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Original Article

Internal Medicine Section

Cardiac Dysfunction in Early Stages of Diabetic Kidney Disease- Fact or Fiction: A Case-control Study

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ABSTRACT

Introduction: The occurrence of kidney dysfunction in diabetics promotes early cardiac dysfunction. The timing of Diabetic Kidney Disease (DKD) and the impact of the stage of DKD on cardiac dysfunction is far from elucidated in current literature.

Aim: To evaluate the association between the early stages of DKD and cardiac dysfunction by echocardiography.

Materials and Methods: The present descriptive, case-control study was conducted in the Pondicherry Institute of Medical Sciences (PIMS), Kalapet, Puducherry, India, from November 2018 to November 2020. All diabetic patients between 25-60 years, who attended the Medicine Outpatient Department (OPD) or were admitted into the medical wards, were screened, among which 280 subjects were selected for the study. Patients with Estimated Glomerular Filtration Rate (eGFR) of more than 45 mL/min/1.73m^2 were characterised as cases and those with eGFR of more than 90 mL/min/1.73m^2 were controls. Echocardiographic parameters were recorded. Chi-square test, Mann-Whitney U test, and unpaired t-test were used for statistical analysis. Multivariate logistic regression analysis was done using an odd's ratio to assess the association between early DKD and cardiac dysfunction.

Results: The number of diabetics with early kidney disease (cases) were 139 and without kidney disease (controls) were 141. The mean age of the cases was 54.63±4.84 years and the controls were 52.61±7.916 years. The number of males among the cases and controls were 68 (48.92%) out of 139 and 96 (68.08%) out of 141, respectively. The prevalence of systolic dysfunction among diabetic patients with early kidney disease was 12.23% (17/139) and diastolic dysfunction was prevalent in 99.28% (138/139). Systolic dysfunction was 9.68 times more common in cases (n=139) than in controls (n=141). Women had a 2.6 times higher likelihood, and hypertension had (an independent association which was) a 2.6 times higher likelihood of developing cardiac dysfunction in the early stages of DKD.

Conclusion: Systolic cardiac dysfunction is significantly higher (9.68 times more common) in those with early DKD when compared to those without kidney disease; with female gender and systemic hypertension as independent and significant risk factors.

Keywords: Diabetic cardiomyopathy, Diabetic nephropathy, Renocardiac syndrome

INTRODUCTION

Type 2 diabetes mellitus, heart failure and chronic kidney disease are the three important pandemics of the 21st century. Type 2 diabetes mellitus affects more than 400 million people worldwide and India contributes up to 49% of it [1]. Diabetes mellitus is related to the development of kidney disease which is termed Diabetic Kidney Disease (DKD) and is associated with all causes of cardiovascular mortality [2]. Varying degrees of kidney dysfunction is found in 50.4% of the patients with diabetes mellitus [3]. Of around 1,20,000 incident cases of End-stage Renal Disease (ESRD), half are attributed to diabetes [4]. Type 2 diabetes mellitus is also a powerful risk factor for the development of heart failure. It renders the person two to four times more susceptible to cardiac dysfunction; and two-thirds of all deaths due to heart failure, have type 2 diabetes mellitus [3].

Flash pulmonary oedema, cardiac failure, and sudden cardiac death are more common, among patients with diabetes mellitus, especially those with DKD. This has been called "The Reno Cardiac Syndrome" in recent times [5]. Hyperglycaemia of diabetes mellitus, through advanced glycation products, augment Left Ventricular (LV) stiffness and LV mass, resulting in LV diastolic dysfunction without impeding global LV function [5]. Advanced Glycation end Product (AGP) deposition results in cross-linking of collagen in the myocardial architecture and causes myocardial fibrosis [5,6]. Both these processes lead to diastolic dysfunction. The occurrence of kidney dysfunction in diabetics promotes early cardiac dysfunction thus setting up a vicious cycle [7]. A study has documented this condition as diastolic dysfunction and another has documented as an isolated systolic dysfunction [8,9]. So far, hardly any studies have looked for cardiac dysfunction in early diabetic nephropathy and quantified it. Also, the impact of the stage of DKD on cardiac dysfunction is far from elucidated in current literature. What is known about this is that the hazard ratio for heart failure in those with diabetic nephropathy is 2.22 (95% Confidence interval, 1.51-3.27) [10]. LV diastolic dysfunction and E/E' are predictors of death in patients with diabetic nephropathy [11].

Perhaps early detection and treatment of cardiac dysfunction in DKD could diminish morbidity and mortality too. So, this study aimed to evaluate the association between the early stages of DKD and cardiac dysfunction (by echocardiography). The primary objective was to determine the proportion of patients with cardiac dysfunction among those with early stage DKD. The secondary objective was to determine the magnitude of cardiac dysfunction and the associated risk factors.

MATERIALS AND METHODS

This descriptive, case-control study was conducted in the Pondicherry Institute of Medical Sciences (PIMS), Kalapet, Puducherry, India, from November 2018 to November 2020. The approval of the Institutional Research and Ethics Committee was obtained (RC/18/72).

Sample size calculation: The prevalence of cardiovascular disease in patients with mild renal impairment (glomerular filtration rate >50 mL/min) was assumed to be 30% [12]. A total of 280 patients were required to establish the association between DKD and cardiac dysfunction with 95% confidence interval and 7% precision. A total of 536 patients were screened, 296 were selected and 16 repeat

entries were removed from the database during the final analysis. Thus, 280 participants were included in the study.

Inclusion criteria: All diabetic patients {fasting plasma glucose ≥126 mg% or random plasma glucose ≥200 mg% or glycated haemoglobin (HbA1c) ≥6.5} between 25-60 years who attended the medicine OPD or were admitted into the medical wards were screened.

Estimated GFR (eGFR) was calculated using the CKD-EPI formula [13]:

In men (eGFR)=141×min (S_{Cr}/κ, 1)$^{\alpha}$×max (S_{Cr}/κ, 1)$^{-1.209}$

In women (eGFR)= 141×min (S_{Cr}/κ, 1)$^{\alpha}$×max (S_{Cr}/κ, 1)$^{-1.209}$×1.018

Participants whose GFR was more than 45 mL/min/1.73 m^2 BSA were included in the study. Glucose profile and urine albumin excretion were done in all recruited patients; who then underwent a Master's 2 Step Stress Test before echocardiography.

Exclusion criteria: Patients who failed the test, and who were on drugs that suppress myocardial function were excluded from the study.

The patients were divided into cases and controls:

Cases: Patients with eGFR of more than 45 mL/min/1.73m^2 were characterised as cases and

Controls: Patients with eGFR of more than 90 mL/min/1.73 m^2 were controls.

Study Procedure

Echocardiographic parameters were recorded in the case report form. The treatment of participants was decided by the treating physician. Glucose profile and urine albumin excretion were done in all recruited patients; who then underwent a Master's 2 Step Stress Test before echocardiography.

Echocardiography was done using Philips i33 Echocardiography machine. Diastolic dysfunction was evaluated by pulsed doppler echocardiography according to recommendations of the American Society of Echocardiography. Pulsed-wave Doppler (PWD) derived transmitral inflow velocities were obtained in the apical 4-chamber view, with the sample volume placed at the mitral valve leaflets' tips. Measurements included the transmitral early diastolic rapid filling (E-wave) and atrial contraction late filling (A-wave) velocities to calculate the E/A ratio, Isovolumetric Relaxation Time (IVRT) and Deceleration Time (DT).

For Tissue Doppler Imaging (TDI), the mitral annulus velocity was obtained with a 2 mm sample volume on the lateral side and septal side of the mitral annulus. Diastolic dysfunction was labeled according to the standard guidelines. LV overall ejection fraction (systolic function) was calculated by modified Simpson's method, and LV Ejection Fraction (LVEF) ≥50% was considered normal. Echocardiography was done by the principal investigator and 10% of the total sample size was scrutinised by an expert. Left ventricular diastolic dysfunction was assessed as [14]:

- Grade 1: Mitral E/A ratio ≤0.8;
- Grade 2: Mitral E/A ratio >0.8 but less than 2;
- Grade 3: Mitral E/A ratio ≥2

In 2D echocardiography, the following parameters were measured with TDI: Inter ventricular septal thickness, posterior wall thickness, LV diastolic diameter, LV systolic diameter, fractional shortening, Left Atrial (LA) diameter, end diastolic volume, end systolic volume, LVEF, time to peak filling rate, E/A ratio, DT, IVRT, LA length in systole and diastole, LA area in systole and diastole, LA volume, Tissue doppler in the lateral and septal wall, E/E' (E' denotes the mitral annular early diastolic velocity).

The following parameters were included:

E/E' >14, Septal E'< 7 cm/s, Lateral E' <10 cm/s, LA Volume >34 mL/m^2, E <50 cm/s, E> 50 cm/s, E/A: >2, E/A: 0.8-2, E/A: <0.8, DT >240 ms, IVRT >90 ms.

E/A Ratio

The rapid early diastolic filling was measured by echocardiography and denoted by E. The late diastolic filling was measured as atrial systole A. Based on the patterns obtained on the transmitral doppler inflow, the different stages of diastolic dysfunction were ascertained. This is represented as the E/A ratio.

E/E' Ratio

E' denotes the mitral annular early diastolic velocity. E represents the rapid early diastolic ventricular filling. E/E' represents the best measure of mean LV end-diastolic pressure in a normal heart.

STATISTICAL ANALYSIS

Data were entered into Microsoft Excel and analysed using the Statistical Package for the Social Sciences (SPSS) software for windows. Descriptive statistics like mean and standard deviation were used for quantitative variables and frequency or percentage for qualitative variables. Chi-square test, Mann-Whitney U test, and unpaired t-test were used for association. The p-value ≤0.05 was considered significant. Multivariate logistic regression analysis was done using an odd's ratio to assess the association between early DKD and cardiac dysfunction.

RESULTS

In total sample, early-stage DKD (cases) was identified in 139 (25.93%) participants among whom the majority were males. The mean age was 53.6 years. The mean creatinine was within normal limits but the mean Low Density Lipid Cholesterol (LDL-C) and Glycated Haemoglobin (HbA1c) were high [Table/Fig-1,2].

Variable	Cases n (%)	Controls n (%)	p-value
Age (years)			
25-34	0	3 (2.12)	0.315*
35-44	5 (3.5)	22 (15.6)	
45-54	49 (35.25)	37 (26.24)	
≥55	85 (61.15)	79 (56.02)	
Mean±SD age in years	54.63±4.84	52.61±7.91	
Gender			
Male	68 (48.92)	96 (68.08)	0.001*
Female	71 (51.07)	45 (31.9)	
Smoking			
Yes	28 (20.14)	30 (21.27)	0.815**
Alcohol			
Yes	27 (19.42)	28 (19.85)	0.927**
Duration of diabetes			
<5 years	43 (30.94)	52 (36.87)	0.921**
≥5 years	96 (69.06)	89 (63.12)	
Hypertension			
Yes	52 (37.41)	26 (18.43)	<0.001**
No	87 (62.58)	115 (81.56)	
Coronary artery disease			
Yes	19 (13.66)	5 (3.54)	<0.001**
No	120 (86.33)	136 (96.45)	

[Table/Fig-1]: Distribution of demographic variables among cases (n=139) and controls (n=141).
*Mann-Whitney U test applied, **Chi-square test used, p-value ≤0.05 was considered statistically significant

The prevalence of systolic dysfunction among the cases was 12.23% (95% CI: 7.8-18.7) and diastolic dysfunction was prevalent in 99.29% [Table/Fig-3].

The mean±SD age among the cases was 54.63±4.84 years and for controls was 52.61±7.916 years. The majority of the cases were females (51.08%) in the age group of >55 years (61.15%). Among controls, the majority were males (68.1%) in the age

Parameter	Cases (Mean±SD)	Controls (Mean±SD)	p-value
FBS (mg/dL)	179.46±68.48	183±60.12	0.325*
PPBS (mg/dL)	268.60±98.63	271.77±91.2	0.524*
Urea (mg/dL)	32.42±10.94	25.46±8.07	<0.001*
Creatinine (mg/dL)	1.129±0.25	0.705±0.14	<0.001*
HbA1c (%)	8.934±2.03	8.749±1.83	0.512*
HDL (mg/dL)	33.59±9.16	33.02±8.57	0.573*
LDL (mg/dL)	126.86±26.29	112.57±29.79	<0.001*
TGL (mg/dL)	200.20±40.06	185.59±50.56	<0.001*
TCL (mg/dL)	238.76±46.52	218.49±48.01	<0.001**
Urine ACR (mg/dL)	0.264±0.14	0.246±0.12	0.294*

[Table/Fig-2]: Distribution of biochemical variables among cases (n=139) and controls (n=141).
FBS: Fasting blood sugar; PPBS: Postprandial blood sugar; HbA1c: Glycosylated haemoglobin; HDL: High density lipoprotein; LDL: Low density lipoprotein; TGL: Triglycerides; TCL: Total cholesterol; ACR: Albumin creatinine ratio.
*Mann-Whitney U test applied, **Chi-square test applied, p-value ≤0.05 was considered statistically significant

Cardiac dysfunction	n (%)	Confidence interval
LV systolic dysfunction	17 (12.23)	7.8-18.7
LV diastolic dysfunction*		
Grade 1	10 (7.2)	4-12.8
Grade 2	123 (88.49)	82.8-93.3
Grade 3	5 (3.6)	1.6-8.2

[Table/Fig-3]: Proportion of cardiac dysfunction among cases (n=139).
*One patient had indeterminate LV diastolic dysfunction; LV: Left ventricular

group of >55 years (56.03%). This age difference was statistically insignificant. There were 48.92% and 68.1% males in the cases and controls, respectively, this gender difference was statistically significant. 20.14% cases and 21.28% controls had nicotine dependence; 19.42% cases and 19.86% controls had alcohol dependence. Neither was statistically significant.

Among the cases, 69.06% had diabetes for >5 years, 37.41% had hypertension and 13.67% had Coronary Artery Disease (CAD). In the control group, 63.12% had diabetes for >5 years, 18.4% had hypertension and 3.55% had CAD. The cases had a longer duration of diabetes which was statistically insignificant. The association between hypertension and CAD, with early DKD, was statistically significant.

The fasting blood sugar, postprandial blood sugar, HbA1c levels, and urine albumin creatinine ratio were comparable between the groups. However total cholesterol, LDL cholesterol, and triglycerides levels were significantly higher among the cases [Table/Fig-2,4].

Multivariate logistic regression analysis was applied to determine the independent role played by important predictors which resulted in cardiac dysfunction in diabetics with early stages of DKD. Hypertension, CAD and dyslipidemia did not contribute to the development of cardiac dysfunction. However, cardiac dysfunction in women with diabetes and early stages of DKD showed a 3.4 times higher likelihood of developing cardiac dysfunction [Table/Fig-5].

Diabetes and hypertension are closely related to CAD. To understand the independent risk involved with the risk factors, a subgroup analysis excluding CAD was performed which showed that women had a 2.6 times higher likelihood; and hypertension had a 2.6 times higher likelihood of developing cardiac dysfunction in the early stages of DKD. Similarly, elevated LDL levels' association was established with statistical significance but the Odd's ratio was nearly one [Table/Fig-6]. Also, systolic dysfunction was 9.68 times more common in cases than in controls [Table/Fig-7].

DISCUSSION

The association of cardiac dysfunction in ESRD is well established, but at what stages of DKD and how the stage of DKD is related

Parameter	Cases {Mean±SD/ n (%)}	Controls {Mean±SD/ n (%)}	Odd's ratio	Confidence interval	p-value
Age (in years)	54.63±4.84	52.61±7.916	1.05	1.01-1.09	0.315
Gender (male)	68 (48.92)	96 (68.1)	0.45	0.27-0.73	0.001*
Duration (>5 yrs)	96 (69.06)	89 (63.12)	1.30	0.79-2.14	0.294
Hypertension	52 (37.41)	26 (18.44)	2.64	1.53-4.56	<0.001*
Coronary artery disease	19 (13.67)	5 (3.55)	4.31	1.56-11.88	0.005*
Smoking	28 (20.14)	30 (21.28)	0.93	0.52-1.66	0.815
Alcohol	27 (19.42)	28 (19.86)	0.97	0.54-1.76	0.927
Low density lipoproteins (mg/dL)	126.86±26.29	112.57±29.79	1.02	1.01-1.03	<0.001*
Triglycerides (mg/dL)	200.20±40.06	185.59±50.56	1.01	1.00-1.01	0.009*
Total cholesterol (mg/dL)	238.76±46.52	218±48.01	1.01	1.00-1.02	0.001*
HbA1c (%)	8.934±2.03	8.749±1.83	1.05	0.93-1.19	0.424

[Table/Fig-4]: Association between demographic and biochemical parameters and cardiac dysfunction.
*p-value ≤0.05 was considered statistically significant

Parameter	Odd's ratio	Confidence interval	p-alue
Gender (male)	0.29	0.161-0.509	<0.001*
Hypertension	1.78	0.922-3.447	0.09
Coronary artery disease	2.79	0.858-9.068	0.09
LDL (mg/dL)	1.01	0.999-1.028	0.06

[Table/Fig-5]: Multivariate regression analysis.
*p-value ≤0.05 was considered statistically significant

Parameter	Odd's ratio	Confidence interval	p-value
Gender (male)	0.38	0.229-0.646	<0.001*
Hypertension	2.48	1.380-4.466	0.002*
LDL (mg/dL)	1.02	1.007-1.027	0.001*

[Table/Fig-6]: Subgroup analysis after removal of subjects with established Coronary Artery Disease (CAD) (cases -120, controls -136).
*p-value ≤0.05 was considered statistically significant

Parameters	Cases (n)	Controls (n)	Odd's ratio	p-value
Systolic dysfunction				
Ejection fraction <50%	17	2	9.68 (2.19-42.77)	<0.001*
Diastolic dysfunction				
Grade 1	10	11	1	
Grade 2	123	129	1.05 (0.43-2.56)	0.916
Grade 3	5	1	5.50 (0.55-55.49)	0.148
Indeterminate	1	0		

[Table/Fig-7]: Association with cardiac dysfunction in cases versus controls.
*p-value ≤0.05 was considered statistically significant

to major or minor cardiovascular events is still not sufficiently researched. Hence, the present study aimed to study and assess the prevalence of cardiac dysfunction in the early stages of DKD.

Among cases, 12.23% had systolic dysfunction, and a majority (88.49%) had grade 2 diastolic dysfunction. Diabetic cardiomyopathy is a discrete clinical entity that can develop irrespective of the traditional risk factor of CAD and hypertension [15]. Cardiomyopathy can present phenotypically as either diastolic or systolic dysfunction [16]. It is therefore likely that this cardiac dysfunction signifies diabetic cardiomyopathy.

A prospective case-control study by Patil VC et al., observed 54.33% (n=69) of the cases to have significant diastolic dysfunction similar to this study, but the cases in this study included diabetic subjects with early kidney disease and controls included diabetic

subjects without early kidney disease [8]. In contrast, a study by Ernande L et al., was the first to observe systolic dysfunction despite normal diastolic function, emphasises that diastolic dysfunction should not be considered the first marker of preclinical diabetic cardiomyopathy [9]. Contrarily, systolic strain abnormality may be proposed as the first indicator of diabetic cardiomyopathy and as a therapeutic target. But in this study, there were greater proportions of diabetics with simultaneous diastolic and systolic dysfunction. Ernande L et al., also found a 47% prevalence of diastolic dysfunction, with 33% being a grade I and 14% being grade II; but this study had a higher prevalence of grade 2 diastolic dysfunction [9]. The high variability in the prevalence of diastolic dysfunction (23-75%) is due to variability in study subjects' and differences in the methods adopted for determination.

A study by Di Bonito P et al., found TDI helpful in detecting cardiomyopathy early in diabetics and lesser duration of diabetes despite normal cardiac functions; which was associated with insulin resistance [17]. Similarly, another study by Otsuka T et al., found LV diastolic dysfunction even in patients with early stages of CKD [18]. These subtle changes due to kidney disease could be detected by TDI as in this study too. By TDI method, a few authors have shown both diastolic and systolic cardiac dysfunction in diabetics [8,19,20]. However, most of the subjects in those studies had hypertension and obesity which could have contributed to diastolic dysfunction. Most of those studies used the TDI technique in diabetics to evaluate early cardiomyopathy as did this study.

Secondary Objective

The secondary objective was to determine the risk of cardiac dysfunction among diabetics with early stage kidney disease. To ascertain this, the proportion of cardiac dysfunction among those with and without early kidney disease was compared. Systolic cardiac dysfunction was significantly higher in those with early DKD with female gender and systemic hypertension as independent and significant risk factors.

A study by Fiseha T and Tamir Z found the prevalence of CKD to be 46.9% in participants above 60 years and 22.6% in those below 60 years; also, the prevalence of CKD was lower in men (14.8%) than in women (36.9%) which concurs with this study [21]. In contrast to this study, Ravindran R et al., found the prevalence of nephropathy among diabetics to be 13%. A lower prevalence was due to the exclusion of patients with uncontrolled hypertension [22].

Ravindran R et al., and Anjana RM et al., found smoking and alcohol consumption to be risk factors for diabetes [22,23]. Unnikrishnan RI et al., also recorded a significant correlation between smoking and the development of diabetic nephropathy and their findings were in contradiction to this study [24]. The contradiction is probably because this study focussed on patients with early DKD. This meant a shorter duration of diabetes mellitus. Had the duration of diabetes been longer an association may have been observed?

In a study by Veeramani Kartheek As and Srinivas Reddy VC, 97.4% of patients with albuminuria had statistically significant LVH, also there was an association between the findings of 2D-Echo and lipid profile; an elevated serum cholesterol level of >200 mg/dL correlated well with systolic dysfunction (15.38%), diastolic dysfunction (41.67%) and a combined systolic and diastolic dysfunction (10%) all of which were statistically significant [25]. In this study, a higher prevalence of global hypokinesia in patients with elevated total serum cholesterol value of >200 mg/dL was noted, with statistical significance. Furthermore, on univariate analysis, systolic dysfunction was 9.68 times more common in cases than in controls.

Earlier studies, have shown hypertension and diabetes (despite the influence of the kidneys) to have a profound effect on cardiac function emphasising interorgan dependence [25-27]. A few other studies chiefly Chinese, have reported the development of diabetic complications such as CAD, heart failure, stroke and ESRD with the onset of diabetes rather than the onset of DKD [28-30]. Univariate analysis of demographic and biochemical parameters among cases and controls showed female gender, hypertension and CAD to pose a greater risk of developing diastolic dysfunction. Also, elevated urea levels and dyslipidaemia (elevated LDL and TCL) contributed to diastolic dysfunction. These findings suggest that uraemia and hyperlipidaemia increase the risk of cardiac dysfunction in patients with early renal disease. So, it may be inferred that treatment of dyslipidemia could play a role in retarding the progression of cardiac dysfunction in patients with early diabetic nephropathy. On performing a multivariate logistic regression analysis, it was observed that the female gender is a statistically significant risk factor. Hypertension, CAD and dyslipidemia as risk factors were statistically insignificant.

The occurrence of LV diastolic dysfunction before the onset of systolic dysfunction in the presence of early stages of kidney disease has been documented by Otsuka T et al., in the Japanese population [18]. In a Danish Study by Poulsen MK et al., impaired cardiac relaxation has been observed in the diabetic population [31]. Both those studies suggested that age, female gender, and uncontrolled hypertension may contribute to the development of cardiac dysfunction. An Indian study by Chandey M et al., observed that diastolic dysfunction was present in 81% of the studied population, of which 43.2% were males and 56.7% were females. Thirty-five out of 45 (77.8%) males and 46 out of 55 (83.6%) females had diastolic dysfunction, although LV diastolic dysfunction was more prevalent in females [32]. To address this association between early stage DKD and the development of cardiomyopathy; and to exclude the dependent variable of CAD, a subgroup analysis was done which concurred with the established data; that is, age, female gender, and hypertension contributed to the development of cardiomyopathy.

Diabetes is a robust risk factor not only for cardiovascular disease but also for the progress of CKD [33]. The risk of early-stage renal disease increases by 12-fold with diabetes [34]. Roughly 40% of diabetics have signs of CKD upon screening for decreased eGFR and albuminuria [35]. Even though subjects with CKD, mostly those with DKD, frequently have concomitant traditional risk factors for cardiovascular disease, these do not fully explain the augmented incidence of cardiovascular events and mortality [36]. In addition, a few traditional risk factors such as dyslipidemia, systemic hypertension, and obesity have shown an inverse association with cardiovascular disease in subjects with advanced CKD. Hence, through this study, it was found that there exists an increased prevalence of cardiomyopathy in diabetic patients with early kidney disease, especially in those with modifiable risk factors of systemic hypertension, CAD and dyslipidemia; and the non modifiable risk factor i.e., female gender.

Limitation(s)

Asymptomatic/symptomatic CAD was not ascertained by coronary angiography.

CONCLUSION(S)

Systolic cardiac dysfunction was present in 12.23% of patients and diastolic cardiac dysfunction in nearly 90% of those with type 2 diabetes mellitus and early-stage kidney disease (ASE Guidelines 2017). Systolic cardiac dysfunction is significantly higher (9.68 times more common) in those with early DKD when compared to those without kidney disease with female gender and systemic hypertension as independent and significant risk factors. Controlling modifiable risk factors of systemic hypertension and dyslipidemia could play an important role in reducing cardiac dysfunction. The very high risk (Odd's ratio of 3.4) associated with the female gender needs more exploration to determine if additional interventions like physical exercise and weight reduction will be beneficial.

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