

Comparison between brain natriuretic peptide and calcitonin gene-related peptide in children with dilated cardiomyopathy and controls

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ABSTRACT

Background: Dilated cardiomyopathy (DCM) is revealed with the left ventricular dilatation and systolic dysfunction. **Objective:** This study was performed to determine the level of calcitonin gene-related peptide (CGRP) and brain natriuretic peptide (BNP) in children with DCM and controls and comparison of these two biomarkers in patients. **Materials and Methods:** This study was performed from April 2014 to March 2015 on patients with DCM. The levels of BNP and CGRP were measured by ELISA, and final amounts of biomarkers were compared with the echocardiographic finding. **Results:** In this study, the mean age was 10.567 ± 5.50 and 12.135 ± 4.626 years for controls and cases, respectively ($P = 0.321$). The majority of echocardiographic indices in the left and right heart had different means in cases and controls ($P < 0.05$). Means of BNP were 213.814 ± 309.601 and 2.76 ± 1.013 for case and control, respectively ($P < 0.001$). Means of CGRP were 2.278 ± 1.586 and 1.488 ± 0.501 for cases and controls, respectively, ($P = 0.001$). In the patients group, however, no significant relationship was observed between CGRP level and Ross classification but observed a direct relationship of Ross classification with BNP ($\chi^2 = 15.845$, $P < 0.05$). **Conclusions:** The present research was performed on DCM patients and showed that most echocardiographic parameters, mean of CGRP and mean of BNP increased in patients compared to healthy children. The severity of illness based on the Ross classification showed significant and positive correlation with BNP level but not with CGRP. Probably, it could be concluded that BNP would be a better biomarker in DCM patients.

Key words: Brain natriuretic peptide, calcitonin gene-related peptide, children, dilated cardiomyopathy

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INTRODUCTION

Dilated cardiomyopathy (DCM) is identified with systolic dysfunction and dilatation of left ventricle that may cause ventricular arrhythmia, atrioventricular block, syncope, and finally sudden death. Yearly incidence is 0.57 per 100 000 with the distribution of 0.66 and 0.47 for males and females in children. This term is ranged from 4 to 40 in infants that are much higher than in children.¹ Calcitonin gene-related peptide (CGRP) neurotransmitter peptide 37 is an amino acid that extracted from calcitonin gene and commonly

increases in nervous and cardiovascular systems. A positive inotropic and chronotropic effect of calcitonin has been observed on the heart, and it is the strongest endogen vasodilator peptide that has been known so far.² Inconsistent results reported about CGRP levels in congestive heart failure (CHF) with low information regarding regulation of CGRP function.³⁻⁵ Cardiac sensory nerves play a defensive role in the heart through the expulsion of CGRP and nitric oxide. CGRP plays a protective role in myocardial injuries,

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including ischemia recirculation and cardiotoxic agent doxorubicin. CGRP in addition of having great power in vasodilator, it also has beneficial effects on the heart by local downregulation of tumor necrosis factor- α and upregulation of insulin-like growth factor.⁶ Brain-type natriuretic peptide (BNP) is a natriuretic hormone secreted from the cardiac ventricular myocytes in response to an increase in ventricular wall stretch and filling pressures. Natriuretic peptides are useful markers in a variety of cardiac diseases in children and adolescents.⁷ These peptides may be useful for screening of asymptomatic high-risk patients such as aged persons, hypertensive, diabetics, and coronary artery disease.⁸ The cutoff point of BNP in children is higher than adults and is a reliable test for diagnosis of functional and structural disorders of the cardiovascular system.⁹ These peptides are used to diagnose the CHF and may have advantages in screening of asymptomatic high-risk patients. BNP is a reliable test for diagnosis of functional and structural disorders of coronary heart disease (CHD).¹⁰ It resulted that CGRP constituted potential therapeutic for the treatment of cardiomyopathy on diabetic rats in long-term.¹¹ Moreover, it pointed that CGRP measures are related to the overload pulmonary volume in children with CHD, and it can be a cause of CHF and increases with severity.³ The most common cause of CHF is CHD with pulmonary volume overload in infants and children. It also plays an important role in CHF pathogenesis secondary to CHD. Pulmonary volume overload may have a strong role in the regulation of CGRP in children with CHF.^{3,5} In CHF patients, it has been concluded that an increase in BNP level is associated with blood volume increase. Therefore, high secretion of BNP is due to pulmonary hypertension and cyanosis. BNP levels are increased in most types of CHD with both volume and pressure overload of left or right ventricle.¹² Accordance with a variety in DCM studies and this fact that most of them are about the role of BNP and CGRP in the diagnosis, we decided to perform a study with the aim of using BNP and CGRP to diagnose DCM in children to specify the diagnostic value of these two biomarkers with comparison of control group.

MATERIALS AND METHODS

This study was performed on 37 DCM patients from February 2014 for 1 year. Thirty healthy children were matched in age and weight with patients. Hemoglobin <10 g/dl, endocrine, metabolic, valvular disorders, dysrhythmia, and heart block were exclusion criteria. For the control participants, if echocardiography diagnosed any type of heart diseases, they were excluded from the study and replaced with new one based on conditions. Participants aged from 1 to 18 years. Children over 2 years measured weight using RASA mark made in Iran by an error of 100 g, and for children under 2 years, MIKA mark recumbent weighting scale made in Japan with error of 10 g was applied. Height of patients was measured in the recumbent position using a calibrated and flat wooden

table while that of the children above 2 years old was measured in the standing position with a scale ruler. Heart failure stratification was performed by modified Ross classification. Patients were normal in respect to Na, K, Ca, blood urea nitrogen, and creatinine. Three milliliters of blood was drawn from the patients in fasting at 8 am. Samples were centrifuged at 5°C with a round of 3000 g for 10 min. The separated serum was kept in -80°C refrigerator. The levels of BNP and CGRP were measured by ELISA kits. Echocardiography findings were measured by MyLab 60 made in Italy. Data analysis was performed by SPSS 20.0 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.) using test of normality at first with Kolmogorov-Smirnov. In the case of normality, independent *t*-test and one-way ANOVA were used, otherwise same nonparametric tests applied. For the relationship between variables, Pearson correlation was used. In all tests, the significant level considered <0.05 .

RESULTS

In this study, 67 children were recruited in case (37) and control (30). The age range was from 1 to 18 years. The mean age was 11.933 ± 7.625 and 13.568 ± 6.517 years for control and case, respectively, in which *t*-test results nonsignificant difference ($t = 0.946$, $P = 0.348$). The mean weight was 35.133 ± 18.471 and 28.702 ± 10.553 kg in control and case groups, respectively ($t = -1.79$, $P = 0.078$). The mean height was 128.700 ± 29.200 and 127.405 ± 18.712 cm in control and case groups, respectively ($t = -0.22$, $P = 0.827$). Since the sample size is larger than 50, we use the Kolmogorov-Smirnov normality test for variables in the study. The null hypothesis for the test of normality stated that the actual distribution of the variable is equal to the expected distribution, i.e. the variable is normally distributed. Since the probability associated with the test of normality for all variables except weight, left ventricular end-diastolic volume (LVEDV), fractional shortening (FS), left peak E velocity, body mass index, and right isovolumic contraction time (ICT) is less than or equal to the level of significance (0.05), we reject the null hypothesis and conclude that these variables are normally distributed. Therefore, for these variables, all applied tests would be parametric. Table 1 shows the results of independent *t*-test to compare the means of normal distributed echocardiographic parameters of left and right heart in case and control groups. The results showed that mean LVEDV for case and control groups was 66.108 ± 22.129 and 39.279 ± 14.782 with significant level in different ($t = -5.687$, $P < 0.001$) and same trends for means of case and control for left peak E velocity with 85.974 ± 17.759 and 101.558 ± 19.648 , respectively ($t = -3.406$, $P = 0.001$). An examination of the findings in Tables 2 and 3 shows that the results of the nonparametric Mann-Whitney U-test applied to the variables in left and right in the case and control groups revealed a statistically significant

Table 1: Echocardiographic parameters of the left and right heart

Parameters	Group	Mean±SD	t	P
Left ventricular end-diastolic volume Control	Case 39.27867±14.78177	66.10811±22.12908	5.687	<0.001
Fractional shortening Control	Case 33.33333±3.735508	35.40541±8.067285	1.2972	0.199
Left peak E velocity Control	Case 101.5586±19.64822	85.97405±17.75868	-3.4057	0.001
Left peak A velocity Control	Case 57.54533±15.81358	55.37649±15.50389	-0.5643	0.574
Right isovolumic contraction time Control	Case 0.0272±0.015535	0.034±0.016969	1.6933	0.095

SD – Standard deviation

Table 2: Results of the Mann-Whitney U-test to compare the groups' values of the left heart parameters

Parameters	Group	Mean±SD	Mean rank	Sum of ranks	Mann-Whitney U-test	Significant (two-tailed)
Height	Case	127.405±18.712	32.797	1213.5	510.5	0.574
	Control	128.7±29.2	35.483	1064.5		
Left ventricular end-diastolic dimension	Case	46.584±7.713	42.568	1575	238	<0.001
	Control	39.993±4.098	23.433	703		
Left ventricular end-systolic dimension	Case	30.181±7.451	38.716	1432.5	380.5	0.028
	Control	26.517±3.23	28.183	845.5		
Ejection fraction	Case	62.514±13.715	35.986	1331.5	481.5	0.353
	Control	63.533±5.507	31.55	946.5		
Left myocardial performance index	Case	0.549±0.181	45.892	1698	115	<0.001
	Control	0.325±0.051	19.333	580		
Left isovolumic contraction time	Case	0.03±0.01	43.865	1623	190	<0.001
	Control	0.017±0.007	21.833	655		
Left isovolumic relaxation time	Case	0.107±0.026	43.23	1599.5	213.5	<0.001
	Control	0.094±0.012	22.617	678.5		
Left acceleration time	Case	0.054±0.011	33.703	1247	544	0.888
	Control	0.054±0.008	34.367	1031		
Left deceleration time	Case	0.123±0.014	35.581	1316.5	496.5	0.456
	Control	0.121±0.015	32.05	961.5		
Left E/A velocity ratio	Case	1.657±0.757	28.757	1064	361	0.014
	Control	1.842±0.461	40.467	1214		
Left atrium/aorta ratio	Control	1.252±0.294	33.662	1245.5	542.5	0.875
	Case	1.203±0.15	34.417	1032.5		
Left pre-ejection period	Control	0.128±0.156	44.703	1654	159	<0.001
	Case	0.094±0.101	20.8	624		
Left pre-ejection period/ejection time	Control	0.357±0.058	44.743	1655.5	157.5	<0.001
	Case	0.294±0.039	20.75	622.5		
Left Ejection time	Control	0.25±0.026	27.865	1031	328	0.004
	Case	0.263±0.02	41.567	1247		
Left interventricular septal dimension in diastole	Case	6.319±1.294	40.243	1489	324	0.003
	Control	5.43±0.887	26.3	789		
Left ventricular posterior wall dimension in diastole	Case	4.211±1.222	41.149	1522.5	290.5	0.001
	Control	3.343±0.507	25.183	755.5		
Left interventricular septal dimension in systole	Case	9.276±1.761	39.365	1456.5	356.5	0.012
	Control	8.283±1.08	27.383	821.5		
Left interventricular septal dimension in systole	Case	4.251±1.246	41.662	1541.5	271.5	<0.001
	Control	3.363±0.524	24.55	736.5		
Left ventricular mass index	Case	27.0069±10.64840	43.92	1625.00	188.000	<0.001
	Control	16.4649±5.47652	21.77	653.00		

SD – Standard deviation

difference at the level in some of them. The rank average of the left ventricular end-diastolic dimension (LVEDD) of the case group was 42.568, while the participants in the

control group had an LVEDD score rank average of 23.433 with the $P < 0.001$, which shows statistically significant different [Table 4]. The mean ranks of the right E/A velocity

Table 3: Results of the Mann–Whitney U-test to compare the groups’ values of right heart parameters and biomarkers

Parameters	Group	Mean±SD	Mean rank	Sum of ranks	Mann-Whitney U-test	P
Height	Case	127.405±18.712	32.797	1213.5	510.5	0.574
	Control	128.7±29.2	35.483	1064.5		
Myocardial performance index	Case	0.582±0.147	47.378	1753	60	<0.001
	Control	0.316±0.05	17.5	525		
Right isovolumic relaxation time	Case	0.11±0.022	40.176	1486.5	326.5	0.004
	Control	0.096±0.012	26.383	791.5		
Right acceleration time	Case	0.134±0.197	30.068	1112.5	409.5	0.063
	Control	0.07±0.019	38.85	1165.5		
Right deceleration time	Case	0.128±0.012	38.689	1431.5	381.5	0.027
	Control	0.12±0.018	28.217	846.5		
Right peak E velocity	Case	68.413±17.158	40.203	1487.5	325.5	0.004
	Control	57.706±14.139	26.35	790.5		
Right E/A velocity ratio	Case	1.408±0.478	33.216	1229	526	0.714
	Control	1.397±0.307	34.967	1049		
Right peak A velocity	Case	50.366±13.852	40.203	1487.5	325.5	0.004
	Control	42.119±9.916	26.35	790.5		
Right pre-ejection period	Case	0.085±0.015	43.054	1593	220	<0.001
	Control	0.076±0.008	22.833	685		
Right pre-ejection period/ejection time	Case	0.34±0.06	45.973	1701	112	<0.001
	Control	0.289±0.03	19.233	577		
Right ejection time	Case	0.246±0.021	27.365	1012.5	309.5	0.002
	Control	0.264±0.024	42.183	1265.5		
Calcitonin gene-related peptide	Case	2.2779±1.58587	40.97	1516.00	297	0.001
	Control	1.4478±0.50102	25.40	762.00		
Brain natriuretic peptide	Case	213.814±309.601	48.419	1791.5	21.5	<0.001
	Control	2.76±1.013	16.217	486.5		
Age	Case	12.135±4.626	36.122	1336.5	476.5	0.321
	Control	10.567±5.5	31.383	941.5		

SD – Standard deviation

Table 4: Ross classification impact on age and biomarkers in patients

Parameters	DCM	Mean±SD	n	Mean rank	χ^2	P
CGRP	1	3.2500±2.34438	10	20.95	1.286	0.733
	2	2.9556±1.94429	9	20.56		
	3	2.5100±1.50366	10	18.25		
	4	2.4875±2.06566	8	15.75		
BNP	1	97.130±155.2863	10	12.7500	15.8453	0.0012
	2	76.656±76.4345	9	14.2778		
	3	133.050±102.7770	10	19.4500		
	4	614.925±452.6220	8	31.5625		

CGRP – Calcitonin gene-related peptide; DCM – Dilated cardiomyopathy; SD – Standard deviation; BNP – Brain natriuretic peptide

ratio were 33.216 and 34.967 in the case and control groups, respectively, with the $P = 0.714$, in which not enough power to reject equality of mean ranks [Table 5]. Note that the test statistic is corrected for the existence of ties in the ranks of the BNP ($\chi^2 = 15.845, P < 0.05$) and CGRP ($\chi^2 = 297, P < 0.05$) data; there exists enough evidence to result that there is a difference in the Mann–Whitney test scores. Table 4 shows Ross classification impact on BNP and CGRP in patients. CGRP with mean ranks of 20.95, 20.56, 18.25, and 15.75 for severity of classes 1, 2, 3, and 4 in the order given shows no significant relationship with Ross classification.

However, according to Table 4, BNP shows that influenced by the level of disease’s severity significantly ($\chi^2 = 15.8453$ and $P = 0.001$). Table 5 shows that with BNP increasing, CGRP decreases but not significantly in bout patients and all population. LVEDV has appositive and significant correlation ($r = 0.447, P < 0.001$) with BNP in the case of considering all population but not with CGRP. It is observed that there is no significant correlation in the case of patients, except a few parameters. In patients, it is observed that just interventricular septal dimension in systole (IVSDS) has a correlation with CGRP. At the end of the analysis, from 10 patients in Group 1, two patients died due to disease progression. All nine participants in the second groups survived until the end of follow-up. In Group 3, one patient died and one had heart transplantation (from 10 patients). And finally, for the fourth group, from eight patients, two received heart transplantation, one with three chambers peacemaker (died), and two individuals withdraw the study.

DISCUSSION

The current study provided that LVEDD, left ventricular end-systolic dimension (LVESD), ICT, LVEDV, myocardial performance index (MPI), ICT, IRT, IVSDS, peak E velocity,

Table 5: Correlation of echocardiographic parameters and biomarkers in patients

Echocardiographic parameters	Patients population			
	CGRP		BNP	
	PC	P	PC	P
Left ventricular end-diastolic volume	-0.180	0.287	0.322	0.052
Left ventricular end-diastolic dimension	0.079	0.642	-0.057	0.737
Left ventricular end-systolic dimension	0.057	0.738	-0.136	0.422
Ejection fraction	0.035	0.836	0.118	0.487
Fractional shortening	0.052	0.762	0.101	0.551
Left myocardial performance index	0.041	0.809	-0.268	0.108
Left isovolumic contraction time	-0.170	0.315	0.305	0.066
Left isovolumic relaxation time	-0.251	0.134	-0.408	0.012
Left acceleration time	0.096	0.572	-0.035	0.839
Left deceleration time	-0.043	0.803	0.049	0.774
Left peak E velocity	-0.172	0.308	0.360	0.028
Left E/A velocity ratio	0.049	0.774	0.277	0.097
Left peak A velocity	-0.214	0.203	0.012	0.942
Right myocardial performance index	0.034	0.841	0.188	0.264
Right isovolumic relaxation time	0.076	0.656	0.008	0.962
Right acceleration time	-0.168	0.319	-0.021	0.904
Right deceleration time	-0.174	0.304	-0.106	0.531
Right peak E velocity	0.145	0.393	-0.154	0.362
Right E/A velocity ratio	0.284	0.089	-0.068	0.689
Right peak A velocity	-0.130	0.442	-0.123	0.469
Left atrium/aorta ratio	-0.062	0.716	0.059	0.727
Left pre-ejection period	0.300	0.072	-0.150	0.374
Left pre-ejection period/ejection time	0.003	0.987	-0.069	0.684
Left ejection time	0.071	0.675	0.119	0.483
Right pre-ejection period	0.061	0.721	0.035	0.839
Right pre-ejection period/ejection time	0.058	0.735	0.020	0.905
Right ejection time	-0.002	0.992	0.017	0.923
Left interventricular septal dimension in diastole	0.210	0.212	-0.112	0.508
Left ventricular posterior wall dimension in diastole	0.141	0.405	-0.161	0.342
Left interventricular septal dimension in systole	0.375	0.022	0.008	0.962
Left ventricular posterior wall dimension in systole	0.170	0.314	-0.117	0.491
Right isovolumic contraction time	-0.059	0.730	-0.271	0.105
Body mass index	0.028	0.870	0.120	0.478
Left ventricular mass index	0.188	0.266	-0.120	0.479

CGRP – Calcitonin gene-related peptide, BNP – Brain natriuretic peptide; PC – Pearson correlation

pre-ejection period/ejection time (PEP/ET), ET, interventricular septal dimension in diastole, left ventricular posterior wall dimension in diastole (LVPWDD), and left ventricular posterior wall dimension in systole (LVPWDS) in the left heart and MPI, IRT, deceleration time (DT), E, A (peak A velocity), PEP/ET, PEP, and ET in the right heart were significantly different between two case and control groups. The results showed that CGRP level and BNP were higher among patients, but it was very stronger significant in BNP. Increased BNP may approve the presence of DCM due to diastolic dysfunction and probably systolic dysfunction as well but without differentiation power between systolic and diastolic types.

Noori in a study concluded a significant difference in the levels of IRT, DT, PEP, ET, PEP/ET, and MPI of the right heart between case and control groups. For the other echocardiography parameters such as ICT, E, A, and E/A, nonsignificant difference was observed, which is similar with the present findings in all echocardiography parameters, except peak E velocity and peak A velocity in the left heart. In our study, we resulted that the findings comparatively is similar with the Noori's outcomes.¹³ In the years 2012 and 2013, Noori carried out studies on the cardiac and pulmonary dysfunction in asymptomatic beta-thalassemia major patients. In the study, the right and left side heart functions compared in patients with thalassemia major, patients with thalassemia intermedia, and control groups resulted that MPI in both right and left heart was significantly higher in patients than controls, which was similar with our finding in this specific situation. PEP/ET ratio was different in case and controls significantly with similar outcome of the present study. Ejection fraction, in both studies, showed a significant difference that was similar with the present study. For acceleration time in left and right heart, there was not reported a significant difference. Mean of ICT as a parameter of left heart was different in case and control comparison significantly which was similar with our findings. Isovolumic relaxation time (IRT) was significantly different in both studies. In the present study, we received to the conclusion of a significant difference in both left and right heart. DT had significant difference in two case and control groups in Noori studies that agree with right heart. In brief, these two studies by Noori show similar patterns with the results of the present study.^{14,15} Left ventricular mass index (LVMI) as a left heart parameter had significant different values in case and control groups.^{16,15} The results of the late studies were similar with the present study findings. Noori reported that echocardiographic parameters of left ventricle such as ICT, MPI, ET, PEP/ET, DT, AT, IRT, LVEDD, LVESD, and EF in patients and control groups were significantly different. However, in the present study, the results were a little dissimilar. It means that for all the mentioned parameters, we found same results except DT, AT, and EF. Echocardiographic parameters of right ventricle such as MPI (higher in patient), peak A velocity (higher in patient), PEP (higher in patient), and ET (higher in case) in patients were statistically different compared with controls, which was similar with our findings. However, for the E/A (higher in case) parameter, we found disagreement with the Noori study which was not significantly different in case and controls.¹⁷ Jefferies and Towbin reported that DCM is characterized with left ventricular dilatation and is accompanied with systolic dysfunction. However, diastolic dysfunction may also be seen and both ventricles may develop insufficiency, and also there is mortality risk due to ventricular arrhythmia, atrioventricular block, syncope, and sudden death.¹ In our patients, we received to the conclusion that BNP had strong relationship with three of

echocardiographic parameters and severity of illness, which was consistent with Jefferies' results. NT-pro-BNP could be introduced for continuous left ventricle dysfunction in children with cardiomyopathy or myocarditis. However, the normal level in improved children may not demonstrate any residual heart disease.⁹ This result was similar to our findings comparatively when we used BNP instead of NT-pro-BNP. Consequently, to diagnose the heart failure, BNP has been approved by FDA. Similarly, we found an association between BNP and MPI that showed systolic and diastolic dysfunction.¹⁸ Koch *et al.* demonstrated that in children with congenital heart disease, the plasma level of BNP was associated with ventricular function and reflects the ventricular overload injury. Hence, the normal BNP may show compensatory phase.¹⁹ Our results were similar with Koch when we assessed children with DCM. In both studies, the major problem was due to volume overload. Mariano-Goulart *et al.* reported that an increase in BNP level in patients with systolic ventricular dysfunction would be considered as a risk factor for right ventricular dysfunction.²⁰ According to our finding, the BNP level was higher in high severity level of disease based on Ross classification. Kremastinos *et al.* said in their report "plasma level of BNP and NT-Pro-BNP is increased in major thalassemia patients and when left ventricular dysfunction is developing the predictive value of NT-pro-BNP would be better than BNP for diagnosis of latent left ventricular diastolic dysfunction." Moreover, in the related study by Kremastinos *et al.*, they were also proposed that NT-pro-BNP was increasing by age.^{21,22} In our study, a significant difference in mean age and BNP level was observed in the various severity of disease such that in higher severity, the mean age and the mean BNP were higher. Niedner found a relationship between BNP and severity of congenital heart disease;²³ however, in our study, we resulted that increasing of BNP was correlated with severity of DCM. The results of various studies on CGRP have reported that CGRP infusion had meaningful positive clinical impacts on patients with heart failure during multiple mechanisms. These results proposed that heart failure would be treated by CGRP. The findings of the present study showed a significant positive correlation between CGRP and left ventricular dilatation dysfunction (LVDD), LVESD, LVPWDD, and LVPWDS, which was comparable with the results of the study conducted by Jianping in animal model.²⁴ Marangoni *et al.* conducted an animal model study on rats and resulted that FS, E/A, IVRT, LVDD, left ventricular systolic dysfunction (LVSD), intraventricular septum in diastole (IVSD), intraventricular septum in systole (IVSS), and DT were higher in the cases compared with controls. In the current study, similar results were obtained regarding IVDD, IVSD, LVSD, IVSS, and IVRT while the two groups were not significantly different in respect to FS, E/A, IVRT, and DT.²⁵ Hsu JH expressed that CGRP level was related to pulmonary artery systolic pressure. Hsu *et al.* reported an association between CGRP and heart failure

due to CHD and pulmonary artery pressure. Hsu *et al.* also pointed CGRP was related to the severity of the disease.³ A study was carried out on CHD patients who had left to right shunt by Zhang *et al.* The research was different with ours in terms of cardiomyopathy improvement. They measured CGRP and endothelin plasma levels in CHD patients with pulmonary hypertension. They resulted that the level of CGRP increased in patients with pulmonary hypertension. These results were comparable with our findings for showing higher CGRP levels in the patients with DCM.²⁶ Xin *et al.* studied the relationship between right heart echocardiographic findings and CGRP in major thalassemia patients and reported that CGRP was inversely correlated with right ventricle MPI and pulmonary hypertension; however, in another study resulted that there were no correlations between CGRP and pulmonary hypertension in CHD patients.^{27,28} Nonetheless, the current study results showed significant positive correlations in both left and right hearts. Besides, no significant relationship was found between CGRP and MPI in the case group, and there was a direct correlation between IVSS and CGRP level in the left heart.

CONCLUSIONS

The present research was performed on DCM patients and showed that the majority echocardiographic parameters, mean of CGRP and mean of BNP increased in patients compared to healthy children. The severity of illness based on the Ross classification showed significant and positive correlation with BNP level but not with CGRP. Probably could be concluded that BNP would be a better biomarker in DCM patients.

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Conflicts of interest

There are no conflicts of interest.

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