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Original Research Paper

A Gender based comparative analysis of type 2 diabetes mellitus: A case of chronic kidney disease patients (Gender comparison: CKD type 2 diabetes)

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ABSTRACT:
Diabetes Mellitus and Diabetes Mellitus related kidney diseases caused approximately 2 million deaths. Prevalence of type 2 Diabetes Mellitus is increasing in both genders, men are found to be diagnosed at a younger age and lower body fat mass when compared to women There are variances amongst men and women regarding Diabetes Mellitus with regards to comorbidities, the appearance of complications and the initiation of and adherence to therapy. The same is applicable to Chronic Kidney Diseases. Globally, diabetes has been observed to be the utmost cause of Chronic Kidney Diseases. Owing to this strong differentiation between males and females, it important to assess how parameters vary between males and females as has been discussed in the present research. To enrich it further, the research compared the parameters amongst males and females in two groups- one group on dialysis and other group not on dialysis. Blood sugar fasting was less in both males and females who were on dialysis. Haemoglobin did not differ much between males and females in both groups wherein it was less in females of both the groups when compared to males. Serum creatinine was found to be more in females of the group "not on dialysis" while it was more in males of the group "on dialysis". At the end, the study has presented the implications and future scope of the research

Keywords: Diabetes Mellitus, Type 2 Diabetes Mellitus, Chronic Kidney Diseases, Blood sugar

INTRODUCTION:

Diabetes and kidney diseases are the leading causes of death and morbidity globally. All over the world, Diabetes Mellitus (DM) is the fastest growing chronic disease. It is a leading cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation. As per World Health Organization, DM and DM related kidney diseases caused approximately 2 million deaths [1]. Chronic DM hyperglycaemia and hypertension are few of the main causes of Chronic Kidney Diseases (CKD) [2]. Globally, diabetes has been observed to be the utmost cause of CKD [3]. Chung et al., (2023) [4] in their research stated that CKD affects 37 million adults in the United States. The research observed that 44% of the T2DM patients have CKD. From 1990 to 2017, mortality rates, years of life lost (YLL), years lived with disability (YLD), and disability-adjusted life years (DALY) due to CKD have tremendously increased. Diabetes and hypertension were the main causes that contributed majorly to loss of years of healthy life in men and women [5]. Late diagnosis of CKD is a major concern in many countries. It is seen that the diagnosis is mainly completed in the last stage of CKD. This leads to delay in dialysis and kidney transplantation, thus leading to rise in mortality rates [6]. Diabetes related kidney disease (DKD) develops in 40% of the patients with T2DM. The treatment of DKD through Renin-angiotensin system (RAS) blockade differs between men and women. Women have lower albuminuria and better albuminuria responses and overall rates of GFR loss. The responses of these treatments could vary between men and women on the basis of their lifestyles as well [7]. Glucose lowering drugs have benefitted in the treatment of diabetes and CKD. The stats presented in the research of Balkau et al., (2019) show that 31% patients were treated with insulin only, 28% with combinations of insulin and another drug, 42% with non-insulin glucose-lowering drugs. 40% of stage 3 CKD patients used metformin. 53% patients at stage 3 of CKD used insulin while 59% of men and 77% of women from stage 4 and 5 used insulin for treating CKD. Men and women had the same median age while Body mass Index (BMI) was 3.3 kg/m^2 higher in women. Thus, the use of insulin has helped in treating CKD and diabetes [8].

Chesnaye et al., (2021) observed renal function of older men and women suffering with CKD stage 4 and

5. And found that renal function declination rate in men (16.2%/year, 95% CI 15.9–17.1%) was faster as compared to women (9.6%/year, 95% CI 6.3–12.1%). Diabetes came out to be a major determinant of renal decline especially in women [9]. The global researches show that CKD is more prevalent in women. Though, end-stage kidney failure and receipt of kidney replacement therapy is higher in men. The prevalence of the most common risk factors which is obesity and hypertension, differ in men and women [10]. Gender-based differences are prominent in DM as discussed in the above section. These differences are visible in microvascular and macrovascular complications of diabetes. These involve pathophysiological mechanisms, epidemiological features and clinical presentation due to the interaction between biological and psychosocial factors [11]. Though prevalence of type 2 DM is increasing in both genders, men are found to be diagnosed at a younger age and lower body fat mass when compared to women. Globally around 17.7 million more men suffer from type 2 DM than women [12].

There are variances amongst men and women regarding DM with regards to comorbidities, the appearance of complications and the initiation of and adherence to therapy. The same is applicable to CKDs. Owing to this strong differentiation between males and females, several researches have been conducted in the past to asses the same (Table 1).

Reference	Ethnic Group	Gender Specific Relation	Microalbuminuria	Low eGFR	End-stage renal disease
Dyck & Tan, (1994) [13]	Canada	Female	Not reported	Not reported	High risk
Gall et al., (1997) [14]	Denmark	Male	High risk	Not reported	Not reported
Lewis et al., (2001) [15]	Multi-ethnic	Female	High risk	Not reported	Not reported
Haroun et al., (2003)[16]	USA	Female	Not reported	Not reported	High Risk in Females
Keane et al., (2003) [17]	Multi-ethnic	Female	High risk	High risk	High risk
Rossing et al., (2004) [18]	Denmark	Male & Female	Not reported	High risk	High risk
Retnakaran et al., (2006) [19]	UK	Male/Female	High risk for male	High risk for female	Not reported
Xue et al., (2007) [20]	USA	Female	Not reported	Not reported	High risk
Yamagata et al., (2007) [21]	Japan	Male	High risk	Not reported	Not reported
Hippisley-Cox & Coupland, (2010) [22]	UK	Female	Not reported	Both Genders	High risk
Penno et al., (2011) [23]	Italy	Male/Female	High risk for male	High risk for female	Not reported
Hoffmann et al., (2011) [24]	Germany	Female	Not reported	Not reported	High risk

Johnson et al., (2011) [25]	USA	Male	Not reported	Not reported	High risk
Yu et al., (2012) [26]	USA	Male/Female	High risk for male	High risk for male	High risk for female
(Jardine et al., 2012) [27]	UK	Male	Not reported	Not reported	High risk
Zoppini et al., (2012) [28]	Italy	Male & Female	Not reported	High risk	Not reported
Altemtam et al., (2012) [29]	UK	Male & Female	Not reported	High risk	Not reported
Tohidi et al., (2012) [30]	Iran	Female	Not reported	High risk	Not reported
Yu et al., (2012) [31]	USA	Male/Female	High risk for male	High risk for male	High risk for female
Jardine et al., (2012) [32]	UK	Male	Not reported	Not reported	High risk
Zoppini et al., (2012) [33]	Italy	Male & Female	Not reported	High risk	Not reported
Altemtam et al., (2012) [34]	UK	Male & Female	Not reported	High risk	Not reported
Nagai et al., (2013) [35]	Japan	Male & Female	High risk	Not reported	Not reported
Elley et al., (2013) [36]	New Zealand	Female	Not reported	Not reported	High risk
van Blijderveen et al., (2014) [37]	Netherland	Male/Female	High risk in Males	High risk in Males and Females	High risk in Females
De Hauteclocque et al., (2014) [38]	France	Male	Not reported	High risk	High risk
Kajiwara et al., (2016) [39]	Japan	Female	Not reported	High risk	Not reported
Ricardo et al., (2019) [40]	USA	Male	High risk in Males	High risk	High risk in Males

It can be inferred from Table 1 that though previous researchers have researched type 2 DM related CKD from gender prospective, Indian ethnicity has not been researched. Further, the case of differentiation for dialysis has also been a neglected. Thus the present research will bridge all these gaps. Thus, the objectives of present research are-

A. To assess gender based differentiation for T2DM related CKD who are not on dialysis

B. To assess gender based differentiation for T2DM related CKD who are on dialysis

MATERIALS AND METHODS:

The present research is a cross sectional research. The sampling method used is non probabilistic sampling. Under non probabilistic sampling, Convenience sampling has been used.

Total 80 patients were considered in this research, 40 patients of T2DM related CKD on dialysis and 40 patients of T2DM related CKD not on dialysis.

The collected data was analysed using SPSS 23.0 software. Central tendency tests have been conducted here. Further, p value has been used for assessment of statistical significance. Here level of significance has been taken to be 10%.

Data Analysis and Interpretation:

Table 1: Comparison of Parameters for T2DM related CKD "Not on Dialysis"

	Total			Males			Females			p-Value
	Range	Mean	SD	Range	Mean	SD	Range	Mean	SD	
Blood Sugar Random (mg/dL)	110-300	204.00	45.526	110-240	184.5000	38.97649	150-300	223.5000	44.84851	0.053<0.1
Blood Sugar Fasting (mg/dL)	110-180	147.10	21.856	110-162	137.7000	17.01666	110-180	156.5000	22.85826	0.051<0.1
Hb	6.4-12	10.02	1.600	6.4-12	10.0400	1.71542	7.4-12	10.0000	1.56844	0.956>0.1
SERUM PROTEIN	5.8-8.1	6.79	.750	5.8-7.5	6.6700	.59451	5.8-8.1	6.9000	.89691	0.508>0.1
ALBUMIN	2.3-5.2	4.01	1.016	2.3-5.1	3.8800	.99755	2.4-5.2	4.1400	1.06999	0.581>0.1
S. UREA	7.1-177	111.08	38.227	7.1-162	104.7100	45.39889	93.3-177	117.4400	30.55975	0.471>0.1
S. CREATININE	1.5-5.9	3.70	1.158	1.5-5.9	3.6600	1.34511	2.3-5.6	3.7400	1.00907	0.882>0.1
SODIUM	3.9-195	131.80	33.833	3.9-154	121.1600	42.02952	130-195	142.4400	19.96058	0.165>0.1
POTASSIUM	4.3-9.5	6.88	1.552	4.3-9.5	6.6600	1.73282	5-9.5	7.0900	1.40669	0.55>0.1
Age	20-65	50.30	13.731	45-65	55.6000	8.16769	20-65	45.0000	16.39783	0.093<0.1
Systolic BP	100-170	135.1500	20.95930	122-170	140.50	18.769	100-166	129.80	22.61661	0.244>0.1

Diastolic BP	39-110	81.4000	17.57810	39-100	81.600	18.392	58-110	81.2000	17.71879	0.955>0.1
BMI	16-30	23.15	3.51	21-30	25	2.83	16-26	21.30	3.23	.024<0.1
HbA1c	5.4-10.1	7.75	1.087	5.4-8.6	7.31	0.948	6.4-10.10	8.19	1.0795	0.083<0.1

For the patients suffering from T2DM related CKD "Not on Dialysis", the number of males are 20 while females are also 20 in number making the male-female ratio to be 1:1.

In the present study conducted on T2DM related CKD patients who were not on dialysis, the mean age of males is 55 and of females is 45. This means females tend to be diabetic from a smaller age when compared to males. In this direction Hossain et al., (2017)[41] stated that since females go through hormonal changes at the time of Menopause and start of menstruation, it effects their glucose regulation capability.

The blood sugar fasting among the males was 137.70 mg/dL while in females was 156.50 mg/dL. This shows that females tend to have higher levels of blood sugar fasting compared to males and was reported to be statistically significant as well (0.053<0.1). In a research conducted by Hossain et al., (2017)[41], also reported that the fasting blood glucose level of female was higher than that of the male in their research. Thus this research supports the findings of the present research.

In a research conducted by Mhundwa et al., (2023) [42] in South Africa, it was found that T2DM is a leading cause of CKD. The main motive with these patients is to control the risk factors such as blood pressure and blood glucose levels. This would help prevent the progression of CKD. It is seen that 22% of the T2DM patients in South Africa are suffering with CKD. T The researcher observed that the rate of CKD was slightly higher in males (29.6%) than in females (22.7%). 17.8% patients achieved a glycosylated haemoglobin of < 7.0%. In the present research, both males and females have approximately equal haemoglobin with 10.04 (ranging between 6.4 and 12) and 10.00 (ranging between 7.4 and 12) respectively which is more than that reported by Mhundwa et al. [42].

On analysing the serum protein levels in present research, among males and females, the results showed a mean of 6.67 among males and 6.90 among females. Similarly, a comparison has been conducted among males and females on levels of albumin, serum urea, serum creatinine, sodium and potassium. Albumin among males was found to be 3.88 (range of 2.3 to 5.1) and among females was 4.14 (range of 2.4 to 5.2). Serum urea in males is 104.71 and in females is 117.44. Thus, serum protein, Albumin and Serum urea were reported to be more in females when compared to males but was reported to be statistically insignificant. Rezende et al., (2017) [43] also reported higher levels of serum protein, Albumin and Serum urea in females when compared to males in T2DM patients.

Serum creatinine was found to be approximately equal in both males and females with mean of 3.66 and 3.74 respectively. A good amount of difference is seen among sodium levels in males and females. Males possess a mean of 121.16 while females possess 142.44 thus displaying sodium levels to be higher in females than in males. But it was reported to be statistically insignificant. This higher level of sodium possessed by females in comparison to males has been reported in multiple researches [44]–[46] . Further, potassium levels again found to be higher in females than males (males-6.66 and females- 7.09). Also, a significant difference (.024<0.1) was found to exist between males and females in terms of BMI wherein BMI of males was found to more than that of females.

Finally, it can be inferred that there exists a significant difference between the age of males and females (p=0.093<0.1) with mean age of males to be 55.6 years while that of females to be 45 years. This shows that females suffer from T2DM related diabetes from younger age when compared to males.

The graphical representation of all the parameters in presented below

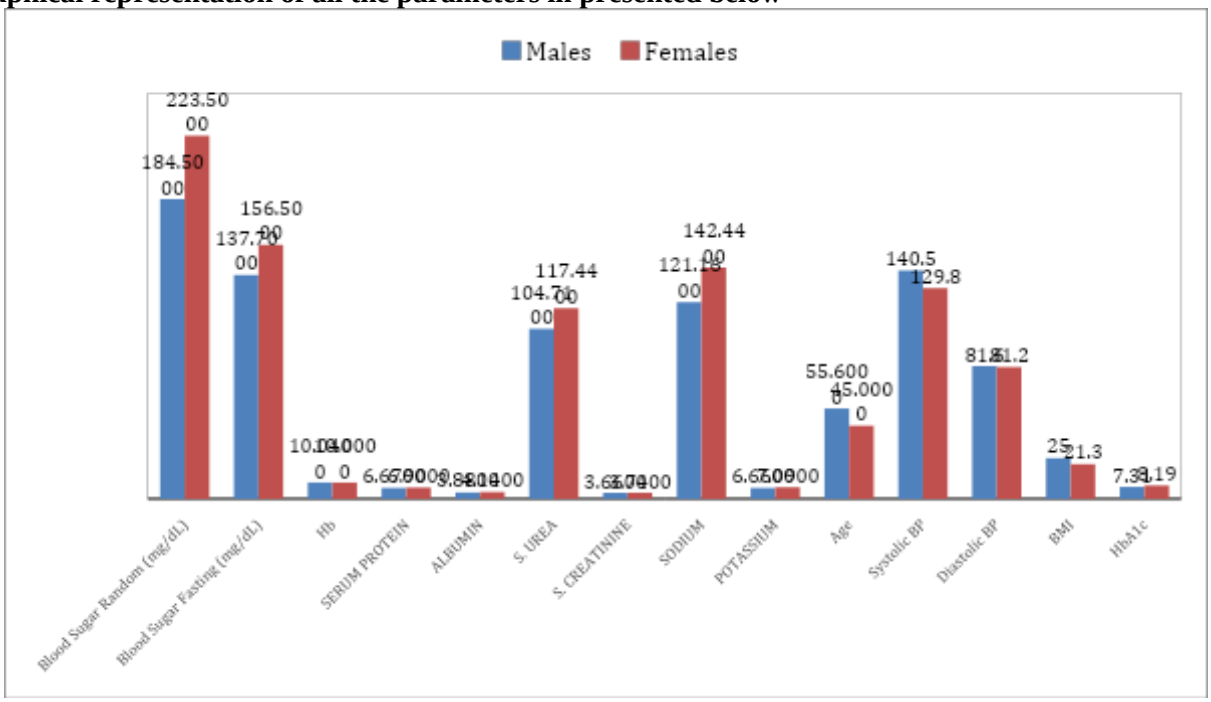

Figure 1: Graphical representation of T2DM related CKD "Not on Dialysis"

Further, Comparison of Parameters for T2DM related CKD "On Dialysis" has been presented in Table 2 below and has been discussed in the subsequent section-

Table 2: Comparison of Parameters for T2DM related CKD "On Dialysis"

	Total			Males			Females			p-Value
	Range	**Mean**	**SD**	**Range**	**Mean**	**SD**	**Range**	**Mean**	**SD**	
Blood Sugar Random (mg/dL)	86-130	106.35	14.626	88-125	106.0667	12.91437	86-130	107.2000	20.76536	0.885>0.1
Blood Sugar Fasting (mg/dL)	103-170	134.75	21.106	105-160	134.2667	18.62973	103-170	136.2000	29.96164	0.865>0.1
Hb	6-12	8.35	1.746	6-12	8.3533	1.83804	6.4-10	8.3400	1.62727	0.989>0.1
SERUM PROTEIN	6.1-7.9	6.92	.569	6.1-7.8	6.8133	.53834	6.4-7.9	7.2400	.59414	0.202>0.1
ALBUMIN	3.1-4.7	3.86	.486	3.1-4.6	3.8400	.47630	3.4-4.7	3.9000	.57009	0.818>0.1
S. UREA	77.8-208.7	152.13	44.669	77.8-208.7	145.4733	47.69661	139.9-201.1	172.0800	29.18539	0.26>0.1

S. CREATINE	6.2-17.4	11.01	3.077	6.2-17.4	11.5533	3.22864	7.1-12.2	9.3800	2.01172	0.178>0.1
SODIUM	131.7-182	150.01	15.369	131.7-174	146.1467	14.10004	142-182	161.6000	14.22322	0.048<0.1
POTASSIUM	3.4-7.2	5.43	.9779	3.4-7.2	5.4733	.95279	4.1-7.2	5.2800	1.15629	0.193>0.1
Age	19-62	46.85	9.842	19-62	46.7333	11.41094	44-49	47.2000	2.04939	0.211>0.1
Systolic	110-179	142.65	20.563	110-179	145.67	22.802	123-140	133.6	7.23	0.115>0.1
Diastolic	70-118	95.30	13.195	70-118	95.87	14.342	83-110	93.6	10.11	0.558>0.1
BMI	18-30	24.75	3.04	18-30	25.20	3.121	19-26	23.4	2.61	0.245>0.1
HbA1c	6.4-8.4	7.29	0.6034	6.5-8.1	7.27	0.5122	6.4-8.4	7.36	0.8961	0.431>0.1

For the patients suffering from T2DM related CKD "On Dialysis", the number of males are 30 while females are 10 in number making the male-female ratio to be 3:1.

In the present study conducted on CKD patients who were on dialysis, the mean age of males is 46.73 and of females is 47.20. This means that there is no difference in age of patients of both genders who suffer form T2DM related CKD and are on dialysis.

The blood sugar fasting among the males was 134.26 mg/dL while in females was 136.20 mg/dL. This shows that males and females who are on dialysis have approximately equal blood sugar fasting even though it was statistically insignificant (0.865>0.1). On the other hand, T2DM related CKD patients who are not on dialysis reported statistically significant difference in blood sugar fasting levels amongst males and females wherein females reported higher levels of blood sugar fasting. It is also observed that T2DM related CKD patients who are on dialysis have lesser blood sugar fasting as opposed to T2DM related CKD patients who are not on dialysis.

Though, both males and females have approximately equal haemoglobin with 8.35 (ranging between 6 and 12) and 8.34 (ranging between 6.4 and 10) respectively though being statistically insignificant. Haemoglobin is also reduced in T2DM related CKD patients on dialysis than the ones who are not.

On analysing the serum protein levels among males and females, the results showed a mean of 6.81 among males and 7.24 among females.

Similarly, a comparison has been conducted among males and females on levels of albumin, serum urea, serum creatinine, sodium and potassium. Albumin among males was found to be 3.84 (range of 3.1 to 4.6) and among females was 3.90 (range of 3.4 to 4.7). Herein the level is slightly more in females when compared to males as was reported in T2DM related CKD patients on not dialysis. The Albumin levels in T2DM related CKD patients on dialysis are comparatively lesser than ones not on dialysis.

Serum urea in males is 145.47 and in females is 172.08 but was found to be statistically insignificant (0.26>0.1). Herein the level is more in females when compared to males as was reported in T2DM related CKD patients on not dialysis A huge difference is seen in serum urea level among males and females when compared between T2DM related CKD patients who are on dialysis and who are not.

Serum creatinine was found to be 11.55 in males and 9.38 in females stating males to posses higher levels in comparison to females. This is also in opposition to the findings of T2DM related CKD patients who are not on dialysis as therein females possessed higher levels of Serum creatinine in comparison to males.

A good amount of difference is seen among sodium levels in males and females. Males possess a mean of 146.14 while females possess 161.60 and was reported to be statistically significant 0.048<0.1. It is seen that sodium levels are higher in females than in males which is common in T2DM related CKD patients on dialysis as well as who are not on dialysis. Though potassium levels again seem to match among both

males and females with 5.47 and 5.28 respectively marking slight increase in males as opposed to T2DM related CKD patients not on dialysis. Finally, no significant difference (p=0.211>0.1) was found to exist between the ages of females and males.

The graphical representation of all the parameters in presented below

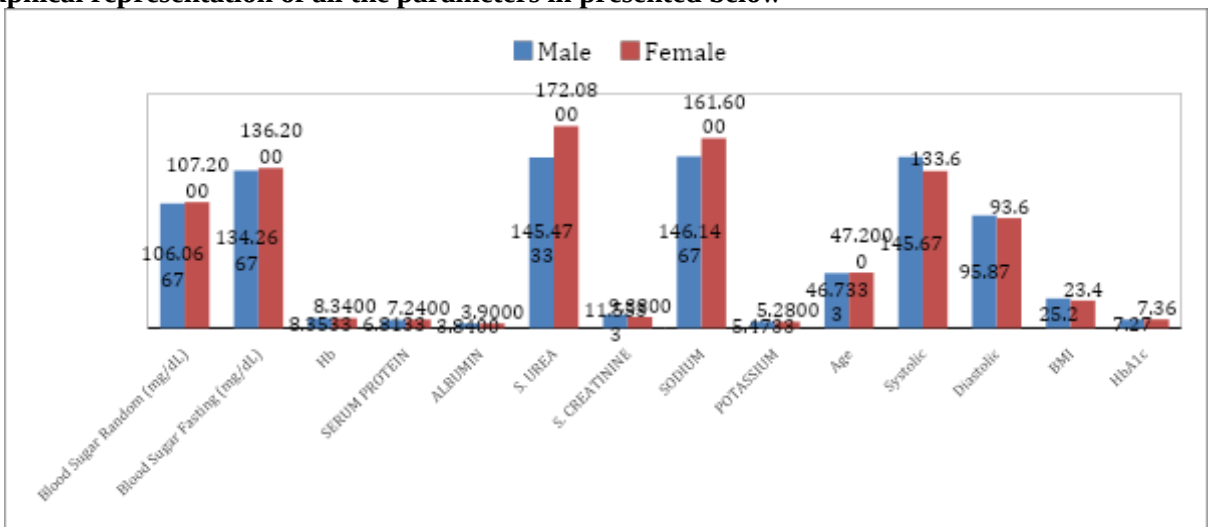

Figure 2: Graphical representation of T2DM related CKD "On Dialysis"

Table 3 below summarizes the comparison between males and females in both the groups while presenting the overall difference as well.

Table 3: Comparison of Parameters for T2DM related CKD "On Dialysis" and "not on dialysis" Summery Table

	T2DM related CKD- Not on Dialysis Females V/S Males	T2DM related CKD- On Dialysis Females V/S Males	Overall Difference Not on Dialysis V/S On Dialysis
Blood Sugar Random (mg/dL)	Higher in females	Higher in females	Higher in non dialysis
Blood Sugar Fasting (mg/dL)	Higher in females	Higher in females	Higher in non dialysis
Hb	Higher in males	Higher in males	Higher in non dialysis
SERUM PROTEIN	Higher in females	Higher in females	Higher in dialysis
ALBUMIN	Higher in females	Higher in females	Higher in non dialysis
S. UREA	Higher in females	Higher in females	Higher in dialysis
S. CREATININE	Higher in females	Higher in males	Higher in dialysis
SODIUM	Higher in females	Higher in females	Higher in dialysis
POTASSIUM	Higher in females	Higher in males	Higher in non dialysis
Age	Mean age of males is more	Mean age of females is more	Mean age more in non dialysis
Systolic	Higher in males	Higher in males	Higher in dialysis
Diastolic	Almost Same	Higher in males	Higher in dialysis
BMI	Higher in males	Higher in males	Higher in dialysis
HbA1c	High in Females	High in Females	Higher in non dialysis

CONCLUSION:

T2DM and CKD are two common chronic conditions that often coexist where in the relationship between T2DM and CKD is bidirectional in a way that T2DM can cause CKD while CKD complicates T2DM. Approximately one-third of the T2DM patients suffer with CKD. As a matter of fact, T2DM and CKD affect both males and females. But there can be gender-specific differences in prevalence, risk factors, disease progression, complications, and management strategies. This makes it important to assess how parameters vary between males and females as has been discussed in the present research. To enrich it further, the research compared the parameters amongst males and females in two groups- one group on dialysis and other group not on dialysis.

Blood sugar fasting is a major parameter for T2DM and related CKD. It was observed that females had higher levels of blood sugar fasting than males in both dialysis and non-dialysis patients. Although, blood sugar fasting was less in both males and females who were on dialysis. Haemoglobin did not differ much between males and females in both groups wherein it was less in females of both the groups when compared to males. Serum creatinine is also an important factor among CKD patients. Serum creatinine was found to be more in females of the group "not on dialysis" while it was more in males of the group "on dialysis". The End-stage renal failure strikes when serum creatinine is doubled in patients from their previous analysis. This doubling of the levels of serum creatinine shows that the patient is losing their kidney function and needs either dialysis or transplantation. Thus, females suffering from T2DM based CKD not on dialysis should monitor their serum creatinine; same is applicable on males of group "on dialysis". With T2DM patients, transplantation is a high risk option and majorly not recommended.

Sodium levels were significantly high in females than males for both dialysis and non-dialysis patients though it was statistically significant only for group "on dialysis".

It was found that all the parameters were higher in females in comparison to males in group "not on dialysis" except for haemoglobin. Further, Serum creatinine, potassium and haemoglobin were higher in males while all other parameters were higher in females in the group "on dialysis".

Thus, the above findings will facilitate in assessment of Prevalence, Risk Factors, Disease Progression, Complications of T2DM related CKD both in patients on dialysis and not on dialysis. Both T2DM and CKD can cause numerous complications which effect males and females differently. Like, diabetic nephropathy might evolve more quickly in males, while women with diabetes might suffer from urinary tract infections owing to anatomical differences. The assessment of differentiation in parameters of T2DM and related CKD can facilitate in assessing and identifying of these complications as well.

For future scope, the present findings should be analysed for treatment and management of T2DM and CKD. Even though treatment and management might be same for both genders, the present research findings can facilitate in understanding differences in both genders in response to therapy and medication side effects.

Statements and Declarations:

Financial interests: Both authors declare that they have no financial interests

Author Contributions: All authors contributed to the study conception and design

Ethics approval: This study was performed in line with the guidelines of King George Medical University, Lucknow, UP, India

Consent to participate: Informed consent was obtained from all individual participants included in the study.

Consent to publish: The authors affirm that human research participants provided informed consent for publication of the paper

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