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Non-Alcoholic Fatty Liver Disease Associated with Aortic Valve Sclerosis in Patients with Type 2 Diabetes Mellitus

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Abstract

Background: The association of non-alcoholic fatty liver disease (NAFLD) with aortic valve sclerosis (AVS) is gaining prominence in the context of both non-diabetic and type 2 diabetic populations. While AVS was once dismissed as an incidental echocardiographic observation, it's now recognized as a potential risk factor for adverse cardiovascular outcomes. Concurrently, NAFLD's ramifications extend beyond liver-associated complications, encompassing cardiovascular and renal anomalies. **Aims & Objectives:** This research aimed to unearth the correlation between NAFLD and AVS in patients with Type 2 Diabetes Mellitus, primarily focusing on the presence or absence of AVS in the context of ultrasonographically diagnosed NAFLD. **Methods**: A cross-sectional assessment spanning 12 months was undertaken at the Kempegowda Institute of Medical Sciences, Bangalore, including 100 patients diagnosed with both NAFLD and type 2 diabetes. Comprehensive evaluations, encompassing clinical assessments, blood tests, ultrasonography, and 2DECHO, formed the research's backbone. **Findings**: Among the cohort, 49% demonstrated a normal echocardiogram, while 51% exhibited signs of sclerotic aortic valve. Notably, male gender exhibited a significant correlation with 2D ECHO findings (p=0.046). Lipid profiles showed marked differences, particularly in triglycerides and LDL levels, between the two groups, with p-values less than 0.05. Other parameters showcased minimal variances, but the lipid profile variations were significantly high in the AVS group. **Conclusion**: The study underscores the tangible link between NAFLD and lipid irregularities in the backdrop of AVS in type 2 diabetic patients. Such findings accentuate the need for vigilant monitoring and targeted interventions for this demographic, given the overarching cardiovascular implications.

Keywords: NAFLD, Aortic Valve Sclerosis, Type 2 Diabetes Mellitus, Echocardiogram, Lipid Profile.

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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) has emerged as a public health problem of epidemic proportions worldwide. The prevalence of NAFLD in patients with type 2 diabetes ranges from approximately 50 to 70% [1–4]. NAFLD is associated not only with liver-related mortality and

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morbidity but also with abnormalities of cardiac structure and function [5-8] and an increased risk of developing cardiovascular disease (CVD), atrial fibrillation and chronic kidney disease [9-12].

Studies have demonstrated that NAFLD is related to aortic valve sclerosis—both in the general population and in patients with type 2 diabetes. A study done by Markus MR et al [13] has shown that NAFLD on ultrasonography is also associated with a greater prevalence of aortic valve sclerosis (AVS), independently of several CVD risk factors [13]. AVS shows some epidemiologic and histopathologic similarities to coronary atherosclerosis [14]. In addition, a large number of prospective studies have suggested a strong association between AVS and increased CVD morbidity and mortality in both nondiabetic and type 2 diabetic individuals [15–17].

AIMS AND OBJECTIVES:

- To determine the association between Nonalcoholic Fatty Liver Disease and Aortic Valve Sclerosis in Type 2 Diabetes Mellitus.

MATERIALS AND METHODS:

Study design: Cross Sectional study
Study period: 12 months
Place of study: Kempegowda institute of medical sciences, Bangalore
Study population: Patients admitted to the hospital with Type 2 Diabetes mellitus in the department of general medicine, Kempegowda institute of medical sciences will be taken up for the study after considering the inclusion and exclusion criteria.

Inclusion criteria:

- Age>18 years
- All patients admitted to the hospital with NAFLD
- Type 2 Diabetes Mellitus

Exclusion criteria:

- Patients on pioglitazone therapy
- Patients who had a pre-existing history of myocardial infarction, angina, coronary revascularization procedures, congestive heart failure, moderate-to-severe valvular heart disease, malignancy, cirrhosis and kidney failure.
- Those with excessive alcohol consumption (i.e., >30 g/day of alcohol for men and >20 g/day for women, respectively), viral hepatitis or other secondary causes of chronic liver disease
- 12-lead standard resting electrocardiogram will be performed in all patients to exclude the presence of silent myocardial ischemia

Methodology:

After obtaining approval and clearance from the institutional ethics committee, the patients fulfilling the inclusion criteria will be enrolled for the study after obtaining informed consent. A pre-tested semi-structured questionnaire was used to collect the socio-demographic characteristics of the study participants by interview method. All Relevant laboratory and radiological investigations were done. The presence of AVS was defined as focal or diffuse thickening and calcification of the aortic leaflets without restriction of leaflet motion on echocardiography. A trans-aortic peak instantaneous velocity ≥2.5 m/s was considered as aortic stenosis. Hepatic steatosis was diagnosed on the basis of characteristic ultrasonographic features, i.e., evidence of diffuse hyper-echogenicity of the liver relative to the kidneys, ultrasound beam attenuation and poor visualization of intra-hepatic vessel borders and diaphragm

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RESULTS:

Table 1: Patient characteristics

Patient characteristics		
Age, Mean ± SD		52.22±14.734
Sex, n (%)	**Male**	53 (53%)
	Female	47 (47%)
Associated comorbidities, n (%)	**HTN**	45 (45%)
	CKD	4 (4%)
	CVA	1 (1%)

Figure 1: Incidence of NAFLD

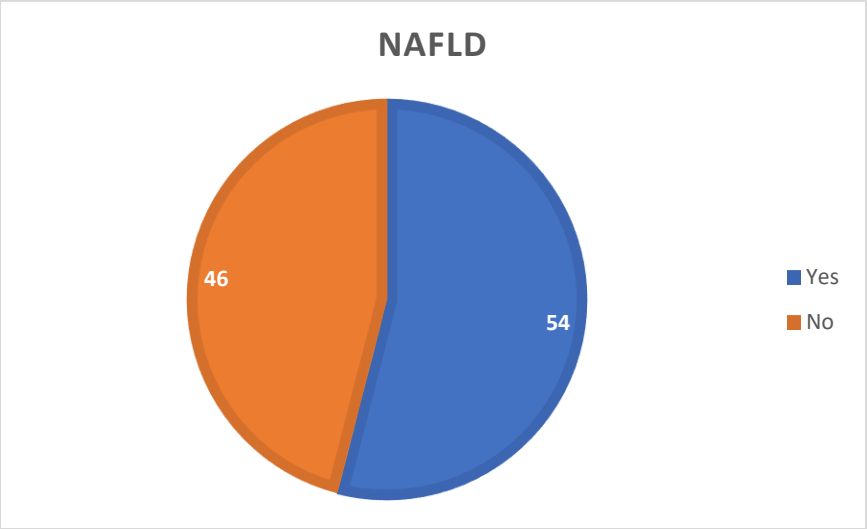
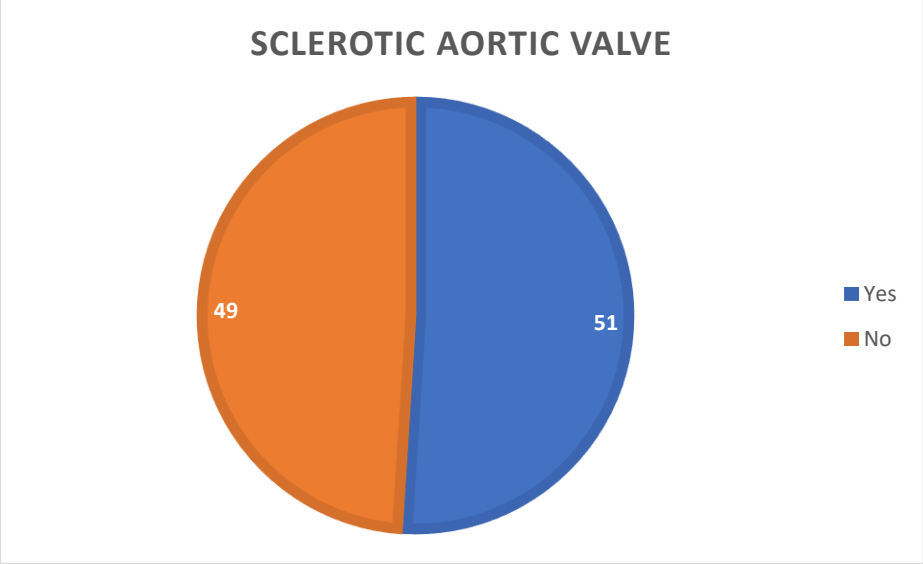


Figure 2: Incidence of Sclerotic Aortic Valve



ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

Figure 3: Association of NAFLD with Sclerotic Aortic Valve

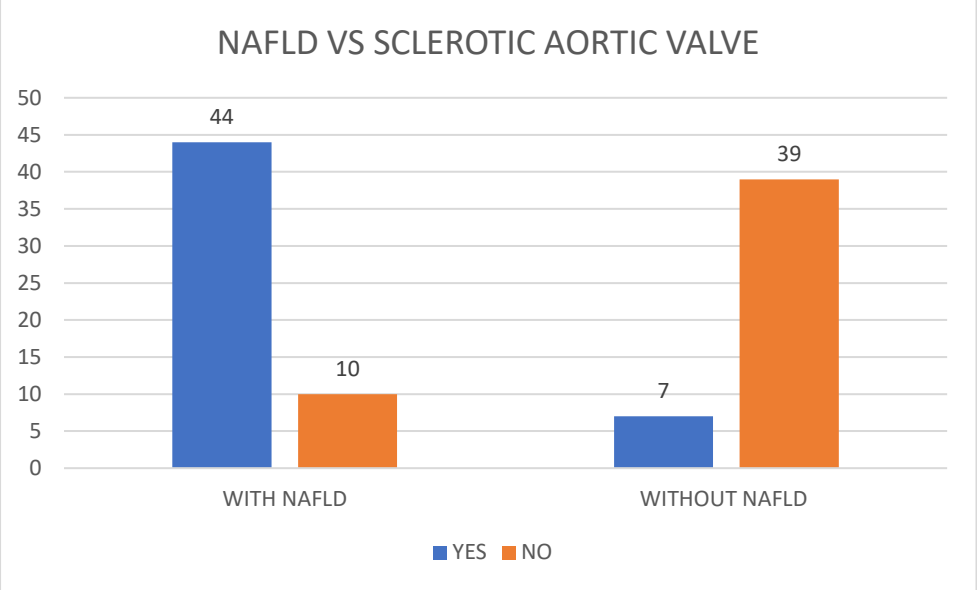


Table 2: Odds Ratio for NAFLD to develop SAV

	95% Confidence Interval	
Odds Ratio	**Lower**	**Upper**
3.199	2.142	4.257

Study participants with NAFLD are at 3.199 times at risk of developing Sclerotic Aortic Valve disease than those without NAFLD.

DISCUSSION:

It is known that AVS is a powerful predictor of adverse CVD outcomes, independently of traditional risk factors, both in patients without diabetes and in those with type 2 diabetes [15-17]. The underlying mechanisms responsible for the observed association between NAFLD and AVS remain speculative and require further study. Speculatively, the most plausible explanation for our findings is that the association between NAFLD and AVS is a simple epiphenomenon of shared CVD risk factors and co-morbidities or, alternatively, a marker of ectopic fat deposition in other organs such as the myocardium or pericardium. Bonapace S et al [18] in their study found a strong, graded relationship between the presence and severity of NAFLD and AVS that was independent of multiple CVD risk factors. It is also plausible to assume that NAFLD, especially its necro-inflammatory form (NASH), is not only a simple marker of AVS in type 2 diabetes but also may be, at least in part, involved in its pathogenesis. This process may occur through the contribution of NAFLD per se to systemic and hepatic insulin resistance and/or through the systemic release of several pathogenic mediators from the steatotic and inflamed liver, such as increased reactive oxygen species, advanced glycation end products, C-reactive protein, plasminogen activator inhibitor-1, transforming growth factor-beta and other pro-inflammatory, pro-coagulant and pro-fibrogenic factors [18]. Notably, several case-control studies have shown that these potential mediators of vascular injury are remarkably higher in patients with NAFLD than in those without the disease [2-9].

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CONCLUSION:

Our findings add evidence that hepatic steatosis and aortic valve sclerosis are interrelated. The release of proatherogenic substances by the steatotic liver or its contribution to insulin resistance and dyslipidemia may contribute to the development of calcification and sclerosis of the aortic valve. Further studies are needed to corroborate these findings in independent samples, and to better elucidate the responsible mechanisms for this association. It is also important to determine whether improvement in NAFLD (or future treatments for NAFLD) will ultimately delay or prevent the development and progression of AVS.

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ISSN: 0975-3583,0976-2833 VOL15, ISSUE 08, 2024

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