

# Complete Blood Count Parameters in Recurrent Pediatric Idiopathic Epistaxis

## Rekürren İdiyopatik Pediatrik Epistaksiste Tam Kan Sayımı Parametrelerinin Yeri

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**ABSTRACT Objective:** The aim of this study was to investigate the relationship between complete blood cell count (CBC) parameters and pediatric recurrent idiopathic epistaxis. **Material and Methods:** The patient records of the children with epistaxis were retrospectively analyzed. The records of the patients with recurrent idiopathic epistaxis were included. Complete blood count results of the patients at of least two visits for epistaxis were retrieved from the hospital records. Mean platelet volume (MPV), red blood cell distribution width (RDW), platelet, hemoglobin, hematocrit, lymphocyte, leucocyte, neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) levels of these patients were compared with age-matched and gender-matched controls. **Results:** A total of 153 patients had at least two visits with epistaxis and 107 of these were diagnosed with recurrent idiopathic epistaxis patients. There was no statistical difference in terms of age and gender between the groups. MPV, RDW, lymphocyte levels were higher and platelet, hemoglobin, hematocrit, leucocyte, NLR and PLR levels were lower in recurrent idiopathic epistaxis patients. No statistically significant difference was detected between the groups according to the permutational non-parametric MANOVA ( $p>0.05$ ). **Conclusion:** Complete blood count is one of the most common laboratory test for evaluation of epistaxis in children. Although MPV, RDW, NLR and PLR are easily measured as a part of the CBC, their importance in epistaxis is not adequately presented. MPV, RDW, NLR and PLR have been identified as markers of inflammation and associated with an ample amount of diseases. However in this study we have concluded that there was no association between CBC parameters and recurrent pediatric idiopathic epistaxis.

**Keywords:** Epistaxis; children; complete blood cell count; mean platelet volume

**ÖZET Amaç:** Bu çalışmanın amacı, tam kan sayımı (TKS) parametreleri ile pediatrik rekürren idiyopatik epistaksis arasındaki ilişkiyi araştırmaktır. **Gereç ve Yöntemler:** Epistaksisi olan çocukların hasta kayıtları retrospektif olarak incelendi. Rekürren idiyopatik epistaksisi olan hastalar çalışmaya dahil edildi. En az iki kez burun kanaması nedeniyle başvuran hastaların TKS sonuçları, hastane kayıtlarından elde edildi. Bu hastaların ortalama trombosit hacmi (OTH), eritrosit dağılım genişliği (EDG), trombosit, hemoglobin, hematokrit, lenfosit, lökosit, nötrofil/lenfosit oranı (NLO) ve trombosit/lenfosit oranı (TLO) düzeyleri benzer yaş ve cinsiyetteki sağlıklı bireylerle karşılaştırıldı. **Bulgular:** Toplamda 153 hastanın epistaksis tanısı ile birden fazla başvurusu vardı. Bunlardan 107'si rekürren idiyopatik epistaksis tanısı almıştı. Gruplar arasında yaş ve cinsiyet açısından istatistiksel fark yoktu. Rekürren idiyopatik epistaksis hastalarında OTH, EDG, lenfosit düzeyleri yüksek, trombosit, hemoglobin, hematokrit, lökosit, NLO ve TLO düzeyleri düşüktü. Ancak gruplar arasında istatistiksel olarak anlamlı bir fark yoktu ( $p>0,05$ ). **Sonuç:** Tam kan sayımı, çocuklarda epistaksinin değerlendirilmesinde en yaygın kullanılan laboratuvar testlerinden biridir. Her ne kadar OTH, EDG, NLO ve TLO, TKS'nin bir parçası olarak kolayca ölçülse de, burun kanamasındaki önemi yeterince ortaya konmamıştır. OTH, EDG, NLO ve TLO, inflamasyon belirtileri olarak tanımlanmıştır ve birçok hastalıkla ilişkilendirilmiştir. Ancak bu çalışmada TKS parametreleri ile rekürren pediatrik idiyopatik epistaksis arasında bir ilişki olmadığı sonucuna varılmıştır.

Recurrent idiopathic epistaxis in children is defined as repeated nosebleeds in patients up to the age of 16. These children have repeated nosebleeds with no specific cause.<sup>1</sup> Up to 9% of children may have recurrent nosebleeds, usually originating from the anterior septum. Local inflammation, mucosal drying and nose picking are the initiating factors for recurrent epistaxis.<sup>2</sup>

There is no clear definition related with further laboratory investigation in pediatric epistaxis for bleeding disorders.<sup>3</sup> However complete blood cell count (CBC) is one of the most used laboratory test for evaluation of epistaxis in children. Recurrent nosebleeds may cause blood loss. It is also associated with inflammation. Therefore clues of inflammation and blood loss must be searched with CBC.

Mean platelet volume (MPV) is a simple way to determine platelet function. It shows the average size of platelets. Higher MPV means bigger platelets and greater hemostatic efficiency because of the ability of producing greater amounts of vasoactive and thrombotic factors. In healthy individuals with an unremarkable CBC, MPV can be useful in predicting an increased bleeding risk.<sup>4-6</sup>

Red blood cell distribution width (RDW) is a routine component of the CBC. It means the variability of the size of the red blood cells in the blood. A high RDW means a large variation in red blood cell (RBC) sizes, and a low RDW means a more homogeneous population of RBCs. Elevated RDW level is known as a marker of chronic inflammation. Several studies have demonstrated the role of RDW in inflammatory diseases and pathophysiological conditions.<sup>4,5,7,8</sup>

White blood cell (WBC) count and its subtypes are known as inflammatory markers.<sup>9</sup> Neutrophil to lymphocyte ratio (NLR) was defined as a potential marker to determine inflammation.<sup>10</sup> It is a simple ratio between the absolute neutrophil and the absolute lymphocyte counts. Platelet to lymphocyte ratio (PLR) is another marker offered for determining inflammation and thrombotic events. NLR and PLR are used as index for differential diagnosis or prognostic prediction of various diseases.<sup>11-13</sup>

Many factors can effect MPV, RDW, NLR, PLR and the other CBC parameters and these CBC parameters were evaluated in an ample amount of diseases. The aim of this study was to investigate the relationship between CBC parameters and pediatric recurrent idiopathic epistaxis.

## MATERIAL AND METHODS

The medical records of the children with epistaxis under 16 years of age (1 January 2009 to 30 June 2016) were retrospectively reviewed. Most of the patients seen for a single visit did not undergo laboratory testing so that the patients with at least two visits for epistaxis were included in the study. The visits within two months were regarded as a single visit.

Only the patients with recurrent idiopathic epistaxis were included in the study. Exclusion criteria were epistaxis with defined reasons (such as intranasal masses, trauma etc.), obesity, hematological disorders, history of autoimmune diseases and systemic diseases as renal or hepatic insufficiency, acute or chronic infection. Patients with abnormal blood parameters (such as anemia, leukocytosis, leukopenia, and thrombocytopenia) and concomitant diseases (such as chronic adenotonsillar disease, cardiovascular disorders, asthma, allergic rhinitis) were excluded from the study. Patients who did not have any CBC results were also excluded.

Complete blood count results were retrieved from the hospital records database. If the same patient had undergone more than one laboratory testing, only the first CBC result was used. Blood samples were collected in dipotassium ethylenediaminetetraacetic acid (EDTA) tubes. An automatic blood counter (Cell-Dyne 3700, Abbott, Abbott Park, IL, USA.) was used for whole blood counts. All blood samples were analyzed within 30 minutes after sampling. Time interval between blood sampling and CBC measurement were calculated from computerized patient database.

Complete blood count of the patients with recurrent epistaxis were compared with age-matched and gender-matched controls. Control group was

consisted from the patients with normal physical examination and no chronic diseases.

## STATISTICAL ANALYSIS

For statistical calculations, Statistical Package for the Social Sciences software (SPSS for Windows, version 15.0, SPSS Inc., Chicago, IL) was used. The distribution of discrete variable (age) according to groups were analyzed by crosstab analysis with frequencies, ratios and chi-square test. Normally distributed continuous variable age was analyzed by two-independent samples t-test and non-normal distributed continuous variable time interval between blood sampling and CBC measurement was analyzed by Mann-Whitney U test.

Continuous response variables required two-level one-factor MANOVA. However, some assumptions were violated for performing MANOVA. Such as, Box's M ( $M=556.309$ ,  $F=9.614$ ,  $p<0.001$ ), some Levene tests for leucocyte ( $F=4.744$ ,  $p=0.031$ ), RDW ( $F=5.566$ ,  $p=0.019$ ) and the violation of multivariate normality assumption. Therefore, non-parametric MANOVA analysis (NP-MANOVA) were performed by F statistics.<sup>14</sup>

$$F = \frac{SS_A / (a-1)}{SS_W / (N-a)} = \frac{(SS_T - SS_W) / (a-1)}{SS_W / (N-a)}$$

where

$$SS_T = \frac{1}{N} \sum_{i=1}^{N-1} \sum_{j=i+1}^N d_{ij}^2, \quad SS_W = \frac{1}{n} \sum_{i=1}^{N-1} \sum_{j=i+1}^N d_{ij}^2 \varepsilon_{ij}$$

and

$a$ : the number of groups,  $n$ : the number of observations in each group,  $N$ : Total number of observations ( $N=an$ ), represents the  $ij$ -element of the distance matrix.

The p-value was calculated by comparing observed F value with permutationally generated distribution. In our study, 10000 permutations were done. For this study, a specific PNP-MANOVA program was written by using SPSS Syntax editor.

## RESULTS

A total of 153 patients had at least two visits with epistaxis and the study was completed with 107 patients.

**TABLE 1:** Male to female ratio of groups.

Group	Gender		Total
	Female	Male	
Study group	44 49.4%	63 50.4%	107 50.0%
Control	45 50.6%	62 49.6%	107 50.0%
Total	89 41.6%	125 58.4%	214 100.0%

\*Chi-square=0.019, p=0.890.

Mean age of the patients in study group and the control group was  $91.2 \pm 4$  and  $91.6 \pm 2$  months, respectively. Male to female ratio of the study group was 63/44, whereas it was 62/45 for the control group. Mean time interval between blood sampling and CBC measurement was  $18.6 \pm 8.1$  minutes for the patients and  $17.1 \pm 8$  minutes for control group.

There was no statistical difference in age, sex and time interval between the groups (Table 1, Table 2).

MPV, RDW, lymphocyte levels were higher and hemoglobin, hematocrit, platelet, leucocyte, NLR and PLR levels were lower in study group. However there is no statistically significant difference between groups according to the permutational non-parametric MANOVA ( $p>0,05$ ). Laboratory data is outlined in Table 3.

## DISCUSSION

In the present study, there was no association between CBC parameters and recurrent pediatric idiopathic epistaxis.

Epistaxis is a common disorder. Most of the children experience at least a single epistaxis event in their childhood. However a subset of children experience recurrent episodes of epistaxis. There is no consensus on the frequency or severity of epistaxis recurrences in childhood but it is possible that only the most severe episodes are considered for treatment.<sup>2</sup> There are no parameters for detecting recurrences in the literature.

**TABLE 2:** Results of age distribution and time interval between blood sampling and CBC measurement in groups.

	Group	N	Mean	Std. Deviation	Min.	Median	Max.	Std. Error Mean	Test	p value
Age (Month)	Study group	107	91.42	46.620	9.00	86.00	191.00	4.507	t=0.034	0.973
	Control	107	91.21	46.180	19.00	87.00	189.00	4.464		
Time interval (Minute)	Study group	107	18.68	8.10	4.00	17.00	31.00	0.783	Z=-1.428	0.153
	Control	107	17.14	8.06	3.00	16.00	30.00	0.779		

CBC: Complete blood cell count.

MPV, RDW, NLR and PLR have been identified as markers of inflammation.<sup>15</sup> Complete blood count is often ordered for excluding bleeding secondary to systemic diseases. Although MPV, RDW, NLR and PLR are easily measured as a part of the CBC, their importance in epistaxis has not been adequately presented.

In previous studies, MPV was found to be associated with a lot of cardiac and non-cardiac diseases. Platelet activation is a link in the pathophysiology of diseases prone to thrombosis and inflammation. Higher MPV levels known to be associated with more thrombosis shows increased platelet activation. Main function of platelets is hemostasis but platelets also release inflammatory mediators. So increased platelet activation is also associated with inflammation. And high levels of MPV are associated with low-grade inflammatory diseases.<sup>16-18</sup> Montague et al. mentioned that *Staphylococcus aureus* colonization causes chronic low-grade inflammation with irritation. They also reported that digital trauma cause septal neovascularization in children with recurrent epistaxis.<sup>19</sup> However this theory is not supported in our study.

Mean platelet volume measurement is affected by the type of anticoagulant (EDTA or citrate), time interval between blood sampling and MPV analysis, and the temperature at which MPV is measured, MPV increases over time in EDTA tube and it is accepted that platelet swelling in EDTA tubes can be minimized by analyzing the samples within less than 1 hour.<sup>17-20</sup> In our hospital CBC measurements are performed at room temperature and in EDTA tubes. The time interval between blood sampling and CBC

**TABLE 3:** Comparison of the CBC parameters for study and control group.

Parameters	Group	N	Mean	Standard Deviation
Hemoglobin	Study group	107	12.88	0.959
	Control group	107	13.11	0.910
Hematocrit	Study group	107	38.28	2.812
	Control group	107	39.41	2.878
Leukocyte	Study group	107	7426.63	1768.741
	Control group	107	7557.18	1496.211
Neutrophile	Study group	107	3223.67	1130.567
	Control group	107	3497.54	1120.319
Lymphocyte	Study group	107	3351.47	1250.468
	Control group	107	3231.40	1167.151
RDW	Study group	107	15.47	1.437
	Control group	107	15.16	1.885
MPV	Study group	107	6.94	1.027
	Control group	107	6.63	0.890
PLT	Study group	107	320084.11	71094.956
	Control group	107	330529.90	73146.960
PLR	Study group	107	114.13	101.425
	Control group	107	120.43	96.069
NLR	Study group	107	1.15	0.889
	Control group	107	1.38	1.708

F=1.122, p=0.282.

RDW: Red blood cell distribution width; MPV: Mean platelet volume;

PLT: Platelet; PLR: Platelet to lymphocyte ratio; NLR: Neutrophil to lymphocyte ratio.

analysis was calculated from the software program and it was within acceptable bounds (18.6±8.1 minutes for patients and 17.1±8 minutes for control group).

Red blood cell distribution width (RDW) is a parameter reflecting erythrocyte morphology which is calculated by dividing the standard deviation (SD) of erythrocyte volumes for the mean corpuscular volume (MCV). Results are

more widely expressed as a percentage. Relationships among RDW, inflammation, neurohormonal and cardiovascular risk factors have been shown. It has recently been suggested as a predictor of prognosis in a variety of disorders. Higher RDW is associated with poor outcomes and increased risk of mortality due to any medical cause from any medical condition. Higher RDW may mirror a profound dysregulation of homeostasis and may reflect a chronic inflammatory state.<sup>21-24</sup>

Bezgin et al. analyzed MPV and RDW values of pediatric epistaxis patients. They found that RDW values of epistaxis patients were lower when compared with controls. However there was no statistically difference between the groups with regard to MPV values. They speculate that lower RDW may increase bleeding tendency by disrupting thrombotic activities.<sup>25</sup> Also Kemal et al. studied MPV and RDW levels of patients complaining from recurrent epistaxis in adults and detected lower MPV and RDW levels.<sup>4</sup> In our study MPV and RDW values were higher than those of control group but this difference was not statistically significant. The different results may be explained by younger age of our study population and difference of patient selection criteria.

Neutrophil count is a marker of ongoing non-specific inflammation and lymphocyte count is a marker of regulatory pathways. As a combination of these two independent inflammation markers, NLR is a powerful simple marker of inflammation.<sup>9,26</sup> Levels of NLR were detected higher in patients with Bell palsy, idiopathic sudden sensorineural hearing loss (ISSNHL), cardiovascular diseases, oncological diseases and inflammatory diseases. It has also been offered as a valuable index for predicting adverse clinical outcomes for many disorders like ISSNHL.<sup>9,27,28</sup>

Platelet lymphocyte ratio (PLR) is also offered as an inflammatory marker. Recent studies show that a high PLR reflects inflammation, atherosclerosis and platelet activation. Many patho-

physiological conditions may alter platelet and lymphocyte counts separately. NLR and PLR are suggested as a more stable marker which describes 2 inversely associated predictors and immune pathways.<sup>29-31</sup> In this study, the difference between NLR and PLR levels of epistaxis patients and control group was not statistically significant.

The study has some limitations. First is a being retrospective study. Also these findings can be result or reason of epistaxis. Answer of this question is not clear. Study population is consist of children visited hospital for epistaxis more than once. So this population may reflect only the severe epistaxis patients. It may not be the same in all pediatric epistaxis cases. However, we can speculate that none of the CBC parameters could be used to predict likelihood of recurrence of epistaxis in childhood.

## CONCLUSION

Complete blood cell count is one of the most common laboratory test for evaluation of epistaxis in children. We aimed to investigate the relationship between CBC parameters and pediatric recurrent idiopathic epistaxis in this study. We have concluded that there was no association between CBC parameters and recurrent pediatric idiopathic epistaxis. The results of our study are somewhat different from the previous literature, and although not significant, these results underline the unreliability of these parameters unless shown otherwise with future studies.

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### Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

### Authorship Contributions

**Idea/Concept:** M. Volkan Akdoğan, Suna Tanrıku, Seda Babakurban, Mahmut Gökdemir; **Design:** M. Volkan Akdoğan,

Seda Babakurban; **Control/Supervision:** M. Volkan Akdoğan, Suna Tanrıku, Seda Babakurban, Mahmut Gökdemir; **Data Collection and/or Processing:** M. Volkan Akdoğan, Suna Tanrıku, Mahmut Gökdemir; **Analysis and/or Interpretation:** M. Volkan Akdoğan, Suna Tanrıku, Seda Babakurban, Mahmut Gökdemir; **Literature Review:** M. Volkan Akdoğan; **Writing the Article:** M. Volkan Akdoğan, Suna Tanrıku, Seda Babakurban, Mahmut Gökdemir; **Critical Review:** M. Volkan Akdoğan, Suna Tanrıku, Seda Babakurban, Mahmut Gökdemir.

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