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# Prevalence of Testosterone Hormone Deficiency and its the Correlation with Other Clinical Parameters in (Chronic Kidney Disease) CKD Patients on Hemodialysis

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## ABSTRACT

**Introduction:** Chronic kidney disease (CKD) is a wide range of metabolic alterations and hormonal disorders leading to endocrine dysfunctions often leads to worse outcomes. One such abnormality is a variable degree of hypogonadism and androgen deficiency.

**Aim:** The present study aim was to study the CKD Patients.

**Methods:** This observational study was conducted on a cohort of 50 CKD patients from June 2020 to July 2020. All clinically stable patients for the last six months and on hemodialysis were included.

**Results:** This observational study consisting of 50 CKD patients with 30 (60%) of them in stage 5, 17 (34%) of them in stage 4, and 3 (6%) of them in stage 3 CKD. Testosterone deficiency was found in 32 (64%) patients.

**Conclusion:** Testosterone is inversely associated with CKD stages, blood urea levels, creatinine is positively associated with haemoglobin level and duration of dialysis.

**Key Words:** Testosterone hormone deficiency, CKD patients, Hemodialysis, Haemoglobin level, Renal, Endocrine dysfunction, Hypogonadism

## INTRODUCTION

One of the common features among renal patients especially chronic kidney disease (CKD) is a wide range of metabolic alterations and hormonal disorders leading to endocrine dysfunctions. [1] These are often associated with worse outcomes. One such abnormality is a variable degree of hypogonadism and androgen deficiency. Testosterone deficiency has been reported to be present in 26-66% of patients with CKD.[2] Androgen deficiency leads to abnormal spermatogenesis, steroidogenesis, erectile dysfunction, decreased libido, and infertility. [3] It has been observed that deterioration of renal function leading to sexual dysfunction is not correctable by even dialysis. Sometimes, they deteriorate and male patients who are on dialysis can become impotent too. [4] Studies have proven that low levels of testosterone have led to many other changes in the body like anaemia, cognitive impairment, cardiovascular disease, and increased mortality. [1,5,6,7] This study was conducted to build on the previous evidence in the Indian scenario. By this study, we aim to estimate the prevalence of testosterone hormone deficiency and its correlation with other clinical parameters in a cohort of CKD patients on hemodialysis at our institute which is a tertiary care centre in the southern part of Maharashtra state.

## METHODS

This observational study was conducted on a cohort of 50 CKD patients from June 2020 to July 2020. All clinically stable patients for the last six months and on hemodialysis were included. Endogenous testosterone level, hemoglobin, urea, creatinine, electrolytes (sodium and potassium), total proteins, albumin, and globulin levels were measured. Written informed consent was taken from all patients. Data entry and analysis was done in SPSS version 22.0 (IBM). Statistical

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significance was considered with a $p < 0.05$. An independent sample t-test was used to determine the difference between laboratory parameters in testosterone deficient and normal groups. Pearson's correlation coefficient and scatter plots were used to determine the relationship between testosterone levels and other clinical parameters as well as the duration of dialysis.

## RESULTS

This observational study consisting of 50 CKD patients with 30 (60%) of them in stage 5, 17 (34%) of them in stage 4, and 3 (6%) of them in stage 3 CKD. The description of the study participants is given in **Table 1**. The mean age of participants in our study was 47.36 ± 14.44 years. Testosterone deficiency was found in 32 (64%) patients. The mean testosterone level was 267.22 ± 152.54 mg/dl. In the testosterone deficient group, it was 174.62 ± 87.42 and in the testosterone normal group it was 431.84 ± 91.09 mg/dl.

On applying, independent sample t-test, there was a significant difference in the laboratory parameters like haemoglobin ($p<0.001$), creatinine ($p=0.045$) and urea ($p=0.013$) in the testosterone deficient and testosterone normal group. **(Table 1)** In the testosterone deficient group, 20 patients belonged to stage 5, 10 belonged to stage 4, and 2 belonged to stage 3 CKD. A difference was observed between CKD stages and testosterone levels and the difference was near significant ($p=0.06$). Also, an inverse correlation was observed between the stage of CKD and testosterone levels ($r = - 0.328$ and $p =0.02$). **[Figure 1]** Correlation was also used to study the relationship between testosterone levels and other parameters. We found a significant positive correlation between haemoglobin levels and testosterone levels ($r=0.744$, $p <0.001$). We also found negative correlation between testosterone levels and blood urea levels ($r = - 0.499$ and $p < 0.001$).This has been represented in scatter plots. **(Figure 2 and 3)** There is a weak correlation ($r=0.261$) between testosterone levels and duration of dialysis but the p-value is near significant ($p=0.067$). **(Figure 4)** There is no correlation between testosterone levels and other parameters.

## DISCUSSION

This observational study consists of 50 CKD patients with 60% of them in stage 5, 34% of them in stage 4, and 6% of them in stage 3 CKD. Endocrine dysfunctions in CKD is associated with the worst outcomes. Testosterone deficiency has been reported to be present in 26-66% of patients with CKD.[2] In men undergoing hemodialysis subnormal total testosterone concentrations have been reported as 44–57%.[1,8,9] In our study the testosterone deficiency was found in 64% of patients. **Albaaj et al.** 2006 reported 26.2% of patients had significantly low testosterone levels and another 30.3% had low-normal levels.[10] **Carrero et al.**, 2009, reported the median value of testosterone as 286 (206 to –346) ng/dl and the deficiency (<288ng/dl) in 52% of men. **Gungor et al.**, 2010 reported the mean testosterone level in their study to be 8.69 ± 4.10 (0.17 to 27.40) and testosterone deficiency (<10 nmol/L) in 66% of the patients of CKD on hemodialysis.[11] **Carrero et al.**, 2011 in another study reported the presence of testosterone deficiency in 44% of the patients and testosterone insufficiency (10– 14 nmol/L) in 33%.[1] **Ekart et al.,** 2014 reported the prevalence of testosterone deficiency to be 13.8% and insufficiency to be 3.5 % in men on hemodialysis for CKD.[12] Cigarrán S et al., 2017, reported mean testosterone levels as 8.81 ± 6.61 ng/ml in CKD patients and testosterone deficiency in 39.5% patients on hemodialysis and 5.6% of peritoneal dialysis.[13] Testosterone levels are correlated with the stage of CKD.[8-16] In our study we found a significant, inverse correlation between stages of CKD and testosterone levels ($r = - 0.328$ and $p =0.02$). In a study by Yilmaz et al., 2011, on 239 referred patients to a renal centre, they reported the prevalence of subnormal testosterone as 17, 17, 34, 38, and 58% in stage 1-5 of CKD.[16]The prevalence was higher in CKD stage 4 and 5 similar to our study. Dhindsa et al., 2015, reported that hypogonadotropic hypogonadism was present across all stages of CKD in the range of 32-46%. In the case of stages 4 and 5 of CKD, around 90% were either hypogonadal and/or had compensated hypogonadism. All these were also typed, 2 diabetics. Khurana et al., 2014, found a 53% prevalence of subnormal testosterone concentrations among 2419 patients with CKD stage 3 or 4.[15]

Testosterone deficiency leads to abnormal spermatogenesis, steroidogenesis, erectile dysfunction, decreased libido, and infertility.[3] Studies have proven that low levels of testosterone have led to many other changes in the body like anaemia, cognitive impairment, cardiovascular disease, and increased mortality. [5,6,7] Our study builds upon this previous evidence. While some studies may show an inverse relation with testosterone levels, we found no relationship between age and testosterone levels. Even Bello et al., 2014, reported no significant interaction between age and serum testosterone levels. In our study, we found a significant positive correlation between haemoglobin levels and testosterone levels. We also found a negative correlation between testosterone levels and blood urea levels. There is a weak correlation between testosterone levels and duration of dialysis but the p-value is near significant. There is no correlation between testosterone levels and other parameters. Previous literature shows testosterone-deficient patients are more likely to be anaemic.[2,5,7] Carrero et al., 2012, reported that patients with testosterone <10 nmol/L were around five times more likely to be anaemic (Hb < 13.0 g/dL) than patients with sufficient testosterone.[17] Ekart et al., 2014 also reported a significant positive correlation between testosterone and haemoglobin in

all male patients (r=0.25). Other studies like Bain et al.[5] and Iglesias et al.[2] also reported similar results. But, some studies like Albaaj et al. and Cigarrán S et al. have also reported no relationship between testosterone and other biochemical parameters like haemoglobin level, parathyroid hormone, creatinine clearance, duration of dialysis.

## CONCLUSION

Our study contributes to estimating the burden of testosterone deficiency in CKD patients and its relationship with other biochemical parameters in patients of hemodialysis. We found that testosterone is inversely associated with CKD stages, blood urea levels, creatinine is positively associated with haemoglobin level and duration of dialysis.

However, our study has certain limitations like a small sample size and the non-availability of a control group. Also, all patients were on hemodialysis so the effect of the dialysis technique cannot be commented upon. Larger studies that can be extrapolated on the patients of hemodialysis are needed.

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**Table 1: Characteristics of study participants (N=50)**

| Variable | Total study participants (N=50) | | Testosterone deficient group ($N_1$=32) | | Testosterone normal group ($N_2$=18) | | p-value (independent sample t-test) |
|---|---|---|---|---|---|---|---|
| | Mean ± S.D | Range | Mean ± S.D | Range | Mean ± S.D | Range | |
| Age (years) | 47.36 ± 14.44 | 20 - 75 | 47.31 ± 14.66 | 20-72 | 47.44 ± 14.46 | 20 - 75 | 0.976 |
| Haemoglobin (g/dl) | 7.79 ± 2.07 | 4.20 - 12.50 | 6.43 ± 0.96 | 4.20 - 8.20 | 10.19 ± 1.027 | 8.20-12.50 | **<0.001** |
| Blood Urea (mg/dl) | 129.60 ± 47.53 | 34 - 230 | 141.91 ± 44.02 | 34 - 230 | 107.72 ± 46.77 | 35 - 212 | **0.013** |
| Creatinine (mg/dl) | 9.34 ± 3.38 | 2.80 - 18.20 | 10.06 ± 3.46 | 4.30- 18.20 | 8.07 ± 2.92 | 2.80 - 17.80 | **0.045** |
| Sodium (mEq/L) | 134.34 ± 6.20 | 122 - 150 | 133.69 ± 6.02 | 122 - 148 | 135.50 ± 6.51 | 122 - 150 | 0.326 |
| Potassium (mmol/L) | 4.65 ± 0.91 | 2.80 - 6.80 | 4.77 ± 0.98 | 2.80 - 6.80 | 4.43 ± 0.75 | 2.90 - 6.30 | 0.206 |
| Total proteins (g/dl) | 6.11 ± 0.66 | 4.20 - 8.10 | 6.13 ± 0.69 | 4.20 - 8.10 | 6.06 ± 0.60 | 4.90 - 7.20 | 0.711 |
| Albumin | 3.09 ± 0.62 | 1.80 - 4.10 | 3.10 ± 0.64 | 1.90 - 4.10 | 3.07 ± 0.62 | 1.80 - 4.00 | 0.869 |
| Globulin | 3.02 ± 0.68 | 1.50 - 4.50 | 3.03 ± 0.63 | 1.90 - 4.40 | 2.99 ± 0.79 | 1.50 - 4.50 | 0.836 |
| Serum testosterone (mg/dl) | 267.22 ± 152.54 | 10.19 - 634.50 | 174.62 ± 87.42 | 10.19 - 289.12 | 431.84 ± 91.09 | 326.64-634.50 | **<0.001** |
| Duration of dialysis (Months) | 29.80 ± 26.47 | 4 - 120 | 26.19 ± 22.48 | 6 - 96 | 36.22 ± 32.095 | 4-120 | 0.201 |

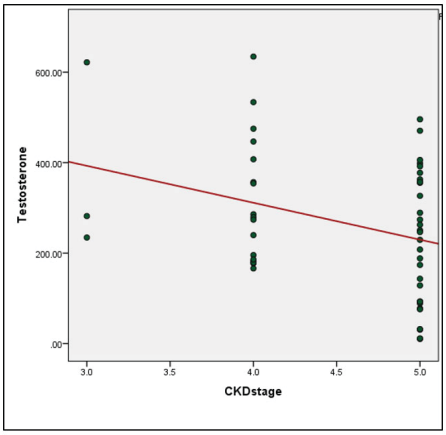


**Figure 1:** Scatter plot showing the inverse correlation between CKD stage and testosterone levels in study participants.

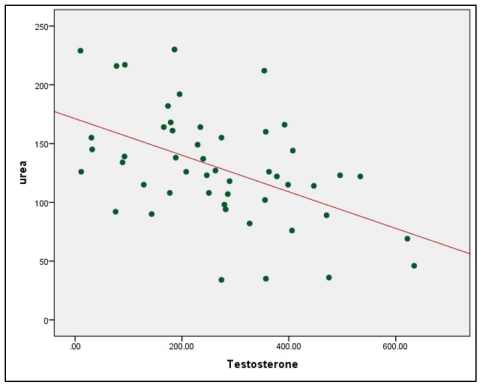


**Figure 3:** Scatter plot showing an inverse correlation between testosterone levels and blood urea levels in study participants.

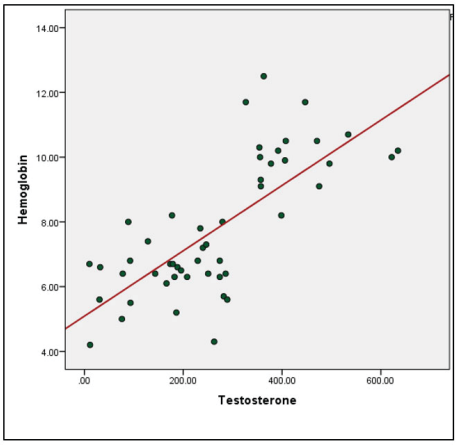


**Figure 2:** Scatter plot showing a positive correlation between hemoglobin levels and testosterone levels in study participants.

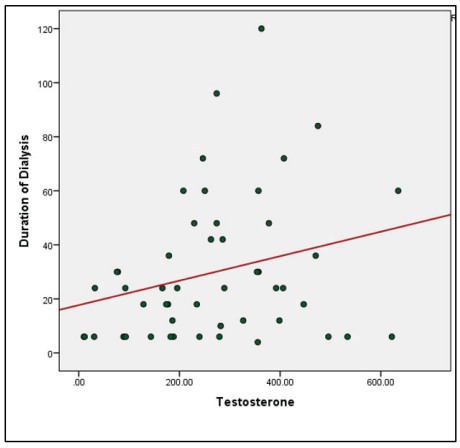


**Figure 4:** Scatter plot showing a positive correlation between the duration of dialysis and testosterone levels in study participants.