A Study of Estimated Glomerular Filtration Rate and Urine Albumin To Creatinine Ratio In Subjects With CVD In Type 2 Diabetes Mellitus

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ABSTRACT
BACKGROUND:
Chronic kidney disease is one of the major complication in patients with Type2 DM. Renal impairment can manifest as decrease eGFR, progression from microalbuminuria to proteinuria.
However albuminuria may be absent in cases with abnormal eGFR.
There were studies trying to explore the relationship between eGFR and albuminuria on the prognosis of type 2 DM patients. A strong synergistic and individual association was found with progression of disease to ESRD.
Whether eGFR and UACR have similar predictive value on CVD in patients with Type 2 Diabetes Mellitus needed to studied. Hence this study aims at evaluating the eGFR and UACR in subjects with CVD in Type 2 Diabetes Mellitus.
OBJECTIVES:
To study the relationship between eGFR and risks for CVD in Type 2 Diabetes Mellitus
To study the relationship between Urine Albumin-Creatinine ratio and risks for CVD in Type 2 Diabetes Mellitus
METHODS:
In 100 subjects with Type 2 Diabetes Mellitus and CVD attending outpatient department / admitted at K R Hospital mysuru, detailed history was taken and clinical examination was done after taking informed consent.
Age, gender, presenting complaints and signs, diagnosis relevant investigations were recorded. HbA1C, renal function test was done eGFR calculated.
Early morning spot urinary albumin creatinine ratio was measured.
RESULTS:
In the present study of 100 subjects of Type 2 Diabetes Mellitus with CVD 36 were female and 64 were male, female to male sex ratio is 1:1.7. Maximum number of the study subjects were having type 2 DM since 1-5 years. 36% of study subjects were having eGFR 30-59 ml/min/1.73m^2. Most of the study subjects (51%) were having a UACR of less than 0.5. Correlation between HbA1C and eGFR was significant with a p value of less than 0.005. As the HbA1C is increasing eGFR decreases according to our study.
CONCLUSION:
These results suggest that incorporation of quantitative information about albuminuria into staging systems based on eGFR useful information about risk for diabetic ESRD. Increased UACR levels were closely related to the increase in risks for renal, cardiovascular events and all-cause mortality in patients with type 2 diabetes, whereas the association between high levels of UACR and reduced eGFR was a strong predictor for renal events.
CVD events and eGFR drop increased exponentially, while UACR showed positive predictive linear relationships, and the risks started even in high-normal albuminuria. UACR was further modified according to eGFR level, with risk progressed with CKD stage. Combining eGFR and UACR level was more accurate in predicting risk of CVD/mortality. The findings call for more aggressive screening and intervention of microalbuminuria in diabetic patients.
KEY WORDS: *Type 2 Diabetes Mellitus, CVD- Cardiovascular disease, HbA1C-glycosylated haemoglobin, Egfr- estimated glomerular filtration rate, UACR- Urine Albumin Creatinine Ratio.*

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I.   Introduction

Diabetes mellitus is a metabolic disorder, due to relative or absolute lack of insulin resulting in elevated blood glucose levels associated with long term microvascular and macrovascular

complications.Number of people with diabetes rised from 108 million in 1980 to 422 million in 2014. Incidence is rised from 4.7% in 1980 to 8.5% in 2014

Diabetes mellitus is the most common cause of end stage renal disease (ESRD) and it has been estimated that 592 million people worldwide will have Diabetes mellitus by 2035.

Between 20-40 % of patient of type 2 Diabetes will develop nephropathy, the incidence being related in part to disease duration.

Between 10-20%type 2 Diabetic patients with nephropathy will progress to ESRD. Glomerulonephritis and interstitial nephritis which appeared to be the common causes of CKD in developing countries earlier is now replaced by diseases like Diabetes mellitus- 41% and hypertension -23%.

India, the second most populous country has the most diabetics in the world with 60 million cases (2015,WHO)

Chronic kidney disease is one of the major complication in patients with Type2 DM. Renal impairment can manifest as decrease eGFR, progression from microalbuminuria to proteinuria.

However albuminuria may be absent in cases with abnormal eGFR.

There were studies trying to explore the relationship between eGFR and albuminuria on the prognosis of type 2 DM patients. A strong synergistic and individual association was found with progression of disease to ESRD.

Whether eGFR and UACR have similar predictive value on CVD in patients with Type 2 Diabetes Mellitus needed to studied. Hence this study aims at evaluating the eGFR and UACR in subjects with CVD in Type 2 Diabetes Mellitus.

II. Objectives

To study the relationship between eGFR and risks for CVD in Type 2 Diabetes Mellitus

To study the relationship between Urine Albumin-Creatinine ratio and risks for CVD in Type 2 Diabetes Mellitus

Methodology

SOURCE OF DATA:

Observation method of primary source of information includes subjects >18 years with Type 2 Diabetes Mellitus with CVD attending outpatient department / admitted at Krishnarajendra Hospital, Mysore from January 2018 to June 2019.

Secondary source of information from published articles, journals, books, case sheets, related website is used in planning, developing synopsis and during dissertation as supporting document.

STATISTICALMETHODS:

Sample size: Using estimation set up technique for the level of significance =5% and allowable error over 10%, the inflated sample size is estimated as 40, using the formula   n = 4PQ / d2

Where P is the prevalence, Q is 1-P and d = 10% = .01 (margin of error) Statistical methods applied. Both descriptive and inferential statistics were employed for data analysis.

The **Descriptive statistics** procedure displays uni-variate summary statistics for several variables in a single table and calculates standardized values. Variables can be ordered by the size of their means alphabetically, or by the order in which the researcher selects the variables.

In the present study following descriptive statistics have been employed

Frequencies

Percentages

Mean

Standard deviation

Inferential statistics

Chi-square test

The chi-square test procedure tabulates a variable into categories and computes a chi-square statistic. This goodness-of-fit test compares the observed and expected frequencies in each category to test either that all categories contain the same proportion of values for that each category contains a user specified proportion of values.

Crosstabs (Cramer's V)

The crosstabs procedure forms two-way and multi-way tables and provides a variety of tests and measures of association for two-way tables. The structure of the table and whether categories are ordered determine what test or measure to use.

Cramer's V as a measure of association between rows and columns was employed.

III. Method Of Collection

Sampling procedure:

After taking informed written consent; history and clinical examination was done of all selected cases according to proforma

Patients with Type 2 Diabetes Mellitus with CVD satisfying inclusion and exclusion criteria are registered in the study

Age, gender, presenting complaints and signs, diagnosis relevant investigations were recorded

Early morning spot Urinary Albumin Creatinine ratio was measured

All the data were entered in a data collection sheet in an Excel format and analysed using SPSS Software.

Numerical values were reported using mean and standard deviation.

Categorical valueswere reported using number and percentages.

Statistical significance will be shown by Chi-square test.

Probability (p) value less than 0.05 was considered a statistically significant.

INCLUSION CRITERIA

Age > 18 years who has given informed written consent

Patients attending outpatient department / admitted with type-2 DM with CVD

EXCLUSION CRITERIA

Patients diagnosed to have Type 1 DM
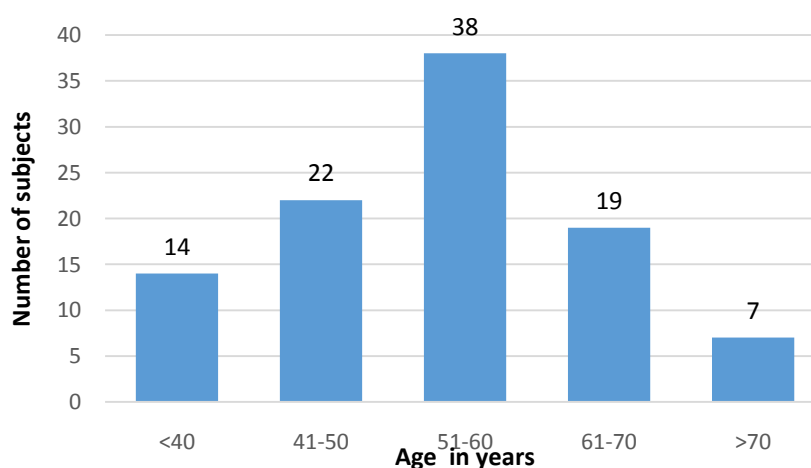
Patients diagnosed to have Heart Failure

Patients with Hepatorenal syndrome

IV. Results

Table 1: Age distribution among study subjects with Type 2 DM and CVD

Age In Years	Number of subjects	Percentage of subjects (%)
<40	14	14
41-50	22	22
51-60	38	38
61-70	19	19
>70	7	7
Total	100	100

Figure 1: Age distribution among subjects

In present study maximum number of subjects were in the age group 51-60 years 38%.

22% subjects were in the age group 41-50 years, 19% subjects were in age group 61-70 years, 14% subjects in age group <40 years and minimum number of subjects 7% were in the group >70 years. Among 100 subjects average mean age is 54.95+12.76.

Table 2: Gender distribution among study subjects

Sex	Number of subjects	Percentage of subjects
Female	36	36
Male	64	64
Total	100	100

Males were more (64%) as compared to females (36%) among study subjects
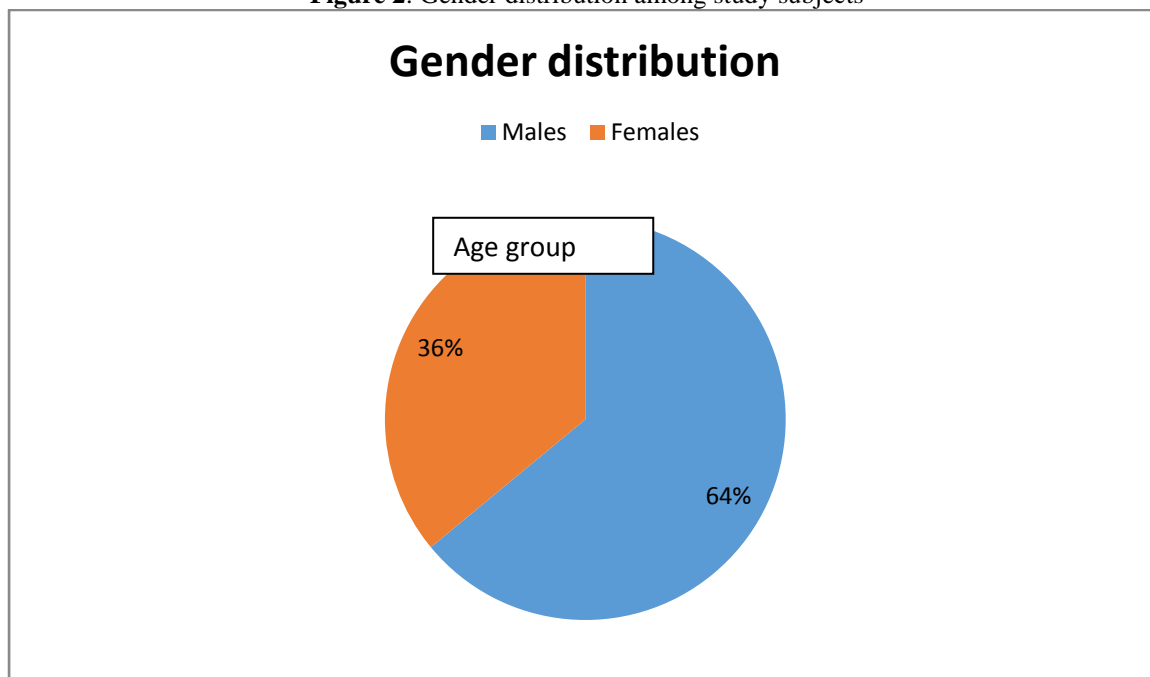
Figure 2: Gender distribution among study subjects

Table 3: Body Mass Index among study subjects

BMI in kg/m^2	Number of subjects	Percentage of subjects
<25	69	69
25-30	24	24
>30	7	7
Total	100	100

Most of the subjects (69%) were having BMI of less than 25.
24% subjects were having BMI between 25 and 30.
7% of the subjects were having BMI more than 30
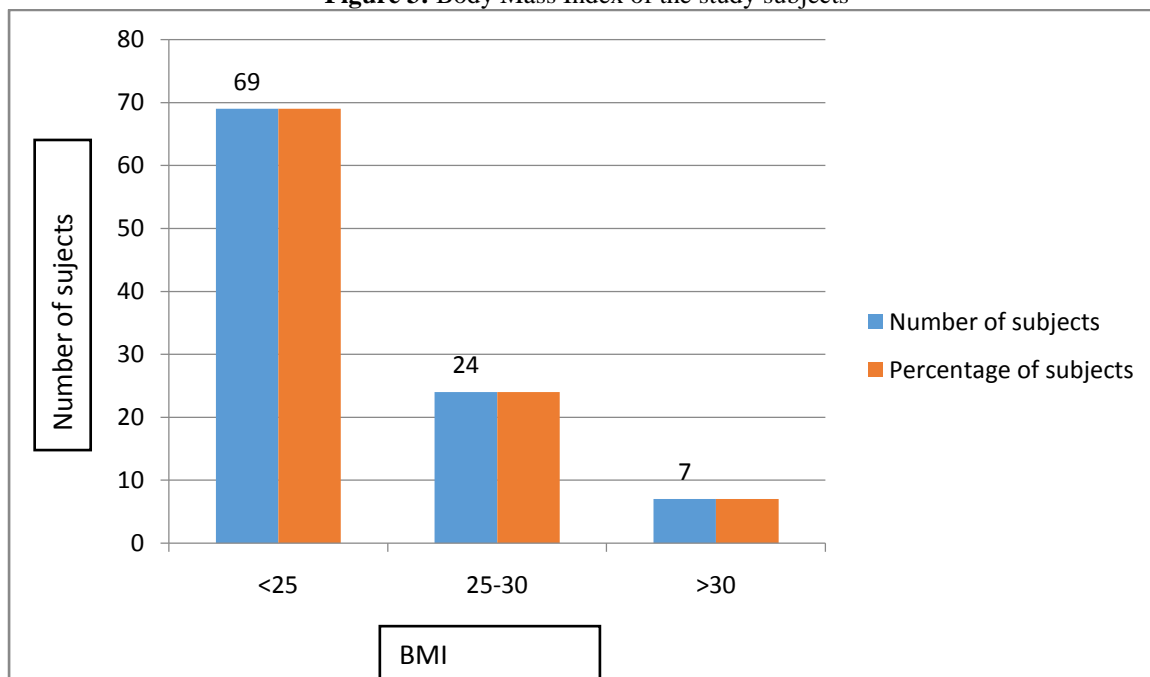
Figure 3: Body Mass Index of the study subjects

Table 4: Duration of Type 2 DM in study subjects

Duration of Type 2 Diabetes mellitus	Number of subjects	Percentage of subjects
Newly detected	3	3
1-5	49	49
6-10	36	36
11-15	4	4
16-20	8	8

Maximum number of subjects (49%) were having Type 2 DM since 1 to 5 years. 36 percentage were having Type 2 DM since 6 to 10 years.
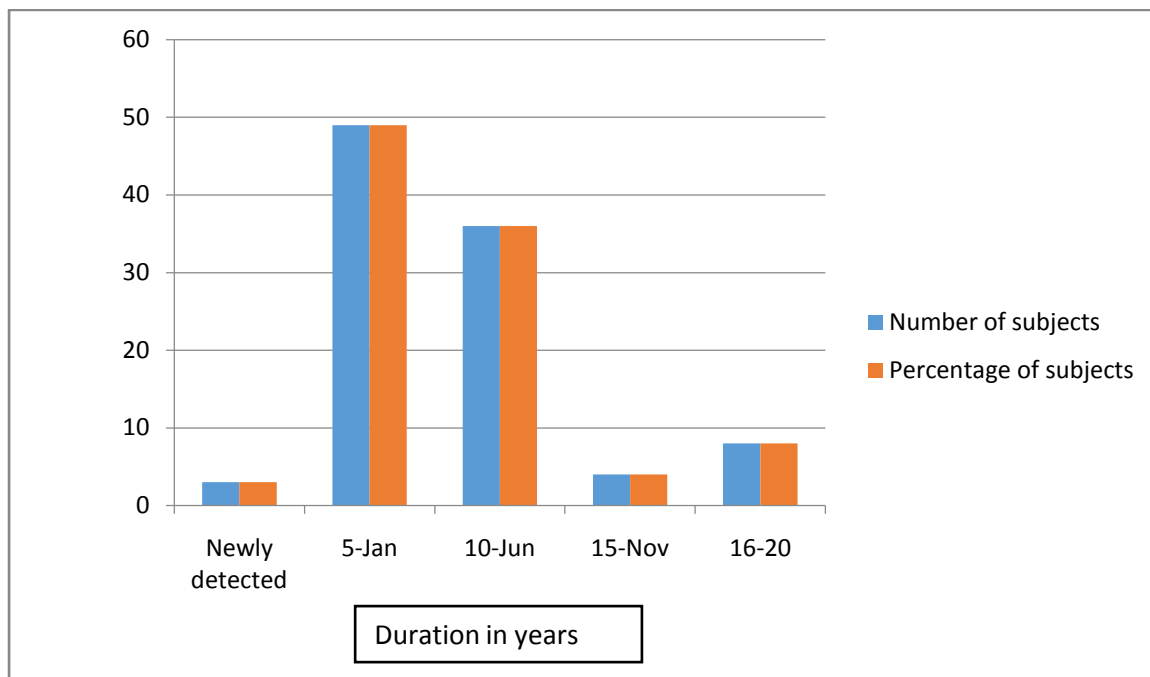
Figure 4: Duration of Type 2 DM among study subjects

Table 5: Estimated Glomerular Filtration Rate (eGFR) in study subjects

eGFR	Male	Female	Total
>90	15	6	21
75-89	5	2	7
60-74	4	1	5
30-59	23	13	36
15-29	9	6	15
<15	9	8	17

Most of the subjects (36%) were having an eGFR between 30 to 59.
21% were having eGFR more than 90

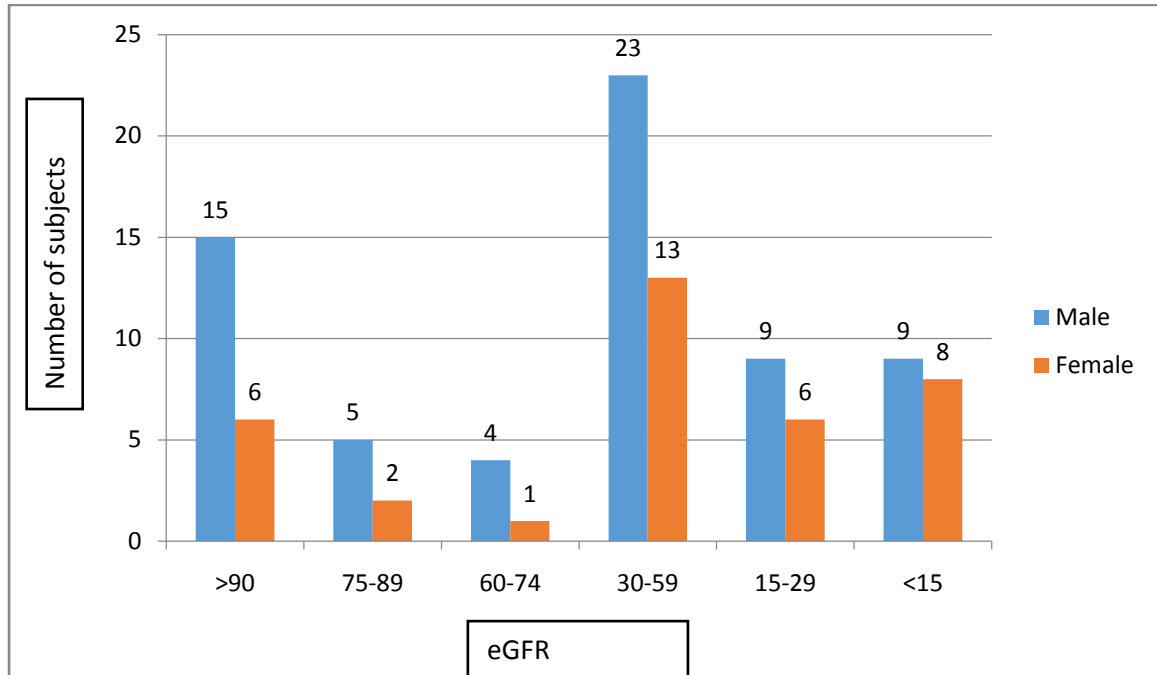**Figure 5:** Estimated GFR of study subjects

Table 6: Urine albumin creatinine ratio (UACR) of study subjects

UACR	Number of subjects	Percentage of subjects
<0.5	51	51
0.5-0.9	31	31
1-1.4	7	7
1.5-1.9	6	6
>2	5	5

Most of the study subjects (51%) were having a UACR of less than 0.5. 31% were having an UACR of 0.5 to 0.9

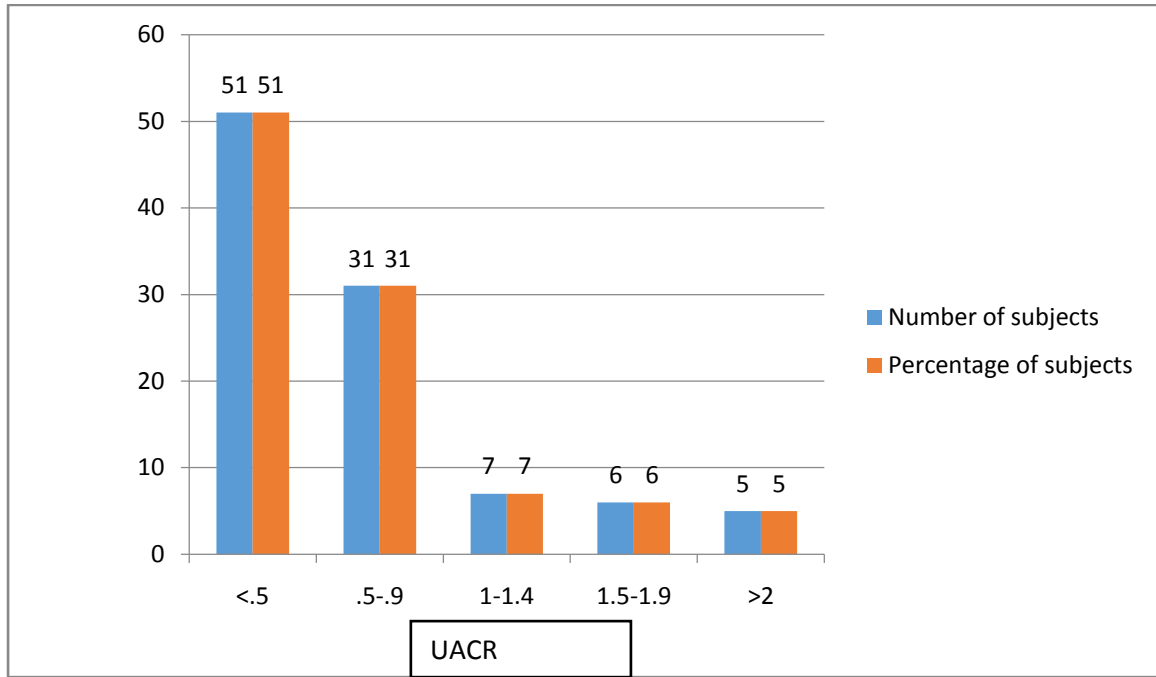**Figure 6:**Urine albumin creatinine ratio (UACR) of study subjects

Table 7: Correlation between HbA1C and eGFR

eGFR (ml/min/1.73m^2)	HbA1c <6.5 (Number of subjects)	HbA1c >6.5 (Number of subjects)	Total (Number of subjects)
>90	0	20	20
60-89	1	11	12
30-59	6	30	36
15-29	2	13	15
<15	5	12	17

Correlation between HbA1C and eGFR was significant with a p value of less than 0.005. As the HbA1C is increasing eGFR decreases according to our study

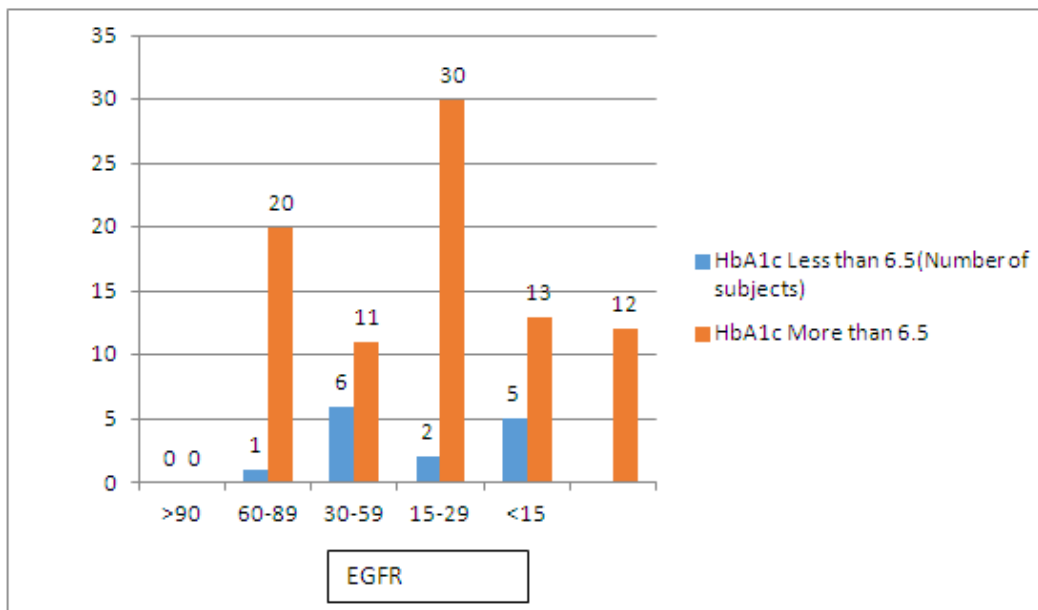**Figure 7:** Correlation between HbA1C and eGFR

Table 8: Correlation of mean age and eGFR in the study subjects

eGFR (ml/min/1.73m^2)	Mean age in years
>90	73.5±10.71
60-89	49.41±15.73
30-59	55.21±12.75
15-29	53.82±11.65
<15	61.38±10.83

In the present study subjects with Egfr <15 were in the mean age group of 61.38±10.83

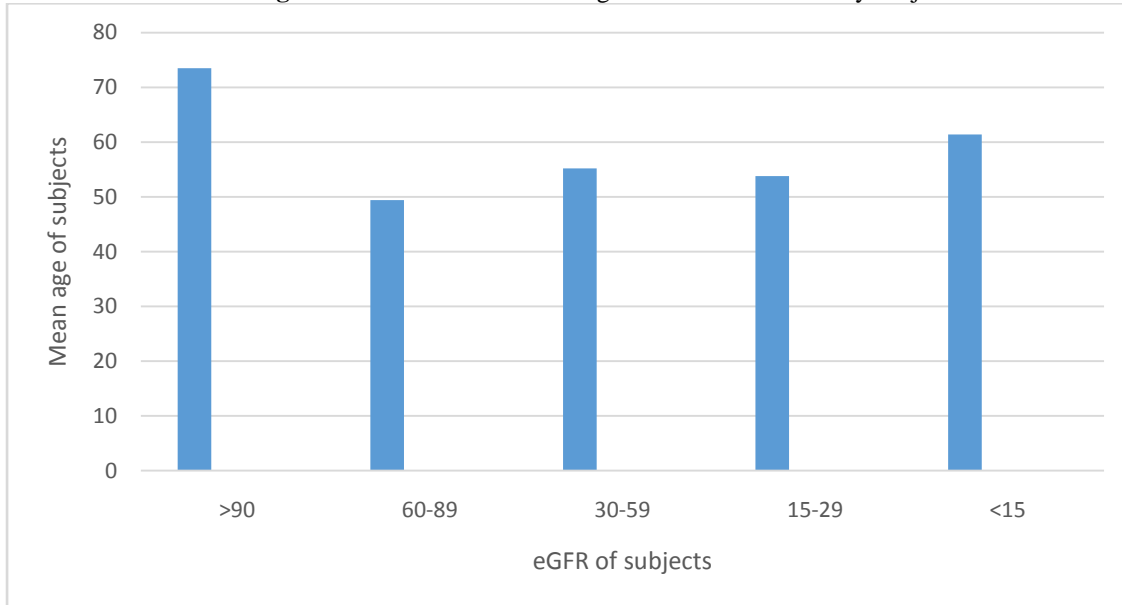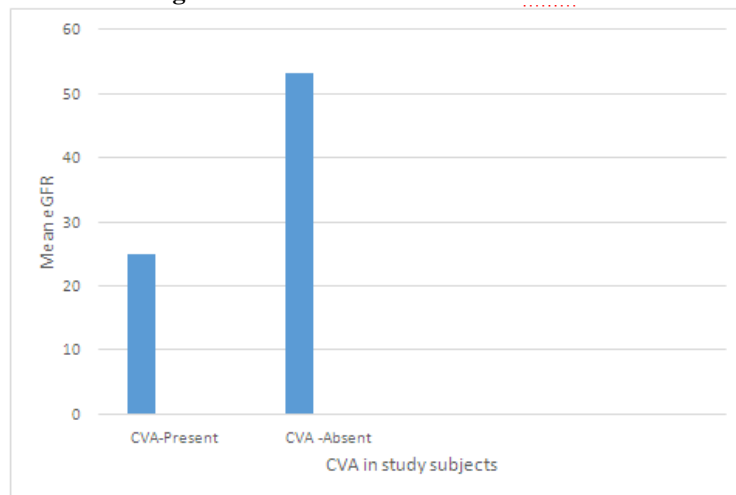**Figure 8:** Correlation of mean age and eGFR in the study subjects

Table 9: Correlation of CVA with eGFR

CVA	Number of subjects	Mean eGFR (ml/min/1.73m^2)
Present	12	24.90±13.68
Absent	88	53.32±35.97

In the present study eGFR is less in subjects with cerebrovascular accident with type 2 DM and CVD

Figure 9: Correlation of CVA with eGFR

V.   Discussion

Table 10: Mean Agedistributioncomparedtootherstudies

Study	Mean Age in years
Presentstudy	54.95
Colman sui etal	52.2
Brad C. Astor et al	48.8

The mean age in this study is 54.95 years which is comparable with previous studies conducted by Colman et al and Brad C. Astor et al in which mean age in study subjects were 52.2 and 48.8 years.

Table 11: Agedistributioncomparedtootherstudies

eGFR	Mean age in years		
	Colman et al	Brad C. Astor et al	Present study Total
>90	60.49	38.5	73.5
60-89	70.37	52.8	49.417
30-59	76.21	70.4	55.21
15-29	79.28		53.8
<15	76.89		61.38

Mean age according to Egfr was compared with other stuides like Colman et al and Brad C. Astor et al

Table 12: Genderdistributioncomparedtootherstudies

eGFR	Gender distribution			
	Colman et al		Present study Total	
	Male %	Female %	Male %	Female %
>90	53.3	46.7	21.9	16.7
60-89	56.4	43.6	14.1	8.3
30-59	66.6	33.4	35.9	36.1
15-29	70.1	29.9	14.1	16.7
<15	63.9	36.1	14	22.2

The present study is compared for gender distribution with other studies like Colman et al

Table 13: HbA1C and Egfr compared with other studies

eGFR	HbA1C	
	Colman et al	Present study
>90	7.40	10.14
60-89	7.14	9.66
30-59	6.96	8.56
15-29	6.63	7.9
<15	6.58	8.26

Table 14: BMI and Egfr compared with other studies

eGFR	BMI		
	Colman et al	Brad C. Astor et al	Present study Total
>90	25.57	26.2	24.14
60-89	25.43	27.1	25.35
30-59	25.07	27.6	22.99
15-29	24.86		23.34
<15	24.66	-	23.86

Table 15: Diastolic blood pressure and Egfr compared with other studies

	Diastolic blood pressure	
eGFR	Colman et al	Present study Total
>90	75.57	96
60-89	76.62	96.66
30-59	73.83	90.27
15-29	67	95.33
<15	67.9	96.70

Table 16: Mean eGFR is compared with other studies

	Mean eGFR	
eGFR	Colman et al	Present study Total
>90	114.74	117.06
60-89	77.79	72.74
30-59	50.34	41.58
15-29	24.30	21.53
<15	10.59	9.21

VI. Conclusion

These results suggest that incorporation of quantitative information about albuminuria into staging systems based on eGFR useful information about risk for diabetic ESRD. Increased UACR levels were closely related to the increase in risks for renal, cardiovascular events and all-cause mortality in patients with type 2 diabetes, whereas the association between high levels of UACR and reduced eGFR was a strong predictor for renal events.

CVD events and eGFR drop increased exponentially, while UACR showed positive predictive linear relationships, and the risks started even in high-normal albuminuria. UACR was further modified according to eGFR level, with risk progressed with CKD stage. Combining eGFR and UACR level was more accurate in predicting risk of CVD/mortality. The findings call for more aggressive screening and intervention of microalbuminuria in diabetic patients.

Table 17: UACR and eGFR compared with other studies

	UACR	
eGFR	Colman et al	Present study Total
>90	5.32	2.49
60-89	11.03	3.7
30-59	25.51	6.92
15-29	42.97	8.86
<15	25.47	8.68

Table 18: Duration of Diabetes compared with other studies

	Duration of Diabetes	
eGFR	Colman et al	Present study Total
>90	5.74	5.3
60-89	7.35	7.45
30-59	9.34	5.36
15-29	10.14	6.6
<15	9.2	7.58

In the present study duration of Diabetes is maximum in Egfr <15 is 7.58 is compared with other studies like Colman et al Egfr<15 is 9.2

VII. Summary

In the present study of 100 subjects of Type 2 Diabetes Mellitus with CVD 36% were female and 64 % were male,

Female to male sex ratio is 1:1.7. The mean age of presentation in our study is 35.9 years.

Most of the subjects (69%) were having BMI of less than 25.

24% subjects were having BMI between 25 and 30.

7% of the subjects were having BMI more than 30

Maximum number of subjects (49%) were having Type 2 DM since 1 to 5 years. 36 percentage were having Type 2 DM since 6 to 10 years.

Most of the subjects (36%) were having an eGFR between 30 to 59.

21% subjects were having eGFR more than 90

Most of the study subjects (51%) were having a UACR of less than 0.5.

31% were having an UACR of 0.5 to 0.9

Correlation between HbA1C and eGFR was significant with a p value of less than 0.005. As the HbA1C is increasing eGFR decreases according to our study

In the present study subjects with Egfr <15 were in the mean age group of 61.38±10.83

In the present study eGFR is less in subjects with cerebrovascular accident with type 2 DM and CVD

LIMITATIONS OF THE STUDY

Study subjects were not followed up.

In study group risk factors were not studied.

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