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Research Article

Association of genetic markers with cardiomyopathy

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ABSTRACT

Background: Cardiomyopathy is an anatomic and pathologic diagnosis associated with muscle or electrical dysfunction of the heart. Cardiomyopathies represent a heterogeneous group of diseases that often lead to progressive heart failure with significant morbidity and mortality. Cardiomyopathy and myocarditis resulted in 443,000 deaths in 2013 up from 294,000 in 1990. Objective: The main objective of the present study is to observe the association of cardiomyopathy and genetic markers such as red cell enzymes namely, Esterase D [ESD] and Super oxide dismutase [SOD] and plasma proteins namely, Haptoglobin [HP] and Group specific component [GC] systems.
Methods: In the present study, fifty cases presenting cardiomyopathy and fifty cases of age and sex matched healthy controls were included. Red cell enzymes were determined by standard agarose gel electrophoresis. Plasma samples were typed using PAGE electrophoresis. The statistical significance of differences between patients and controls were tested. Analysis of the data was carried out using Epi Info 5 software. Relative risk was calculated by the random-effects method. For odds ratio, confidence interval was calculated. The significance level was 5%.
Results: The inter group heterogeneity for ESD and SOD of red cell enzymes and GC system of plasma proteins was found to be a significant value (ESD: $\chi 2$ =10.2564; d.f. = 2; 0.01>p>0.001; SOD: $\chi 2$ = 11.1120; d.f. = 2; 0.01>p>0.001; GC: $\chi 2$ = 15.5044; d.f. = 2; p>0.001), when observed between cardiomyopathy patients and controls. Thus, all the examined groups were deviating from Hardy-Weinberg equilibrium indicating a significant association between cardiomyopathy and these red cell enzymes and plasma protein markers. There was a predominant occurrence of Haptoglobin 2 phenotype in patients when compared to controls. Risk estimates show significant association with both ESD and GC systems with an increased risk of 100% and more, indicating that individuals with ESD (2-2 and 2-1) and GC (2-1) phenotypes are more likely to get the disease when compared with the other phenotypes of the ESD and GC systems.
Conclusions: Out of seven genetic markers, four markers (ESD, SOD, HP and GC) are found to be significant i.e. they show some relation with the cardiomyopathy which influences the disease. Furthermore studies on genetic markers, to be attempted in future, would certainly enlighten us to assess the role of these polymorphic systems in different cardiomyopathies.

Keywords: Cardiomyopathy, Red cell enzymes, Plasma proteins, Polymorphism

INTRODUCTION

Cardiovascular disease (CVD) includes all diseases and conditions of the heart and blood vessels. The main types of CVD are: coronary heart disease, stroke, heart failure and cardiomyopathy, acute rheumatic fever and rheumatic heart disease, peripheral vascular disease and congenital heart disease.

Cardiomyopathy is a disease where the heart muscle becomes enlarged, thickened or stiff, reducing the effectiveness of the heart and causing heart failure. This is characterized by left and right ventricular failure in which some may be asymptomatic for years and others have acute onset. In this disorder, stroke volume and cardiac output are decreased and atypical chest pain occurs at rest. It is a progressive and chronic disease. It occurs in only 10-20 per 100,000 populations resulting in about 30,000 deaths/ year. The recent revision of the definition of a cardiomyopathy by the World Health Organization recognizes that ventricular dysfunction can result from a failure to correct volume or pressure overload in valve disease or to control hypertension. Loss of myocardium caused by coronary artery disease also leads to severe ventricular dysfunction. All of these end stage conditions are categorized as specific cardiomyopathies. The second form of cardiomyopathy is caused by intrinsic disorders of the myocardium itself and is subdivided on the basis of the pathophysiology. Such a functional rather than an etiological classification has drawbacks but reflects our current state of knowledge. The different functional abnormalities produce characteristic changes in ventricular shape are easily recognized in short axis echocardiographic planes by pathologists.[1] The 4 main types of cardiomyopathies are: Dilated cardiomyopathy (DCM), where both ventricles are involved, Hypertrophic cardiomyopathy (HCM), usually die by age 40 and Restrictive cardiomyopathy (RCM), the rarest form of cardiomyopathy and Arrhythmogenic RV (ARVC). As cardiomyopathy progresses, the heart becomes weaker and less able to pump blood through the body resulting in heart failure , arrhythmias, systemic and pulmonary edema and, more rarely, endocarditis.

Genetics of cardiomyopathy:

Dilated cardiomyopathy (DCM):

DCM refers to enlargement of the heart, which often affects all four chambers, especially late in the disease. Family-based studies of first-degree relatives during the past few decades have established that familial dilated cardiomyopathy (also known as familial DCM, or FDC) can be identified in 20 to over 50 percent of patients diagnosed with IDC by clinical screening of family members. Most familial DCM is transmitted in an autosomal dominant inheritance pattern, although all inheritance patterns have been identified (autosomal recessive, X-linked, and mitochondrial). During the past 15 years, familial DCM genetic studies have identified mutations in over 30 genes.

Hypertrophic cardiomyopathy (HCM):

The majority of HCM cases are caused by an inherited gene from parent to child. If a parent has HCM, his or her child will have a 50% chance of inheriting the HCM gene. This pattern of inheritance is called autosomal dominant. The disease does not skip generations. However, the manifestation of the disease varies greatly even in the same family. This means that one family member may have the HCM gene and develop severe symptoms, when another family member with the same gene may never develop any or only mild clinical signs of HCM. To date, disease-causing gene mutations have been identified in approximately two thirds of HCM cases, and some 50% of idiopathic familial DCM cases. Inherited cardiomyopathies show a wide range of clinical presentation within the same family, often with incomplete and age-dependent penetrance.

A number of genetic polymorphisms exist in human beings, which manifest variable susceptibilities towards pathogenesis and etiology of a particular disease. Some genetic markers might be serving some hidden important biological functions for understanding biological significance of polymorphisms in man. Special attention is being diverted towards the relationship between the genetic markers and human diseases. A biochemical marker will influence disease susceptibility which implies that some product related to gene determining biochemical trait or possibly the product of some closely linked genes take part in the complex mechanism influencing diseases. Biochemical genetic markers are of considerable importance in disease association studies. The existence of genetically determined polymorphisms of red cell enzymes and plasma proteins has led to more number of investigations into the possible correlations between these genetic markers and human diseases. We report here the polymorphism data of seven genetic markers: Esterase D (ESD) and Superoxide Dismutase (SOD), Haptoglobin (HP), Caeruloplasmin (CP), Group Specific Component (GC), Transferrin (TF) and Albumin (ALB). The main objective of the present study is to determine whether these genetic markers are predictors of Cardiomyopathy.

METHODS

Blood samples from a total of 50 Cardiomyopathy patients and 50 healthy normal individuals of both sexes were collected. The samples were collected from local hospitals of Visakhapatnam city, North Coastal Andhra Pradesh, South India. In this study seven genetic markers were studies. Of which, plasma proteins include Albumin (ALB), Haptoglobin (HP), Caeruloplasmin (CP), Group Specific Component (GC), Transferrin (TF) and red cell enzymes include: Esterase D (ESD) and Superoxide Dismutase (SOD). 3ml of intravenous blood samples were collected in sterile test tubes containing EDTA solution as an anticoagulant. The samples were brought to the laboratory in a thermos flask containing ice, within few hours of sample collection. The Plasma was separated. Fresh and clear hemolysates were prepared according to standard procedures and stored until further use. The plasma protein markers - Group Specific Component (GC), Transferrin (TF) and Albumin (ALB) were typed by acrylamide gel electrophoresis[2] and

Haptoglobin (HP) and Caeruloplasmin (CP) as described by Clark.[3] Esterase-D (ESD) and Superoxide dismutase (SOD) were typed by agarose gel electrophoresis described by Wraxall and Stolorow.[4]

The allele frequencies were estimated by maximum likelihood method[5] and statistical heterogeneity was tested using the standard χ^2 test.[6] Analysis of the data was carried out using Epi Info 5 software. Odds ratios and 95% confidence interval (95% CI) were calculated to assess the strength of the relationship between the biochemical markers and Cardiomyopathy. Pooled odds ratios and relative risk were calculated by the random-effects method of DerSimonian and Laird.[7] Estimates from the random effects model incorporate the variability among studies and represent a more conservative approach. For odds ratio, confidence interval was calculated. Increased risk was calculated using the formula: Increased Risk = (Relative Risk – 1.00) x 100. The significance level was 5%.

Multifactor Dimensionality Reduction (MDR) analysis was performed using MDR software (v. 3.0.2) to study case-control data, gene-gene interactions, and gene-environment interactions.[8,9] Best models with possible combinations of the polymorphisms were considered based on 10-fold cross validation and maximum testing accuracy. Once MDR identifies the best combination of factors, the final step is to determine which multifactor levels (genotypes) are high risk and which are at low risk using the entire data set. This final evaluation is conducted with a threshold ratio that is determined by the ratio of the number of affected individuals divided by the number of unaffected individuals in the data.

RESULTS

Biochemical markers include several enzyme markers and plasma proteins which play an important role in usual metabolism of human beings. Distribution of phenotypes and allele frequencies of genetic markers are shown in Table 1and 2 respectively.

Enzyme markers:

The present study includes enzyme markers Esterase D and Superoxide Dismutase.

In the present study, the frequency of the 1 and 2 alleles of ESD in controls were 81% and 19% with observed genotype frequencies of 68%, 26% and 6% for 1-1, 2-1 and 2-2 respectively. The frequency of ESD*1 and ESD*2 alleles in patients were 62% and 38% with observed genotype frequencies of 36%, 52% and 12% respectively. The study group showed the predominant occurrence of 2-1 phenotype in cardiomyopathy patients. The homogeneity test for goodness of fit between observed and expected phenotypes is statistically non-significant in both patients (χ^2 = 0.53623; d.f = 1; 0.50 > p > 0.30) and controls (χ^2 = 1.2142; d.f = 1; 0.30 > p > 0.20). The inter group heterogeneity was found to be (χ^2 = 10.2564; d.f. =2; (0.01>p>0.001), significant value when observed between cardiomyopathy patients and controls, indicating that patients group deviate from Hardy Weinberg equilibrium.

Considering SOD system, the frequency of the SOD*1 and SOD*2 alleles in patients were 90% and 10% with observed genotype frequencies of 80% and 20% for 1-1 and 2-1 respectively. On the other hand the electrophoretic separation for red cell superoxide dismutase among controls revealed the presences of normal SOD 1-1 phenotype. The inter group heterogeneity was found to be a significant value (χ^2 = 11.1120; d.f. =2; (p>0.001), when observed between cardiomyopathy patients and controls.

Plasma proteins:

The plasma protein, haptoglobin system in patient group showed the predominant occurrence of Haptoglobin 2-2 phenotype (54%) when compared to controls (32%). The frequency of HP*1 and HP*2 alleles in patients are 36% and 64% and in controls it was 25% and 75% respectively. The chi- square test for homogeneity was found to be significant in controls (χ^2 = 7.5612; d.f = 1; 0.01 > p > 0.001) and non-significant in patients (χ^2 = 0.72016; d.f = 1; 0.50 > p > 0.30). The inter group heterogeneity test is statistically non- significant (χ^2 = 5.0970; d.f = 2; 0.10 > p>0.50**),** when observed between cardiomyopathy patients and controls.

Considering GC system in the present study, the patient group showed the predominant occurrence of GC 2-1 phenotype (34%) when compared to controls (10%). The allelic frequency in patient group was 95% of GC*1 allele and 5% of GC*2 allele, and the control group showed 73% of GC*1 allele and 27% of GC*2 allele. The chi- square test for homogeneity was found to be non-significant in patients (χ^2 = 0.94522; d.f = 1; 0.50 > p > 0.30) and controls (χ^2 = 0.1388; d.f = 1; 0.80 > p > 0.70). The inter group heterogeneity was found to be (χ^2 = 15.5044; d.f. =2; (p>0.001), significant value when observed between cardiomyopathy patients and controls**.**

In this study transferrin (TF), Caeruloplasmin (CP) and Albumin (ALB) locus were found to be monomorphic with the common allele C, B and N phenotypes respectively. Therefore, no association was observed between cardiomyopathy patients and TF, ALB and CP systems.

Test of association of ESD, HP and GC phenotypes with the disease condition compared to the control group, the odds ratio and relative risks for each genotype versus the other two are shown in Table 3.

Table 1: Distribution of red cell Enzyme and plasma protein phenotypes in cardiomyopathy patients and controls.

System	Phenotype	Cardiomyopathy Patients		Controls	
		Observed	**Expected**	**Observed**	**Expected**
ESD	1-1	18.00	19.22	34.00	32.81
	2-1	26.00	23.56	13.00	15.39
	2-2	6.00	7.22	3.00	1.80
	Total	**50.00**	**50.00**	**50.00**	**50.00**
Chi-square (χ^2)			**χ^2=0.5362** (0.50>p>0.30)		**χ^2=0.5362** (0.50>p>0.30)
SOD-A	1-1	40.00	40.50	50.00	-
	2-1	10.00	9.00	-	-
	2-2	00.00	0.50	-	-
	Total	**50.00**	**50.00**	**50.00**	-
Chi-square (χ^2)			**χ^2=0.6172** (0.50>p>0.30)	-	
HP	1-1	2.00	3.13	2.00	6.48
	2-1	21.00	18.75	32.00	23.04
	2-2	27.00	28.12	16.00	20.48
	Total	**50.00**	**50.00**	**50.00**	**50.00**
Chi-square (χ^2)			**χ^2=0.72016** (0.50>p>0.30)		**χ^2=7.5612** (0.01>p>0.001)
GC	1-1	28.00	26.65	45.00	45.13
	2-1	17.00	19.71	5.00	4.75
	2-2	5.00	3.64	0.00	0.12
	Total	**50.00**	**50.00**	**50.00**	**50.00**
Chi-square (χ^2)			**χ^2=0.94522** (0.50>p>0.30)		**χ^2=0.1388** (0.80>p>0.70)
TF	C	50.00	-	50.00	-
ALB	N	50.00	-	50.00	-
CP	B	50.00	-	50.00	-

Table 2: Distribution of red cell enzyme and plasma protein allele frequencies in cardiomyopathy patients and controls.

System	Allele	Patients	Controls	Intergroup Heterogeneity
ESD	1	0.6200 ± 0.3432	0.8100 ± 0.0392	
	2	0.3800 ± 0.3432	0.1900 ± 0.0392	10.2564
SOD	1	0.9000 ± 0.0300	1.0000 ± 0.0000	
	2	0.1000 ± 0.0300	-	11.1120
HP	1	0.2500 ± 0.0433	0.3600 ± 0.0480	
	2	0.7500 ± 0.0433	0.6400 ± 0.0480	5.0970
GC	1	0.7300 ± 0.0444	0.9500 ± 0.0218	
	2	0.2700 ± 0.0444	0.0500 ± 0.0218	15.5044
TF	C	1.0000 ± 0.0000	1.0000 ± 0.0000	-
ALB	N	1.0000 ± 0.0000	1.0000 ± 0.0000	-
CP	B	1.0000 ± 0.0000	1.0000 ± 0.0000	-

Table 3: Test of association, relative risk and odds ratio estimates of ESD, HP and GC phenotypes in disease and control groups.

System	Phenotype combinations	Control (n)	Cardiomyopathy				
			(n)	RR	OR	95%CI	χ^2 values
ESD	1-1 vs. 2-1 + 2-2	34	18	0.53	0.26	0.11-0.65	10.26
	2-1 vs. 1-1 + 2-2	13	26	2.00	3.08	1.23-7.83	7.10
	2-2 vs. 1-1 + 2-1	03	06	2.00	2.14	0.44-11.60	1.10
HP	1-1 vs. 2-1 + 2-2	02	02	1.00	1.00	0.10-10.47	0.00
	2-1 vs. 1-1 + 2-2	32	21	-	0.41	0.17-0.98	4.86
	2-2 vs. 1-1 + 2-1	16	27	1.69	2.49	1.02-6.13	4.94
GC	1-1 vs. 2-1 + 2-2	45	28	0.62	0.14	0.04-0.46	14.66
	2-1 vs. 1-1 + 2-2	05	17	3.40	4.64	1.41-16.14	8.39
	2-2 vs. 1-1 + 2-1	00	05	-	-	-	5.26

In ESD system, patients with homozygotes 2-2 phenotype and heterozygotes 2-1 phenotypes were at an increased risk of cardiomyopathy, with an overall odds ratio of 3.08 (95% C.I: 1.23-7.83, p = 0.007) by the method of Der Simonian and Laird. Risk estimates also show a significant association of ESD 2-2 and 2-1 phenotypes with cardiomyopathy (RR = 2.00) individuals. The result shows an increased risk of 100% more, indicating that ESD 2-2 and 2-1 individuals are two times more likely to get the disease when compared with the other phenotype of the ESD system.

An increased predisposition of homozygous HP 2-2 phenotype was observed in individuals with cardiomyopathy ($\chi 2$ = 4.9400*). Homozygous 2-2 individuals were at increased risk of cardiomyopathy, with an overall odds ratio of 2.49 (95% Confidence Interval: 1.02 - 6.13). Risk estimates show a significant association of HP 2-2 phenotype with cardiomyopathy individuals (RR = 1.69).

An increased predisposition of heterozygous GC 2-1 phenotype was observed in individuals with cardiomyopathy ($\chi 2$ = 8.3900*). Heterozygous 2-1 individuals were at increased risk of cardiomyopathy, with an overall odds ratio of 4.64 (95% Confidence Interval: 1.41 –16.14). Risk estimates show a significant association of GC 2-1 phenotype with cardiomyopathy individuals (RR = 3.40). The result shows an increased risk of 100% and more, indicating that individuals with 2-1 phenotype are three times more likely to get the disease when compared with the other phenotypes of the GC system.

In the cell in the figure, the left bands represent the disease case, and the right bands represent the control case. High-risk combinations are depicted as darkly shaded cells, low-risk combinations as lightly shaded cells (Figure 1).

Table 4: Results of MDR analysis on genetic factors.

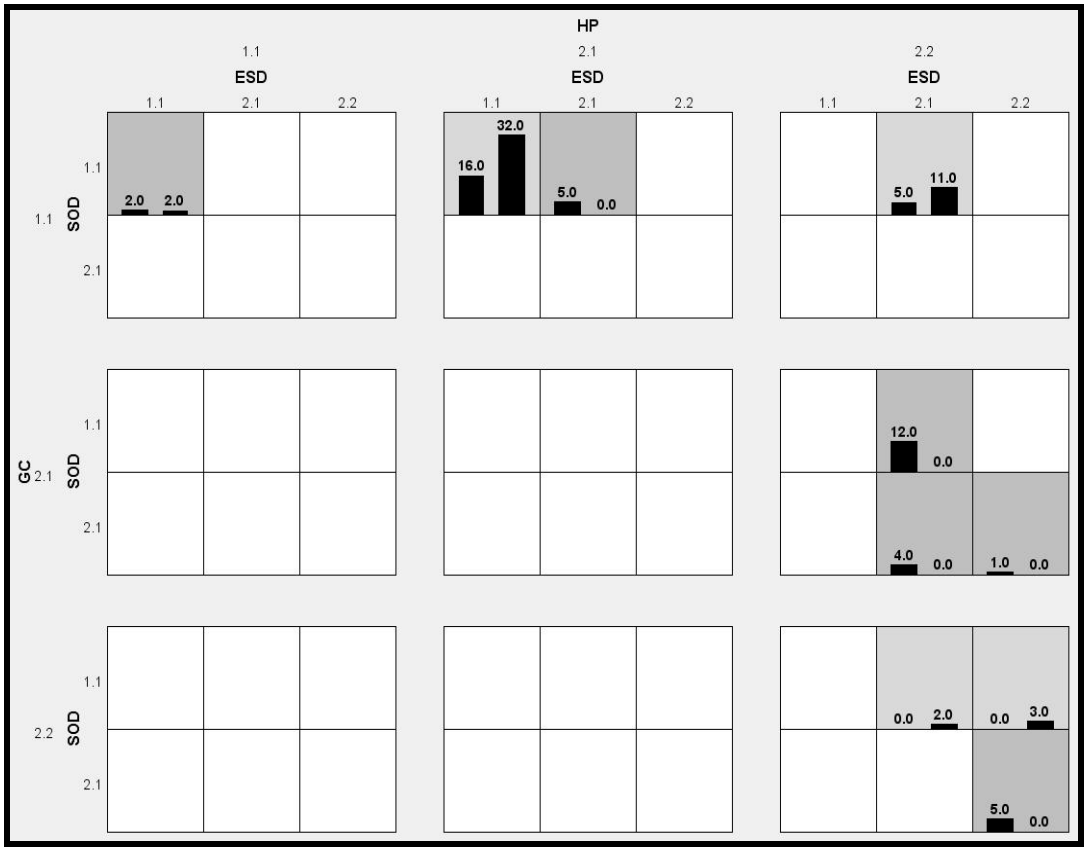
No. of loci	Polymorphism Model	Testing Accuracy	CVC	Prediction error (%)
1	GC	0.61	9/10	39.0
2	SOD, GC	0.69	9/10	31.0***
3	ESD, HP, GC	0.70	9/10	30.0***
4	ESD, SOD, HP, GC	0.76	10/10	24.0***

***P≤0.001 based on 1000 permutations.

MDR software was used to analyse the interaction of the 4 factors that may affect the cardiomyopathy, and the results were detailed in Tables 4 and 5. We found that the cross-validation (CV) consistency of the four-factor model (ESD, SOD, HP and GC) was maximal (10/10), and the accuracy of the test samples was the highest (0.76). Permutation testing was used to perform a hypothesis test and evaluate its statistical significance. Thus, the two-factor, three-factor and four-factor interaction models were the best models, which shows that there was an interaction between the four SNP's (p<0.001). Thus the 2-way, 3-way and 4-way models are found to be significant. Table 5 summarizes the four locus genotype combinations associated with high risk and with low risk, along with the corresponding distribution of cases and of controls, for each multilocus genotype combination.

Table 5: Distribution of high-risk and low-risk genotypes in the best four locus model.

Pattern	Multilocus–genotype combinations				Number of		Case/ control ratio	Association with cardiomyopathy
	ESD	SOD	HP	GC	cases	controls		
1	1.1	1.1	1.1	1.1	2	2	1.0	High-risk
2	1.1	1.1	2.1	1.1	16	32	0.5	Low-risk
3	2.1	1.1	2.1	1.1	5	0	∞	High-risk
4	2.1	1.1	2.2	1.1	5	11	0.4	Low-risk
5	2.1	1.1	2.2	2.1	12	0	∞	High-risk
6	2.1	1.1	2.2	2.2	0	2	0.0	Low-risk
7	2.1	2.1	2.2	2.1	4	0	∞	High-risk
8	2.2	1.1	2.2	2.2	0	3	0.0	Low-risk
9	2.2	2.1	2.2	2.1	1	0	∞	High-risk
10	2.2	2.1	2.2	2.2	5	0	∞	High-risk



*In the cell in the figure, the left bands represent the disease case, and the right bands represent the control case. High-risk combinations are depicted as darkly shaded cells, low-risk combinations as lightly shaded cells.

Figure 1: An MDR Analysis of the four-factors (ESD, SOD, HP, GC) - interaction model of cardiomyopathy.

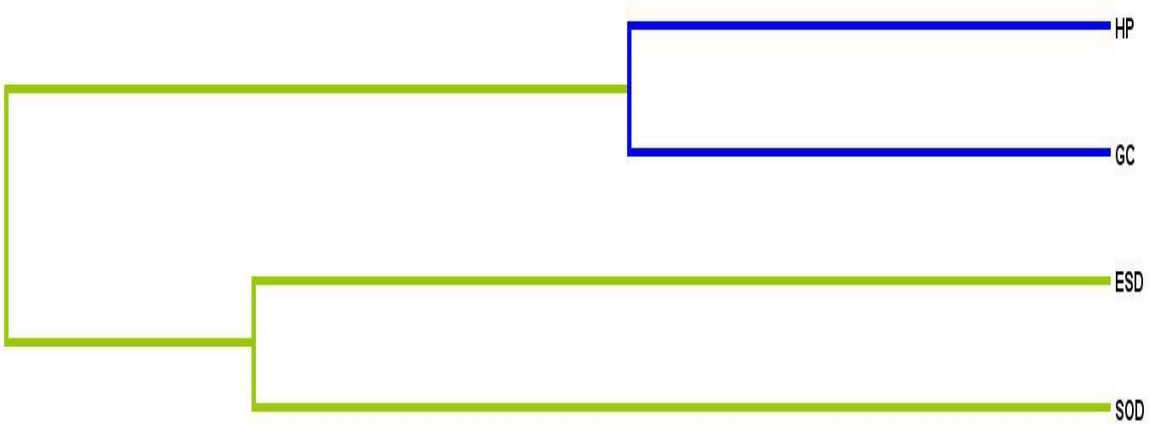


Figure 2: A tree diagram of the interactions among three factors (ESD, SOD, HP and GC) for cardiomyopathy, as analyzed by MDR.

The cell is labeled as either high risk if the case–control ratio reaches or exceeds a predetermined threshold (for example, 1) and low risk if it does not reach this threshold (Fig. 1). The interaction information analysis revealed a strong synergism between the four SNPs markers ESD, SOD, HP and GC, contributing to cardiomyopathy. The dendrogram (Fig. 2) depicts the location of longitudinal connecting bars indicating the strength of the dependence: Green bars represent weaker associations and Blue bars represent stronger associations.

DISCUSSION

The human Esterase D gene, has been localized cytogenetically to the same sub band of chromosome 13q 14:11. Esterases belong to the family of nonspecific enzymes that catalyze the hydrolysis of esters. Human ESD is the dimeric enzyme in that it displays several phenotypes as a result of the expression of co-dominant autosomal alleles, primarily allele ESD 1 and ESD 2. The activity of ESD enzyme depends on the normal function of the ESD gene. Consequently, absence, complete or partial inactivation, deletion of one ESD allele, mutation or other alternations in ESD sequences will result in decreasing of ESD activity. In our study the chi square test for heterogeneity was found to be significant when observed between cardiomyopathy patients and controls.

The enzyme superoxide dismutase (SOD), catalyses the dismutation of superoxide into oxygen and hydrogen peroxide. As such, it is an important antioxidant defense in nearly all cells exposed to oxygen. SOD catalyses the destruction of the O_2- free radicals. It protects oxygen metabolizing cells against harmful effects of superoxide free-radicals. Fridovich[10] reported that SOD, is a genetic marker acts as an antioxidant and catalyses the dismutation of oxygen radicals to yield hydrogen peroxide and oxygen, which has been implicated as being essential in defence against the potential toxicity of oxygen. Two identifiable isoenzymes SOD A, a cytoplasmic, soluble, Cu-Zn containing enzyme and SOD B, a mitochondrial, insoluble, Mn. containing enzyme is encode by genes localized on 6q25.3 and 21q22.1 chromosomes respectively. The SOD system was found to be a significant in our study, when observed between cardiomyopathy patients and controls.

Haptoglobin is positive acute phase protein that binds free hemoglobin and removes it from the circulation to prevent kidney injury and iron loss following hemolysis. Also, by binding free hemoglobin, hemoglobin functions as an antioxidant. In addition, haptoglobin acts as a potent immunosuppressor of lymphocyte function and modulates the helper T-cell types 1 and 2 (Th 1/Th2) balance within the body. In our results, HP 2-2 phenotype shows odds of two fold compared to the HP 1-1 phenotype. Likewise, in the Strong Heart Study (SHS) among American Indians with CVD-DM, the HP 2-2 phenotype showed odds of almost fivefold (OR=4.96, 95% CI=1.85–3.33) compared to the HP 1-1 phenotype.[11] Chapelle et al showed that following a myocardial infraction, the severity and extent of myocardial damage was much greater in patients with HP 2-2 than in those with HP 1-1 or HP 2-1.[12] Our findings are inconsistent with a recently reported prospective study from Andhra Pradesh demonstrating increased cardiac mortality in patients with the HP 2-2 phenotype.[13] The group-specific component (GC) is the major vitamin D-binding protein in plasma. The gene encoding GC is linked, on human chromosome 4, to the albumin and alpha-fetoprotein genes. The GC system was found to be a significant in our study, when observed between cardiomyopathy patients and controls.

CONCLUSION

Cardiomyopathies are a heterogeneous group of heart muscle disorders responsible for a great deal of morbidity and mortality. It forms a major issue not only for the

prevention of the disease but also for its cure. There are various biochemical and molecular applications for its identification and diagnosis. The present study undergone through the biochemical approach was to identify the association of various red cell and plasma protein markers based on qualitative studies in cardiomyopathy patients. Out of seven genetic markers, four markers (ESD, SOD, HP and GC) are found to be significant i.e. they show some relation with the cardiomyopathy which influences the disease. However, it may be concluded that the results detected in the present study need to be tested on a larger scale.

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REFERENCES

1. Davies MJ. The cardiomyopathies: an overview. St George's Hospital Medical School, Histopathology Department, London, UK, Heart. 2000;83:469–474.
2. Clark JT. Simplified "Disc" (Polyacrylamide) electrophoresis. Ann NY Acad Sci. 1964;121:428-36.
3. Kitchin, FD, Bearn AG. The electrophoretic patterns of normal and variant phenotypes of the Group Specific Components (GC) in human serum. Amer J Hum Genet. 1966;18:201-14.
4. Wraxall BGD, Stolorow MD. The simultaneous separation of the enzymes Glyoxylase-I, Esterase-D amd Phosphoglucomutase. J Forens Sci. 1986;31:1439-49.
5. Balakrishnan V. Hardy-Weinberg equilibrium and allele frequency estimation. In: Malhotra KC (Ed) Statistical Methods in human population genetics, IBRAD, ISI and ISHG, Calcutta. 1988; pp.39-93.
6. Taylor GL, Prior AM. Blood groups in England II distribution in the population. Ann Eugen. 1938;8:356 –61.
7. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7:77–88.
8. Ritchie MD, Hahn LW, Moore JH. Power of multifactor-dimensionality reduction for detecting gene-gene in teractions in the presence of genotyping error, missing data, phenocopy, and genetic heterogeneity. Genet Epidemiol. 2003;24:150–7.
9. Moore JH. Computational analysis of gene-gene interactions using multifactor dimensionality reduction. Expert Rev Mol Diagn. 4:795–803.
10. Fridovich I. Superoxide radical: an endogenous toxicant. Annu Rev Pharmacol Toxicol. 1983;23:239–57.
11. Levy AP, Roguin A, Hochberg I, et al. Haptoglobin phenotype and vascular complications in diabetes. N Eng J Med. 2000;343:969–70.
12. Chapelle JP, Albert A, Smeets JP, Marechal JP, Heusghem C, Kulbertus HE. Effect of the haptoglobin phenotype on the size of a myocardial infarct. N Engl J Med. 1982;307:457–63.
13. Sushma M, Ramesh M, Geethakumari K, Laxmipathi T, Sudhakar G. Association of genetic markers of cardiovascular disease with type 2 diabetes. International Journal of Current Research. 2013:5(12):4041-4.

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