

İNTİHAR GİRİŞİMİ OLAN ERGENLERDE PERİFERİK İNFLAMASYON PARAMETRELERİNİN DEĞERLENDİRİLMESİ

EVALUATION OF PERIPHERAL INFLAMMATION PARAMETERS IN ADOLESCENTS WITH SUICIDE ATTEMPTS

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ÖZET

AMAÇ: Hematolojik parametreler, psikopatoloji ve inflamasyon arasındaki ilişkiyi göstermek için kullanılabilen periferik inflamasyon belirteçleridir. Bu çalışmada intihar girişiminde bulunan ergenleri sağlıklı ergenlerle hematolojik parametreler açısından karşılaştırmayı amaçladık.

GEREÇ VE YÖNTEM: Ekim 2018 - Mart 2020 tarihleri arasında Çocuk Acil Servisine başvuran 765 ergenin hemogram kayıtları geriye dönük olarak değerlendirildi. Kontrol grubu, benzer yaş ve cinsiyet özelliklerine sahip, yukarıda belirtilen dönemde çocuk hastalıkları polikliniğinde muayene edilen, organik veya psikopatolojik herhangi bir tanısı olmayan ergenlerin hemogram kayıtlarından oluşturuldu. Dışlama kriterleri uygulandıktan sonra intihar girişimi olan 95 vaka ve 95 kontrol grubu çalışmaya dahil edildi. Vaka ve kontrol grupları istatistiksel olarak nötrofil/lenfosit oranı (NLR), trombosit-lenfosit oranı (PLR), monosit/lenfosit oranı (MLR), ortalama trombosit hacmi (MPV) ve eritrosit dağılım genişliği (RDW) parametreleri açısından karşılaştırıldı.

BULGULAR: İntihar girişimi olan ergenlerde NLR ve MLR değerleri kontrol grubuna göre anlamlı olarak yüksek saptandı. Diğer parametreler açısından gruplar arasında istatistiksel olarak anlamlı bir fark saptanmadı. NLR ve MLR parametreleri açısından ek psikiyatrik tanılara göre ayrılan olgu grubunun üç alt grubu arasında istatistiksel olarak fark yoktu. Ancak NLR, bu üç alt grupta kontrol grubuna göre anlamlı olarak daha yüksek bulundu.

SONUÇ: İntihar girişiminde bulunan ergenlerin NLR ve MLR parametreleri kontrol grubuna göre daha yüksek saptandı. İntihar girişimi olan ergenlerde inflamatuvar parametrelerin değerlendirilmesi ile ilgili daha kapsamlı araştırmalara ihtiyaç vardır.

ANAHTAR KELİMELEER: Ergen, İntihar girişimi, NLR.

ABSTRACT

OBJECTIVE: Haematological parameters are peripheral inflammation markers that can be used to demonstrate the relationship between psychopathology and inflammation. In this study, we aimed to compare adolescents who attempted suicide with healthy adolescents in terms of haematological parameters.

MATERIAL AND METHODS: The haemogram records of 765 adolescents admitted to the Paediatric Emergency Service between October 2018 and March 2020 were retrospectively evaluated. The control group was created from the haemogram records of adolescents who had similar age and sex characteristics, who had been examined in paediatric outpatient clinics during the above-mentioned period and who did not have any organic or psychopathological disorder. After implementation of the exclusion criteria, 95 adolescents with suicide attempts and 95 healthy adolescents were included in the study. The case and control groups were statistically compared in terms of neutrophil/lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte/lymphocyte ratio (MLR), mean platelet volume (MPV) and red cell distribution width (RDW) parameters.

RESULTS: It was found that in adolescents with suicide attempts, NLR and MLR values were significantly higher than in the control group. There was no significant difference between the groups in terms of other parameters. In terms of NLR and MLR parameters, there was no statistical difference among the three subgroups of the case group separated according to the psychiatric diagnoses. However, NLR was found to be significantly higher in comparison with the control group of these three subgroups.

CONCLUSIONS: The NLR and MLR parameters of adolescents who attempted suicide were higher than those of the control group. There is a need for more comprehensive studies on the evaluation of inflammatory parameters in adolescents who have attempted suicide.

KEYWORDS: Adolescent, Suicide attempt, NLR.

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INTRODUCTION

Presently, suicide is an important public health issue. Every year approximately 800.000 individuals in the world die because of suicide. Suicidal deaths are the third most common cause of deaths in those aged 15-19 years (1). Suicidal mortality rates have declined in the recent years, considering all age groups in the Western countries. However, there is no similar decrease in suicidal mortality rates in adolescents and young adults (2, 3). Suicide attempts may be 20 times higher than suicidal mortality rates (4, 5). The presence of psychopathologies such as depression and substance use disorder are the causes for most suicide attempts resulting in death; thus, the relationship between suicide and psychiatric disorders is important (6). In addition, common impulsiveness and aggressive behaviour in adolescents and young adults contribute to this situation (7).

Suicidal thoughts and suicide attempts are one of the most common psychopathologies among adolescents (8). Both suicidal attempts and deaths pose an emotional burden for patients and their families. Therefore, it is important to identify the risk factors associated with suicide in a timely and reliable manner. Neuro-inflammatory processes associated with psychiatric disorders are of interest to researchers. Variables such as infections, autoimmune diseases, vitamin deficiencies, traumatic brain injury and stress can cause suicidal behaviour via inflammatory mediators. One of the biological causes of suicide is neuroinflammation (9).

Haemogram is a simple, inexpensive and easy-to-apply laboratory test that is used worldwide. Neutrophil/lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte/lymphocyte ratio (MLR), mean platelet volume (MPV) and red cell distribution width (RDW) are haematological parameters that can be used as peripheral inflammation markers (10, 11). NLR, MLR, PLR, MPV parameters are especially investigated in psychiatric disorders. While the differences in terms of NLR have been stated in the studies performed, there is not enough evidence in terms of other parameters. In a study conducted in patients with major depressive disorders, NLR levels in the case group were higher

than the control group, indicating neuroinflammation as the aetiology of the disorder (12). In addition, high NLR values have been reported in patients diagnosed with bipolar affective disorder and schizophrenia (11, 13, 14). The NLR value is a valuable, repeatable and cost-effective strategy to determine the risk of suicide (15, 16). Thrombocytosis and/or increase in platelet volume indicates platelet reactivity. Reactive platelets also play a role in inflammation (17). Increased RDW levels indicate ineffective erythrocyte production. This can also be a consequence of systemic inflammation (18). Current studies on peripheral inflammation parameters and psychopathologies in children and adolescents are also related to other psychopathologies such as autism, obsessive-compulsive disorder, attention deficit / hyperactivity disorder, early-onset schizophrenia and depression (10, 19 - 24).

Literature review of studies on haemogram parameters in individuals who attempted suicide showed that these studies included mostly adult age groups. Suicide attempts as a common psychopathology in adolescents may vary than that in adults in terms of causes and clinical appearance. The aim of this study was to compare the haematological parameters of adolescents who attempted suicide with those in the control group.

MATERIALS AND METHODS

Patients who were brought to the paediatric emergency room of Konya Training and Research Hospital for suicide attempts between October 2018 and March 2020 based on the hospital registration system were screened. In total, there were 765 patients, and 659 of these patients who were not evaluated by a child psychiatrist after a suicide attempt were excluded from the study. Further, 11 of the remaining 106 patients were excluded because they received medical treatment for their existing psychiatric disorder. Finally, 95 adolescents with suicide attempts were included in the study, and they were divided into three main groups. These groups were those with an additional diagnosis of depression [33 individuals (34.7%)], non-depressed psychiatric disorders (anxiety disorders, attention deficit hyperactivity disorder, conduct disorder

etc.) [32 individuals (33.7%)] and those who had no psychopathology detected [30 individuals (31.6%)]. Depression and other psychopathologies were diagnosed by the child psychiatrist according to DSM-V diagnostic criteria after consultation with the patient and his family.

The control group comprised 95 adolescents who were paired with the case group according to the age, gender and those who applied for routine control to the children's health and diseases outpatient clinic on similar dates. Those with known haematological, rheumatological, psychiatric, neurological and infectious diseases were excluded from the study.

The haematological parameters of the patient and control groups were recorded in the SPSS programme. NLR, PLR and MLR were calculated using the programme. First, the case and control groups were compared; then, the case group was divided into three subgroups according to concomitant psychopathologies, and the control subgroups matched one-to-one were compared. Finally, the case subgroups and the entire control group were compared.

Ethical Committee

This retrospective case-control study was conducted after the study approval was obtained from the Konya Training and Research Hospital Medical Specialization Board (date:08.05.2020, number:38-18).

Statistical Analysis

Statistical analyses were performed using The SPSS 19 (IBM Inc., USA) software. Descriptive statistics of the categorical variables included in the study were presented as frequencies and percentages, while numerical data was shown as means and standard deviations. The normal distribution of the data was checked using the Kolmogorov-Smirnov Test between two main groups and Shapiro Wilk test between subgroups. These differences were compared between two groups with abnormal distribution using Mann-Whitney-U test. All statistical analyzes were performed formulating two-way hypotheses with a 5% significance threshold and a 95% confidence interval.

RESULTS

A total of 190 adolescents aged 12–18 [42 (22.1%) boys and 148 (77.9%) girls] were included in the study (95 in the case group and 95 in the control group). Case and control groups were individually matched in terms of the number, age and gender. The mean age of the total sample was 15.45 ± 1.29 years. The mean ages of the boys and girls were 15.71 ± 1.13 and 15.37 ± 1.33 years, respectively; with no statistically significant difference between them ($p = 0.14$). Sociodemographic characteristics of the groups were shown in **Table 1**.

Table 1: Sociodemographic characteristics of the participants

		Patient group (Mean±SD)	Control group (Mean±SD)
Age	Male	15.71±1.13	15.71±1.13
	Female	15.37±1.33	15.37±1.33
		n (%)	n (%)
Gender	Male	42 (22.1)	42 (22.1)
	Female	148 (77.9)	148 (77.9)

When examining the suicide attempt process, eight (8.4%) cases were planned and 87 (91.6%) were impulsive. Further, 25 (26.3%) were identified as recurring cases of suicide attempts, whereas 70 (73.7%) were identified as the first case of a suicide attempt. Approximately all cases (98.9%) attempted suicide by taking medication. Only one patient (1.1%) had a suicide attempt by hanging. The characteristics of suicide attempts were given in **Table 2**.

Table 2: Characteristics of suicide attempts

Features of suicide attempt	Patient group (n=95), n (%)
Number of suicides	
First suicide attempt	70 (73.7)
Repeated suicide attempts	25 (26.3)
Suicide process	
Planned suicide attempt	8 (8.4)
An impulsive suicide attempt	87 (91.6)
Suicide method	
Taking medication	94 (98.9)
Hanging	1 (1.1)

In the case group, the NLR and MLR values were significantly higher than in the control group ($p < 0.001$ and $p = 0.044$, respectively). There was no significant difference between the groups in terms of other parameters. The data was shown in **Table 3**. In comparison to the subgroups of case and control groups, the NLR value was significantly higher in case subgroups than in the control subgroups ($p < 0.001$). There was no significant difference in terms of other parameters.

Table 3: Laboratory findings for the patient and control group participants

Variables	Patient group (n=95)		Control group (n=95)		p
	Mean	SD	Mean	SD	
NLR	3.60	3.79	1.71	0.83	<i>p</i> <0.001
MLR	0.28	0.18	0.24	0.09	<i>p</i> =0.044
PLR	148.23	100.10	118.16	31.90	<i>p</i> =0.188
MPV	10.10	0.77	10.23	1.09	<i>p</i> =0.736
RDW-CV	13.30	1.38	13.45	1.40	<i>p</i> =0.135

Mann-Whitney-U test

NLR: neutrophil/lymphocyte ratio MLR: monocytes/lymphocyte ratio PLR: platelet-to-lymphocyte ratio MPV: mean platelet volume RDW-CV: red cell distribution width-coefficient of variation

DISCUSSION

In this retrospective case-control study, NLR, MLR, PLR, MPV and RDW parameters that are peripheral inflammation markers were examined in adolescents who attempted suicide. According to the study result, NLR and MLR values were significantly higher than in the control group in terms of suicides in adolescents. In addition, there was no difference in NLR value when divided into subgroups according to case group psychopathology, but subgroups had higher NLR values than the control group.

Currently, research on psychiatric disorders and their inflammatory causes are increasing. In a study by Ozdin et al., NLR, PLR and MLR were evaluated in patients with bipolar affective disorder and schizophrenia (25). According to the study, the levels of inflammatory parameters in schizophrenia and bipolar disorder were found to be higher than in the control group. Moreover, in a study by Inanlı et al., NLR, MLR and MPV values were higher than in the control group during the bipolar disorder manic period (11). In depressive patients, MPV values were significantly higher than in the control group. As a result, it was noted that bipolar disorder is associated with low-grade inflammation, NLR and MLR can be used as a biomarker in patients in manic period and MPV can be used in all bipolar patients. Arabska et al. studied patients with depression and reported that the severity of depression is associated with NLR (26). When comparing patients with initial episode and recurrent depressive attacks, NLR values were higher in the first episode patients. In addition, Rodriguez et al. concluded that inflammatory processes play a role in patients with psychotic disorders (27). NLR is the best marker to assess these disorders. In the study of patients with depression in the childhood age group, NLR and MPV levels were higher than in the control

group, and their high scores on the depression scale was associated with these parameters (22). Similarly, in a study conducted with children diagnosed with attention deficit hyperactivity disorder, NLR and PLR levels were found to be higher in the case group than in the control group. The study also stated that NLR elevation was not affected by age, gender and treatment (24). Similar to adult studies, high NLR levels were also found in a child study examining early-onset schizophrenia cases. As a result of the study, it was concluded that high NLR level may be an inflammation biomarker in schizophrenia (23). In a recent study evaluating adolescents with a suicide attempt, higher NLR, MLR, and PLR values were found in the case group compared to the control group (28).

In the present study, NLR and MLR values were higher in the case group than in the control group. These findings are consistent with the conclusion that inflammatory processes are effective in the formation of psychiatric disorders, both in adults and in the childhood age group. Thus, inflammation might be important among the biological causes of suicidal behaviour.

In studies and reviews that investigated inflammatory changes in suicide, most often the presence of suicide attempts or thoughts in patients were associated with changes in inflammatory cytokines (29-31). In a study by Ayhan et al., NLR values were higher in patients with suicidal behaviour regardless of depression than in the control group (32). However, when the cases were separated according to the presence of depression, no significant difference was observed. They attributed this to the fact that the suicide attempt was associated with low-grade inflammation. Ekinçi et al. found that NLR values in patients with depression and previous a suicide attempt were significantly related to the recent suicide attempt (16). In addition, another marker of inflammation, i.e., CRP, was not associated with suicide attempts. Thus, it was reported that inflammation plays a role in the pathogenesis of suicidal behaviour in patients with depression. However, in a study by Meydaneri et al. in which patients with depression were divided into two groups according to whether they had any suicide attempts, there was no significant difference between the groups in terms of NLR and PLR values (33).

Orum et al. compared patients with violent and non-violent suicide attempts with healthy controls and found that NLR and MPV values were significantly higher in the group with violent suicide attempts (34).

In our study, NLR and MLR values, which are haematological parameters that can be used as inflammation marker, in adolescent age group were higher in the case group than in the control group. In addition, when the case group was classified in terms of psychopathologies, NLR levels were higher than in the control groups. The increase of the NLR level supports the role of inflammatory processes in patients with suicidal attempt in the adolescent age group. However, no difference among the diagnostic subgroups in terms of NLR values suggests a relationship between NLR values and a suicide attempt independent of the underlying diagnosis.

Peng et. al. found no significant difference between adult patients with depression and control groups in terms of PLR value (35). In addition, PLR values vary in suicidal studies. In a study conducted by Velesco et al. (15), PLR values were higher in the case group, whereas in a study by Orum et al. (34), there was no significant difference between the groups. In our study, there was also no significant difference between PLR values. This is due to the fact that NLR levels are more significant than PLR levels in showing subclinical inflammation, as emphasised by some researchers (36). Therefore, it may be more significant to consider NLR levels instead of PLR values in adolescents who have attempted suicide.

In adult studies, MPV levels were found to increase in some psychopathologies (11, 37). Similarly, in a study of depression and inflammation parameters in children, MPV levels were found to be high (22). In addition, there are studies that were conducted in patients with neurodevelopmental disorders such as attention deficit/hyperactivity disorder and autism spectrum disorder; no difference was observed between the groups in terms of MPV levels (38). In Orum et al.'s suicide study, MPV levels were high in a group of violent suicide attempts (34). In our study, there was no significant difference in MPV levels between the groups.

The fact that most suicide attempts in the case group occurred by taking medication or on impulse could explain the lack of difference between the groups.

In terms of RDW levels, there was no difference between the case and control groups in suicidal studies and studies related to childhood depression (22, 34). RDW shows inflammation in organic pathologies rather than psychiatric disorders in the childhood age group (22). In our study, there was no difference between the case and control groups in terms of RDW values in accordance with these findings.

The present study has some limitations. First, this is a retrospective study. There is another drawback that variables such as smoking and body mass index, which can affect inflammatory processes, were not evaluated. The fact that patients with depression were not classified according to the severity of the disorder that can be considered as another limitation; these patients were not classified according to the severity of the disorder due to the lack of a sufficient number of patients diagnosed with depression in our study. Non-depression psychopathologies were evaluated as an inhomogeneous group because they did not reach sufficient numbers. Despite all these limitations, we also showed that inflammatory processes play a role in suicidal aetiology. Other strengths of the study are that individuals with suicidal attempts were evaluated and diagnosed by a child psychiatrist and there were many exclusion criteria.

In conclusion, in the present study, NLR and MLR values were higher in patients with a suicide attempt in the adolescent age group compared to the control group. Therefore, in patients with suicidal attempts, inflammatory processes are important. The clinician can also use the high NLR level as a risk factor to predict a suicide attempt in individuals with suicidal ideation or in patients with a diagnosis of depression. However, to determine which parameters play a role, large-scale studies are needed.

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