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.
Dilated left ventricle in dilated cardiomyopathy
FORMS OF CARDIOMYOPATHY

- Dilated Cardiomyopathy (DCM)
- Hypertrophic Cardiomyopathy (HCM)
- Restrictive Cardiomyopathy (RCM)
- Arrithmogenic right Ventricular Cardiomyopathy (ARVCM)

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

- Cardiotrophin 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

1. Blood samples
2. Trizole added in sample tubes
3. Incubate for 5 minutes and added chloroform
4. Centrifuge at 4oC for 15 minutes
5. Aqueous Phase separated and add isopropyl alcohol
6. Incubate for 10 minutes and then centrifuge for 10 minutes
7. Precipitated RNA form gel like or white pellet
8. RNA wash with 75% alcohol to get rid of impurities
cDNA SYNTHESIS By Rt-PCR

After RNA isolation

cDNA synthesis by adding these in tube

Incubate for 5 minutes

kit

Template RNA

primers
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
cDNA was amplified by using forward and reverse primers

reaction mixture

Master mix, water, cDNA
Forward primer
Reverse primer

RT-PCR

Gene expression analysis
RESULTS

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

<table>
<thead>
<tr>
<th>Etiological attributes</th>
<th>Idiopathic</th>
<th>Nutritional</th>
<th>Multifactorial</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>65%</td>
<td>15%</td>
<td>15%</td>
</tr>
<tr>
<td>Symptomatology</td>
<td>breathless</td>
<td>palpitation</td>
<td>Chest pain</td>
</tr>
<tr>
<td></td>
<td>40%</td>
<td>75%</td>
<td>80%</td>
</tr>
</tbody>
</table>

*Figure 01:* Attributes of disease group

*Figure 02:* Symptomatology of the DCM group.
PHYSICAL ACTIVITY

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control group</th>
<th>DCM group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vigorous</td>
<td>20%</td>
<td>5%</td>
</tr>
<tr>
<td>Moderate</td>
<td>70%</td>
<td>20%</td>
</tr>
<tr>
<td>Sedentary</td>
<td>10%</td>
<td>75%</td>
</tr>
</tbody>
</table>

**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.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Systolic BP (mmHg)</th>
<th>Diastolic BP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>103</td>
<td>78</td>
</tr>
<tr>
<td>DCM group</td>
<td>124</td>
<td>83</td>
</tr>
</tbody>
</table>

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