

EXPRESSION OF CARDIOTROPHIN-1 GENE IN CARDIOMYOPATHIC SUBJECTS



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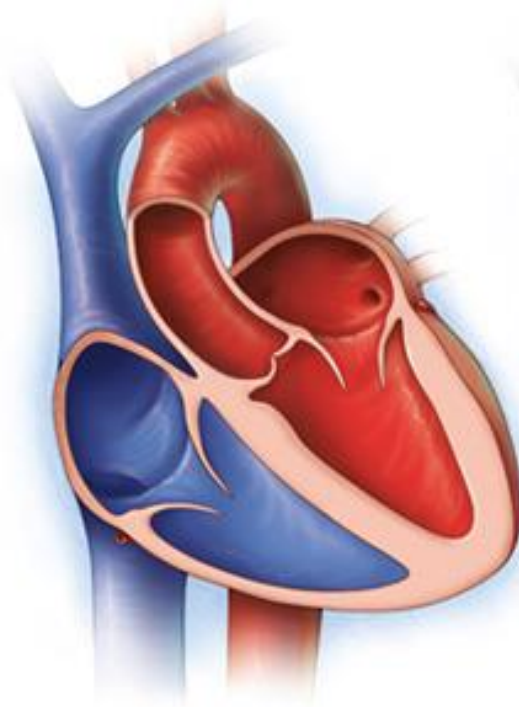
INTRODUCTION

Cardiomyopathy

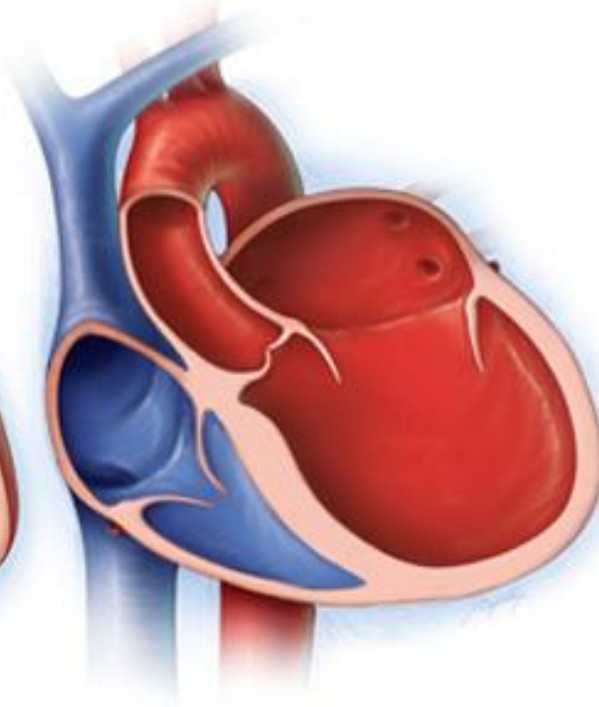
- Chronic disease of the heart muscles
- Cardiac muscles abnormally enlarged
- Loses the ability to pump blood effectively
- Arrhythmias and Heart failure

- Structural and functional abnormalities of the ventricular myocardium.
- Usually starts in the left ventricle and over time can affect the right ventricle.
- It is due to numerous mutations in various genes.

Normal heart



Dilated cardiomyopathy



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Dilated left ventricle in dilated cardiomyopathy

FORMS OF CARDIOMYOPATHY

- Dilated Cardiomyopathy (DCM)
- Hypertrophic Cardiomyopathy (HCM)
- Restrictive Cardiomyopathy (RCM)
- Arrhythmogenic right Ventricular Cardiomyopathy (ARVC)

DCM is the most common type of cardiomyopathy.

PREVALENCE of DCM

- Dilated cardiomyopathy prevalence
 - World: 1:2500
 - Pakistan: 66%
- 0.6% for males and 0.4% for females---in the developing world
(Joanna *et al.*, 2010; Khan *et al.*, 2010; Maron *et al.*, 2006)

CARDIOTROPHIN-I

- Cardiotrophin-1 (CT-1) is a member of the interleukin-6 (IL-6) family of cytokines that can induce hypertrophy of cardiomyopathy.
- CT-1 gene is located on chromosome 16p11.1– 16p11.2 in humans. It encodes 201 amino acids (Jougasaki, 2010).
- Cardiotrophin-1 binds with the gp130/leukemia inhibitory factor receptor.
- It acts via transmembrane signaling glycoprotein.

MECHANISM OF ACTION

It cause defects in ventricular sarcomere assembly, that included

- (i) Disruptions and disorganization of the normal parallel alignment of the thick and thin filaments
- (ii) Larger distances between Z discs and misalignment of Z-band between sarcomeres.

RELATION BETWEEN CARDIOMYOPATHY AND CARDIOTROPHIN-1

- Cardiostrophin is responsible for the change in sarcomere structure.
- It regulates cross-bridge kinetics, and modify their interactions.
- That also affects differentiation and maturation of cardiocytes.
- Its effect can be reversed by transcription factor GATA4 which has an anti apoptotic effect.

AIMS AND OBJECTIVES

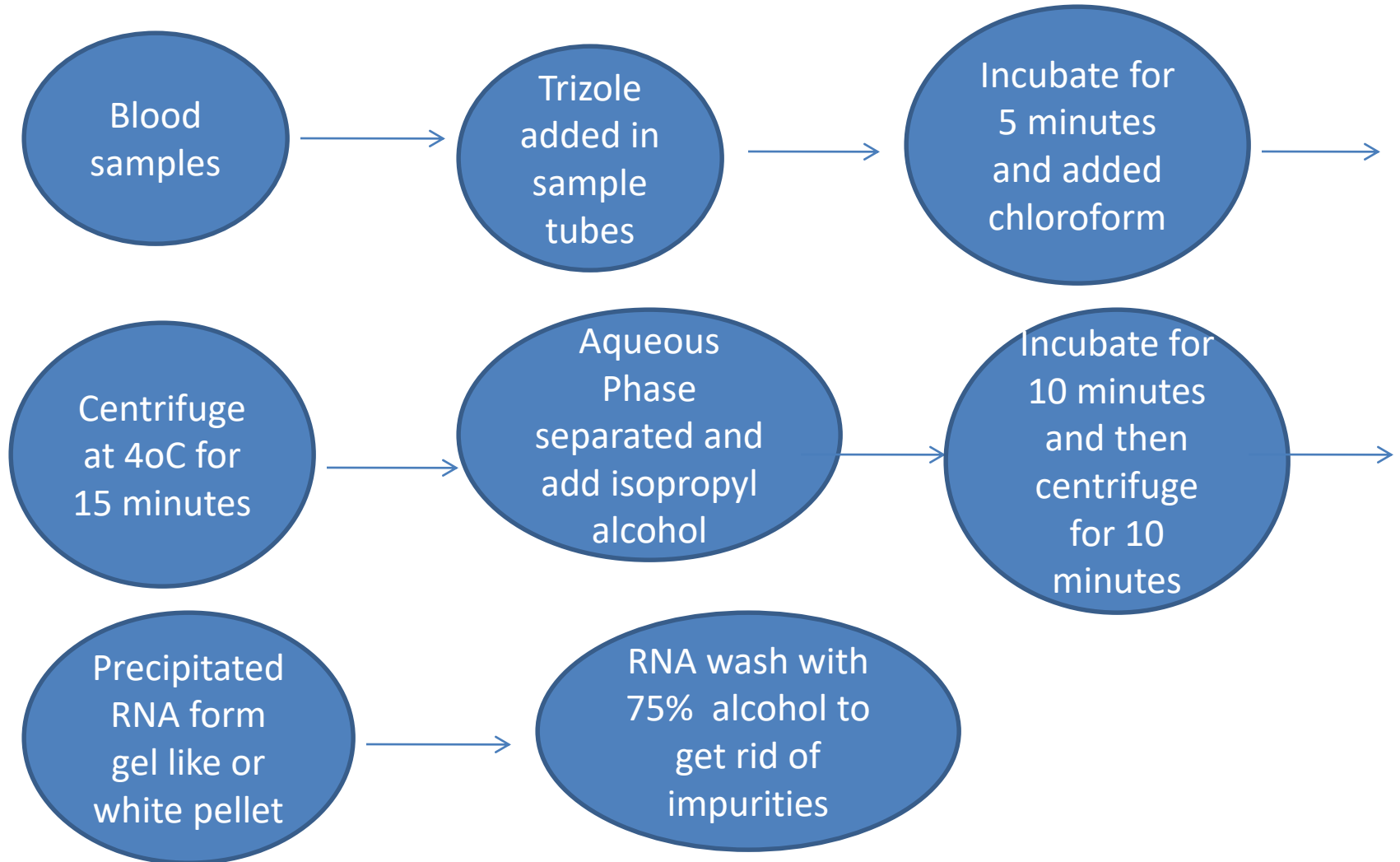
The aim and objective of the study:

- To evaluate the expression of cardiotrophin -1 in dilated Cardiomyopathy subjects.

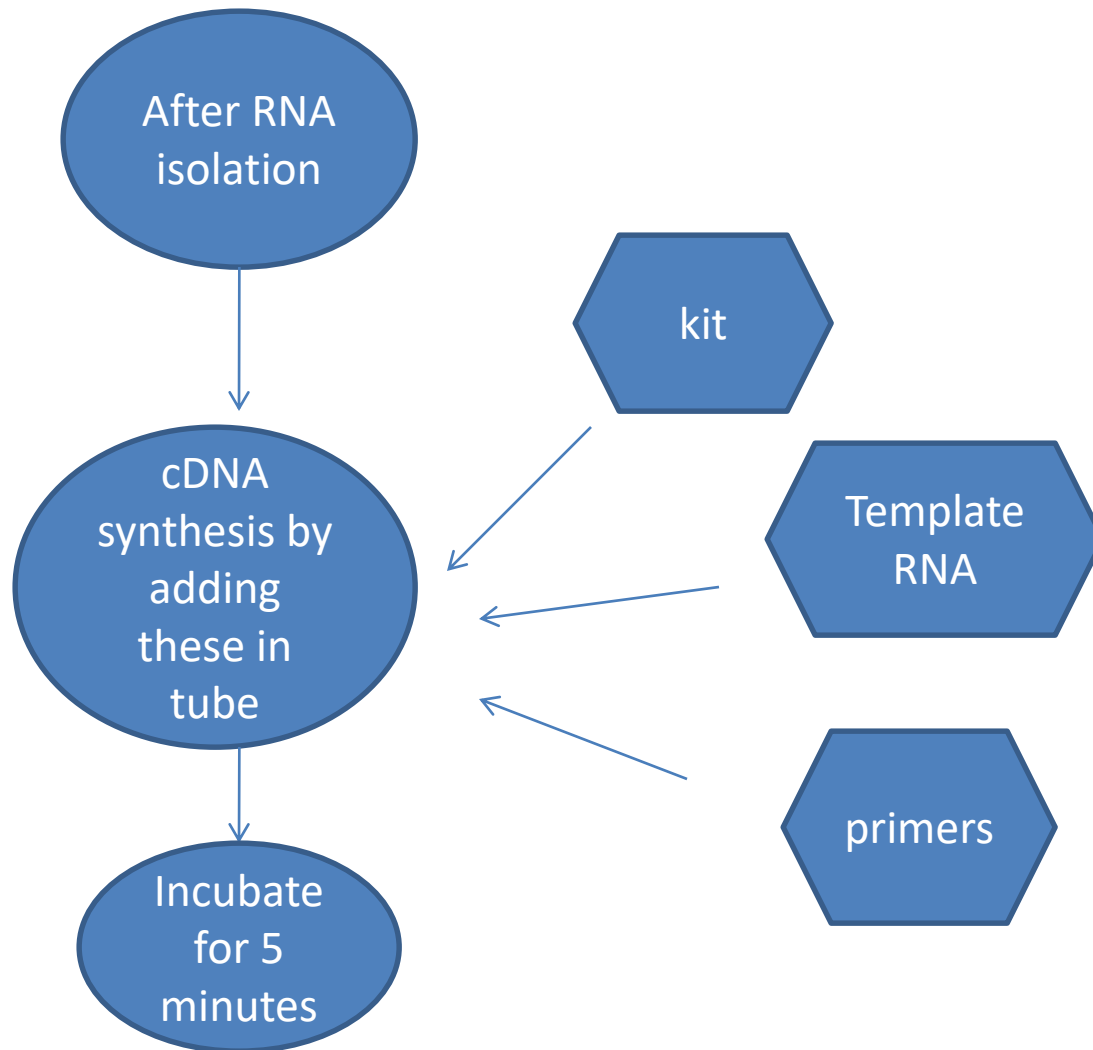
METHODOLOGY

- This study was conducted in Punjab Institute of Cardiology Lahore (PIC). Study population was divided into two groups
 - Control group (n=10): Healthy individuals (During rtPCR run in duplicate)
 - Cardiomyopathy group (n=20): patients with Cardiomyopathy.
- Expression of gene was observed from blood sample by isolating RNA.

RNA ISOLATION BY TRIZOLE METHOD



cDNA SYNTHESIS By Rt-PCR



Chilled on ice and spin gently and place tube on ice

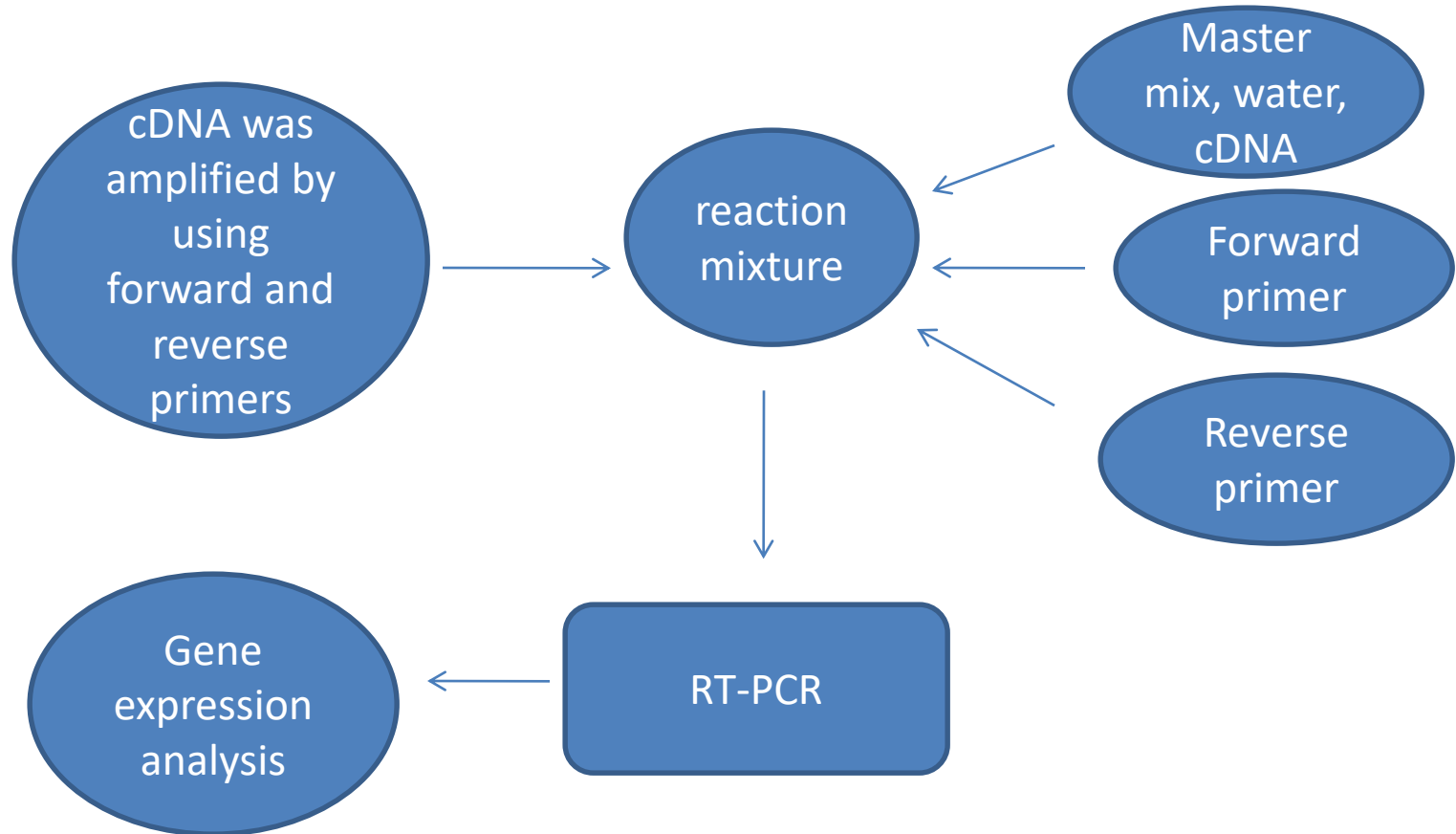


Add components: buffer, Rnase inhibitor, dntp, reverse transcriptase



Spin and incubate for 40 minutes

PCR AND GEL ELECTROPHORESIS



RESULTS

Table: Prevalence of Etiological Attributes and Symptomatology in diseased group.

Etiological attributes	Idiopathic	Nutritional	Multifactorial
	65%	15%	15%
Symptomatology	breathless	palpitation	Chest pain
	40%	75%	80%

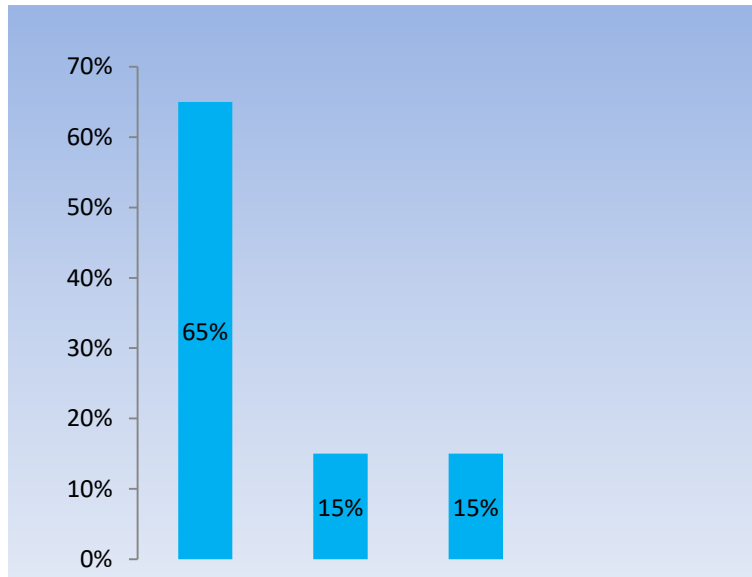


Figure 01: Attributes of disease group

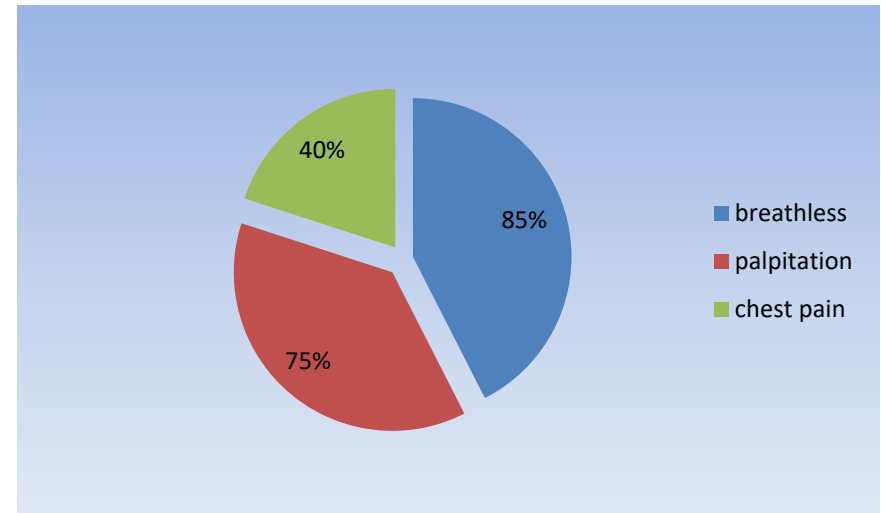


Figure 02: Symptomatology of the DCM group.

PHYSICAL ACTIVITY

Variables	Control group	DCM group
Vigorous	20%	5%
Moderate	70%	20%
Sedentary	10%	75%

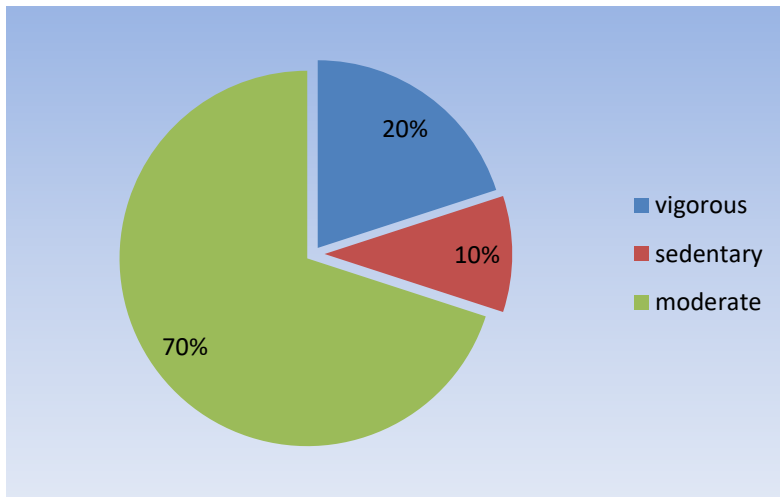


Figure 03: % age distribution in control group.

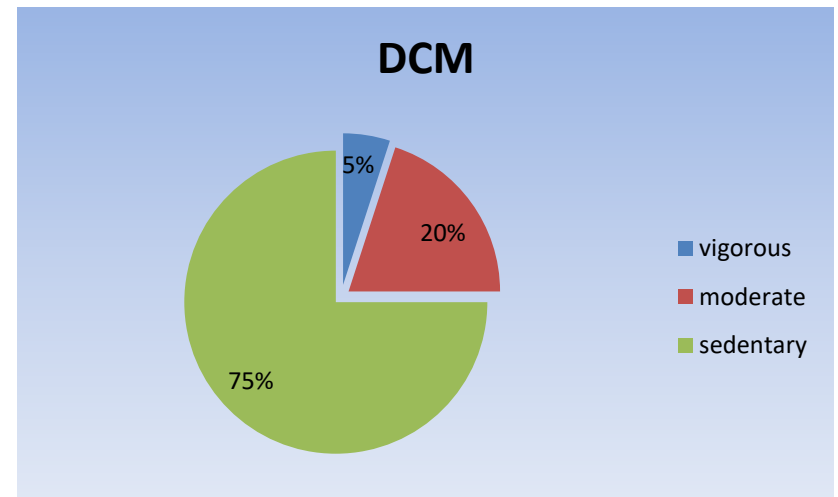


Figure 04: % age distribution in DCM group.

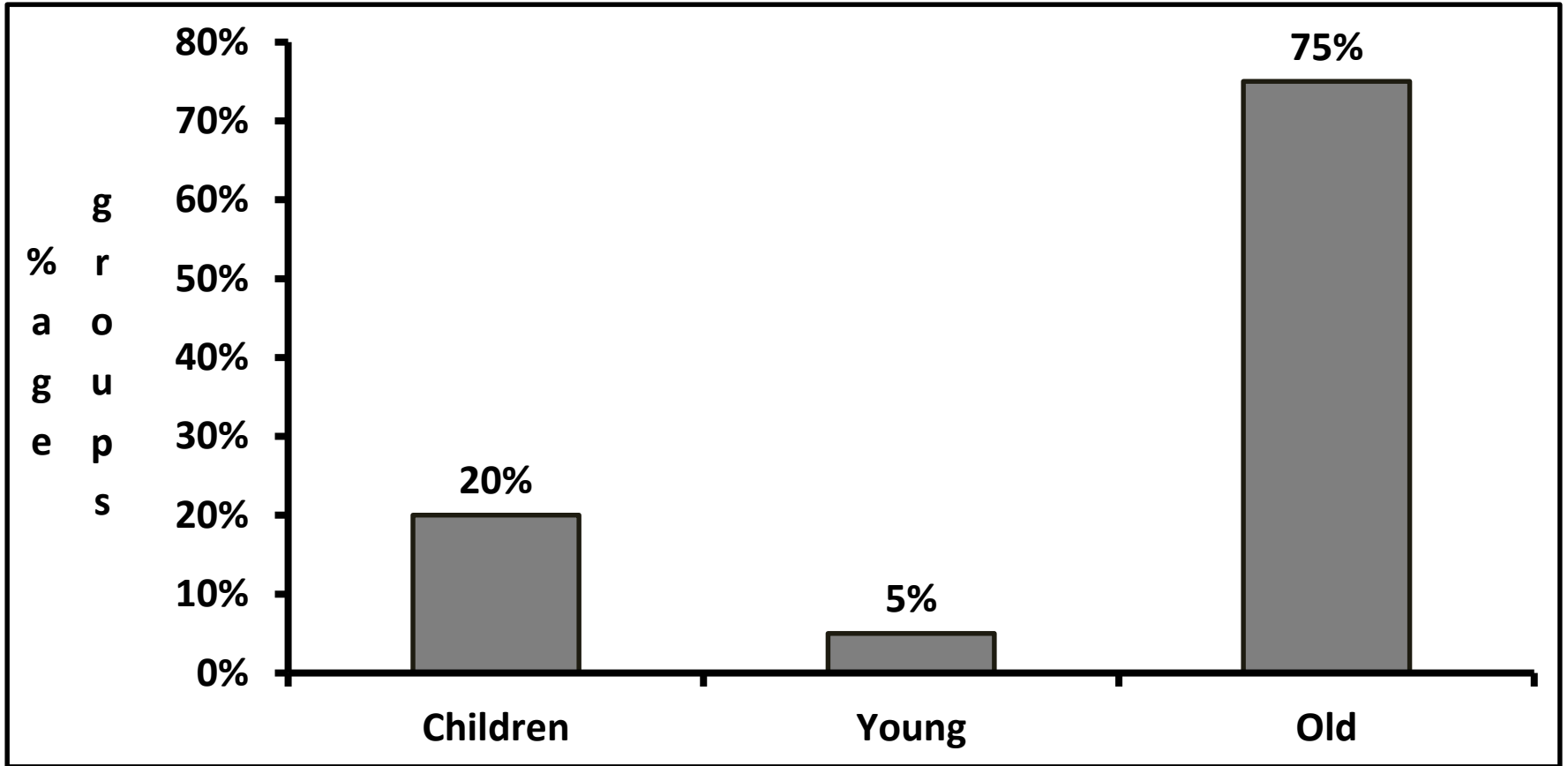


Figure 05: Distribution of age groups in Dilated cardiomyopathy subjects

SYSTOLIC AND DIASTOLIC BP

• **Table:** Prevalence of Systolic and Diastolic BP in both groups.

Groups	Systolic BP (mmHg)	Diastolic BP (mmHg)
Control group	103	78
DCM group	124	83

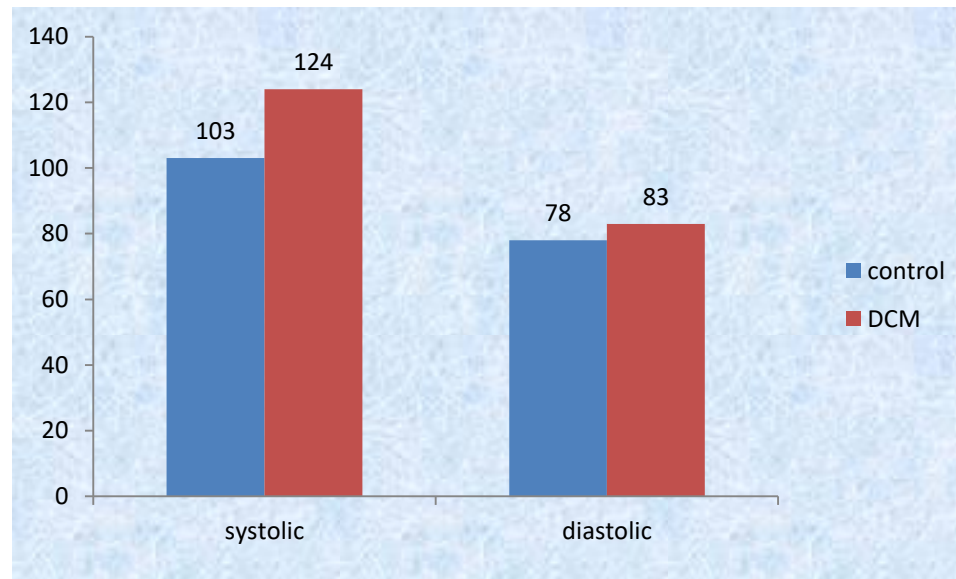


Figure 06: prevalence of systolic and diastolic BP in both groups

GENE EXPRESSION ANALYSIS

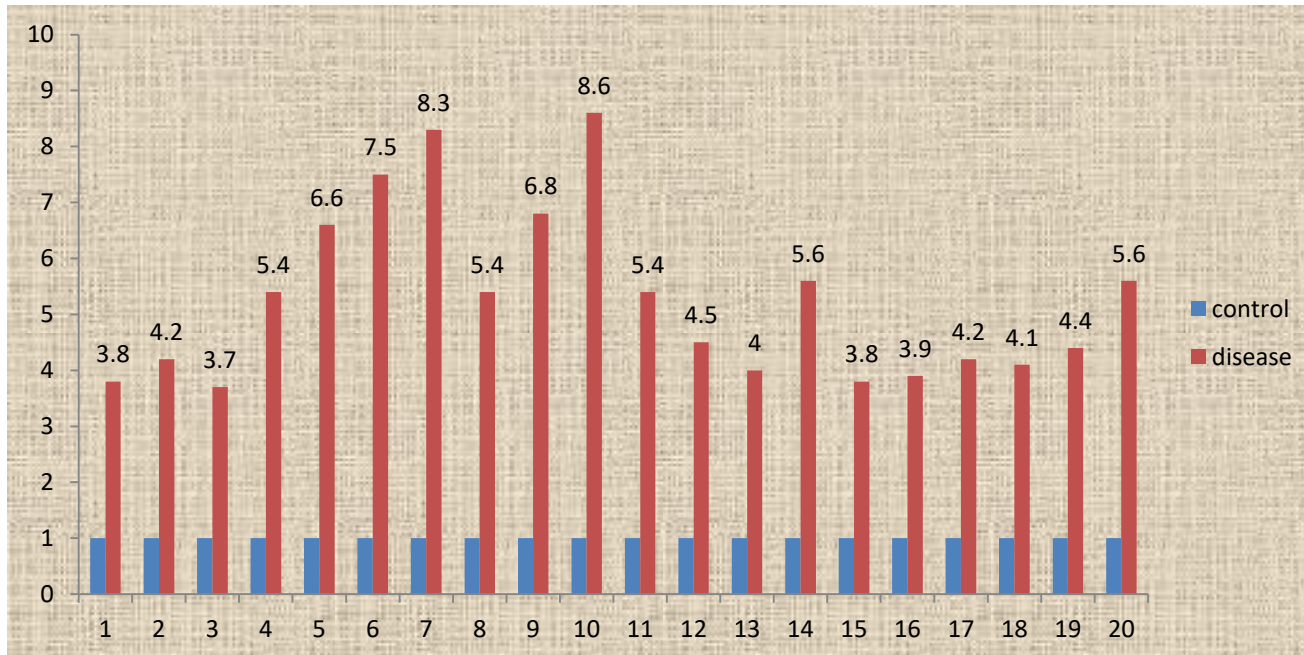


Figure 07: Expression of Cardiotrophin-1 gene in Control and DCM group.

CONCLUSION

- Increased expression of cardiotrophin-1 was observed in cardiomyopathy subjects (6.2 ± 0.657) as compared to Healthy Subjects.



THANK YOU