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STUDY OF PHARMACOLOGICAL MANAGEMENT OF PATIENTS SUFFERING FROM DILATED CARDIOMYOPATHY

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ABSTRACT

Dilated Cardiomyopathy represents a significant health problem as it can lead to progressive refractory heart failure and represents the majority of indications for heart transplantations. In dilated cardiomyopathy, the heart is enlarged, all the chambers are severely dilated and the heart muscle is pale and flabby. A descriptive cross-sectional hospital based study was carried out in the patients admitted with dilated cardiomyopathy at Shahid Gangalal National Heart Centre. The study was carried out for three months from July to October 2014. Structured questionnaire was used as a tool for the collection of information through interview with the patient or care-taker during the hospital stay. The primary data collection included demographic pattern, risk factors, symptoms, diagnostic criteria, blood tests, medication pattern. Among the 100 patients, there were 51 male and 49 female. In the study group, 40% of the patients were smokers and 30% of the patients were drinkers, 43% of the patients were associated with either of the disease hypertension, diabetes mellitus and chronic obstructive pulmonary disease. Among 49 women, 5 women were associated with peripartum and postpartum dilated cardiomyopathy. All patients were presented with dilation of left ventricle. All patients were treated with loop diuretics and were also treated with Aldosterone antagonist, ACE inhibitors, Beta blockers, inotropic agents, Antiplatelet

and statins. The average cost of the treatment of the patients with dilated cardiomyopathy was found to be expensive. The patients were managed pharmacologically to prevent the deterioration of the disease and to treat the underlying symptoms.

KEYWORDS: Dilated Cardiomyopathy, Idiopathic, Peripartum, Mitral, Dilation.

INTRODUCTION

Cardiomyopathies are a heterogeneous group of diseases of the myocardium associated with mechanical and/or electrical dysfunction that usually (but not invariably) exhibit inappropriate ventricular hypertrophy or dilatation and are due to a variety of causes that frequently are genetic. Cardiomyopathies either are confined to the heart or are part of generalized systemic disorders, often leading to cardiovascular death or progressive heart failure–related disability.[1]

Dilated cardiomyopathy (DCM) is characterized by left ventricular dilatation and systolic dysfunction in the absence of hypertension, coronary artery disease, valve disease, congenital heart disease, and other overloading conditions. Left ventricular diastolic dysfunction may coexist, and atrial dilation as well as right ventricular dilation and dysfunction can also develop. It may be idiopathic, familial/genetic, viral and/or immune, alcoholic/toxic, or associated with recognized cardiovascular disease in which the degree of myocardial dysfunction is not explained by the abnormal loading conditions or the extent of ischaemic damage. Dilated cardiomyopathy represents a significant health problem as it can lead to progressive refractory heart failure, and represents the majority of heart transplantation indications.[2]

A large number of cardiac and systemic diseases can cause systolic impairment and left ventricular dilatation, but in the majority of patients no identifiable cause is found-hence the term “idiopathic” dilated cardiomyopathy (IDC). There are experimental and clinical data in animals and humans suggesting that genetic, viral and immune factors contribute to the pathophysiology of Idiopathic Dilated Cardiomyopathy.[3]

Dilated cardiomyopathy is the most common cardiomyopathy worldwide and accounts for 25% of heart failure cases in the USA. Incidence of the disease discovered at autopsy was estimated at 4.5/100 000/year (24 cases), while clinical incidence in the same period was 2.45/100 000/year (13 cases). This is a total incidence of 6.95/100 000 new cases a year.[4]

Dilated cardiomyopathy represents a significant health problem as it can lead to progressive refractory heart failure, and represents the majority of heart transplantation indications. This condition is also associated with a high rate of sudden death due to ventricular arrhythmias and a high mortality rate of 15% to 50% at 5 years. The prevalence of dilated cardiomyopathy in the US population, using diagnostic criteria for advanced disease, was estimated to be 36.5 per 100000 persons.[2]

Though it seems likely that women of reproductive age all over the world have some risk of developing PPCM, good data about incidence are unavailable because so few population-based registries exist. Recent reports suggest an estimated incidence of one case per 299 live births in Haiti, one case per 1000 live births in South Africa, and one case per 2289 live births to one case per 4000 live births in the USA.[5]

In Nepal, an observational study on non-moderate chronic drinkers was carried out at Department of Cardiology, College of Medical Sciences, Bharatpur. Clinical evaluation along with detail sonographic study of heart and liver showed a strongly positive relationship on the coexistence of chronic liver disease and cardiomyopathy among the non-moderate drinkers.[6] DCM is characterized by dilatation and impaired contraction of either the left ventricle or both ventricles, as a result of altered structure or function in diseased cardiomyocytes. Before the heart becomes dilated and weak, there is either an index event (e.g., a myocardial infarction or acute myocarditis) that leads to impaired ventricular contractility, or progression of underlying disease (e.g., severe valvular regurgitation) that leads to ventricular pressure overload causing systolic dysfunction. Because of ventricular systolic dysfunction, gradual compensatory responses of the cardiomyocytes lead to cardiac remodelling. Initially the cardiomyocytes respond by becoming hypertrophied, but the poorly functioning ventricle gradually dilates to handle the progressive volume overload. Hypertrophy is judged as the ratio of LV mass to cavity size; this ratio is decreased in persons with dilated cardiomyopathies. The enlargement of the remaining heart chambers is primarily due to Left Ventricular failure. Progressive dilation can lead to significant mitral and tricuspid regurgitation, which may further diminish the cardiac output and increase end-systolic volumes and ventricular wall stress. In turn, this leads to further dilation and myocardial dysfunction.[7]

MATERIALS AND METHODS

Materials

Structured questionnaire was used as a tool for the collection of information through interview with the patient or care-taker during the hospital stay.

Study Design

The study was cross-sectional descriptive. The patients admitted with dilated cardiomyopathy were included in the study and their emergency and further treatment was studied. Patients were observed for any signs and symptoms of complication during their stay in hospital and the treatment regimen during their stay was studied.

Study Site and Duration

The study was carried out at Shahid Gangalal National Heart centre, Kathmandu, Nepal. The study was carried out for a period of 3 months starting from July 2014 to October 2014.

Study Variables

The study variables included demographic pattern, chief complaints, duration of symptoms, source of admission, risk factors. The risk factors that were defined were pregnancy, smoking habit, drinking habit, obesity, hypertension (previous or newly identified), Diabetes mellitus, and Chronic Obstructive Pulmonary disease.

Sampling Technique and Sample Size

The sampling technique was non-randomized sampling and the samples were collected from the patients who meet the inclusion criteria. The sample size of the study was 100.

Criteria for selection of patients

Inclusion Criteria

All those admitted patients who have been diagnosed with dilated cardiomyopathy.

Exclusion Criteria

The patients with Hypertrophic Cardiomyopathy, Ischemic Cardiomyopathy, Pericardial diseases, Systemic arterial hypertension, Coronary heart disease, Congenital heart disease.

Statistical Analysis

The statistical analysis of the results was performed by the 20th version of SPSS.

Ethical Consideration

An institutional approval was taken from institutional review board of Shahid Gangalal National Heart Centre, and permission from the concerned authorities was taken before the study. Prior to collection of the data, written consent was taken from the patients for the study. The identity of the patient was not disclosed. All the research activities were carried out under the close guidance of supervisor.

RESULT AND DISCUSSION

The study was carried out in 100 patients of whom the demographic pattern was observed, risk factors were analysed, diagnostic criteria was monitored, and the prescription pattern study and cost analysis was done.

Age and Sex distribution

The age group distribution of dilated cardiomyopathy was found to large ranging from 21 years to 93 years. About 34% of the patients belonged to the age group of 70-79 years. The age group of the patients is related to the incidence of the disease, affecting many people in the later stages of life. However, due to large number of risk factors, genetic linkage, co-morbid diseases and idiopathic nature of the disease, no specific distribution of the disease in particular age group was found in this study.

In previous studies carried out in Finland, of the 808 potential cases screened, 118 infants, children and adolescents, representing an average age-specific population of 1.4 million, were definitely identified as having idiopathic cardiomyopathy.[8] However in this study, no patients diagnosed with dilated cardiomyopathy where below the age of 20 years.

The distribution of the disease in both male and female was found to be almost similar. Even though there are no previous study to conclude the incidence of the disease in particular gender, studies in other heart disease has shown that the heart disease is more prevalent in males than in females.[9,10]

Risk Factors

From the study of the 100 patients, the risk factors associated with the disease was found to be smoking habit, drinking habit, hypertension, diabetes, chronic obstructive pulmonary disease, obesity and pregnancy.

The study showed that 40% of the patients were smokers or had the history of smoking. The patients who used to smoke but had stopped smoking for greater than a year were categorised as ex-smokers.[11,12] According to a study carried out among men younger than 55, the relative risk of diffuse hypokinesis was 2.78 for heavy smokers as compared with non-smokers.[13] These results suggest that smoking is related to cardiomyopathy and that the relationships are largely separate from the association of smoking with coronary stenosis. According to a study of the pathophysiology of ciggrate smoking and cardiovascular disease showed that, even though the precise mechanisms responsible remain undetermined, free radical-mediated oxidative stress appears to play a central role in Ciggrate smoking mediated cardiovascular diseases. These free radicals could potentially arise directly from cigarette smoke and indirectly from endogenous sources as well.[14]

A total of 30% of the patients were associated with drinking alcohol on regular basis or occasionally. Among them, male patients were greater in number who had the habit of drinking alcohol. The patients who had habit of drinking alcohol but had stopped drinking for greater than a year were categorised as ex-drinkers.[15] The previous showed that the prevalence of alcoholic women with dilated cardiomyopathy was found to be similar to that of alcoholic men, although women required a lower total lifetime dose of ethanol to develop the disease.[16]

The study showed that 43% of the patients who were diagnosed with dilated cardiomyopathy were associated with either of the risk factors.ie. Hypertension, Diabetes mellitus, Chronic obstructive pulmonary disease. Among them, 2% of the patients had all these risk factors. The study by Coughlin et al showed that diabetics, particularly those with a history of hypertension, may be at increased risk of dilated cardiomyopathy.[17]

Among the women who were diagnosed with dilated cardiomyopathy, the 5 cases were associated with pregnancy. 3 patients had peripartum dilated cardiomyopathy and 2 patients had postpartum dilated cardiomyopathy. The study suggests pregnancy as one of the possible risk factors of dilated cardiomyopathy in women. The patients were considered of having peripartum dilated cardiomyopathy if DCM was seen during third trimester of pregnancy or the first five months postpartum.[1]

Diagnostic Characteristics

The electrocardiography done on patients showed that the 26% patients had the heart rhythm of atrial fibrillation, which is the most sustained cardiac arrhythmia. The study on etiological profile and clinical presentation of patients with atrial fibrillation from a rural area of Bihar showed that 15.15% of patients presented with atrial fibrillation was diagnosed with dilated cardiomyopathy.[18]

The study showed that the patients diagnosed with dilated cardiomyopathy had an ejection fraction of less than 40%. Most patients were diagnosed with ejection fraction of 20% indicating a progression to heart failure. One patient had the ejection fraction of 10% which needed critical support for the heart to pump the blood (Dobutamine, Nor-adrenaline, Oxygen).

Among the patients, mitral regurgitation was detected in 89% of the patients among which 33 patients had mild regurgitation, 36 patients had moderate regurgitation and 19 patients had severe regurgitation. The previous study on dilated cardiomyopathy with mitral regurgitation showed that mitral regurgitation was detected in 57% of the patients which showed that mitral regurgitation is a sensitive marker of decreased survival.[19]

The tricuspid regurgitation was detected in 78% of the patients, among which 45 patients had mild regurgitation, 17 patients had moderate regurgitation and 10 patients had severe regurgitation. The study also showed that the wall motion abnormality was detected in all patients. The abnormality was detected as Global Left ventricular wall hypokinesia. Non-ischemic dilated cardiomyopathy (NICM) is associated with diffuse global hypokinesia on echocardiography. However, NICM also may be associated with segmental wall-motion abnormalities (SWMAs) even in the presence of global hypokinesia, probably secondary to patchy myocardial scars.[20]

The study showed that the left ventricular internal diameter in diastole and systole was increased in majority of the patients. The previous study on epidemiological study of dilated cardiomyopathy in India also showed increased left ventricular internal diameter in diastole and systole.[21] The study of Paul et al showed that left ventricular systolic diameter (LVIDs) was positively correlated with left atrial size. Thus, more the left ventricular systolic dimensions (LVIDs), the more is the left atrial size.

In this study, it was seen that the dilation of left ventricle was prominent in all patients. The dilation of left atrial was seen in 39% of the patients whereas dilation of overall heart was observed in 31% of the patients. A study showed that left atrial size is the principal independent predictor of prognosis in patients with dilated cardiomyopathy in that patients with left atrial dilation had an increase in mortality and a worse clinical outcome compared with those without left atrial dilation.[22] In another study, it was seen that, Patients with dilated cardiomyopathy represent a heterogeneous group with regard to both clinical outcome and the relative degree of left and right ventricular chamber dilation. Patients in the predominant and disproportionate dilation of left ventricle appear to have better overall survival and less severe mitral and tricuspid regurgitation than do patients with a relatively equal degree of left and right ventricular dilation.[23]

PRESCRIPTION PATTERN

All patients were treated with loop diuretics furosemide and or torsemide. According to ACC/AHA guidelines for heart failure, diuretics are recommended in patients with reduced ejection fraction and are the only drugs used for the treatment that can adequately control the fluid retention.

Spironolactone in combination with furosemide was given to 84% of the patients. During monitored treadmill exercise, a significant improvement in ventricular arrhythmia was found in the group receiving spironolactone. The finding on the previous study suggests that aldosterone may contribute to the incidence of ventricular arrhythmia in patients with chronic heart failure, and spironolactone helps reduce this complication.[24]

About 54% of the patients were treated with the combination of Furosemide, Enalapril and Spironolactone. In as study carried to observe the therapeutic effect of the drugs on, the combined treatment of, enalapril, furosemide, spironolactone for chronic congestive heart failure significantly reduced the patients' symptoms, improve the quality of life, which was safe and effective.[25] If dilated cardiomyopathy with low ejection fraction is present, therapy with angiotensin-converting enzyme inhibitors, digoxin, diuretics, beta-blockers and spironolactone is indicated.[26]

About 16% of the patients were administered with carvedilol. In a study to determine the effect of beta-blockers on circulating levels of inflammatory and anti-inflammatory cytokines in patients with dilated cardiomyopathy, the results indicate that the suppression of left

ventricular remodelling and the improvement of prognosis in patients with dilated cardiomyopathies are markedly stronger in the beta-blocker group than in the angiotensin-converting enzyme inhibitor group. Thus, beta-blocker should be added to patients with dilated cardiomyopathy treated with an angiotensin-converting enzyme inhibitor.[27] In another controlled study of the effects of carvedilol in patients with dilated cardiomyopathy, the addition of carvedilol to treatment with digoxin, ACE inhibitors and diuretics are associated with a significant improvement in symptoms and in LV function and suppression of inflammatory cytokines.[28]

Atorvastatin was indicated for 19% patients. In a study of usefulness of atorvastatin in Patients with heart failure due to inflammatory dilated cardiomyopathy and elevated cholesterol levels, the results demonstrate that treatment with atorvastatin in addition to standard therapy for heart failure may significantly improve clinical outcomes in this cohort of patients.[29]

About 51% of the patients were administered multi-vitamins. The previous study showed that thiamine deficiency was significantly more frequent in patients with cardiac disease, occurring in 1/3 of the patients, raising the possibility that the systematic replacement of that micronutrient might contribute to better myocardial performance in patients taking diuretics for prolonged periods.[30]

Even though previous studies have shown high number of cases of ischemic cardiomyopathy, no cases were identified in this study because no history of myocardial infraction was identified during admission and no angiogram was done in majority of the cases.

Cost Analysis

The average cost of cardiac drugs that the patients have to take per day during their hospital stay was found to be Rs. 37.03 and the average cost of other drugs was found to be Rs. 81.67.

Tables and Figures

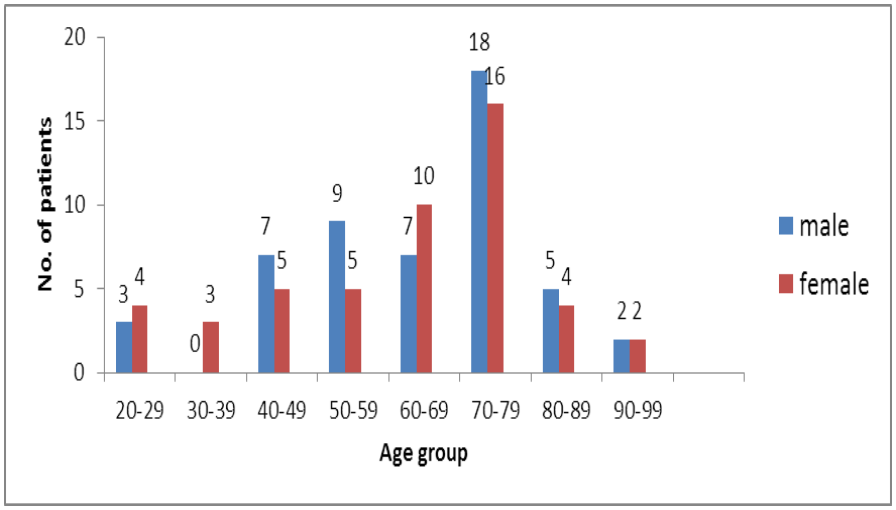

Figure 1: Age and Sex distribution of the study population.

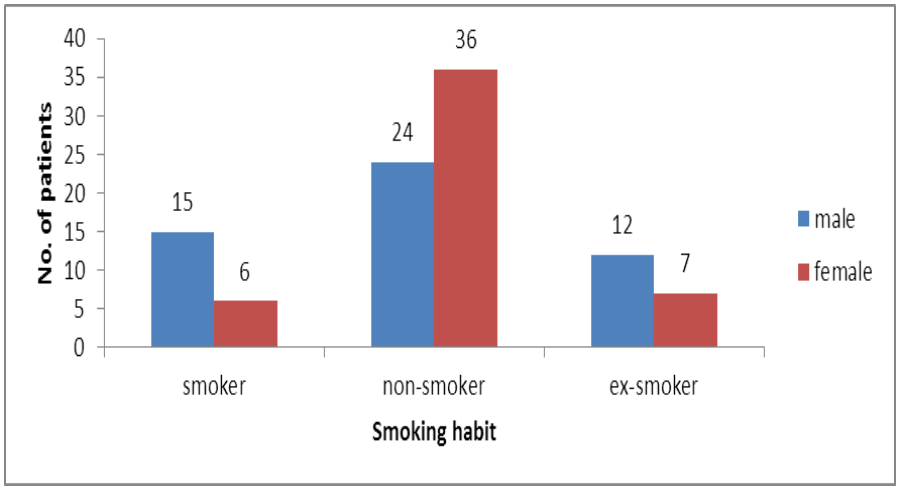

Figure 2: Smoking habit of the study population.

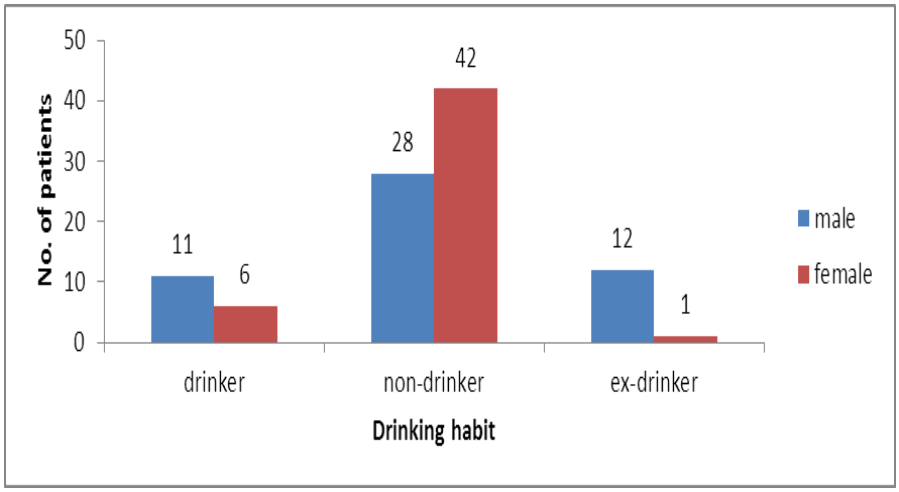

Figure 3: Drinking habit of the study population.

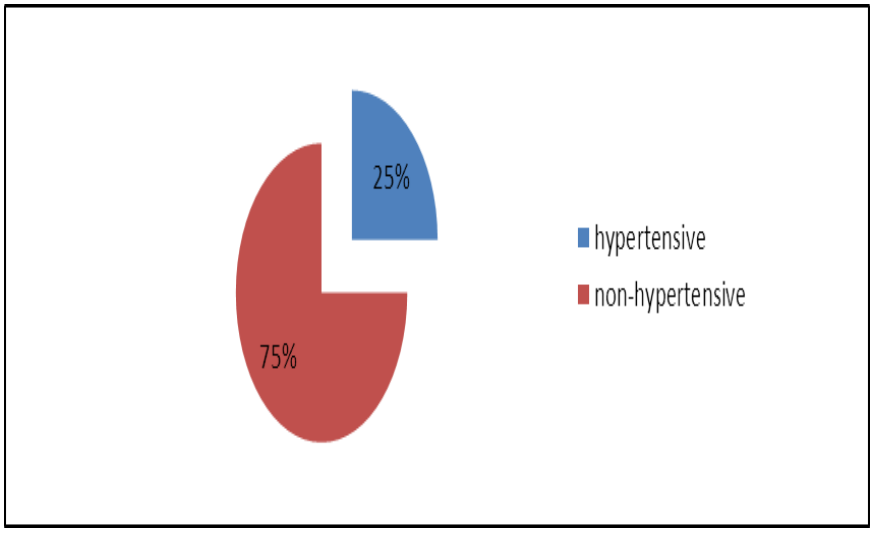

Figure 4: Percentage of hypertensive patients.

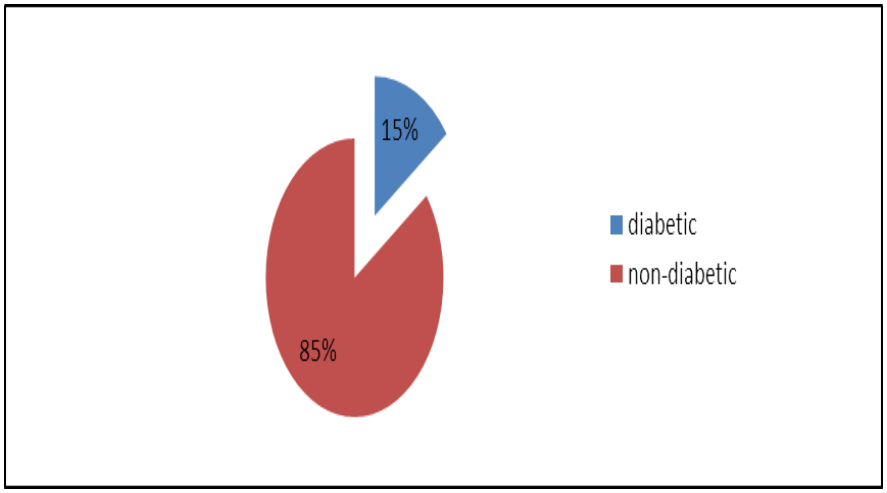

Figure 5: Percentage of diabetic patients.

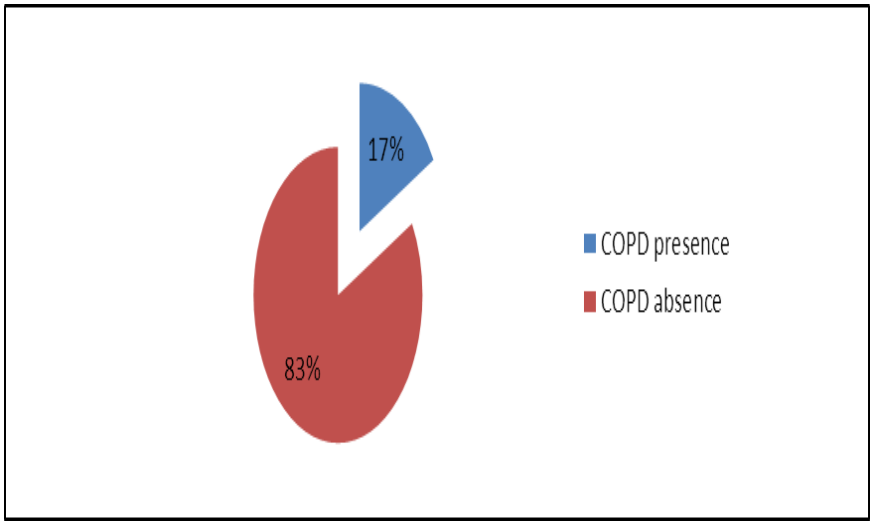

Figure 6: Percentage of chronic obstructive pulmonary disease patients.

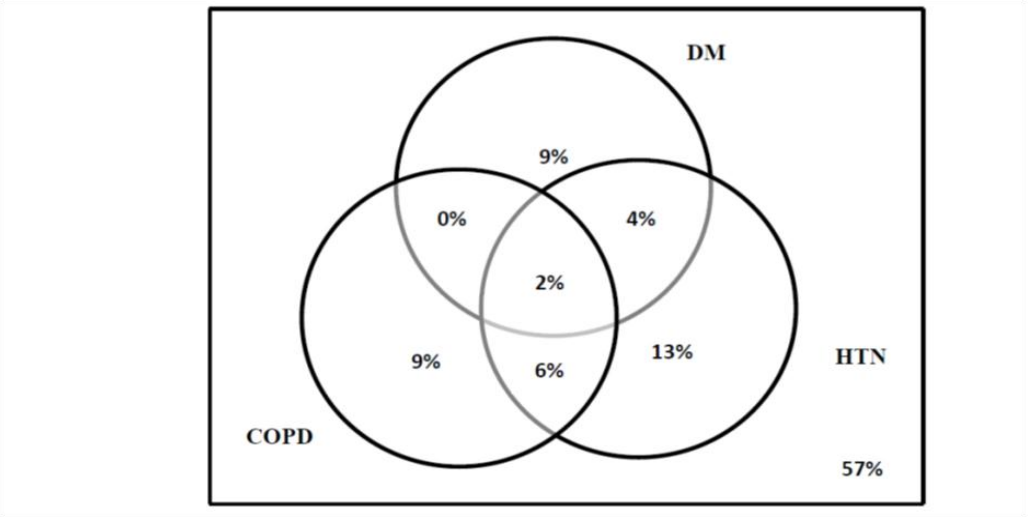

Figure 7: Cumulative risk factors in patients.

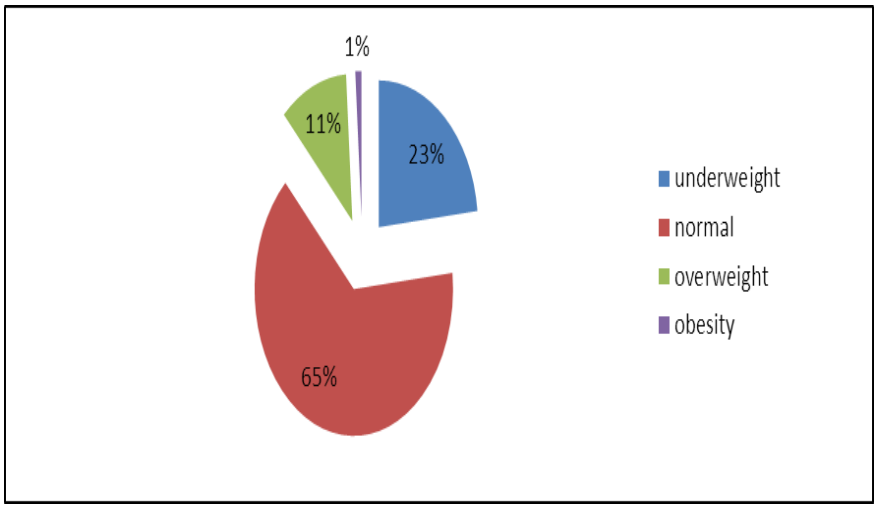

Figure 8: Obesity of the patients.

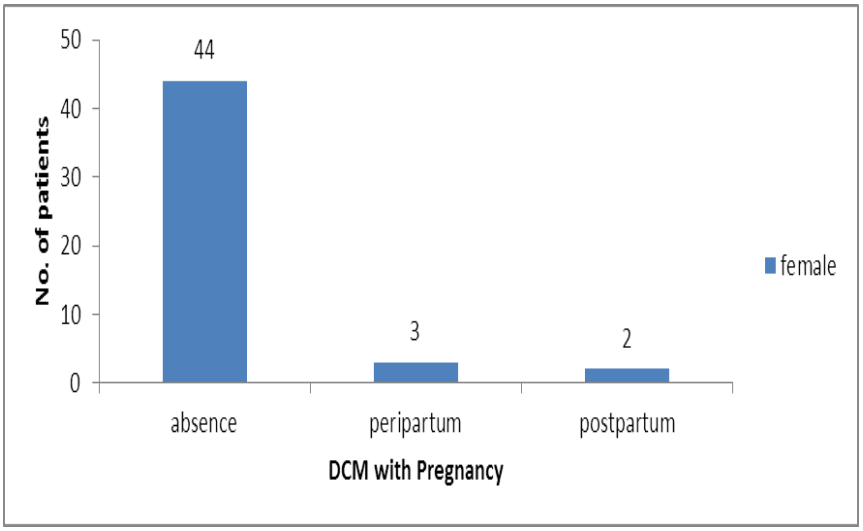

Figure 9: Women having dilated cardiomyopathy along with pregnancy.

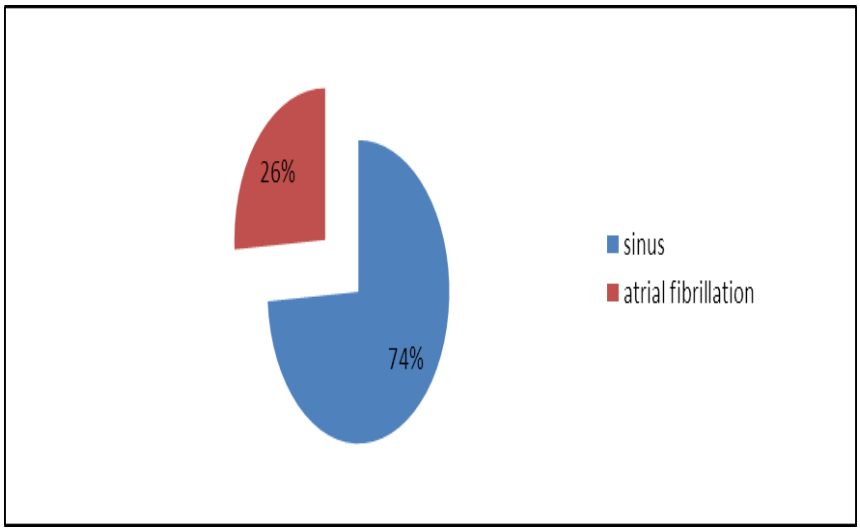

Figure 10: Heart rhythm detected by electrocardiogram.

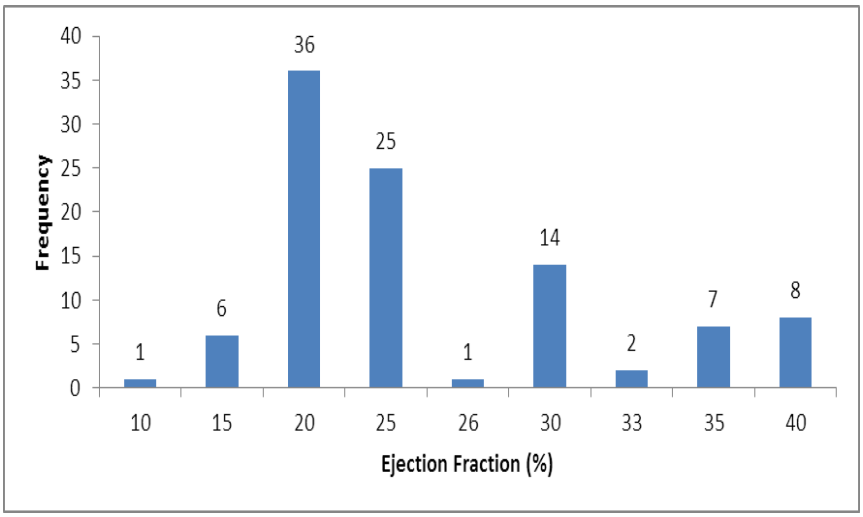

Figure 11: Ejection fraction of the heart.

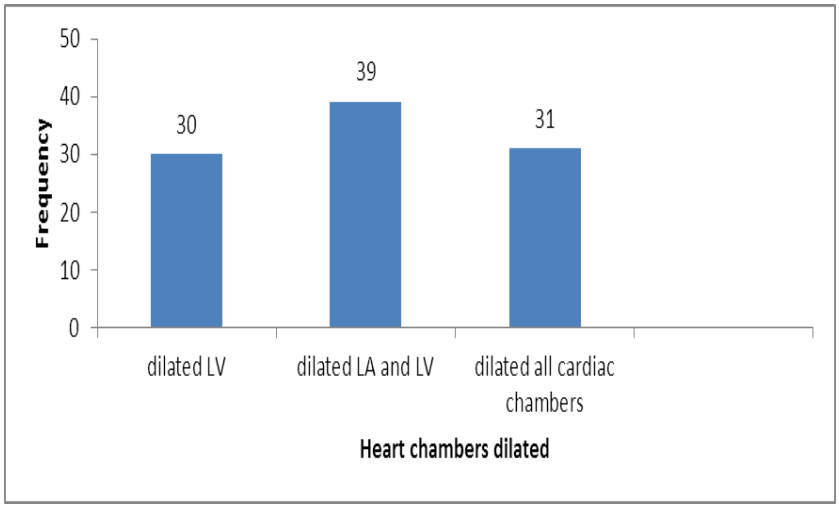

Figure 12: Dilation of heart chambers.

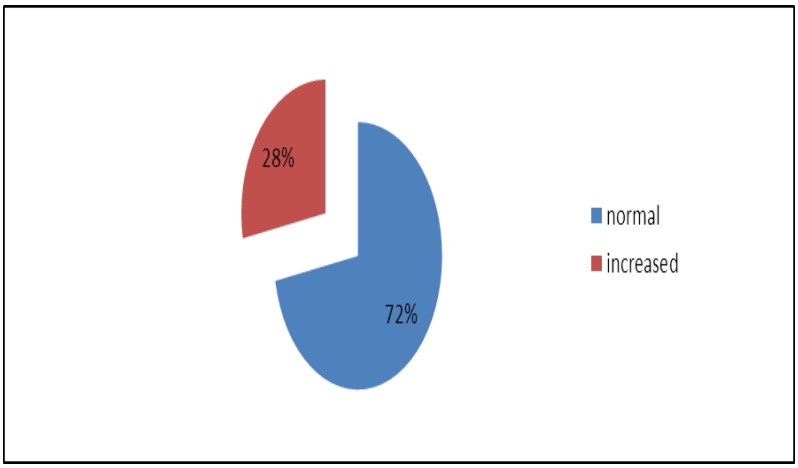

Figure 13: Serum creatinine level in the study population.

Table 1: Age group distribution of study population.

Age group	Frequency of patients	Percent
20-29	7	7%
30-39	3	3%
40-49	12	12%
50-59	14	14%
60-69	17	17%
70-79	34	34%
80-89	9	9%
90-99	4	4%
Total	100	100%

Table 2: Mitral regurgitation of heart in the study population.

Mitral regurgitation	Frequency	Percent
nil	11	11.0%
trivial	1	1.0%
mild	33	33.0%
moderate	36	36.0%
severe	19	19.0%
Total	**100**	**100.0%**

Table 3: Tricuspid regurgitation of the heart in the study population.

Tricuspid regurgitation	Frequency	Percent
nil	22	22.0%
trivial	6	6.0%
mild	45	45.0%
moderate	17	17.0%
severe	10	10.0%
Total	**100**	**100.0%**

Table 4: Left Ventricular Internal Diameter in diastole of the study population.

Left Ventricular Internal Diameter in diastole (LVIDd)		No. of patients	Percent
Normal	less than 5.5 cm	23	23.0%
Increased	5.6-6.5 cm	42	42.0%
	6.6-7.5 cm	25	25.0%
	Greater than 7.5 cm	10	10.0%
Total		**100**	**100.0%**

Table 5: Left Ventricular Internal Diameter in systole of the study population.

Left Ventricular Internal Diameter in systole (LVIDs)		No. of patients	Percent
Normal	less than 4 cm	11	11.0%
Increased	4.1-5 cm	35	35.0%
	5.1-6 cm	34	34.0%
	Greater than 6 cm	20	20.0%
Total		**100**	**100.0%**

Table 6: Drugs given as combination therapy.

Combinations	No. of patients	Percent
Furosemide+ Spironolactone	84	84%
Furosemide+ Enalapril + Spironolactone	54	54%
Furosemide+ Digoxin + Enalapril + spironolactone	27	27%
Aspirin + Enalapril + Furosemide + Spironolactone	25	25%
Aspirin + Furosemide + Losartan + Spironolactone	5	5%
Carvedilol + Enalapril + Furosemide + Spironolactone	8	8%
Furosemide + Digoxin + Enalapril	31	31%
Carvedilol + Enalapril	8	8%
Aspirin+ Atorvastatin	15	15%
Furosemide+ Vitamins	51	51%
Spironolactone + Vitamins	47	47%

Table 7: Cost analysis of medicines given to patients during hospital stay.

	Therapy	Cost
Medicines	Cardiac drug	Rs. 37.03
	Other drugs	Rs. 81.67
Tests	Echocardiography	Rs. 1100
	Electrocardiography	Rs. 170
	X-ray	Rs. 300
	Blood tests (Serum Creatinine, Fasting Sugar, Urea, Haemoglobin, WBC, Platelets, lipid profile)	Rs. 1230

CONCLUSION

The study showed that dilated cardiomyopathy is a very complex disease and is mostly idiopathic. Despite the severity of the disease, no particular therapy is available for the

complete cure of the disease. The management of the disease is done my managing the underlying symptoms. As majority of the cases is likely to go to heart failure, heart transplantation is the only option available to treat the disease till date. The study showed that mostly used drug for dilated cardiomyopathy is diuretics followed by aldosterone antagonist and ACE inhibitors. Various risk factors have been identified through the study which includes smoking, drinking, pregnancy and other associated disease such as hypertension, diabetes and chronic obstructive pulmonary disease. The average cost of the treatment of the patients with dilated cardiomyopathy was found to be expensive.

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