Open Access
Full Length Article

ORIGINAL ARTICLE

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

Erum Afaq[1], Syed Hafeezul-Hassan[2], Muhammad Kashif Nisar[3], Humera Afaq[4], Kishwar Naheed[5]

[1] Assistant Professor Physiology, Liaquat National Hospital and Medical College, Karachi
[2] Head/Professor Physiology, Liaquat National Hospital and Medical College, Karachi
[3] Associate Professor Biochemistry, Jinnah Medical & Dental College, Karachi
[4] Post Graduate Resident Medical Officer, Internal Medicine, Abbasi Shaheed Hospital, Karachi
[5]Assistance professor, Anatomy, Liaquat National Hospital and Medical College, Karachi

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 ≥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

[1] Conceived the topic of research, designed the study, data collection, Literature review and manuscript writing [2] Discussion, Critical review, [3] Data analysis, [4] Critical Review, [5] Compiling results,

Address of Correspondence
Erum Afaq
Email. doc_erum@yahoo.com

Article info.
Received: May 31, 2017
Accepted: July 9, 2017

Cite this article: *Afaq E, Hassan H, Nisar MK, Afaq H, Naheed K. Comparison of Mean Lipid Profile in Calcific Aortic Stenosis Cases and Controls.JIMDC. 2017; 6(3):140-143*

Funding Source: *Nil*
Conflict of Interest: *Nil*

Introduction

Severe calcific aortic stenosis (AS) is one of the most commonly encountered valvular pathologies requiring surgery in developed countries.[1] 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.[2] 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.[3-5] In patients with familial hypercholesterolemia, high cholesterol concentrations are associated with the development of AS.[6,7] 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.[8] That includes elevated LDL cholesterol, lipoprotein (a), hypertension, male gender and smoking.[9] This information can leads the way as lipid lowering drugs may be the treatment of choice for prevention and delay the progression of calcific AS.[10,11]

In Pakistan no such data is available. We designed this retrospective case-control study to evaluate the relationship between altered lipid profilein 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 inducted. 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 brased on their written consent on a detailed prescribed performa. 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,[12] 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 categoric 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 I. 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.[3,13,14] There is also an overlap in the risk factors of

calcific AS and atherosclerosis, among them one is dyslipidemia. [8,15,16] 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.[12] In our study, the cause of triglyceridemia may be due to the presence of coronary artery disease in controls.[17]

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. [18] 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.[19] 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.[20] 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.[21] 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. [21] However, Moura et al 2007 showed higher level of LDL cholesterol in calcific AS patients. [22] 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.[23]

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.

Acknowledgment

Authors acknowledged Muhammad Irfan and Hira Fatima Waseem bio-statisticians in the Department of Statistics, Liaquat National Hospital and Medical College, for their guidance in statistical analysis of the data.

References

1. Heistad DD, Shanahan C, Demer LL. Introduction to the Compendium on calcific aortic valve disease. Circulation research. 2013;113(2):176-8.
2. Parisi V, Leosco D, Ferro G, Bevilacqua A, Pagano G, de Lucia C, Filardi P, Caruso A, Rengo G, Ferrara N. The lipid theory in the pathogenesis of calcific aortic stenosis. Nutrition, Metabolism and Cardiovascular Diseases. 2015;25(6):519-25.
3. Kamath AR, Pai RG. Risk factors for progression of calcific aortic stenosis and potential therapeutic targets. International Journal of Angiology. 2008;17(02):63-70.
4. Rosenhek R, Baumgartner H. Aortic sclerosis, aortic stenosis and lipid-lowering therapy. Expert review of cardiovascular therapy. 2008;6(3):385-90.
5. Wierzbicki AS, Viljoen A, Chambers JB. Aortic stenosis and lipids: does intervention work? Current opinion in cardiology. 2010;25(4):379-84.
6. Retterstol K, Mundal L, Igland J, Tell GS, Holven K, Veierod MB, Leren TP. Incidence of various types of atherosclerotic disease in patients with genotyped familial hypercholesterolemia. Atherosclerosis. 2017;263:e26.
7. Dutta B, Islam A, Ullah M, Zaman A, Karmakar K, Rahman M, et al. Homozygous Familial Hypercholesterolaemia with Valvular Aortic Stenosis and Significant Coronary Artery Disease: A Case Report. Cardiovascular Journal. 2014;6(2):180-3.
8. Ljungberg J, Johansson B, Engström KG, Albertsson E, Holmer P, Norberg M, Berqdahl IA, et al. Traditional Cardiovascular Risk Factors and Their Relation to Future Surgery for Valvular Heart Disease or Ascending Aortic Disease: A Case–Referent Study. Journal of the American Heart Association. 2017;6(5):e005133.
9. Sathyamurthy I, Alex S, Kirubakaran K, Sengottuvelu G, Srinivasan K. Risk factor profile of calcific aortic stenosis. Indian Heart Journal. 2016;68(6):828-31.
10. Rossebo AB, Pedersen TR, Allen C, Boman K, Chambers J, Egstrup K, Gerdts E, et al. Design and baseline characteristics of the simvastatin and ezetimibe in aortic stenosis (SEAS) study. The American journal of cardiology. 2007;99(7):970-3.
11. Shabiti A, Aibibula A, Tuerxun A, Wufuer H. Therapeutic Effect and Mechanism of Action of Abnormal Savda Munziq in Development of Degenerative Atherosclerotic Aortic Valve Disease. Medical Science Monitor. 2017;23:4431-9.
12. Peltier M, Trojette F, Sarano ME, Grigioni F, Slama MA, Tribouilloy CM. Relation between cardiovascular risk factors and nonrheumatic severe calcific aortic stenosis among patients with a three-cuspid aortic valve. The American journal of cardiology. 2003;91(1):97-9.

13. Liberman M, Bassi Evo, Martinatti MK, Lario FbC, Wosniak Jo, Pomerantzeff PMA, Laurindo FR. Oxidant generation predominates around calcifying foci and enhances progression of aortic valve calcification. Arteriosclerosis, thrombosis, and vascular biology. 2008;28(3):463-70.
14. Rajamannan NM, Evans FJ, Aikawa E, Grande-Allen KJ, Demer LL, Heistad DD, Simmons CA, Masters KS, Mathieu P, O'Brien KD, Schoen FJ. Calcific aortic valve disease: not simply a degenerative process. Circulation. 2011; 124(16):1783-91.
15. O'Brien KD. Pathogenesis of Calcific Aortic Valve Disease A Disease Process Comes of Age (and a Good Deal More). Arteriosclerosis, thrombosis, and vascular biology. 2006;26(8):1721-8.
16. Freeman RV, Otto CM. Spectrum of calcific aortic valve disease. Circulation. 2005;111(24):3316-26.
17. Do R, Willer CJ, Schmidt EM, Sengupta S, Gao C, Peloso GM, et al. Common variants associated with plasma triglycerides and risk for coronary artery disease. Nature genetics. 2013;45(11):1345-52.
18. Ortlepp JR, Pillich M, Mevissen V, Krantz C, Kimmel M, Autschbach R, Langebartels G, Erdmann J, Hoffmann R, Zerres K. APOE alleles are not associated with calcific aortic stenosis. Heart. 2006;92(10):1463-6.
19. Le Quang K, Bouchareb R, Lachance D, Laplante M-A, El Husseini D, Boulanger MC, Fournier D, et al. A. Early Development of Calcific Aortic Valve Disease and Left Ventricular Hypertrophy in a Mouse Model of Combined Dyslipidemia and Type 2 Diabetes Mellitus Significance. Arteriosclerosis, thrombosis, and vascular biology. 2014;34(10):2283-91.
20. Park JY, Choi JW, Ryu SK, Song CS. The Impact of Low Level of High Density Lipoprotein Cholesterol on Adverse Clinical Outcomes in Patients with Mild to Moderate Aortic Stenosis. The American Journal of Cardiology. 2013; 111(7):103B.
21. Novaro GM, Sachar R, Pearce GL, Sprecher DL, Griffin BP. Association between apolipoprotein E alleles and calcific valvular heart disease. Circulation. 2003;108(15):1804-8.
22. Moura LM, Ramos SF, Zamorano JL, Barros IM, Azevedo LF, Rocha-Gonçalves F, Rajamannan NM. Rosuvastatin affecting aortic valve endothelium to slow the progression of aortic stenosis. Journal of the American College of Cardiology. 2007;49(5):554-61.
23. Kizer JR, Gefter WB, DeLemos AS, Scoll BJ, Wolfe ML, Mohler 3rd E. Electron beam computed tomography for the quantification of aortic valvular calcification. The Journal of heart valve disease. 2001;10(3):361-6.