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CORRELATION OF DIASTOLIC DYSFUNCTION IN PATIENTS WITH DIABETIC NEPHROPATHY

Medicine

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ABSTRACT

BACKGROUND: India is the diabetes capital with home to 69.1 million people with DM, the second highest number of cases after China. This global burden of diabetes, brings with it the potential for a catastrophic increase in the prevalence of kidney and cardiovascular disease. Although the increased mortality in patients with diabetes traditionally has been attributed to coronary artery disease, more recent studies have emphasized the importance of chronic heart failure (HF) as a common and deadly comorbidity, to which the patient with nephropathy, even in its earliest stages, is especially prone. Diabetes mellitus may be one factor that specifically influences cardiac diastolic function, because diabetes and impaired glucose tolerance selectively accelerate the deterioration of LV diastolic function.

METHODOLOGY: A cross sectional study was conducted in GSL GENERAL HOSPITAL, Rajahmundry over a period of 18 months from Nov 2016 to April 2018 in type 2 diabetes mellitus patients department of general medicine. A total of 150 subjects were observed in this study. This study was done with a view to determine whether there is any association between diastolic dysfunction in type 2DM and Diabetic nephropathy.

RESULTS: Overall Mean age of study participants was 56.98 $\pm$ 10.27 years with a range from 30 to 88 years. In the present study there was significant correlation between age, duration of Type 2 Diabetes, PPBS, HbA1c, UACR, serum creatinine, eGFR, Hb, USG showing renal parenchymal changes, ECG showing LVH, and Diabetic nephropathy with diastolic dysfunction.

CONCLUSION: Results of the present study reveals that there is significant evidence to support the conclusion that microalbuminuria or proteinuria in patients with diabetes is a potential risk factor not only for kidney function impairment but also a marker for high risk of cardiovascular complications.Type 2 DM subjects with and without nephropathy should be screened for sub clinical diastolic dysfunction by echocardiography.These patients should receive a multifactorial treatment and should be monitored carefully to prevent or slow down the progression of both kidney and cardiovascular complications.

KEYWORDS

Diastolic dysfunction, microalbuminuria , type 2 diabetes mellitus

INTRODUCTION :

The incidence of diabetes mellitus (DM) is increasing worldwide and rapidly assuming epidemic proportions.According to International Diabetes Federation estimates, around 415million people had DM in 2015 and this number is expected to rise to 642 million by 2040[1].

India is the diabetes capital with home to 69.1 million people with DM, the second highest number of cases after China[1].

This global burden of diabetes, brings with it the potential for a catastrophic increase in the prevalence of kidney and cardiovascular disease. Although the increased mortality in patients with diabetes traditionally has been attributed to coronary artery disease, more recent studies have emphasized the importance of chronic heart failure (HF) as a common and deadly comorbidity, to which the patient with nephropathy, even in its earliest stages, is especially prone[2,3].

The recognition of such a link between HF and kidney failure in diabetes is supported not only by epidemiologic data but also by shared pathogenic mechanisms that underlie the development of both disorders and give rise to common therapeutic approaches aimed at slowing their progression[2].

Diabetic nephropathy (DN) is the leading cause of end-stage renal disease and the care of patients with diabetes and DN contributes significantly to health care costs. Of patients with type 1 diabetes, approx.20%-30% will eventually develop DN, whereas about 10%-20% of those with type 2 diabetes will do so[4].

Patients with diabetic kidney disease have exceptionally high rates of cardiovascular morbidity and mortality. In fact, the excess mortality among patients with diabetes appears to be largely limited to the subgroup with kidney disease and explained by their high burden of cardiovascular disease. The mechanisms underlying the strong association between diabetic kidney disease and various forms of cardiovascular disease are poorly understood[5].

Diabetes mellitus may be one factor that specifically influences cardiac diastolic function, because several studies have shown that diabetes and impaired glucose tolerance selectively accelerate the deterioration of LV diastolic function. However, little is known about the specific effect of diabetes on LV diastolic function in patients with CRF. Therefore, the present study was designed to examine diastolic function in subjects with non-dialysis CRF, and elucidate whether the etiology (underlying disease) of CRF, especially diabetic nephropathy, per se influences specifically LV diastolic function[6-11].

AIMS AND OBJECTIVES:

The objective of this present study was to determine whether there is any association between diastolic dysfunction in type 2DM and Diabetic nephropathy.

MATERIALS AND METHODS:

Study design: Cross sectional study

Study subjects: All type 2 diabetic subjects who attended the outpatient and inpatient wards of medicine department in GSL General Hospital who satisfied the inclusion criteria were included in the study.

Sample size: 150

Study period: 1st November 2016 to 30th April 2018

Inclusion criteria: All type 2 diabetics above the age of 30 years

Exclusion criteria: Type2 diabetics with Ischemic heart disease
Hypertension
Valvular heart disease
UTIS
Poor transthoracic echo window
Known renal disease/family history of renal disease

METHODOLOGY

All subjects aged above30 years who satisfied the inclusion criteria were included in the study. A pre-structured questionnaire was used to collect the clinical data. Baseline data including age, detailed medical history, past history, family history, drug history and personal history were recorded. Clinical examination and routine and relevant investigations were carried out for all participants.

Weight of the subjects was measured to the nearest 0.1 kg in light clothes on standing bare foot using a well calibrated balance scale. Height of the subject was measured to the nearest 0.5 cm using a wooden scale fixed on the wall while the subject is standing relaxed with bare foot and heels together touching the wall.

Waist circumference was measured at the smallest horizontal circumference between the lower costal margin and iliac crest after normal expiration, and the hip circumference was measured at the point of maximum extension of the buttocks. Waist circumference >90cm for males and 80cm in females was considered as central obesity[12,13].

BMI was calculated as weight in kilograms divided by height in square meters.

Diagnosis of diabetes was made according to WHO criteria or if the subjects were already taking Insulin or oral antidiabetic drugs. Criteria for diagnosis of Diabetes mellitus

1. Fasting plasma glucose 7.0 mmoll (126mg/dl) or
2. 2h plasma glucose 11.1 mmol/l (200mg/dl) during an OGTT[14]

Subjects with systolic pressure more than 130mm Hg and diastolic pressure more than 90 mmHg or those on antihypertensive drugs were considered as hypertensives.

Triglycerides >150mg/dl and HDL<40mg/dl for males and <50mg/dl for females and on specific treatment was taken as dyslipidemia.

Venous blood samples were taken after an overnight fast for fasting blood glucose and 2-hour post glucose blood sugar, glycosylated hemoglobin and lipid profile. Plasma glucose concentration was estimated using the glucose oxidase method. Serum lipids (total cholesterol, triglycerides, LDL cholesterol and HDL plasma cholesterol concentrations) were measured. Cholesterol and triglyceride levels were determined in the serum by commercially available kits on an Erbamannheim -360 analyzer .High –density lipoprotein was measured by using the direct high-density lipoprotein method. Low density lipoprotein and very low density lipoprotein cholesterol were calculated according to the formula of Friedewald et al. LDL cholesterol =cholesterol-[HDL cholesterol+ (o.46xtriglycerides)]

Glycosylated hemoglobin (HbA1c) was estimated by ion exchange resin method using colorimetry.

Albumin creatinine ratio (ACR) was measured by immunoturbidometry using Microalbuminuria test kit provided by ERBA MANHEIM GERMANY. Serum creatinine was done by creatininase enzymatic method, eGFR was calculated using CKD-EPI equation.

ECG recording was obtained for every subject to rule out ischemic heart disease. ECG finding of left ventricular hypertrophy was done byusing Sokolow-lyon index where the sum of S wave in V1 and R wave in V5 or V6 $\geq$35mm, R wave in aVL$\geq$11mm.

Tran thoracic echocardiography was carried out to exclude valvular heart disease and assess both systolic and diastolic cardiac dysfunction. Using Philips ultrasound HD11XE and with a 2-3.5 MHz transducer.According to ASE/EACVI guidelines left ventricular diastolic dysfunction was identified using these parameters

TABLE 1. LV RELAXATION, FILLING PRESSURES, 2D AND DOPPLER FINDINGS IN DIASTOLIC DYSFUNCTION

	Normal	Grade I	Grade II	Grade III
LV relaxation	Normal	Impaired	Impaired	Impaired
LAP	Normal	Low or normal	Elevated	Elevated
Mitral E/A ratio	≥0.8	≤0.8	>0.8 to <2	>2
Average E/e' ratio	<10	<10	10–14	>14
Peak TR velocity (m/sec)	<2.8	<2.8	>2.8	>2.8
LA volume index	Normal	Normal or increased	Increased	Increased

Where LAP-left atrial pressure, mitral inflow velocities were traced and the following variables were derived: E/A ratio represents ratio of peak velocity flow in early diastole (E wave) to peak velocity flow in late diastole caused by atrial contraction (A wave), average E/e' represents peak mitral inflow velocity during early diastole to e'-early diastolic velocity, peak TR velocity- pulmonary artery systolic pressure, LA volume index-left atrial volume index[15].

STATISTICAL METHODS:

Data entry and statistical analysis were performed with the help of Microsoft excel 2007 and SPSS version 21.0.Categorical variables were presented as numbers and percentages. All descriptive data was expressed as Mean+/- standard deviation and percentages. Chi-square test was used to assess the association among different categorical variables.Logistic regression was performed to determine association among continuous and categorical variables.Correlation was performed to find out the relation between different continuous variables.For all statistical analyses $p<0.05$ was considered statistically significant.

RESULTS:

A total of 150 cases with Type 2 Diabetes were included in the present study.

Overall Mean age of study participants was 56.98 $\pm$ 10.27 years with a range from 30 to 88 years.

Overall Mean duration of Type 2 Diabetes was 7.65 $\pm$ 5.81 years with a range from 1 to 30 years.

Overall Mean height of the study participants was 160.13 $\pm$ 7.66 cms with a range from 143 to 182 cms.

Overall Mean weight of the study participants was 66.41 $\pm$ 11.88 kgs with a range from 35 to 106 kgs.

Overall Mean BMI of the study participants was 25.84 $\pm$ 4.24 kg/m^2 with a range from 14.5 to 42.20 kg/m^2.

Overall Mean waist circumference of the study participants was 87.88 $\pm$ 9.64 cms with a range from 64 to 106 cms.

Overall Mean Waist to Hip ratio of the study participants was 0.898 $\pm$ 0.109 with a range from 0.7 to 1.07.

Overall Mean Hb of the study participants was 10.62 $\pm$ 1.74 gm% with a range from 7.0 to 16.2 gm%.

Overall Mean FBS of the study participants was 169.26 $\pm$ 45.282 mg/dl with a range from 88 to 409 mg/dl.

Overall Mean PPBS of the study participants was 256.69 $\pm$ 71.64 mg/dl with a range from 152 to 550 mg/dl.

Overall Mean HbA1C of the study participants was 9.112 $\pm$ 1.36 % with a range from 7.0 to 12.8%.

Overall Mean UACR of the study participants was 43.525 $\pm$ 60.03 mg/g with a range from 3.4 to 317 mg/g.

Overall Mean serum creatinine of the study participants was 1.59 $\pm$ 1.25 with a range from 0.4 to 8.7 mg/dl.

Overall Mean EGFR of the study participants was 73.65 $\pm$ 40.428 ml/min/m^2 with a range from 7 to 162 ml/min/m^2.

table2. GENDER DISTRIBUTION IN STUDY POPULATION

SEX	Frequency	Percent
FEMALE	71	47.3
MALE	79	52.7
Total	150	100.0

Out of 150 cases, 36 cases (24%) in stage II, 29 cases in stage IV (19.3%) and only 2 cases (1.3%) were in stage III nephropathy respectively. Around 55% cases do not have nephropathy.

Table3. Distribution Of Patients With Usg Evidence Of Renal Parenchymal Changes In Study Population

USG FINDING	Frequency	Percent
GRADE 1-2	30	20.0
GRADE 2-3	29	19.3
GRADE 3-3	1	0.7
NAD	90	60.0
Total	150	100.0

Table4. DISTRIBUTION OF PATIENTS WITH DIASTOLIC DYSFUNCTION ON 2D ECHO IN STUDY POPULATION

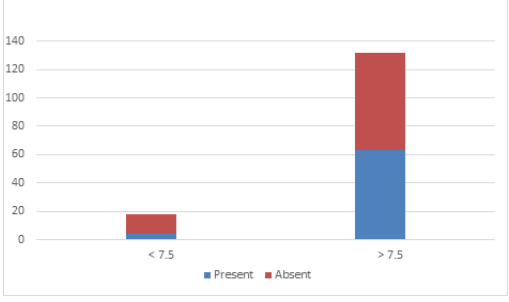
2D ECHO FINDING	Frequency	Percent
DIASTOLIC DYSFUNCTION	77	51.3
NORMAL	73	48.7
Total	150	100.0

Out of 150 cases, 82 (54.7%) had dyslipidemia which accounts to more than half.

Table5.association Between Hba1c And Nephropathy In Study Population

HbA1C	Nephropathy		
	Present	Absent	Total
< 7.5	4 (22.2%)	14 (77.8%)	18
>7.5	63 (47.7%)	69 (52.3%)	132
Total	67	83	150

Chi square=4.169, df=1, P value=0.0412(significant)



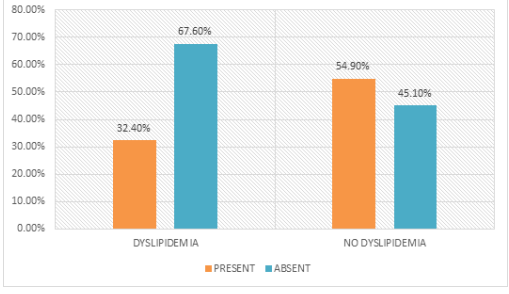
Graph1. Association Between Hba1c And Nephropathy In Study Population

Out of 150 cases, 18 cases had HbA1C <7.5% and 132 cases were having HbA1C>7.5%. Around 22.2% of the cases with HbA1C<7.5% had nephropathy as compared to 47.7% of cases with HbA1C>7.5%. This shows a better association between HbA1C and nephropathy. This difference was found to be statistically significant on chi square test (P value <0.05).

Table6. association Between Dyslipidemia And Nephropathy Status In Study Population

			Nephropathy Status		Total
			Present	Absent	
Dyslipidemia	Absent	Count	22	46	68
		Percent	32.4%	67.6%	100.0%
	Present	Count	45	37	82
		Percent	54.9%	45.1%	100.0%
Total		Count	67	83	150
		Percent	44.7%	55.3%	100.0%

Chi square = 7.631, df = 1, P value = 0.006 (Significant)



Graph 2.association Between Dyslipidemia And Nephropathy Status In Study Population

Out of 150 cases, 82 cases had dyslipidemia and 68 cases were having normal lipid levels. Around 55% of the cases with dyslipidemia had nephropathy as compared to 32.4% of cases with normal lipid levels. This shows a better association betweendyslipidemia and nephropathy. This difference was found to be statistically significant on chi square test (P value <0.05).

Out of 150 cases, 82 cases had dyslipidemia and 68 cases were having normal lipid levels. Around 53.7% of the cases with dyslipidemia had diastolic dysfunction as compared to 48.5% of cases with normal lipid levels. This shows an association between dyslipidemia and diastolic dysfunction. However, this difference was not found to be statistically significant on chi square test (P value >0.05)

Table7. Association Between Usg Evidence Of Renal Parenchymal Changes And Diastolic Dysfunction In Study Population

			Diastolic Dysfunction		Total
			Present	ABSENT	
USG	Grade 1-2	Count	18	12	30
		Percent	60.0%	40.0%	100.0%
	GRADE 2-3	Count	20	9	29
		Percent	69.0%	31.0%	100.0%
	GRADE 3-3	Count	0	1	1
		Percent	0.0%	100.0%	100.0%
	NAD	Count	39	51	90
		Percent	43.3%	56.7%	100.0%
Total		Count	77	73	150
		Percent	51.3%	48.7%	100.0%

Chi square = 7.871, df = 3, P value = 0.049 (Significant)

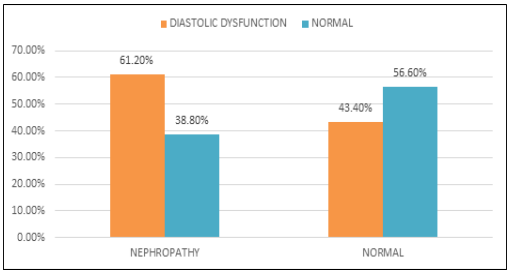
From the above table it was found that, 60% of cases with grade 1-2 and 69% of cases with grade 2-3 on ultrasound had diastolic dysfunction as compared to 43.3% cases with normal ultrasound findings. This difference was also found to be statistically significant on chi square test (P value <0.05).

Out of 150 cases, 51 cases showed LVH on ECG and 99 cases had normal findings on ECG. Among those cases with LVH on ECG, 82.4% had diastolic dysfunction as compared to 35.4% cases who had normal ECG findings. This shows an association between abnormal ECG findings and diastolic dysfunction and it was also found to be statistically significant (P value <0.05).

Table8. association Between Nephropathy Status And Diastolic Dysfunction In Study Population

			Diastolic Dysfunction		Total
			PRESENT	ABSENT	
Nephropathy Status	Present	Count	41	26	67
		Percent	61.2%	38.8%	100.0%
	Absent	Count	36	47	83
		Percent	43.4%	56.6%	100.0%
Total		Count	77	73	150
		Percent	51.3%	48.7%	100.0%

Chi square = 4.713, df = 1, P value = 0.03 (Significant)



Graph 3.association Between Nephropathy Status And Diastolic Dysfunction In Study Population

Out of 150 cases of type 2 Diabetes mellitus, 67 cases had nephropathy and 83 cases did not have nephropathy. Among 67 cases with nephropathy, 41 cases (61.2%) had diastolic dysfunction whereas 36 out of 83 cases (43.4%) without nephropathy had diastolic dysfunction. This shows a better association between presence of nephropathy and diastolic dysfunction. Also this association was found to be statistically significant on chi square test (P value <0.05).

Table 9. Comparison Of Study Variables And Nephropathy

Study Variable	Nephropathy Status	N	Mean	SD	t	P value
AGE	PRESENT	67	58.57	10.37	1.710	0.089
	ABSENT	83	55.70	10.07		
Duration Of T2dm	PRESENT	67	10.70	6.83	6.525	0.001
	ABSENT	83	5.19	3.17		
Height	PRESENT	67	160.54	7.25	.579	0.564
	ABSENT	83	159.81	8.007		
Weight	PRESENT	67	64.60	10.2	-1.693	0.093
	ABSENT	83	67.88	12.9		
BMI	PRESENT	67	25.03	3.74	-2.108	0.037
	ABSENT	83	26.49	4.52		
Waist Circumference	PRESENT	67	88.85	8.83	1.113	0.267
	ABSENT	83	87.09	10.23		
WHR	PRESENT	67	0.86	0.09	-3.775	0.001
	ABSENT	83	0.92	0.11		
Hb	PRESENT	67	10.17	1.60	-2.926	0.004
	ABSENT	83	10.98	1.77		
FBS	PRESENT	67	175.61	55.03	1.551	0.123
	ABSENT	83	164.13	35.04		
PPBS	PRESENT	67	269.01	84.4	1.910	0.05
	ABSENT	83	246.73	57.9		
HbA1C	PRESENT	67	9.09	1.02	-.145	0.885
	ABSENT	83	9.12	1.58		
UACR	PRESENT	67	84.56	70.77	9.5213	0.0001
	ABSENT	83	10.4	5.38		
Serum Creatinine	PRESENT	67	2.51	1.37	10.935	0.003
	ABSENT	83	0.84	0.23		
EGFR	PRESENT	67	37.54	24.9	-16.517	0.001
	ABSENT	83	102.80	23.3		

- Mean age of cases with nephropathy was 58.5 years and without nephropathy was 55.7 years. On unpaired t test this difference was not found to be statistically significant (P value >0.05)
- Mean duration of type 2 DM among cases with nephropathy was 10.7 years and among cases without nephropathy was 5.19 years. On unpaired t test this difference was found to be statistically significant (P value <0.05). This shows that cases with more duration of type 2 DM had more risk of nephropathy.
- Mean height of cases with nephropathy was 160.54 cms and without nephropathy was 159.81 cms. On unpaired t test this difference was not found to be statistically significant (P value >0.05)
- Mean weight of cases with nephropathy was 64.6 kgs and without nephropathy was 67.88 kgs. On unpaired t test this difference was not found to be statistically significant (P value >0.05)
- Mean BMI of cases with nephropathy was 25.03 and without nephropathy was 26.49. On unpaired t test this difference was found to be statistically significant (P value <0.05)
- Mean waist circumference of cases with nephropathy was 88.85 cms and without nephropathy was 87.09 cms. On unpaired t test this difference was not found to be statistically significant (P value >0.05)
- Mean WHR of cases with nephropathy was 0.86 and without nephropathy was 0.92. On unpaired t test this difference was found to be statistically significant (P value <0.05)
- Mean Hb of cases with nephropathy was 10.17 gm% and without nephropathy was 10.98 gm%. On unpaired t test this difference was found to be statistically significant (P value <0.05)
- Mean FBS of cases with nephropathy was 175.6 mg/dl and without nephropathy was 164.13 mg/dl. On unpaired t test this difference was not found to be statistically significant (P value >0.05)
- Mean PPBS of cases with nephropathy was 269.01 mg/dl and without nephropathy was 246.73 mg/dl. On unpaired t test this difference was not found to be statistically significant (P value is 0.05)
- Mean HbA1C of cases with nephropathy was 9.09 and without nephropathy was 9.12. On unpaired t test this difference was not found to be statistically significant (P value >0.05)
- Mean UACR of cases with nephropathy was 84.56 and without nephropathy was 10.4. On unpaired t test this difference was found to be statistically highly significant (P value <0.01)
- Mean serum creatinine of cases with nephropathy was 2.51 and without nephropathy was 0.84. On unpaired t test this difference was found to be statistically highly significant (P value <0.01)
- Mean EGFR of cases with nephropathy was 37.54 and without nephropathy was 102.8. On unpaired t test this difference was found to be statistically highly significant (P value <0.01)

Table10.comparison Of Study Variables And Diastolic Dysfunction

Variable	Diastolic Dysfunction	N	Mean	SD	t	P value
Age	PRESENT	77	58.82	10.64	2.282	0.024
	ABSENT	73	55.04	9.56		
Duration Of T2dm	PRESENT	77	8.84	6.17	2.627	0.010
	ABSENT	73	6.4	5.15		
Height	PRESENT	77	160.84	8.06	1.168	0.245
	ABSENT	73	159.38	7.18		
Weight	PRESENT	77	65.9	12.44	-.491	0.624
	ABSENT	73	66.9	11.31		
BMI	PRESENT	77	25.44	4.40	-1.184	0.238
	ABSENT	73	26.26	4.05		
Waist Circumference	PRESENT	77	87.83	10.16	-0.068	0.946
	ABSENT	73	87.93	9.13		
WHR	PRESENT	77	0.9	0.104	.288	0.774
	ABSENT	73	0.89	0.11		
Hb	PRESENT	77	10.33	1.70	-2.116	0.036
	ABSENT	73	10.92	1.73		
FBS	PRESENT	77	174.10	40.91	1.349	0.179
	ABSENT	73	164.15	49.24		
PPBS	PRESENT	77	268.3	67.91	2.068	0.040
	ABSENT	73	244.4	73.85		
HbA1C	PRESENT	77	9.49	1.24	3.709	0.006
	ABSENT	73	8.7	1.36		
UACR	PRESENT	77	61.9	76.4	4.0504	0.0001
	ABSENT	73	24.1	23.4		
Serum Creatinine	PRESENT	77	1.85	1.46	2.710	0.008
	ABSENT	73	1.31	0.90		
EGFR	PRESENT	77	63.82	38.29	-3.148	0.002
	ABSENT	73	84.01	40.28		

- Mean age of cases with diastolic dysfunction was 58.8 years and without diastolic dysfunction was 55.04 years. On unpaired t test this difference was found to be statistically significant (P value <0.05)
- Mean duration of type 2 DM among cases with diastolic dysfunction was 8.84 years and among cases without diastolic dysfunction was 6.4 years. On unpaired t test this difference was found to be statistically significant (P value <0.05). This shows that cases with more duration of type 2 DM had more risk of diastolic dysfunction.
- Mean height of cases with diastolic dysfunction was 160.8 cms and without diastolic dysfunction was 159.3 cms. On unpaired t test this difference was not found to be statistically significant (P value >0.05)
- Mean weight of cases with diastolic dysfunction was 65.9 kgs and without diastolic dysfunction was 66.9 kgs. On unpaired t test this difference was not found to be statistically significant (P value >0.05)
- Mean BMI of cases with diastolic dysfunction was 25.4 and without diastolic dysfunction was 26.2. On unpaired t test this difference was not found to be statistically significant (P value >0.05)
- Mean waist circumference of cases with diastolic dysfunction was 87.83 cms and without diastolic dysfunction was 87.93 cms. On unpaired t test this difference was not found to be statistically significant (P value >0.05)
- Mean WHR of cases with diastolic dysfunction was 0.9 and without diastolic dysfunction was 0.89. On unpaired t test this difference was not found to be statistically significant (P value >0.05)
- Mean Hb of cases with diastolic dysfunction was 10.33 gm% and without diastolic dysfunction was 10.92 gm%. On unpaired t test this difference was found to be statistically significant (P value <0.05)
- Mean FBS of cases with diastolic dysfunction was 174.1 mg/dl and without diastolic dysfunction was 164.1 mg/dl. On unpaired t test this difference was not found to be statistically significant (P value >0.05)
- Mean PPBS of cases with diastolic dysfunction was 268.3 mg/dl

and without diastolic dysfunction was 244.4 mg/dl. On unpaired t test this difference was found to be statistically significant (P value <0.05)

- Mean HbA1C of cases with diastolic dysfunction was 9.49 and without diastolic dysfunction was 8.7. On unpaired t test this difference was found to be statistically significant (P value <0.05)
- Mean UACR of cases with diastolic dysfunction was 61.9 and without diastolic dysfunction was 24.1. On unpaired t test this difference was found to be statistically highly significant (P value <0.01)
- Mean serum creatinine of cases with diastolic dysfunction was 1.85 and without diastolic dysfunction was 1.31. On unpaired t test this difference was found to be statistically highly significant (P value <0.01)
- Mean EGFR of cases with diastolic dysfunction was 63.82 and without diastolic dysfunction was 84.01. On unpaired t test this difference was found to be statistically highly significant (P value <0.01)

DISCUSSION:

Comparing glycemic indices FBS, PPBS, HbA1C in Type 2 diabetics with nephropathy with other studies

In the present study majority of patients had higher FBS, PPBS and HbA1C values, the mean FBS value was 175.6±55.03 mg/dl (p=0.123), and the mean PPBS value was 269.01±84.4 mg/dl (p=0.05), and the mean HbA1C value was 9.09±1.02 %, when HbA1C compared with <7.5% and >7.5% (p<0.05) and it was statistically associated with diabetic nephropathy.

The above data has been compared with other studies like CURE study by Unnikrishnan et al where the mean FBS was 183.6±70.2 mg/dl (p<0.0001) and the mean HbA1C was 9.5±2.3 % (p<0.0001)[16], in a study by Sanjeev Kumar et al where the mean FBS was 211.52±27.85 mg/dl (p<0.0001), mean HbA1C was 8.37±0.83 %, (p<0.0001)[17], in a study by Retnakaran et al where the mean FBS was 147.6 mg/dl (p<0.0001) and the mean HbA1C was 6-8% (p=0.0004)[18], in a study by Debbarma et al where the mean FBS was 230.81±111.66 mg/dl (p=0.21), the mean PPBS was 362.24±143.02 mg/dl (p=0.01), the mean HbA1C was 8.9±2.4 (p=0.02)[19], in a study by Prataap K Chandie Shaw et al where the mean HbA1C was 7-9 % (p=0.3)[20], in a Japanese study by Yuko watanabe et al HbA1C when compared with eGFR (p=0.008) and albuminuria (p=0.03) there was significant association seen[21].

The present study was in correlation with the above mentioned studies and there was significant association between the high glycemic indices like HbA1C in type 2 diabetics with nephropathy and high values of FBS and PPBS were present but not significantly associated with nephropathy. This shows that uncontrolled hyperglycemia had increased risk for nephropathy in type 2 diabetes patients.

Comparing dyslipidemia in Type 2 diabetics with nephropathy with other studies

In the present study group the prevalence of dyslipidemia or abnormal lipid levels in diabetics was 54.7% and in Type 2 diabetics with nephropathy it was 54.9% (p=0.006) which shows a significant association between dyslipidemia and nephropathy.

The above data was compared with other studies like Jayapalreddy et al where there was a prevalence of 81.5% with abnormal lipid levels in patients with diabetic nephropathy[22], this was also compared with another study GALL MA et al where elevated serum lipids was a risk factor for the development of diabetic nephropathy[23], in another study by Debbarma et al where the total cholesterol (p=0.01), LDL cholesterol(p=0.009) and triglycerides (p=0.224) were higher in microalbuminuria group than normoalbuminuria group and the differences were statistically highly significant except for HDL in males (p=0.154) and triglycerides(p=0.224)[19], in a study by Prataap K Chandie Shaw et al there was no significant association between abnormal lipid levels and nephropathy[20], in a study by Retnakaran et al (UKPDS 74) where dyslipidemia (total cholesterol (p=0.04), HDL cholesterol (p=0.02), LDL cholesterol (p=0.08), triglycerides (p<0.0001)) had a significant association with albuminuria or nephropathy[18], in a Japanese study by Yuko watanabe et al dyslipidemia has no significant association with eGFR (p=0.26) but had a significant association with albuminuria (p<0.005[21].

The present study was in correlation with the above studies and shows that abnormal elevated serum lipid levels or dyslipidemia had a significant association with diabetic nephropathy.

Comparing renal parameters UACR, serum creatinine, and eGFR in Type 2 diabetics with nephropathy with other studies

In the present study group mean urine albumin creatinine ratio (UACR) was 84.6±70.8 mg/g (p=0.0001), and the mean serum creatinine was 2.51±1.37 mg/dl (p=0.003), and the mean eGFR was 37.54±24.9 ml/min/m^2 (p=0.001), which shows that the renal parameters which were mentioned shows statistically significant association with the nephropathy.

The above data was compared with other studies like DCCT where gender specific equations of ACR shows a cut off of micro albuminuria and macro albuminuria in males was 19.1 mg/g and 143.5 mg/g, in females was 29.0 mg/g and 217.4 mg/g, and eGFR mean was 84.5±17.1 ml/min/m^2 (p<0.001), and serum creatinine mean was 0.95±0.3 mg/dl (p<0.001), and these values are found to be significantly associated[24], in a study by Fisher et al the mean eGFR was 43±13 ml/min/m^2 and median ACR was 46 mg/g[25], in a Japanese study by Yuko watanabe et al the mean ACR with respect to albuminuria was 261.5 mg/g (p<0.001), and with respect to eGFR strata it was not significantly associated, and in that study mean eGFR and mean serum creatinine when compared to eGFR strata they were significantly associated but with respect to albuminuria they were not significantly associated[21], in various other studies like Sanjeev kumar et al mean serum creatinine was 1.76±0.59 mg/dl (p<0.0001) and was significantly associated with nephropathy[17], in Debbarma et al mean serum creatinine was 1.08±0.18 mg/dl (p=0.01) and shows a significant association with nephropathy[19], in Prataap K et al mean serum creatinine was 0.86 mg/dl and shows significant association with macro albuminuria (p=0.00093) and not significantly associated with microalbuminuria (p=0.20), in Prataap K et al south Asians showed an eGFR of 100ml/min and Europeans showed an eGFR of 90ml/min/m^2[20], in CURE study ACR showed a significant association with macro albuminuria (p=0.043) but not significantly associated with microalbuminuria[16].Levey et al studied role of eGFR in chronic kidney disease in predicting prognosis, eGFR was one of the important indicator of reserved renal function and indicator of prognosis[26].

The present study was in correlation with above studies and shows that rise in UACR and serum creatinine and a decline in eGFR shows a significant association with diabetic nephropathy. This may be related to longer duration of diabetes and its complications.

In the present study there was significant correlation between Duration of Type 2 Diabetes, BMI, WHR, HbA1c <7.5% and >7.5%, UACR, serum creatinine, eGFR, dyslipidemia, Hb, USG showing renal parenchymal changes, and diastolic dysfunction with nephropathy.

The present study was showed a significant association between the duration of diabetes mellitus and diastolic dysfunction, which means that longer the duration of diabetes there was increase in prevalence of diastolic dysfunction.

The present study showed that uncontrolled hyperglycemia which was better indicated by the glycemic indices like FBS, PPBS and HbA1c was associated with diastolic dysfunction.

The present study showed that abnormal lipid levels were seen in patients with diastolic dysfunction but not significantly associated

The present study showed nephropathy detecting renal parameters in a diabetic patient like UACR, serum creatinine, eGFR and USG showing renal parenchymal changes were all independently associated with diastolic dysfunction in Type 2 diabetes patients.

The present study showed significant association between anemia and diastolic dysfunction. Hemoglobin measurement was an inexpensive tool in diabetes patients at increased risk of cardiac dysfunction.

The present study was in correlation with the studies by J. Miyazato et al and showed increased prevalence of diastolic dysfunction in diabetics with nephropathy.

The present study was in correlation with studY by J. Miyazato et al and showed that left ventricular hypertrophy in diabetic patients was significantly associated with diastolic dysfunction and was an independent risk factor for diastolic dysfunction.

In the present study there was significant correlation between age, duration of Type 2 Diabetes, PPBS, HbA1c, UACR, serum creatinine, eGFR, Hb, ecg showing LVH and Diabetic nephropathy with diastolic dysfunction.

CONCLUSION:

- Results of the present study reveals that there is significant evidence to support the conclusion that microalbuminuria or proteinuria in patients with diabetes is a potential risk factor not only for kidney function impairment but also a marker for high risk of cardiovascular complications.
- Type 2 DM subjects with and without nephropathy should be screened for sub clinical diastolic dysfunction by echocardiography.
- These patients should receive a multifactorial treatment and should be monitored carefully to prevent or slow down the progression of both kidney and cardiovascular complications.

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