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Evaluation of Pro-BNP in Children with Acute Rheumatic Fever

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ABSTRACT

Objective: Acute rheumatic fever (ARF) is an autoimmune disorder associated with beta-hemolytic streptococcus infection (Group A). While acute carditis is the most significant manifestation of the disease, its involvement typically occurs on the skin, in the joints, heart, and central nervous system. Additionally, B-type natriuretic peptide (BNP) is an important myocardial function and prognosis marker. In this study, we examine the BNP levels in a children's cohort who were diagnosed with ARF clinical signs.

Material and Methods: All patients with ARF were enrolled in Pediatric Cardiology. Thirty-three patients, aged 5-15 years (mean age 11.06 ± 2.18 years), with ARF, were examined, and their findings were compared to 41 children (mean age; 10.78 ± 2.87 years) who had previously developed ARF, as well as an additional 43 children (mean age; 9.53 ± 2.99 years) who had pain but no systemic and congenital heart disease. Furthermore, ARF patients were also assessed in subgroups such as carditis, chorea, and arthritis. Doppler echocardiographic examination was performed on all the patients. Pro-BNP levels were measured in patients with ARF after diagnosis and before treatment, and they were compared with patients who had previously had ARF and control groups upon admission. Pro-BNP levels were measured with a chemiluminescent assay. Comparisons were analyzed with variance analysis (ANOVA), post-hoc Tukey HSD, t-test analysis, and Pearson correlation.

Results: The Pro-BNP values were 308.18 ± 402.65 pg/ml in patients with active ARF while Pro-BNP values were 84 ± 135.75 pg/ml, 64.82 ± 50.37 pg/ml in patients who previously had ARF and control group, respectively ($p< 0.001$). Pro-BNP values were higher in active carditis patients than in other subgroups. A positive correlation was found between Pro-BNP and ASO, CRP, ESR, and thrombocytes whereas there was a negative correlation between BNP and hemoglobin. Pro-BNP values decreased significantly with active carditis (101.12 ± 100.01 pg/ml) after treatment ($p= 0.003$).

Conclusion: Unlike other cardiac enzymes, Pro-BNP revealed a statistical correlation with acute phase reactants, platelet count, and antistreptolysin O (ASO). Thus, this study proved that an increased Pro-BNP might be helpful for diagnosing patients with inflammation and cardiac involvement.

Keywords: Acute rheumatic fever, Pro-BNP, congestive heart failure, child

ÖZ

Akut Romatizmal Ateşli Çocuklarda Pro-BNP'nin Değerlendirilmesi

Giriş: Akut romatizmal ateş (ARA) A grubu beta hemolitik streptokok enfeksiyonuna karşı gelişen otoimmün reaksiyon ile ilişkili bir hastalıktır; deri, eklem, kalp ve santral sinir sistemi tutulumu ile meydana gelir. Akut kardit hastalığın en önemli klinik tipidir. B-tip natriüretik peptid (BNP) miyokard fonksiyonları ve prognoz belirleyicisi olarak önemi iyi bilinmektedir. Bu çalışmada ARA kliniği ile başvuran çocuklarda BNP düzeylerini değerlendirdik.

Gereç ve Yöntemler: Çalışma prospektif olarak çocuk kardiyoloji servisinde yapıldı. Çalışmada 5-15 yaşları arasında (ortalama yaş 11.06 ± 2.18 yıl) ARA olarak değerlendirilen 33 hasta ve bunların bulguları ile daha önce ARA tanılı 41 çocuk (ortalama yaş 10.78 ± 2.87 yıl) ve daha önceden sistemik ve konjenital kalp hastalığı olmayan göğüs ağrısı olan 43 çocuk (ortalama yaş 9.53 ± 2.99 yıl) değerlendirildi. Bununla birlikte ARA hastaları kardit, korea ve artrit olarak altgruplarda değerlendirildi. Tüm hastalara doppler ekokardiyografik inceleme yapıldı. Pro-BNP tüm ARA hastalarında tedavi öncesi ve ARA geçirmiş olanlar vekontrol grubundan başvuru anında incelemesi yapıldı. Pro-BNP düzeyleri kemilüminesant tekniğiyle değerlendirildi. İstatistiksel analizlerde varyans analizi (ANOVA), post-hoc Tukey HSD, t-test analizi ve Pearson korelasyon kullanıldı.

Bulgular: Pro-BNP düzeyleri aktif ARA hastalarında 308.18 ± 402.65 pg/ml bulunurken, sırasıyla geçirilmiş ARA ve kontrol grubunda 84 ± 135.75 pg/ml ve 64.82 ± 50.37 pg/ml bulundu ($p< 0.001$). Pro-BNP düzeyleri aktif kardit altgrubunda en yüksek bulundu. Pro-BNP ile ASO, CRP, ESH, trombosit sayısı arasında pozitif korelasyon bulunurken, hemoglobin ile negatif korelasyon bulundu. Aktif karditlilerde pro-BNP değerleri (101.12 ± 100.01 pg/ml) tedavi sonrasında istatistiksel olarak düştü ($p= 0.003$).

Sonuç: Pro-BNP, diğer kardiyak enzimlerden farklı olarak akut faz reaktanları, trombosit sayısı ve antistreptolizin O (ASO) ile istatistiksel korelasyon gösterdi. Sonuçta, bu çalışma artmış pro-BNP'nin enflamasyon ve kardiyak tutulum u olan hastalarda tanıda yardımcı olabileceğini göstermiştir.

Anahtar Kelimeler: Akut romatizmal ateş, Pro-BNP, konjestif kalp yetmezliği, çocuk

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INTRODUCTION

Acute rheumatic fever (ARF) is an autoimmune disorder caused by infection with specific strains of beta-hemolytic *streptococci* (Group A), and it is the cause of 25-40% of cardiovascular disorders in all age groups. When cases with no clinical symptoms are included, this rate is thought to reach 90% (1). Troponin-I and CPK-MB are used in conjunction with echocardiographic (ECHO) data as laboratory indicators of acute cardiac injury (2). However, brain natriuretic peptide (BNP), a cardiac hormone, has been reported to be an essential marker that provides information regarding myocardial function and prognosis (3). BNP is used to determine heart failure caused by ventricular dysfunction and associated volume and pressure overload, as well as ischemic cardiac injury following MI, and to determine the prognosis in diastolic dysfunction, primary pulmonary hypertension, stable angina pectoris, congestive heart failure, and myocardial infarction. It is also used in the evaluation of cardiomyopathy and congenital heart diseases in children (3-5). However, studies on its role in ARF patients are scarce, and the purpose of this study was to examine the effect of BNP in children with ARF.

MATERIALS and METHODS

One hundred seventeen children, who presented to Kahramanmaraş Sütçü İmam University, Department of Pediatrics, Cardiology and Emergency clinics between August 2008 and June 2009 with chest pain and ARF symptoms without any other systemic disease or congenital heart disease were prospectively analyzed.

Patients between 5-15 years of age, whose parents signed an informed consent form were included in the study.

Each patient's age, gender, weight, height, body mass index, vital signs, presence of acute disease, admission symptoms, history of previous ARF and recent throat infection, treatments applied, and family history were recorded.

In patients with a preliminary diagnosis of ARF, Pro-BNP test was requested in addition to routine telecardiography, electrocardiography, complete blood count (CBC), CRP, erythrocyte sedimentation rate, throat culture, and ASO. ASO titers above 320 Todd IU/ml were considered positive in our study. The Immulite® 2000 (Siemens Healthcare Diagnostics) device was used to measure pro-BNP using the chemiluminescence method. Pro-BNP values above 70 pg/ml were considered positive. Cardiac evaluation was performed with Doppler echocardiography in patients with suspected ARF. PR interval prolongation was defined as PR interval values of longer than 0.16 seconds on electrocardiograms in the 5-15 age group.

Children with pathological mitral valve regurgitation on echocardiogram, together with other valve insufficiency and negative acute phase reactants, were considered to have previously experienced ARF or have ARF sequelae, regardless of ARF history. Patients with active RF were grouped as G_1, and patients with previous ARF were grouped as G_2. Patients who presented with chest pain and had no known organic disease were included in the control group (G_3).

ARF was diagnosed using Jones criteria, which included two major or one major and two minor criteria, as well as indicators of previous group A streptococcal infection (throat culture positivity or ASO positivity). Sydenham's chorea was diagnosed by excluding the causes of chorea in the other pediatric age group. Carditis was confirmed by echocardiography. Doppler echocardiography was used to detect valve alterations and characteristics.

Patients diagnosed with acute rheumatic fever were evaluated in subgroups of acute carditis, acute chorea, and acute arthritis. Patients with acute carditis (moderate-severe) were hospitalized with 2 mg/kg/day (maximum 60 mg/day) methyl-prednisolone treatment for two weeks. Based on the acute inflammation findings and the patients' responses, the prednisolone dose was cut in half in the third week, and the steroid was tapered off by the fourth week, while 80 mg/kg/day (maximum 3000 mg/day) acetylsalicylic acid (ASA) was added to the treatment, which was continued for 3-4 weeks. Prednisolone was discontinued and patients were evaluated with echocardiography. Pro-BNP, CK-MB, and Troponin-I were tested.

SPSS 16.0 (SPSS Inc., Chicago, IL, USA) software was used for statistical analysis. The values of the groups were given as mean ± standard deviation (SD), median (range), ratios, and percentages. Differences between groups were identified by analysis of variance (ANOVA) and post-hoc Tukey HSD ($p< 0.05$). T-test was used to evaluate independent samples, $p< 0.05$ was considered significant. Pearson correlation test was used for the relations between Pro-BNP, CK-MB, and Troponin-I among themselves and with other variables. $p< 0.05$ was considered statistically significant for the test results.

Ethics committee approval for the study was obtained from the Ethics Committee of Kahramanmaraş Sütçü İmam University Faculty of Medicine at the meeting numbered 2009/1 dated 08.01.2009.

RESULTS

A total of 117 children, 50 boys, and 67 girls, were included in the study. Thirty-three of the cases were in the ARF group (G_1), 41 in the previous ARF group (G_2), and 43 in the control group (G_3) (Table 1). Although there was no significant difference between the groups in terms of age

Table 1. Distribution of the number of patients and demographic data by groups

	Acute rheumatic fever (G_1) (n= 33)				Previous ARF (G_2) (n= 41)	Control group (G_3) (n= 43)
	Acute carditis (n= 18)	Acute chorea (n= 10)	Acute arthritis (n= 5)	**(G1) (n= 33)**		
Girls (n)	9	6	0	**15**	**27**	**25**
Boys (n)	9	4	5	**18**	**14**	**18**
Age (years)*	11.17 ± 2.7	11.9 ± 2.18	9 ± 1.87	**11.06 ± 2.18**	**10.78 ± 2.87**	**9.53 ± 2.99**

*Mean ± SD.

and gender distribution (p> 0.05), chorea was detected more frequently in girls.

In G_1, symptoms at initial examination included abnormal movement, joint swelling, fever, joint pain, chest pain, and abdominal pain, as well as cardiac murmur. Body temperature (underarm) of G_1 cases was 36.75 ± 0.69°C at admission.

In G_1 patients, among the major criteria, carditis was observed in 19, arthritis in 14, and chorea in 10, while erythema marginatum and subcutaneous nodules were not seen in any patient. However, one patient with carditis also had chorea and seven also had arthritis. The incidence of major criteria was 57.6% for carditis, 42.4% for arthritis, and 30.3% for chorea. History of joint pain (arthralgia), which is among the minor criteria, was found in 81.8% of the patients in the ARF group. Findings of throat infection were seen in 18% of G_1 patients, but no growth was detected in throat cultures.

Hemoglobin (Hb) and hematocrit (Htc) levels of the acute group were found to be lower than the control group (G_3) (p< 0.05). Furthermore, patients in the acute phase and G_2 were found to have higher leukocyte counts than G_3 (p= 0.003 and p= 0.003), but no difference was identified between ARF subgroups. Thrombocytosis was detected in 50% of patients with acute carditis, 40% of patients with acute arthritis, and 10% of patients with acute chorea. Among the signs of acute inflammation, erythrocyte sedimentation rate (ESR) was found to be 53.21 ± 32.29 mm/h in G_1 patients, and ESR was higher in patients with acute carditis (p< 0.001) and arthritis (p= 0.02) than in the group with chorea. Furthermore, 75.8% of the ARF patients had positive CRP values, with the acute carditis group having statistically significantly higher CRP than the chorea group (p= 0.005), while the carditis group was not different from the arthritis group (p> 0.05) (Tables 2,3).

In the G_1 group, a negative correlation was found between Hb and Pro-BNP (Figure 1) (p= 0.001), while a positive correlation was found with MVC (p= 0.015), ESR (p= 0.0001), and CRP (p= 0.0001) (Figure 2). In addition, a positive correlation was found with the TR gradient (p= 0.004) and TR pressure (p= 0.002) in this group of patients.

When active cases were examined separately, pro-BNP levels were found to be higher in the active carditis group than in the chorea (p< 0.001) and arthritis (p= 0.004) groups (Table 3). There was no statistical correlation between Pro-BNP taken before treatment and demographic criteria (age, height, weight) and vital signs (fever, heart rate, systolic and diastolic arterial pressure) (p> 0.05), but a positive correlation was found with ASO (p= 0.012).

Table 2. Laboratory data

	ARF (G1)	Previous ARF (G2)	Control group (G3)
Hemoglobin (mg/dl)*	11.73 ± 1.36 [1]	12.66 ± 1.62	**13.13 ± 1.4 [1]**
Hematocrit (%)*	35.75 ± 3.51 [2]	37.54 ± 4.65	**38.99 ± 3.21 [2]**
Leukocytes (number/mm³)*	9556.1 ± 2517.4 [a]	9480.2 ± 3549.5 [3]	**7414.4 ± 1680.6 [3,a]**
Platelets (K/µl) *	347120 ± 108601[o]	328720 ± 118066	**283260 ± 65925[o]**
ASO value (Todd/IU) *	798 ± 404	643 ± 501	-
CRP (mg/dl) *	62.76 ± 68.53	21.69 ± 37.53	-
ESR (mm/hr) *	**53.21 ± 32.29**	**36.73 ± 40.68**	

*: Mean ± SD
[1] (between G_1 and G_3): p= 0.001
[2] (between G_1 and G_3): p= 0.005
[3] (between G_2 and G_3): p= 0.003
[a] (between G_1 and G_3): p= 0.003
[0] (between G_1 and G_3): p= 0.021

Table 3. Laboratory data of ARF subgroups

	Acute carditis	Akut chorea	Acute arthritis
Hemoglobin (mg/dl)*	11.36 ± 1.43	12.5 ± 1.14	11.54 ± 1.05
Hematocrit (%)*	35.12 ± 3.73	37.45 ± 2.87	34.62 ± 3.15
Leukocytes (number/mm³)*	10199 ± 2760.9	7816 ± 1067.6	10720 ± 2147.6
Platelets*	390110 ± 98982 [1]	267400 ± 92007 [1]	351800 ± 97127
ESR (mm/hour)*	72.5 ± 26.45 [2]	26.4 ± 24.8 [2,3]	37.4 ± 14.08 [3]
CRP (mg/dl)*	92.56 ± 71.69 º	11.9 ± 23.82 º	57.2 ± 62.83
ASO value (Todd/IU)*	908 ± 412	671 ± 424	656 ± 243
Pro-BNP (pg/ml)* (n= 33)	497.09 ± 464.12 [1] (18)	63.6 ± 66.984 (10)	117.22 ± 125.45 (5)
CK-MB (%)* (n= 26)	3.6 ± 3.27 (16)	2.77 ± 1.49 (7)	1.71 ± 2.75 (3)
Troponin I (ng/ml)* (n= 26)	0.27 ± 0.289 (17)	0.2 (7)	0.2 (2)

*: Mean ± SD.
[1] (Between acute chorea and acute carditis): p= 0.021.
[2] (Between acute chorea and acute carditis): p< 0.001.
[3] (Between acute chorea and acute arthritis): p= 0.02.
[4] (Between acute chorea and acute carditis): p= 0.01.
º (Between acute chorea and acute carditis): p= 0.005.

Table 4. Pro-BNP, CK-MB and Troponin-I values by groups

	G_1	G_2	G_3
Pro-BNP (pg/ml) * (n= 114)	308.18 ± 402.65 (33) [1,2]	84.26 ± 135.75 (41) [2]	**64.82 ± 50.37 (40) [1]**
CK-MB (%)* (n= 95)	3.16 ± 2.75 (26)	3.51 ± 2.76 (26)	**5.37 ± 5.76 (43)**
Troponin I (ng/ml) * (n= 96)	**0.245 ± 0.233 (26)**	**0.22 ± 0.094 (28)**	**0.239 ± 0.129 (42)**

*: Mean ± SD.
[1] (between G_1 and G_3): p< 0.001.
[2] (between G_1 and G_2): p< 0.001.

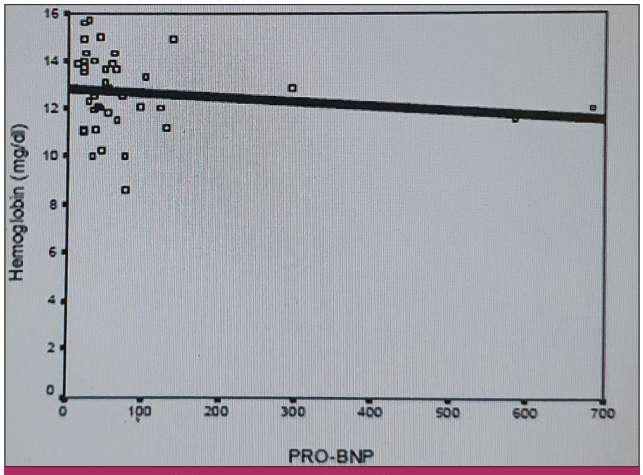

Figure 1. Hemoglobin-Pro-BNP relationship in G_1 group.

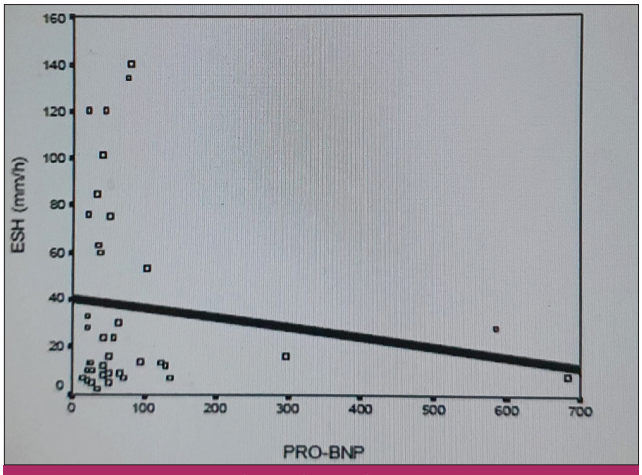

Figure 2. ESH-Pro-BNP relationship in the G_1 group.

The PR interval was greater than 0.16 sec in 30% of the G_1 patients. One patient in the G1 group had left ventricular hypertrophy, while three patients in the G_2 group had left ventricular hypertrophy alterations.

The most frequently involved valves were the mitral, tricuspid, aortic, and pulmonary valves, in order of frequency. Second and third degree mitral valve regurgitation was detected in 18 of 30 patients with acute carditis. Pericardial effusion was detected in one case with valve regurgitation.

Left ventricular end-diastolic diameter (LVEDd) was 44.45 ± 4.82 mm in the G_1 group, 44.24 ± 6.61 mm in the G_2 group, and 38.53 ± 4.2 mm in the G_3 group. While the increase in LVEDd was seen in 4.7% of the patients in the control group, this increase was found to be 40% in the previous ARF group and 35.5% in the ARF group. The change in the mean LVEDd was statistically significantly different between the G_3 and G_2, and G_1 groups ($p< 0.001$). (Figures 3-8)

Pro-BNP was 308.18 ± 402.65 pg/ml in the G_1 group, 84.26 ± 135.75 in the G_2 group, and 64.82 ± 50.37 pg/ml in the G_3 group. It was found to be significantly higher in the G_1 group compared to other groups ($p< 0.001$).

When the ARF subgroups were evaluated separately, pro-BNP was found to be higher in the acute carditis group (497.09 ± 464.12 pg/ml) than in the chorea group (63.6 ± 66.98) and arthritis group (117.22 ± 125.45) ($p< 0.001$). In addition, a positive correlation was found between pro-BNP and other signs of inflammation such as CRP ($p< 0.001$), ESR ($p< 0.001$), and platelet count ($p= 0.019$).

There was no statistically significant difference between the G_1 group and the other groups in terms of CK-MB and Troponin I ($p> 0.05$), and a positive correlation was found between CK-MB and Troponin I (Figure 8).

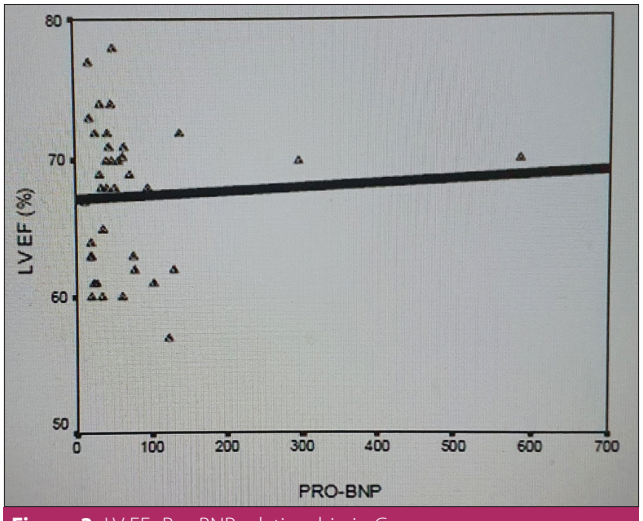

Figure 3. LV EF- Pro-BNP relationship in G_1 cases.

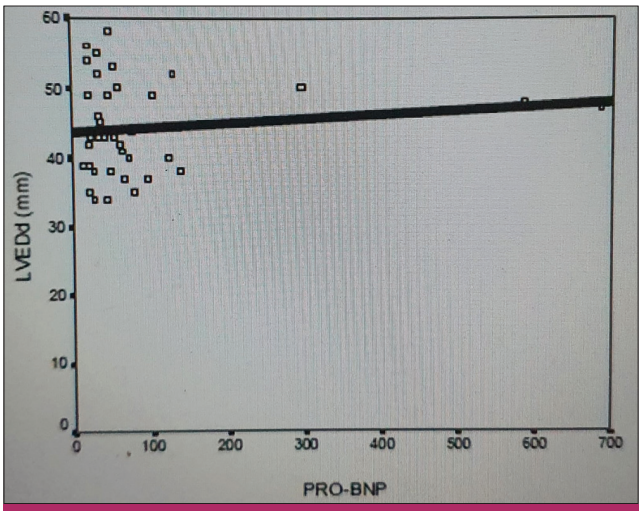

Figure 4. LVEDd- Pro-BNP relationship in G_1 cases.

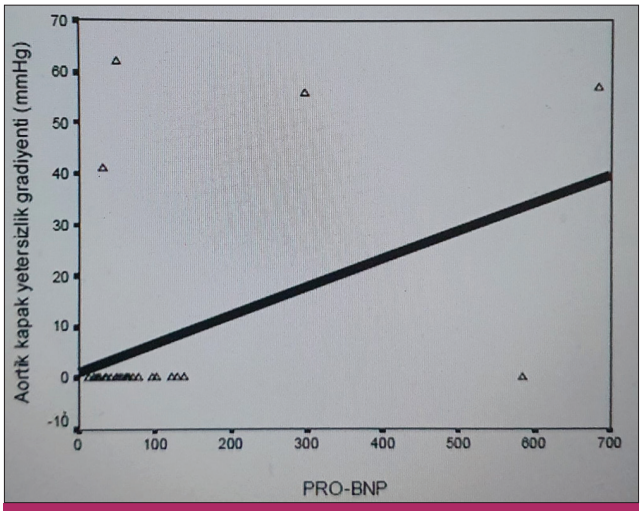

Figure 5. Aortic valve insufficiency flow-Pro-BNP relationship in G_1 cases.

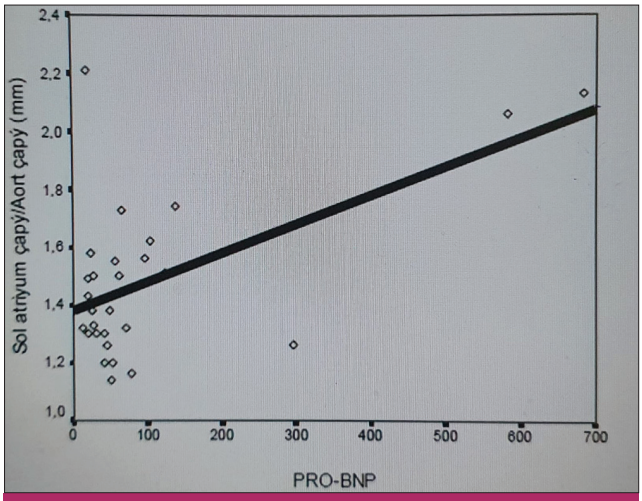

Figure 6. Left atrial diameter/aortic diameter ratio-Pro-BNP relationship in G_1 cases.

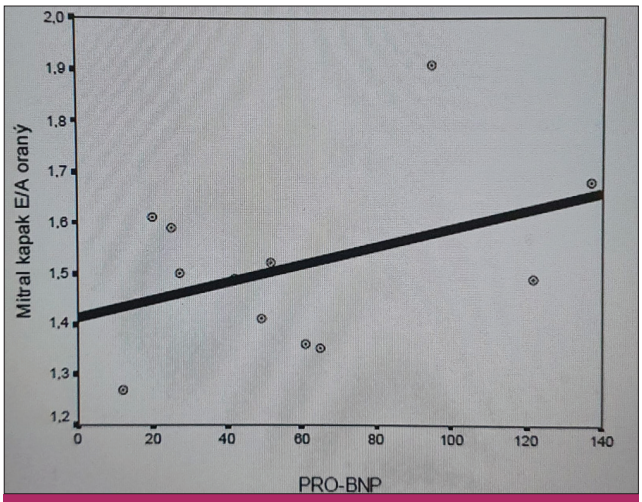

Figure 7. Pro-BNP- mitral valve E/A ratio relationship in G_1 cases.

Figure 8. Troponin-CPK-MB relationship in G_1 cases.

In patients with acute carditis, a positive correlation was found between Pro-BNP and ASO (p= 0.026), ESH (p= 0.025) and CRP (p= 0.043) before treatment; while a negative significant correlation was detected between Pro-BNP and hemoglobin (p= 0.015). When patients with acute carditis were evaluated after treatment, Pro-BNP levels were found to be significantly lower (101.12 ± 100.01 pg/ml) (p= 0.003).

DISCUSSION

In our study, 54.5% of the cases were boys and 45.5% were girls. The mean age of ARF cases included in the study was 11.06 ± 2.18 years which was consistent with previous studies conducted in Türkiye (6-12).

The most common complaints at admission were joint swelling, joint pain, cardiac murmur, abnormal movement, fever, and chest pain in only one patient and abdomen pain in another. Similarly, the most common complaints in previous studies were joint pain and fever (8,9,11,13). In our study, the frequency of abnormal movement was observed to be higher than in other studies (6,8,9,11,12,14). This is because patients with complaints like arthritis are treated in a variety of settings, whereas patients with neurological issues are referred to our facility.

Arthritis is the most prevalent major finding of ARF in developed countries, with a frequency of 55-85% documented in the literature (4,6,8,10-12). Arthritis was found in 42% of the patients in our study. ARF arthritis primarily affects the peripheral major joints, while small joints and the axial skeletal system are rarely involved (15). The most common joint involvement in our analysis was the ankle (65%), followed by the knee (60%).

The mitral valve was the most commonly involved in rheumatic carditis (65-70%), with another 25% having both aortic and mitral involvement (11). According to reports, right-sided heart valves are infrequently affected, and tricuspid valve involvement occurs in 10% of cases (16). Among clinical symptoms, the rate of carditis in studies in our country ranged between 38% and 74.3% (7,9,10). Gungor et al. (11) reported a carditis rate of 82.2%. Again in Türkiye, in the largest series of 377 cases between 1993 and 2017, Erdem et al. reported carditis as the most common major finding with 83.6% (17). In our study, the most common major finding in the group was carditis with a rate of 57.6%. According to Karasalan et al. (6), the mitral valve was the most commonly involved with 57%, Olguntürk et al. (10) reported 98% mitral valve, 24.9% aortic valve involvement, and Erdem et al. (17) reported 54.9% mitral valve, 34% mitral and aortic valve involvement. In our study, as in the literature, the mitral valve was the most commonly affected, accounting for 91% of all cases. Although right heart valve involvement is less common, tricuspid valve involvement was found more frequently in our study. Pericarditis with clinical manifestations was detected only in 5-10% of patients (18). In our study, pericardial effusion was found in only one case.

Sydenham's chorea, which is found in 10-15% of patients, is characterized by involuntary jerky movements of the face and extremities, muscle weakness, and deterioration of speech and balance. It is the most prevalent type of acquired chorea in children. It is known as an often benign, self-limiting clinical condition with no sequelae (19). In studies conducted in various parts of the world, the rate of chorea was reported to be between 28-52% (20). In studies covering the years 1982-2002 in Türkiye, the reported rate ranged from 4% to 17.9% (6,7,9,10). Erdem et al. (17) reported this rate as 13.5% in their more recent study spanning the years 1993 to 2017. The rate

of chorea in our study was 30.2%. Although the findings of our study do not correspond to the rates provided in earlier studies in our country in terms of acute chorea, they are compatible with the findings of studies conducted abroad.

Leukocytosis, a sign of inflammation, was seen in 27.3% of the ARF patients. El-Eissa et al. (21) and Lenk et al. (7) found higher rates of 94% and 95.5% respectively. The delayed onset of chorea compared to other early signs of ARF may be attributed to differences in the reference range for leukocytosis, the effect of patients' age on leukocyte count, and the treatments used before presenting to clinics. Elevated ESR and CRP, which are other indicators of inflammation, were found to be 66.7% and 75.8%, respectively. In a study by Olgunturk et al. (10), ESR and CRP were 89.5% and 72.7%, respectively. Bostan et al. (9) reported ESR and CRP as 66% and 100%. Gungor et al. (11) found statistically significant leukocytosis and CRP elevation in patients with arthritis when compared with the control group. Again, this low rate can be attributed to the fact that chorea, a late finding of ARF, constitutes approximately 1/3 of all our cases.

An increase in LVEDd was detected in 40% of the RHD patient group (G_2). The increase in LVEDd in these cases can be related to the patients' long periods of not using inotropic drugs, as well as probably recurring attacks that remained unnoticed.

BNP is known to be elevated in many congenital and acquired heart diseases (22). Studies have suggested that using BNP and NT-pro-BNP as diagnostic tools in cardiac failure in children with cardiomyopathy or CHF may be beneficial (23). Again, it was discovered that Pro-BNP increased in the early period in studies conducted by Kotby et al. (24) in children with acute RHD and by Çimen et al. (25) in 24 children with acute RHD in our country. In our study, Pro-BNP levels were found to be significantly higher in the ARF group compared to the control group ($p< 0.001$). This can be attributed to the fact that LVEDd was greater than the control group and EFs were lower.

It has been proposed that because the ventricles are the primary source of BNP in the heart, it is more sensitive and specific than other natriuretics in ventricular diseases (26). BNP is released from living myocytes as a result of increased ventricular surface tension. BNP values were found to be highest in patients with decompensated heart failure, less elevated in compensated patients, and lowest in healthy individuals (27). Increased BNP levels in the asymptomatic and early stages of heart failure are considered indicators of this peptide's sensitivity in early diagnosis. In studies with Ugandan children with latent RHD, the NT-Pro-BNP level was not greater than in the healthy control group (28).

In a study involving adult patients, it was reported that Pro-BNP increased in patients with severe mitral valve stenosis (29). In addition, it has been shown that levels in serum change with the severity of the disease in patients with chronic rheumatic valve disease (30). In a study of 18 cases, Mehrotra et al. (31) found that Pro-BNP was higher in patients with subclinical carditis than in patients without carditis and that it may be used as a marker of carditis. It was also observed that there was no difference between the first carditis attack and recurrent attacks (24). Pro-BNP level, which was found to be statistically significantly higher in acute carditis cases in our study, was not statistically significant in the previous ARF group compared to the control group ($p> 0.05$). In addition, it was observed in our study that Pro-BNP acts as an inflammation marker. Because in our study, a significant positive correlation was found between acute phase reactants (increase in CRP, ESR, and leukocyte count)- which are indicators of inflammation- platelet count, and ASO, which is an indicator of immunological response, and pro-BNP, particularly in the ARF group ($p< 0.05$).

It has been demonstrated that NT-Pro-BNP levels return to normal within 6-8 weeks of carditis treatment (25). In our study, when patients with acute carditis were examined following treatment, Pro-BNP levels were found to be significantly decreased.

CONCLUSION

In conclusion, studies on the role of Pro-BNP in children with ARF are scarce in the literature. In cases with active carditis, a significant correlation was found between Pro-BNP and LVEDd, EF, valve pathologies as well as acute inflammation indicators such as CRP, ESR, platelet count, and ASO, which is an indicator of streptococcal infection. It would be beneficial to routinely use Pro-BNP elevation, which is an indicator of myocardial injury, for ARF diagnosis, treatment, and follow-up.

Ethics Committee Approval: This study was approved by the Kahramanmaraş Sütçü İmam University Faculty of Medicine Ethics Committee (Decision Number: 1, Date: 08.01.2009).

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