Cardiomyopathies in Children

Clinical, Epidemiological and Prognostic Evaluation

Arman BILGIÇ, M.D.,* Nazan ÖZBARLAS, M.D.,**
Süheyla ÖZKUTLU, M.D.,* Sema ÖZER, M.D.,***
and Şencan ÖZME, M.D.*

SUMMARY

In this article, the clinical and epidemiological characteristics of 137 children with cardiomyopathy admitted to the Hacettepe Pediatric Cardiology Unit were studied and the prognosis was evaluated after a follow-up period of 24±5 months. It was found that the highest proportion of patients were residents of Ankara, followed by the Northern and the Central Anatolian regions, and consanguinity between their parents was more common than the proportion for Turkey as a whole. Most of the patients had dilated cardiomyopathy (78.9%) and the age at which symptoms appeared varied according to the type of cardiomyopathy. A high proportion of patients came to the hospital with complaints of dyspnea and a decrease in effort capacity. The most common findings on the physical examination were hepatomegaly and tachycardia. Electrocardiographic and echocardiographic evaluations were made for all patients and cardiac catheterization and endomyocardial biopsy were performed when necessary. The outcome was as follows: 34.5% improved, 45.7% remained stable, 9.5% deteriorated and 10.3% died.

Additional Indexing Words:
Cardiomyopathy Infancy Childhood

CARDIOMYOPATHY is a heart muscle disease of unknown etiology.[1] According to etiological classification, cardiomyopathy is divided into 2 groups, namely cardiomyopathy and specific myocardial disease.[2] There are various hypotheses about the etiology of the disease.

The etiological research on the disease has attracted considerable interest in recent years, primarily due to success achieved in the replacement

From the Department of Cardiology, Hacettepe University, Institute of Child Health, Ankara, Turkey.

* Professor of Pediatrics and Pediatric Cardiology.

** Resident in Pediatric Cardiology.

*** Associate Professor of Pediatrics and Pediatric Cardiology.

Address for reprints: Arman Bilgiç, M.D., Department of Pediatric Cardiology, Hacettepe University, Ankara 06100, Turkey.

Received for publication April 21, 1990.

Accepted June 22, 1990.

therapy of cardiomyopathies associated with metabolic disorders (carnitine deficiency) and trace element deficiency (selenium).[3)-5)] It is also noteworthy that considerable success has been achieved in the therapy of the disease through heart transplantation, compared with less satisfactory results obtained through medical therapy.

The aim of this study is to show the epidemiological and clinical aspects and the prognosis of patients with cardiomyopathy who applied to the Pediatric Cardiology Unit at the Hacettepe University Medical Faculty during the last 5 years. The Hacettepe University Hospital is a reference center in Ankara, the capital of Turkey. The country is divided into geographical regions by administrators and researchers and Ankara is situated in the Central region. A similar regional division is used in this study.

Materials and Methods

Data for 137 patients who were diagnosed as having cardiomyopathy between September 1984—September 1989 were used for the study. Patients with specific myocardial disease were excluded. The disease was diagnosed using clinical, electrocardiographic, telecardiographic and echocardiographic findings. Cardiac catheterization was performed on 11 patients and endomyocardial biopsy was obtained in 6 patients. Together with epidemiologic, clinical and laboratory data, control registers of the patients were also included for prognostic evaluation and the most recent conditions of some of the patients were noted based on correspondence with their parents.

The types of cardiomyopathy were identified as dilated, hypertrophic and restrictive according to the echocardiographic findings. Prognosis was analyzed under four headings: improvement, stable, deterioration, exitus. Patients with improved clinical, tele and electrocardiographic findings as well as patients with normal or subnormal myocardial function were defined as having improved. Patients with stability in the above findings were classified as stable and patients who showed deterioration in their findings were included in the deteriorated category.

For the analysis of the data the Statistical Package for the Social Sciences (SPSS) computer program was used. For the evaluation of statistical significance t-tests were performed.

Results

Patients with cardiomyopathy constituted 0.5% of all patients who

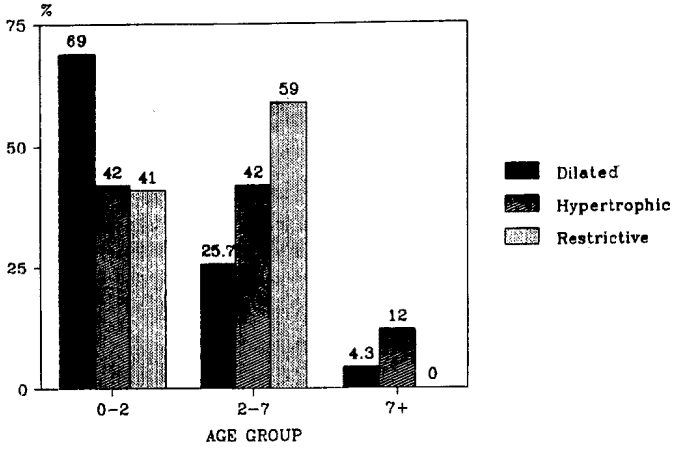

Fig. 1. Cardiomyopathy types and the age groups at the onset of symptoms.

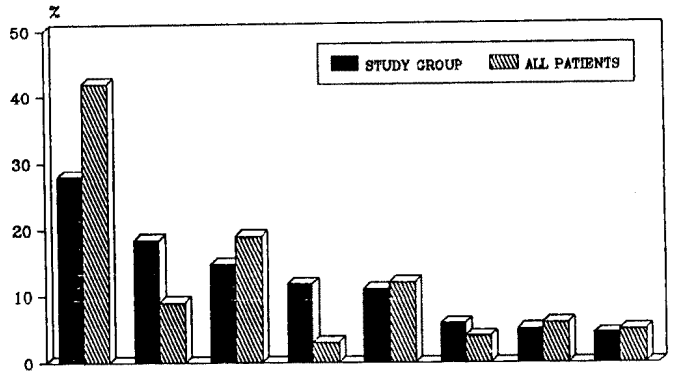

Fig. 2. Regional distribution of patients in the study group and all patients coming to the Pediatric Cardiology Unit.

Regions (from left side: Ankara, Northern, Central, Southeastern, Southern, Marmara, Aegean, Eastern)

came to the Pediatric Cardiology Unit during the 5-year period under consideration.

Of the 137 patients, 75 were male and 62 were female, 105 (78.9%) had dilated, 12 (9.1%) had hypertrophic and 16 (12%) had restrictive types of cardiomyopathy. The sex ratio of patients was not found to be significantly different from normal except for those patients with hypertrophic cardiomyopathy (M/F: 3/1).

The average age of admission to the hospital was 50 ± 8 months (range 15 days—15 years); the age at the onset of symptoms was 28 ± 5 months (range 15 days—10 years), and it was found that the patients were usually brought to the hospital 8 ± 1.2 months after the beginning of symptoms.

Table I. Distribution of Patients Who Were Admitted to the Cardiology Unit between 1984-1989 According to Place of Residence

	Patients with cardiomyopathy (%)	All patients (%)	t	p
Ankara	27.9	42.1	3.68	*<0.01*
Northern	18.4	9.0	2.83	*<0.01*
Central	14.7	18.2	1.42	>0.1
Southeastern	11.8	3.0	3.19	*<0.01*
Southern	11.0	12.3	0.38	>0.5
Marmara	5.9	4.2	0.95	>0.5
Aegean	5.1	6.1	0.50	>0.5
Eastern	4.4	5.1	0.34	>0.05

Table II. Initial Symptoms and Types of Cardiomyopathy

Symptoms	Dilated		Hypertrophic		Restrictive	
	n	%	n	%	n	%
No symptoms	—	0	2	20.0	—	0
Dyspnea	63	60.0	4	34.0	8	50.0
Fatigue	21	20.0	5	42.0	7	43.8
Palpitation	14	13.3	—	0	3	18.8
Coughing	24	22.9	—	0	2	12.5
Sweating	11	10.5	—	0	1	6.3
Edema	10	9.5	—	0	3	18.8
Abdominal distension	8	7.6	1	9.0	5	31.3
Fever	7	6.7	—	0	1	6.3
Cyanosis	9	8.6	—	0	3	18.8
Syncope	3	2.9	1	9.0	—	0
Chest pain	—	0	2	20.0	—	0

Figure 1 shows the age at the onset of symptoms according to the type of cardiomyopathy.

Information on the place of residence of patients was also considered in the analysis. It was found that 27.9% of the patients were from Ankara, followed by 18.4% from the Northern region and 14.7% from the Central region of Turkey. However, the distribution of all patients coming to the Pediatric Cardiology Unit in the last 5 years is significantly different from our study group; the main differences arising from the higher percentages of patients coming from the Northern ($t=2.83$, $p<0.01$) and Southeastern regions ($t=3.19$, $p<0.01$) in our study group (Fig. 2 and Table I).

The proportion of patients with parents of first degree consanguinity was found to be 20.2% compared with the national proportion of 14.6% ($p>0.1$).[6] This proportion was 23.8% for children with dilated cardio-

Table III. Initial Physical Findings and Types of Cardiomyopathy

Findings	Dilated		Hypertrophic		Restrictive	
	n	%	n	%	n	%
Tachycardia	89	84.8	4	33.0	11	68.8
Hepatomegaly	73	69.5	4	33.0	10	62.5
Murmur	37	35.0	12	100.0	6	37.0
Edema	3	2.9	—	0	3	18.8
Splenomegaly	11	10.5	—	0	3	18.8
Ascites	2	1.9	—	0	4	25.0
Cyanosis	5	4.8	—	0	2	12.5
Arrhythmia	10	9.0	—	0	—	0

myopathy, 18% for children with hypertrophic and 18.8% for children with restrictive cardiomyopathy. It was found that siblings of 6 patients had previously been diagnosed as having cardiomyopathy and parents of 2 patients reported that they had had other children who died because of cardiac failure. These 8 patients made up 5.9% of all patients; 7 of these were found to have consanguinity between their parents; 40.8% of the patients with dilated cardiomyopathy had had nonspecific respiratory diseases previously. The distribution of symptoms according to the type cardiomyopathy is shown in Table II. The findings of physical examination are shown in Table III.

On the first x ray, 89.6% of the patients had cardiomegaly. The most frequent finding on the electrocardiograms was biventricular hypertrophy (89.6%) and 48.7%, 25.5% and 11.7% of the patients were found to have left ventricular hypertrophy, ST-T changes and voltage suppression, respectively. Sixteen of the children (15%) with dilated cardiomyopathy were found to have arrhythmia whereas this finding was not encountered in children with other types.

Echocardiography was performed for the purposes of diagnosis, classification and follow-up. The ejection fraction was less than 50% for 96.4% of children with the dilated type and 25% of children with the restrictive type at their first presentation.

Cardiac catheterization was performed on 11 patients, of whom 10 were identified as having restrictive cardiomyopathy. One was found to have obstructive hypertrophic cardiomyopathy.

Digoxin was administered to 80% of the patients and this was combined with diuretics, corticosteroids or verapamil wherever necessary. Four patients with the hypertrophic type of cardiomyopathy received beta-blockers.

Table IV. Types of Cardiomyopathy and Prognosis

	Improved		Stable		Deteriorated		Exitus	
	n	%	n	%	n	%	n	%
Dilated	37	38.5	39	40.6	9	9.4	11	11.5
Hypertrophic	2	25.0	6	75.0	—	—	—	—
Restrictive	—	—	7	20.0	2	20.0	1	10.0
Total	39	34.5	52	45.7	11	9.5	12	10.3

The average follow-up duration was 24±5 months; 56.9% of the patients were followed for periods of more than 1 year and 24.1% were followed for more than 3 years, while 14.5% could not be followed.

The clinical course of the 116 patients who were followed up is shown in Table IV, according to the type of cardiomyopathy.

It is noteworthy that, of the 12 patients who died, 9 died within the first 7 months after the beginning of symptoms.

In addition to cardiomyopathy, 1 patient had a ventricular septal defect and 1 patient had coarctation of the aorta. Of 11 patients on whom cardiac catheterization was performed, 3 were found to have pulmonary hypertension and 2 had mitral insufficiency. These were thought to be components of the cardiomyopathy.

Cerebrovascular embolic phenomenon was found in 3.8% of the dilated type and 12% of the restrictive type of cardiomyopathy.

Discussion

In this study, clinical and epidemiologic characteristics of patients with cardiomyopathy were analyzed. Of the 137 patients, 78.9% were found to be of the dilated type, 12% of the restrictive and 9.1% of the hypertrophic type. Studies done after 1980 have stressed that hypertrophic cardiomyopathy follows a better clinical course than previously reported. A study carried out in Italy based on 4 year screenings has reported the proportion of asymptomatic patients to be 72%.[7] It is only possible to identify the asymptomatic group with careful screening; therefore it may be considered that the low percentage of the hypertrophic type in our study can be attributed to the lack of screening and that the study group reflects symptomatic patients.

The hypertrophic type of cardiomyopathy is known to be twice as common in males as compared with females.[8] However, in our study, the sex ratio for this type of cardiomyopathy was found to be 3: 1 and no sex dif-

ference was found for the other types.

It was found that there is some variation in the age at the time of onset of the initial symptoms according to the type of cardiomyopathy. An interesting finding was that 69% of the dilated type had had symptoms before 2 years of age. It is possible that a significant proportion of these patients had endocardial fibroelastosis. Endocardial fibroelastosis can be differentiated from the dilated type only with histopathological analyses and for 95% of cases this disease of infancy shows dilated type characteristics from the clinical and hemodynamic standpoints.[8]

When all patients who applied to the Pediatric Cardiology Unit during the same period as our study group were compared, it was found that there were higher proportions of patients coming from the Northern and Southeastern regions among patients with cardiomyopathy. The differences are statistically significant (Northern region: $t=2.83$, $p<0.01$ and Southeastern region: $t=3.19$, $p<0.01$). This result raises the possibility of the existence of environmental factors in the etiology of cardiomyopathy. The differences for the other regions were not found to be statistically significant, except for Ankara. The difference between Ankara's two proportions in favour of all patients coming to our Pediatric Cardiology Unit is probably due to the fact that the university is in Ankara and therefore patients residing in Ankara have easier access to the hospital. Patients with specific diseases come to the university from other regions only by being referred by other health institutions.

The higher proportion of first degree consanguinity between the parents of patients in our study group (20.2%) compared with the relevant figure for Turkey as a whole (14.6%)[6] and the existence of this condition for 7 of 8 patients with siblings who had cardiomyopathy can be regarded as evidence in support of the influence of genetic factors on the disease, although the difference between the proportions was not found to be statistically significant. In our study 5.7% of patients with the dilated type had had siblings with cardiomyopathy, whereas this figure was zero for the hypertrophic type. It is known that the prevalence of the familial form is about 50–70% and that the genetic pattern is autosomal dominant with high penetration for the hypertrophic type.[9] For the dilated type, although the genetic pattern has not been identified until now, it is reported that familial forms are not as rare as previously thought.[10] Our inability to identify any familial form for the hypertrophic type could therefore be due to the lack of familial screening and the identification of asymptomatic patients.

In 40.8% of patients with dilated type, nonspecific respiratory disease was found to precede cardiomyopathy, and this supports the etiological role

of either viral infections or immune reactions initiated by viruses. The proportion with similar findings was found to be 33% in Germany and 50% at the Mayo Clinic, U.S.A.[11]

Arrhythmia was found in 15% of the patients, all of these being the dilated type. This figure is close to the proportion found in Germany (23%).[11] None of the patients with hypertrophic cardiomyopathy was found to have arrhythmia, possibly because Holter monitoring was not applied to the patients which would have enabled the identification of intermittent arrhythmias.

It is generally reported in studies on the subject that a third of patients with dilated cardiomyopathies die, another third improve and that the remaining 1/3 remain stable.[12] The ratio of improvement for our study group is in accordance with the literature but the low exitus rate could be due to the following: 14.5% of patients could not be followed up, only 56.9% of patients were followed up for more than 1 year and all of the 11 patients (9.5%) whose conditions had deteriorated were followed up for less than 6 months and information on their latest condition could not be obtained.

It is reported by various regional hospitals that hypertrophic cardiomyopathy is a disease with a better prognosis than previously thought.[7],[13] The lack of cases of exitus for this type of the disease in our study group supports that finding.

The Hacettepe Faculty Hospital is a reference center and therefore our findings on cardiomyopathy can be regarded as reflecting at least partly the situation for Turkey as a whole. Consanguinous marriages constitute a significant proportion of marriages in Turkey and this increases the importance of cardiomyopathy as a disease with familial forms. It is known that medical therapy of the disease has not yielded satisfactory results and that cardiac transplantation is considered a better solution. Hence more studies on the etiology of the disease are needed, genetic counselling should be improved, familial forms should be more thoroughly researched, and regional characteristics of the disease should be studied.

References

1. Report of WHO Expert Committee: Cardiomyopathies, World Health Organization Technical Report Series, Geneva, 1984
2. Brandenburg RO, Chazov E, Cherian G, et al: Report of the WHO/ISFC task force on definition and classification of cardiomyopathies. Circulation **64**: 437A, 1981
3. William GD, Palacios IF, Fallon JT, Aretz HT, Mills J: Active myocarditis in the spectrum of acute dilated cardiomyopathies. New Eng J Med **312**: 885, 1985
4. Limas CJ, Limas C: HLA antigens in idiopathic dilated cardiomyopathy. Br Heart J **62**:

379, 1989

5. Ino T, Sherwood G, Benson LN, Wilson G, Freedom RM, Rowe RD: Cardiac manifestations in disorders of fat and carnitine metabolism in infancy. J Am Coll Cardiol **11**: 1301, 1988
6. Hacettepe University Institute of Population Studies: 1988 Turkish population and health survey, Ankara, Turkey, April 1989
7. Spirito P, Chiarella F, Carratino L, Berisso MZ, Bellotti P, Vecchio C: Clinical course and prognosis of hypertrophic cardiomyopathy in an outpatient population. New Eng J Med **320**: 749, 1989
8. Barry JM: Cardiomyopathies. *in* Heart Disease in Infants, Children and Adolescents, ed by Adams FH, Emmanouilides GC, Riemenschneider TA, Williams and Wilkins, Baltimore, p 940–964, 1989
9. Editorials: The genetics of hypertrophic cardiomyopathy. Ann Int Med **105**: 610, 1986
10. Schmidt MA, Michels VV, Edwards WD, Miller FA: Familial dilated cardiomyopathy. Am J Med Gen **31**: 135, 1988
11. Schmaltz AA, Apitz J, Hort W: Dilated cardiomyopathy in childhood: Problems of diagnosis and long-term follow-up. Eur Heart J **8**: 100, 1987
12. Griffin ML, Hernandez A, Martin TC, Goldring D, Bolman RM, Spray TL, Strauss AW: Dilated cardiomyopathy in infants and children. J Am Coll Cardiol **11**: 139, 1988
13. Shapiro LM, Zezulka A: Hypertrophic cardiomyopathy: A common disease with a good prognosis. Br Heart J **50**: 530, 1983