ($n=41$)	10.8 (9.8–13.8)	
Without systemic involvment ($n=30$)	11.38 (9.65–13.25)	
WBC ($\times 10^3$/uL)		6.61 (5.58–7.93)
All IgAV group ($n=71$)	10.19 (8.14-13)*	
Severe course ($n=12$)	12.1 (10.35–14.13)* #	
Mild course ($n=59$)	9.9 (7.6–12.9)*	
Systemic involvment ($n=41$)	11.86 (9.1–13.3)* ^	
Without systemic involvment ($n=30$)	9.45 (7.5–11.23)*	
Neutrophils ($\times 10^3$/uL)		3.47 (2.32–4.12)
All IgAV group ($n=71$)	6.04 (4.51–8.78)*	
Severe course ($n=12$)	7.7 (5.7–9.95)* #	
Mild course ($n=59$)	5.6 (4.11–8.02)*	
Systemic involvment ($n=41$)	6.74 (5.45–9.34)* ^	
Without systemic involvment ($n=30$)	4.8 (3.26–6.41)*	
Lymphocytes ($\times 10^3$/uL)		2.4 (1.95–2.14)
All IgAV group ($n=71$)	2.92 (2.23–3.93)*	
Severe course ($n=12$)	2.6 (2.03–4)	
Mild course ($n=59$)	2.93 (2.3–3.96)*	
Systemic involvment ($n=41$)	2.79 (2.08–3.4)	
Without systemic involvment ($n=30$)	3.21 (2.4–4.46)*	
CRP (mg/l)		0.6 (0.23–0.99)
All IgAV group ($n=71$)	8.21 (3.53–21.99)*	
Severe course ($n=12$)	13.3 (5.1–37.66)*	
Mild course ($n=59$)	8.2 (2.98–15.7)*	
Systemic involvment ($n=41$)	10.04 (5.04–32.57)*	
Without systemic involvment ($n=30$)	6.65 (1.64–11.27)*	
NLR		1.22 (0.97–1.91)
All IgAV group ($n=71$)	1.903 (1.31–3.06)*	
Severe course ($n=12$)	2.79 (1.63–4.2)*	

Table 3 (continued)

Parameter	IgAV	Control group
Mild course ($n=59$)	1.8 (1.28–2.84)*	
Systemic involvment ($n=41$)	2.77 (1.59–3.93)* ^	
Without systemic involvment ($n=30$)	1.61 (1.15–1.96)	
PLR		126.79 (95.47-152.32)
All IgAV group ($n=71$)	121.58 (89.6–147.6)	
Severe course ($n=12$)	136 (220−95.3)	
Mild course ($n=59$)	129.6 (387.7-85.76)	
Systemic involvment ($n=41$)	139.64 (96.34–160.43)^	
Without systemic involvment ($n=30$)	100.89 (79.96–131.3)	
MPR		0.029 (0.024–0.037)
All IgAV group ($n=71$)	0.023 (0.02–0.03)*	
Severe course ($n=12$)	0.021 (0.019–0.03)*	
Mild course ($n=59$)	0.025 (0.02–0.031)*	
Systemic involvment ($n=41$)	0.022 (0.019–0.027)*	
Without systemic involvment ($n=30$)	0.026 (0.022–0.032)	

MPV mean platelet volume, *PDW* platelet distribution width, *NLR* neutrophil/lymphocyte ratio, *PLR* platelet/ lymphocyte ratio, *MPR* mean platelet volume/platelets count ratio

*$p<0.05$ in comparison with control group

#$p<0.05$ children with severe course in comparison with mild course

^$p<0.05$ children with systemic involvment in comparison with children without systemic involvement

Table 4 Logistic regression analysis of the association of WBC, Neutrophil count, NLR, PLR and systemic involvement in IgAV. OR—odds ratio, 95% CI lower and upper limits of the 95% confidence interval for the odds ratio

Parameter	OR	95% CI lower	95% CI upper	*p* value
WBC	1.158	0.999	1.342	0.051
Neutrophil count	1.377	1.104	1.718	**0.005**
NLR	2.274	1.329	3.89	**0.003**
PLR	1.013	1.001	1.024	**0.031**

involvements in IgAV showed that the higher risk of systemic involvement was associated with higher neutrophil counts and higher NLR and PLR (Table 4).

ROC curve analysis revealed that statistically significant predictors of systemic involvement in IgAV children included NLR, PLR and neutrophil counts. The largest AUC (area under the curve) was demonstrated for the NLR (AUC = 0.738, $p<0.0001$), which at the optimal cutoff value determined using the Youden index at the level of 2.73 showed a high specificity (90%). The parameter with the highest sensitivity (75.6%) at the cutoff of 5.45 (Youden index) was the neutrophil count (Table 5). MPR is the statistically least valuable indicator of systemic involvement. The comparison of ROC curves for selected parameters is shown in Fig. 1.

Discussion

In searching for parameters useful for predicting the course of IgAV (risk of systemic involvement) and making decisions about treatment, it is important to know the complex mechanisms responsible for migration and infiltration of neutrophils into the perivascular space, which ultimately contributes to the development of inflammation with their dominant participation [19]. As the ratio of particular types of white blood cells, rather than their total number, is considered to have a higher prognostic value in assessing the severity of inflammation, in our study, we assessed the ratio of neutrophils to lymphocytes as well as PLR and MPR ratios.

Table 5 ROC curves analysis of NLR, neutrophils count, PLR and MPR for predicting systemic involvment

Parameter	Cut-off value	Sensitivity %	Specificity %	AUC	95% CI	*p* value	Youden index
NLR	2.73	53.7	90	0.738	0.623–0.853	**<0.0001**	0.44
Neutrophils	5.45	75.6	60	0.734	0.617–0.852	**0.0001**	0.36
PLR	124.04	65.9	73.3	0.709	0.585–0.833	**0.001**	0.39
MPR	0.023	63.4	63.3	0.506	0.506–0.766	**0.04**	0.27

Bold values are statistically significant

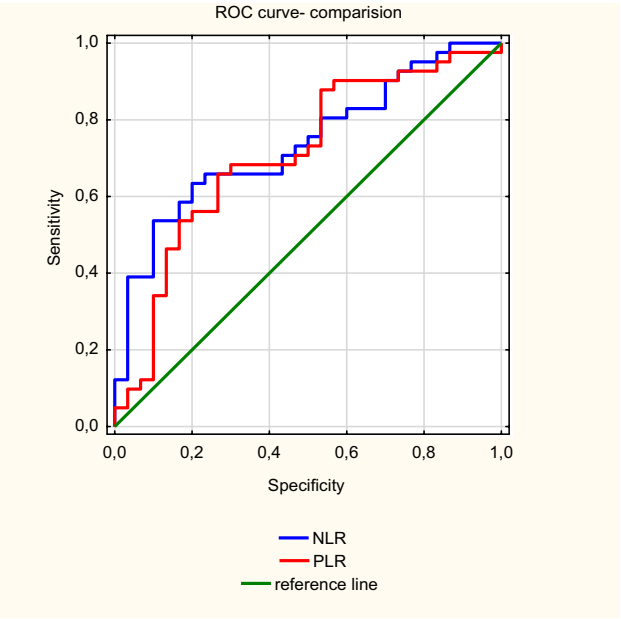

Fig. 1 Comparision of ROC curves of NLR and PLR for predicting systemic involvment in IgAV

The significantly higher neutrophil counts and the value of the NLR in children with IgAV documented in our study confirm their participation in the pathogenesis of the disease. It is known that neutrophils are not only the first effector cells flowing into the site of injury/inflammation removing extracellular pathogens but they also affect the activation, regulation, and function of other cells of the immune system, among others, through the release of cytokines, extracellular traps, and effector molecules [20]. The current research shows that the NLR, showing changes in particular populations in the total leukocyte pool, is associated with higher severity of inflammation and, thus, with a more severe course of the disease [13, 21]. This is confirmed by the results of our research because NLR, like the neutrophils count, was higher in children with the severe course of the disease and/or systemic involvement. Moreover, ROC curve analysis showed that NLR is the best predictor of systemic involvement in children with IgAV with an optimal cutoff value of 2.73 (sensitivity 53.7%, specificity 90%). Previous research by Makay et al. and Hee Hong et al. which showed significantly higher NLR values in the group of patients with GT bleeding coincide with ours (cutoff value 2.82, 81% sensitivity, 76% specificity and cutoff value 2, 86, sensitivity 73%, specificity 68% respectively) [13, 22]. In our study, we also showed elevated PLT and PLR in the group of children with systemic involvement (cutoff value 124.04, sensitivity 65.9%, specificity 73.3%). Similarly, Gayret et al. showed that PLT and PLR are significantly higher in children with GT bleeding but in contrast to the studies of other authors and ours he did not confirm the increase of neutrophils and NLR in this group of patients [14].

Reactive thrombocytosis can be observed in various clinical conditions (acute or chronic infection, trauma, malignancy). The aforementioned cellular shifts associated with the immune response to the ongoing non-specific inflammatory process (neutrophilia, lymphopenia) influence changes in the values of both PLR and NLR. Significantly increased levels of cytokines in the acute phase of IgAV, including TNF-alpha, IL-6, IL-8, are responsible for thrombocytosis, elevated CRP, more severe course of the disease, and a higher risk of renal involvement [23–26]. Three main elements are considered to be a measure of platelet activation: MPV (which determines the average size of platelets and reflects their production in the bone marrow), PDW (index of inhomogeneity of the size of the platelets) and the number of platelets [27]. The healthy population shows an inverse relationship between MPV and platelet count [28]. Reactive thrombocytosis is often accompanied by low MPV and PDW [29]. Activated platelets play an important role in the systemic inflammatory response through the release of inflammatory mediators and the presentation of surface molecules (including P-selectin, E-selectin) that affect their interactions with other cells [30]. Larger platelets are more active, contain more mediators (serotonin, adenosine diphosphate, platelet-derived growth factor, β-thromboglobulin) and show greater expression of adhesion molecules (glycoproteins Ib, and glycoprotein IIb-IIIa) [31]. In addition, due to the presence of a ligand for P-selectin on the surface of neutrophils (PSGL-1, P-selectin glycoprotein ligand-1), the platelets can affect neutrophils and stimulate cytokine synthesis by neutrophils and their migration to surrounding tissues [32]. It has been previously shown that low MPV may correlate with GT bleeding in the course of IgAV [12, 13]. We have not demonstrated such dependencies in our work. MPV and PDW were similar in children with IgAV and did not differ from those observed in healthy children. Data on the usefulness of the MPV in other inflammatory diseases are divergent. In the acute phase of rheumatic diseases, a decrease in MPV [33, 34] or its increase associated with higher activity of juvenile idiopathic arthritis, psoriatic arthritis, SLE may occur [5, 35, 36]. Some studies indicate the usefulness of MPV in monitoring anti-inflammatory therapy in rheumatoid arthritis [37]. Conflicting research results concern vascular diseases, indicating an increase in MPV values in peripheral and coronary artery diseases [38, 39] or a lack of MPV association with coronary disease severity [40]. According to Shin DH et al., larger MPV is not associated with higher platelet reactivity, but indicates their reduced aggregation, because larger platelets may not be fully mature and appear as a result of their accelerated release from the bone marrow [31].

MPR calculated by dividing the MPV by the PLT is suggested to be the better indicator of platelet activation and, thus, the severity of the inflammatory process. The relationship between MPR and prognosis in critically ill patients, in malignancies and in febrile seizures in children [31, 41–43] has been studied so far. In the presented study, the MPR was significantly lower in all IgAV children and in the systemic involvement group. This indicates the usefulness of MPR to predict systemic involvement in IgAV. The ROC curve analysis showed the lowest sensitivity and specificity for this index (63.4% and 63.3%, respectively, $p = 0.04$), which means that it requires further research on a larger group of patients.

It is important that the interpretation of results includes physiological cellular shifts (between the circulating pool and the tissue pool) that occur during bleeding and cause neutrophilia during the first hours [44]. Other factors that may affect the tested ratios, i.e., thyroid dysfunction, diabetes, renal and hepatic failure, are less important in children than in the adult patients (they were not observed in our cohort); however, they should be kept in mind [45]. The causes of thrombocythemia include chronic iron deficiency, hyposplenism, congenital lack of spleen, status after spleen removal, alcoholism, hemolytic anemia [46, 47] and used drugs (antibiotics, corticosteroids, non-steroidal inflammatory drugs). As it is known, in children with IgAV, the incidence is higher in autumn and winter and is usually associated with the infectious factor, which was also confirmed by our research (55% of new cases in the autumn and winter season and 56% occurrence of the infectious trigger factor). Therefore, changes in leukocyte populations reflect the body's response to an ongoing inflammatory process per se and it may be modified by the pharmacological treatment. The logistic regression analysis showed a higher risk of systemic involvement with higher values of NLR and the analysis of ROC curves showed NLR as the best predictor of organ involvement. PLR was also found to be associated with systemic involvement but with lower AUC. That is why NLR is a more valuable indicator to identify patients at higher risk for systemic involvement in the course of IgAV.

In our study group, all patients with renal involvement also presented features of GT bleeding; therefore, it was impossible to assess the above ratios in children with only renal involvement. Ozturk and Ekinci (2 patients with only renal involvement) [44] and Nagy et al. (6 patients with only renal involvement) [48] suggest that IgAV should be considered as systemic involvement or extracutaneous involvement as a determinant of a severe course of the disease. In the group we studied, we additionally applied an objective scale of disease severity, including joint, renal and GT symptoms (Table 1) [16–18]. We did not show a significant difference in NLR, PLR and MPR between the severe and mild group. It may be result from the low number of patients in severe group ($n = 12$) and the fact that to the mild group were classified children with less severe systemic involvement who did not yet meet the point criterion. The limitation of the scale used is related to not including other rare manifestations of IgAV, such as acute scrotum, central nervous system disorders, myositis, myocardial involvement, which may be severe. In addition, it should be analyzed, as suggested by other authors, whether the selected cutoff point in the severity of the disease (4 points) was rightly adopted.

Additionally, it would be valuable to assess the correlation between the extent of skin lesions and the indicators: NLR, PLR, and MPR, which has not been studied so far. In our study group, such an assessment was not possible because of the similar distribution of skin lesions in all patients.

The retrospective character of single-center studies and a small study group may limit the value of statistical analyses. Another limiting factor may result from the different time from the onset of the disease symptoms to the collection of a blood sample; however, it should be noted that the first (pretreatment) peripheral blood count was used for the analysis.

In conclusion, NLR is a more valuable indicator than PLR to identify patients at higher risk of systemic involvement in the course of IgAV. MPR was significantly lower in the systemic involvement group, which also indicates its usefulness in assessing the course of the disease. However, due to the fact that it was characterized by the lowest sensitivity and specificity, its use requires further research. Due to the multitude of factors affecting the results of peripheral blood counts, the above ratios should not be decisive in clinical doubts. As always, clinical observation and individual approach to the patient are most important. It is necessary to determine the cutoff values of the tested ratios, which will allow for selecting patients with GT symptoms who should receive early corticosteroids or isolating patients who require increased supervision (e.g., hospital observation). Further prospective and multicenter studies on the usefulness of the above-mentioned parameters for predicting the severity of the disease and seeking new ratios to facilitate clinical decision making are needed.

Author contributions All authors have: (1) made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; (2) been involved in drafting the manuscript or revising it critically for important intellectual content; (3) given final approval of the version to be published; and (4) agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval Study was approved by Ethics Committee of the Medical University of Silesia in Katowice on 01.07.2014 (KNW/0022/KB1/66/14; KNW/0022/KB1/66/III/14/16/17).

Informed consent All participants signed an informed consent declaration.

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