

## Comparison of Mean Lipid Profile in Calcific Aortic Stenosis Cases and Controls

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### ABSTRACT

**Objective:** This study was aimed to compare the mean lipid profile in calcific aortic stenosis patients and control group.

**Patients and Methods:** Total 202 individuals, 101 cases and 101 controls visiting National Institute of Cardiovascular Disease and various tertiary care hospitals of Karachi from January 2012 to December 2012 were included in this study. Calcific AS patients having the age of  $\geq 60$  years fulfilling the inclusion criteria were selected from echocardiography department and OPD from NICVD. Age and gender match controls were selected from OPD. Lipid profile was done in DDRRL, Ojha Campus. Lipid profile estimates were carried out on HITACHI 902 analyzer using photometry technique.

**Results:** Nonparametric *Mann-Whitney test* showed increase level of Triglyceride in calcific AS patients.

**Conclusion:** Calcific AS patients showed altered lipid profile as compare to control group so dyslipidemia may be involved in its pathogenesis.

**Keywords:** Calcific aortic stenosis, Cholesterol, Dyslipidemias, High density lipoprotein, Low density, lipoprotein, Triglyceride.

#### Author's Contribution

<sup>1</sup> Conceived the topic of research, designed the study, data collection, Literature review and manuscript writing

<sup>2</sup> Discussion, Critical review, <sup>3</sup> Data analysis, <sup>4</sup> Critical Review, <sup>5</sup> Compiling results,

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### Introduction

Severe calcific aortic stenosis (AS) is one of the most commonly encountered valvular pathologies requiring surgery in developed countries.<sup>1</sup> It is postulated that an early lesion in AS is characterized by subendothelial thickening on the aortic side of the leaflet because of accumulation of cellular lipid infiltration and extracellular mineralization, accompanied by a proliferation of smooth muscle cells and lipid-laden foam cells resembling atherosclerotic plaques.<sup>2</sup> There are similarities between risk factors for coronary atherosclerosis and the

development of AS, which suggests that the atherosclerotic process involving aortic valve leaflets eventually brings about or accelerates the thickening of the leaflet structure, leading to significant AS.<sup>3-5</sup> In patients with familial hypercholesterolemia, high cholesterol concentrations are associated with the development of AS.<sup>6,7</sup> Many cardiovascular studies have proved that there is a link between atherosclerotic risk factors and the factors associated with the prevalence and progression of calcific AS.<sup>8</sup> That includes elevated

LDL cholesterol, lipoprotein (a), hypertension, male gender and smoking.<sup>9</sup> This information can lead the way as lipid lowering drugs may be the treatment of choice for prevention and delay the progression of calcific AS.<sup>10,11</sup>

In Pakistan no such data is available. We designed this retrospective case-control study to evaluate the relationship between altered lipid profile in echocardiographically diagnosed patients with calcific AS, who referred to echocardiography department and OPD for further evaluation and to compare the mean values of lipid profile in calcific AS patients and controls.

## Patients and Methods

This study was conducted in National Institute of Cardiovascular Disease (NICVD) and DDRRL, Ojha Campus DIMC, Dow University of Health Sciences (DUHS). Study was approved by ethical review committee of NICVD and DUHS. Patients were selected from echocardiography department and OPD from NICVD. A detailed history was taken and Elderly patients (age ≥ 60 years) having calcific AS were included in the study. For controls, age and gender matched persons without calcific AS were included. Patients having severe aortic regurgitation, history of endocarditis, rheumatoid arthritis, rheumatic fever or rheumatic heart disease and echocardiographic evidence of rheumatic valvular stenosis, chronic renal failure, familial hypercholesterolemia (total cholesterol > 300 mg/dL in adults), cancer, prosthetic valves or patient taking lipid lowering drugs were excluded from the study. The patients were documented based on their written consent on a detailed prescribed form. Study was completed in 2 years after approval from Board of Advanced Scientific Research (BASR) and Funding Committee of Dow University of Health Science. Sample size was calculated with the help of open Epi (<http://www.openepi.com/SampleSize/SSMean.htm>) by taking mean total cholesterol in AS patients as 211 ± 43 mg/dl, mean total cholesterol in patients without aortic stenosis as 193 ± 48 mg/dl,<sup>12</sup> power of 80% and confidence interval of 95%. The calculated sample size was 202 patients, 101 in each case and control groups. Non-probability purposive sampling technique was used.

Fasting blood samples were collected from both the case and control groups for lipid profiling. Lipid profile

estimates were carried out on HITACHI 902 analyzer using photometry technique in DDRRL, Ojha Campus. Data was entered in Microsoft Excel and analyzed using SPSS version 21. Descriptive analysis was done according to the type of variable. Numeric data was analyzed by calculating mean and standard deviation (SD). Frequencies and percentages were calculated for categorical variables. As the data was nonparametric, median and range were taken. The nonparametric *Mann-Whitney test* was used to compare the two groups. P-value less than 0.05 was considered to be statistically significant.

## Results

A total of 202 individuals were recruited in our study. Total 101 elderly people as calcific AS cases and 101 age and gender matched controls. The age and gender distribution among two groups is presented in table 1. The mean age and standard deviation for the cases was 67.09 ± 5.04 and the mean age and standard deviation for controls was 66.72 ± 3.68. There were 63 (62.4%) males and 38 (37.6%) females in the case group and 67 (66.3%) male and 34 (33.7%) females were included in control group.

Histogram and Shapiro-Wilk test were applied to check the normality. As the variables are violating the assumption of normality therefore nonparametric *Mann-Whitney test* was used to compare both cases and controls. Triglyceride level showed significant difference between both the groups as mentioned in table 2.

**Table 1: Demographic profile in cases and controls**

Variables		Cases	Controls
Age (years)	Mean	67.09	66.72
	SD	5.04	3.68
Gender	Males n (%)	63 (62.4)	67 (66.3)
	Female n (%)	38 (37.6)	34 (33.7)

**Table 2: Descriptive statistics of lipid profile in both groups**

Lipid profile (mg/dl)	Cases	Controls	p-Value
	Median (Range)	Median (Range)	
Triglyceride	114 (421)	140 (356)	<0.001
Total Cholesterol	160 (177)	152 (218)	0.739
HDL	39 (40)	40 (34.8)	0.524
LDL	93 (119)	88 (118)	0.087

## Discussion

Multiple studies have shown many similarities in the histopathologic features of atherosclerosis and calcific AS.<sup>3,13,14</sup> There is also an overlap in the risk factors of calcific AS and atherosclerosis, among them one is dyslipidemia.<sup>8,15,16</sup> In this study fasting lipid profile was done among calcific AS cases and controls. There was a difference in the mean triglyceride level in cases and controls with significant p-value <0.05. These findings are in contrast to Peltier et al 2003, who showed a higher level of triglyceride in AS cases.<sup>12</sup> In our study, the cause of triglyceridemia may be due to the presence of coronary artery disease in controls.<sup>17</sup>

Mean total cholesterol showed the insignificant difference in both groups. This finding is consistent with the findings of a study conducted by Ortlepp 2006 and in contrast to the study conducted by Peltier et al who found that there is hypercholesteremia in patients of calcific AS.<sup>18</sup> Models of atherosclerotic disease in rabbits and rats have also been used to determine the effects of hypercholesterolemia on the aortic valve morphology and function.<sup>19</sup> Insignificant values in our study may be due to presence of comorbidities in both groups.

HDL-cholesterol showed insignificant p-value but HDL-cholesterol was decreased in both the groups. The case-control study conducted by Park et al. 2013, showed that decrease in HDL-cholesterol was associated with the AS and its progression.<sup>20</sup> Novaro et al. 2003, showed an insignificant association of HDL-cholesterol with cases and controls. However, in his work patients had a normal level of HDL-cholesterol.<sup>21</sup> In our study, insignificant p-value for HDL-cholesterol might be due to the fact that both groups included female participants above sixty years of age and in females, HDL- Cholesterol decreases as age increases.

Regarding mean LDL-cholesterol, our study showed non-significant p-value. The study was consistent with the results of Novaro et al. 2003, who showed insignificant p-value of LDL cholesterol between cases and controls.<sup>21</sup> However, Moura et al 2007 showed higher level of LDL cholesterol in calcific AS patients.<sup>22</sup> In humans, a strong influence has been observed of the LDL cholesterol levels on the progression of AS, as quantified by electron beam tomography using a volumetric score.<sup>23</sup>

## Conclusion

Calcific AS is a multifactorial disease. The present study concluded that calcific AS patients have altered lipid profile as compared to control group so dyslipidemia may be involved in its pathogenesis. However, in some patients, the presence of coronary artery disease may have produced symptoms, predominantly angina, which incited investigation and hence resulted in bias towards finding an association between aortic stenosis and altered lipid profile.

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