A SURVEY OF PLASMA TESTOSTERONE CONCENTRATION IN MALE PATIENTS WITH CHRONIC KIDNEY DISEASE STAGE III - V

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SUMMARY

Objectives: To evaluate the plasma testosterone level in male patients with chronic kidney disease stage III - V, pre-dialysis. Subjects and methods: A cross-sectional study with a study group of 118 chronic kidney disease patients, pre-dialysis. All patients had done measurement of plasma testosterone by ECLIA method. Results: The average value of plasma testosterone was 9.22 nmol/L. Testosterone levels decreased in 65.3% of patients. Concentration of plasma testosterone in the patients with old ages; severe stage of chronic kidney diseases was lower than that of the patients without above characteristics, p < 0.001. Testosterone levels were possitively correlated with glomerular filtration rate, hemoglobine and serum albumin levels (r = 0.587, 0.565, 0.414, respectively, p < 0.01), negative correlation with serum hs-CRP, r = -0.239, p < 0.05. Conclusion: Decreased plasma testosterone levels were common and associated with old ages, anemia, hypoalbuminia, and severe stage of chronic kidney disease.

** Keywords: Chronic kidney disease; Plasma testosterone; Anemia.*

INTRODUCTION

Chronic kidney disease (CKD) is increasing in the world as well as in Vietnam due to increases of hypertension and diabetes. Organ dysfunction is a common complication of patients with CKD, especially CKD stage III - V. Male and female sexual dysfunction, reduced fertility are common signs in CKD patients. In the early stages of the disease, CKD stage I and II, this disorder was not clearly seen. Reducing levels of sex hormones related to the common sexual and reproductive dysfunction in CKD patients [2, 3]. Some causes of hypogonadism include testosterone hormone: anemia, serum hypoalbumin, or a decrease in glomerular filtration rate. Reducing testosterone levels in men with CKD leads to reducing sexual and reproductive functions, and the quality of life of patients. There have been a number of studies in Vietnam on testosterone levels in patients with maintenance dialysis, or in patients with diabetes, but there have not been many studies in pre-dialysis CKD patients yet. From the above reasons, we carried out the topic with the aims:

- To investigate the plasma testosterone concentration in patients with pre-dialysis chronic renal disease stage III - V.

- To find out the relationship between testosterone and clinical, subclinical characteristics in male patients diagnosed CKD stage III - V.

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SUBJECTS AND METHODS

1. Subjects.

118 patients with CKD stage III - V (patients with glomerular filtration rate [GFR] < 60 mL/min) were diagnosed and treated at 103 Military Hospital.

** Selection criteria:*

- Patients with CKD due to many causes.
- Patients ≥ 18 years old.
- Did not use male hormones instead.
- Agreed to participate in the study.

** Exclusion criteria:*

- Patients with chronic acute renal failure.
- Patients with chronic renal failure accompanied by cancer.
- Patients who were suffering from acute diseases or needed surgery.

2. Methods.

- Research design: Cross-sectional, descriptive study.
- Determining past medical history, present illness and the cause of CKD.
- Blood tests (full blood count and blood chemistry) had done for all patients.
- The patient was calculated GFR by MDRD formula.
- CKD stage was divided according to KDIGO (2012).
- Quantification of plasma testosterone: Taking fasting venous blood, antifreeze then separate the plasma. Quantify testosterone by electroluminescent immunomodulation method. Unit: nmol/L. Diagnose reduce of plasma testosterone concentration based on the Vietnamese biological index (when the concentration is < 10 nmol/L).
- Data is processed by SPSS 22.0 software. The graph is automatically drawn on the machine.

RESULTS AND DISCUSSIONS

1. Characteristics of patients and concentration of plasma testosterone in patients with CKD stage III - V.

** Age characteristics of patients (n = 101):*

< 30 years old: 11 patients (9.3%); 30 to < 40 years old: 20 patients (16.9%); 40 to < 50 years old: 27 patients (22.9%); 50 to < 60 years old: 31 patients (26.3%); ≥ 60 years old: 29 patients (24.6%); X ± SD (year): 49.86 ± 12.99.

The proportion of patients in the age groups was equal. The patient with ≥ 50 years old reached 50%. The results showed that the patients with CKD in the III - V stage often had a higher average age than the previous studies, especially the number of patients aged 60 and older often accounted for about 30 - 40%.

Table 1: The stage of CKD (n = 118).

Stage of CKD	n	Ratio (%)
III	33	28
IV	31	26.3
V	54	45.7
Median GFR (mL/min)	16 (7 - 32.25)	

Because selected patients were those with CKD during the stage III - V, our study

showed a median GFR of 16 mL/min, of which the proportion of patients with CKD stage V accounted for 45.7%. The patients admitted to our hospital due to complications of CKD that was appeared in severe stage of CKD. Our research results were also consistent with other domestic authors' findings.

Table 2: Characteristics of plasma testosterone levels (n = 118).

Characteristics	n	Ratio (%)
Plasma testosterone < 10 nmol/L	77	65.3
Average (nmol/L)	9.22 ± 3.72	
Min	4.57	
Max	18.79	

The results showed that in 118 male patients with CKD in the III - V stage, 65.3% of patients had lower plasma testosterone levels compared to normal values of Vietnamese people. Average testosterone levels were also below normal levels. Thus, lower testosterone level was common in patients with CKD stage III - V. Our research results were also consistent with other authors' findings. Edey M.M et al (2017) had confirmed that testosterone deficiency was common in patients with renal impairment and especially in dialysis patients [7]. Published data showed that up to 40 - 60% of hemodialysis patients exhibited hypogonadism and a lower rate of about 15 - 40% in patients with CKD stage I – IV, in noticeable excess of the general population rate. It can be explained that the production of testosterone naturally decreased with age, and there was an increase in sex hormone-associated globuline, thereby reducing free testosterone. Fugl-Meyer K.S et al (2017) also reported that: At the stage of CKD III - V, a significant increase in LH levels was observed [8]. This suggested that the accumulation of metabolites affected the tests more than the hypothalamus or pituitary function. They are reasons why patients with CKD in the stage of I - IV had lower plasma testosterone levels.

2. Relation between plasma testosterone and clinical and subclinical characteristics in patients with CKD stage I - IV.

Table 3: Testosterone-related age (n = 118).

Age group	Average (nmol/L)	Reduction rate (n, %)
< 30 (n = 11)	13.35 ± 2.86	0 (0)
30 - < 40 (n = 20)	11.48 ± 4.45	9 (45)
40 - < 50 (n = 27)	10.72 ± 3.35	12 (44.4)
50 - < 60 (n = 31)	7.13 ± 2.33	28 (90.3)
≥ 60 (n = 29)	6.93 ± 1.58	28 (96.6)
p	< 0.001	< 0.001

The results of our study showed that the group of patients aged 60 and older had the lowest testosterone levels and a higher reduction in plasma testosterone levels than the younger group. Our results were also consistent with other domestic and foreign authors' findings. After the age of 30, testicular activity decreased by

2% per year and development of gonads, about 20% of men were in their 50s, about 30% of men aged 60 and 50% of men in their 80s had testosterone levels were significantly lower than normal. The decline in testosterone production is associated with age due to many factors causing a spiraling spiral of decline: The number of Leydig cells decline; Leydig cells produce less testosterone; less testosterone is testicularly introduced into the bloodstream in response to LH; the hypothalamus reduces hormone secretion to release FSH and LH (GnRH: Gonadotropin Releasing Hormone), leading to the pituitary gland producing reduced LH making testicles produce less testosterone.

Table 4: Testosterone related to CKD (n = 118).

CKD stage	Average (nmol/L)	Reduction rate (n, %)
III (n = 33)	12.87 ± 3.83	12 (36.4)
IV (n = 31)	8.43 ± 2.93	23 (74.2)
V (n = 54)	7.44 ± 2.23	42 (77.8)
p	< 0.001	< 0.001

The results of our study showed that the more severe CKD, the lower the concentration of testosterone and the higher the rate of patients with lower testosterone levels. This suggests a link to the purification of substances with the function of testosterone-producing cells of the testicles. Decreased testicular size in CKD and detectable histological abnormalities, including vasectomy disorders, interstitial fibrosis and calcification areas.

Table 5: Correlation of testosterone with some indicators (n = 118).

Index	Testosterone (nmol/L)		Correlation equation
	r	p	
GFR (mL/min)	0.587	< 0.001	Testosterone = 0.131*GFR + 6.447
Hemoglobin (g/L)	0.565	< 0.001	Testosterone = 0.075*hemoglobin + 1.218
Serum albumin (g/L)	0.414	< 0.001	Testosterone = 0.261*albumin - 0.864
Serum hs-CRP (mg/L)	-0.239	< 0.05	Testosterone = 9.11 - 0.033*hs-CRP

There was a positive correlation between the concentration of plasma testosterone and GFR, hemoglobin level and serum albumin concentration, $p < 0.01$, negative correlation to hs-CRP, $p < 0.05$.

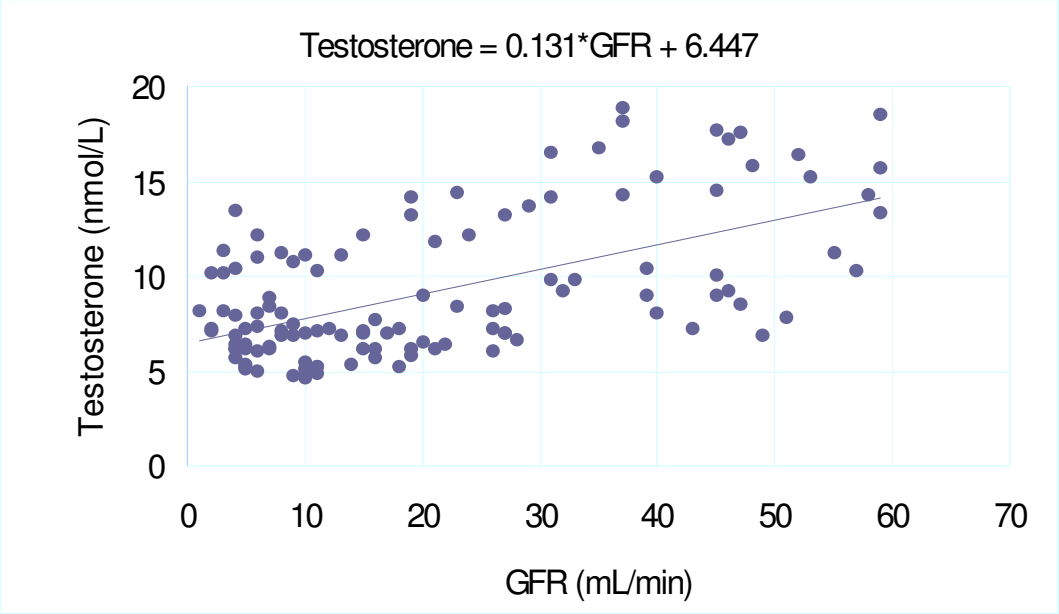

Figure 1: The correlation between plasma testosterone and GFR (n = 118).

There was a positive correlation between testosterone and GFR, r = 0.587, p < 0.001.

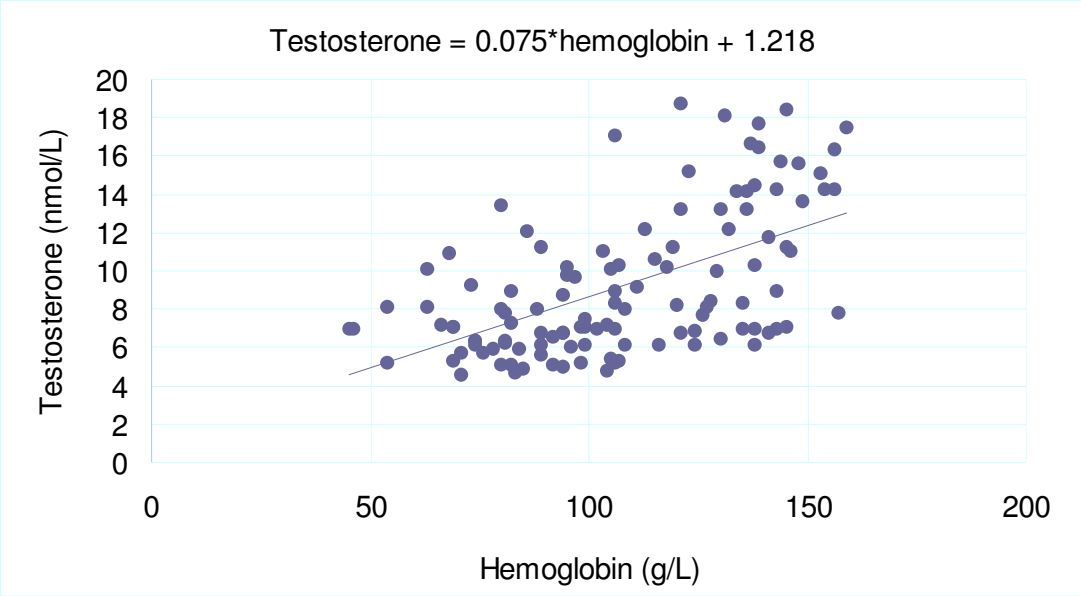

Figure 2: Correlation between plasma testosterone and hemoglobin (n = 118).

There was a positive correlation between testosterone and hemoglobin, r = 0.565, p < 0.001.

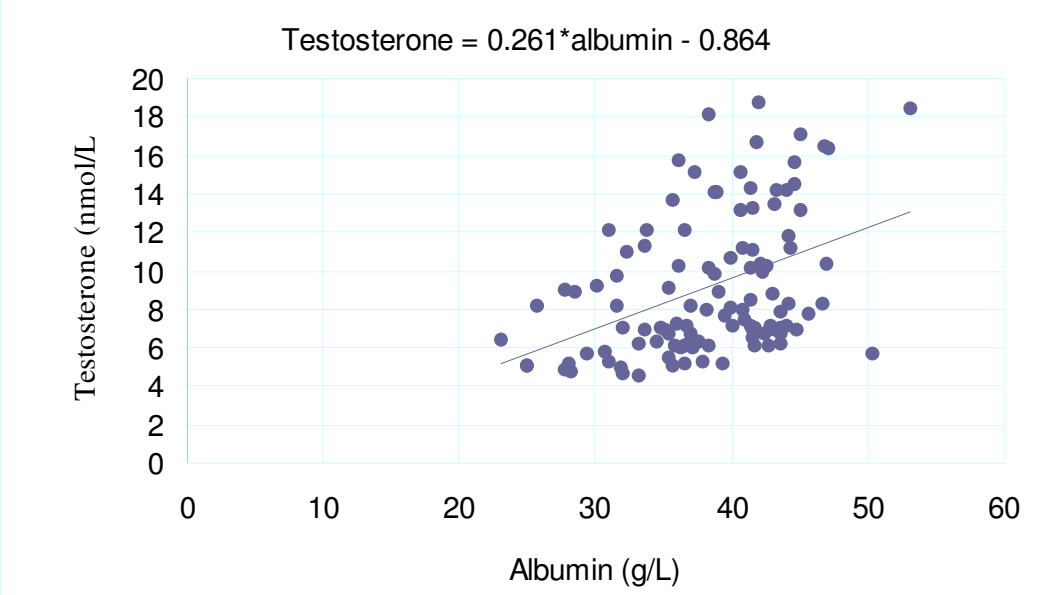

Figure 3: The correlation between plasma testosterone with serum albumin (n = 118).

There was a positive correlation between testosterone and albumin, r = 0.414, p < 0.001.

The factors correlating with testosterone levels related to the pathogenesis of reduced blood testosterone. Although many authors found an association between testosterone levels and anemia, the mechanism of the action of testosterone on increased red blood cell production is unclear [7, 8]. The theory is that the mechanism of testosterone stimulates red blood cells by increasing the production of erythropoietin. Testosterone also acts directly on the bone marrow to increase the number of reactive red blood cells. Testosterone is a steroid compound containing 19 C ($C_{19}H_{28}O_2$) molecular weight of 288 daltons, synthesized from cholesterol or acetyl-CoA. In normal human plasma, there is only 1 - 2% of free testosterone, because most testosterone is associated with albumin (54%) and with a globulin (Sex hormone binding globumin, SHBG) (44%). The free components and combination of testosterone in plasma are always in a dynamic equilibrium. The combined proteins for storage are key, but testosterone is able to penetrate tissues including albumin-associated testosterone. Therefore, changes in serum albumin levels may lead to changes in plasma testosterone levels.

CONCLUSION

Studying plasma testosterone levels of 118 patients with CKD stage III - IV, we had some comments:

- The average level of plasma testosterone was 9.22 nmol/L. Testosterone levels decreased in 65.3% of patients.

- Concentration of testosterone decreased, the rate of patients decreased gradually along with old age groups, stage of CKD, $p < 0.001$. Testosterone levels were possitive correlated with GFR, hemoglobin and serum albumin levels ($r = 0.587$, 0.565, 0.414, respectively, $p < 0.01$), negative correlation with serum hs-CRP, $r = -0.239$, $p < 0.05$.

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