SERUM TESTOSTERONE LEVEL AND RESPONSE TO ANDROGEN DEFICIENCY IN AGING MALES (ADAM) QUESTIONNAIRE IN CHRONIC KIDNEY DISEASE (CKD) - A SINGLE CENTER STUDY

ANSARY EAF[1], ISLAM MN[2], HOSSAIN MB[3], MAMUN MAA[4], TALUKDERM MFA[5], BHUIYAN FK[6], CHOWDHURY MN[7]

Abstract

Introduction: *Abnormalities of serum testosterone level in males are observed in chronic kidney disease (CKD) patients. Erectile dysfunction, decreased libido, infertility in chronic kidney disease (CKD) patients is associated with low serum testosterone. So this study of CKD patients help early recognition of these adverse conditions associated with low serum testosterone level and thus specific actions may be taken earlier.*

Objective: *To evaluate the serum testosterone level and the response of ADAM questionnaire in males with different stages of chronic kidney disease (CKD).*

Method: *This cross sectional study was done From January to December, 2014 in the Department of Nephrology, Dhaka Medical College Hospital. A total of 90 diagnosed cases of adult male with different stages of CKD (CKD stage 3, 4, 5 and 5D) patients along with age matched 88 healthy individuals were included. Every subject was provided the Bangla version of ADAM questionnaire. Serum Testosterone was done by ^{125}I-testosterone RIA system. P values <0.05 was considered as statistically significant.*

Result: *Mean S. testosterone was found 4.29±1.9 ng/ml in CKD patients (group A) and 9.15±1.2 ng/ml in healthy subjects (group B). The mean S. Testosterone difference was statistically significant (p<0.05) between two groups. It was observed that positive response to ADAM questionnaire was found 11.4% in healthy subjects, 10.1% in CKD stage 3, 54.5% in CKD stage 4, 100% in CKD stage 5 and 5D. Among those groups only CKD stage 5 and 5D patients observed low S. testosterone and was found 39.1% and 84.0% respectively.*

Conclusion: *Serum testosterone significantly decreased with progression of CKD stages. Positive ADAM questionnaire also found to be significant in CKD patients.*

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Introduction:

Endocrine abnormalities are a common feature of chronic renal insufficiency (Alice et al. 2002). The altered metabolic milieu in CKD affects the secretion of hormones and the response of target tissues, causing endocrine dysfunctions (Handelsman 1985). As many as 50 to 70% of CKD stage-5 men have been reported to be hypogonadal on the basis of low concentrations of testosterone (Albaaj et al. 2006; Gomez et al. 1980). Alterations of sex steroid production and metabolism (leading to

1. Eusha Ahmad Fidalillah Ansary, Associate Professor, Department of Nephrology, Uttara Adhunik Medical College, Dhaka.
2. Md. Nazrul Islam, Associate Professor, Department of Nephrology, Dhaka Medical College, Dhaka.
3. Md. Bellal Hossain, Indoor Medical Officer, Department of Nephrology, Mymensingh Medical College, Mymensingh.
4. Md. Abdullah Al Mamun, Assistant Registrar, Department of Nephrology, Shaheed Suhrawardy Medical College, Dhaka.
5. Md. Faruq Amin Talukder, Indoor Medical Officer, Kurmitola General Hospital, Dhaka.
6. Ferdous Kamal Bhuiyan, Assistant Professor, Department of Nephrology, Sher-E Bangla Medical College, Barisal.
7. Md. Nizamuddin Chowdhury, Professor and Head, Department of Nephrology, Dhaka Medical College, Dhaka.

Correspondence : Dr. Eusha Ahmad Fidalillah Ansary, Associate Professor, Department of Nephrology, Uttara Adhunik Medical College, Dhaka.

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primary hypogonadism and disturbances of the hypothalamic-pituitary axis) are already seen when moderate reductions in the GFR arise (Richardson & Weinstein 1970). These disorders are not normalized with initiation of maintenance dialysis treatment; instead, they often progress (de Vries et al. 1984). Morley et al. (2000) examined whether certain symptoms are more commonly present in males with low bioavailable testosterone (BT) levels. These were used to evaluate a questionnaire for androgen deficiency in aging males (ADAM). The validity of the ADAM questionnaire to screen for low BT was tested in 316 Canadian physicians aged 40 to 62 years. Low BT levels were present in 25% of this population. None had elevated luteinizing hormone (LH) levels. The ADAM questionnaire had 88% sensitivity and 60% specificity. When the questionnaire was administered twice 2 to 4 weeks apart to 10 men, it was determined that the coefficient of variation was 11.5%. In a second study of 34 ADAM-positive patients, 37% of those with clearly normal BT levels demonstrated some evidence of dysphoria. Finally, in 21 patients who were treated with testosterone, improvement on the ADAM questionnaire was demonstrated in 18 ($P < 0.05$). These data support the concept of a symptom complex associated with low BT levels in aging males. In addition, the ADAM questionnaire appears to be a reasonable screening questionnaire to detect androgen deficiency in males over 40 years of age. So this study of CKD patients help early recognition of these adverse conditions associated with low serum testosterone level and thus specific actions may be taken earlier. And thus, this study has done to evaluate the serum testosterone level and the response of ADAM questionnaire in males with different stages of chronic kidney disease.

Methods:

This Cross sectional study was conducted on 178 subjects, among them different stages of CKD patients 90 and age matched healthy individuals 88 at Department of Nephrology, Dhaka Medical College Hospital, Dhaka. CKD patients of stage 3, 4, 5 (with estimated glomerular filtration rate (eGFR) 30-59 ml/min, 15-29 ml/min, <15 ml/min without dialysis), according to MDRD formula respectively, stage 5D on maintenance hemodialysis were included. Patients having critical illness, taking spironolactone, glucocorticoids, finasteride, cyclophosphamide, cyclosporin A and tacrolimus, age < 20 or >60 were excluded from this study. Every subject was provided the androgen deficiency in aging males (ADAM) questionnaire (Morley, et al. 2000). Bangla version of ADAM questionnaire was made from Bangla Academy. This questionnaire was explained to every subject and completed confidentially. Diagnosis of CKD was confirmed by history, clinical examination, biochemical findings and imaging. All CKD patients were designated as group 'A' (total no. 90), healthy control group were grouped as group 'B' (total no. 88). Clinical and biochemical finding of the CKD patients (group A) was compared with that of the healthy control group (group B).

Data processing and data analysis:

Statistical analyses were carried out by using the Statistical Package for Social Sciences version 16.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentage shown with cross tabulation. Student t-test was used for continuous variables for two groups. For significance of difference Spearman correlation co-efficient test was done between stage of CKD and S. Testosterone of CKD patients. Pearson's correlation coefficient was used to test the relationship between two continuous variables. P values <0.05 was considered as statistically significant.

Results:

Majority 37(41.1%) patients belonged to age 41-50 years. The mean age was found 42.74±10.2 years. More than two third (66.7%) patients had normal (3.2-14.6 ng/ml) S. testosterone and their mean S. testosterone were found 4.29±1.9 ng/ml. Positive ADAM questionnaire was found 62(68.9%) patients (Table-1). It was observed that majority 36(40.9%) subjects belonged to age 41-50 years. The mean age was found 42.8±9.8 years. All subjects had normal (3.2-14.6 ng/ml) S. testosterone and their mean S. testosterone

were found 9.15±1.2 ng/ml. Positive ADAM questionnaire was found 10(11.4%) healthy subjects. It was observed that 22.2% patients of CKD stage 3, 24.4% of CKD stage 4, 25.4% of CKD stage 5 and 27.8% of CKD stage 5D (Figure-1). It was observed that in group A (CKD patients), 60(66.7%) patients had normal (3.2-14.6 ng/ml) S. testosterone and their mean S. testosterone were found 4.29±1.9 ng/ml. In group B (Healthy subjects), all subjects had normal (3.2-14.6 ng/ml) S. testosterone and their mean S. testosterone were found 9.15±1.2 ng/ml. The mean S. testosterone difference was statistically significant ($p<0.05$) between two groups (Table III). A line diagram showed progressive lowering of mean S. Testosterone from healthy to progression of CKD (Figure 2). In this current study it was observed that positive response to ADAM questionnaire was found 11.4% in healthy subjects, 10.1% in CKD stage 3, 54.5% in CKD stage 4, 100% in CKD stage 5 and 5D. Among those groups only CKD stage 5 and 5D patients observed low S. testosterone and was found 39.1% and 84.0% respectively (Figure 3). A strong negative Spearman's rank correlation (r=-0.893; p=0.001) existed between Stages of CKD and S. Testosterone of CKD patients (Figure 4).

Table I

Baseline characteristics of the CKD patients (n=90)

Baseline characteristics	Group-A (n=90)	
	No. of patients	Percent
Age (in year)		
21-30	15	16.7
31-40	21	23.3
41-50	37	41.1
51-60	17	18.9
Mean±SD	42.74	±10.2
S. Testosterone (ng/ml)		
<3.2	30	33.3
3.2-14.6 (normal)	60	66.7
Mean±SD	4.29	±1.9
Result of ADAM Questionnaire)		
Positive	62	68.9
Negative	28	31.1

Table II

Baseline characteristics of the healthy subjects (n=88)

Baseline characteristics	Group-B (n=88)	
	No. of subjects	Percent
Age (in year)		
21-30	14	15.9
31-40	21	23.9
41-50	36	40.9
51-60	17	19.3
Mean±SD	42.8	±9.8
S. Testosterone (ng/ml)		
<3.2	0	0.0
3.2-14.6 (normal)	88	100.0
Mean±SD	9.15	±1.2
Result of ADAM Questionnaire)		
Positive	10	11.4
Negative	78	88.6

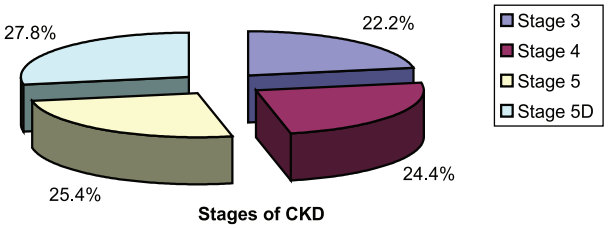

Fig.-1: *Pie chart showing distribution of different stages of CKD patients*

Table III

S. Testosterone distribution between CKD patients and healthy subjects (n=178)

S. Testosterone (ng/ml)	Group A (CKD) (n=90)		Group B (Healthy) (n=88)		P value
	N	%	n	%	
<3.2	30	33.3	0	0.0	
3.2-14.6 (normal)		60	66.7	88	100.0
Mean±SD	4.29	±1.9	9.15	±1.2	0.001[s]

s=significant, P value reached from unpaired |t-test

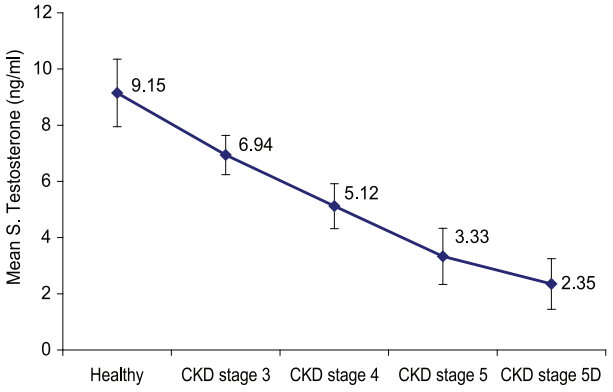

Fig.-2: *Line diagram showing relation of mean S. Testosterone (ng/ml) with different stage of CKD and healthy subjects.*

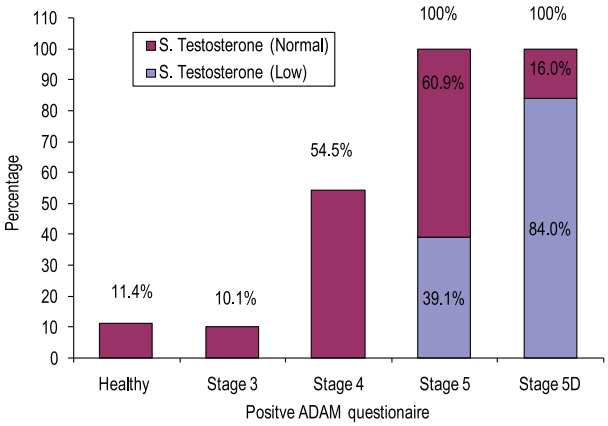

Fig.-3: *Bar diagram showing positive response to ADAM questionnaire with S.Testosterone level in different stages of CKD patients and healthy subjects.*

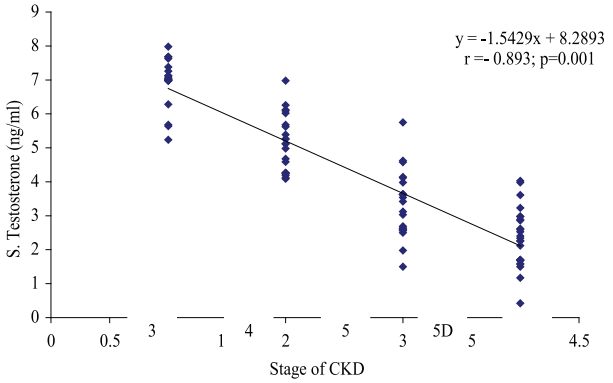

Fig.-4: *Scatter diagram showing negative Spearman's rank correlation (r=-0.893; p=0.001) between different stages of CKD and S. Testosterone of CKD patients.*

Discussion:

This cross-sectional study was carried out with an aim to evaluate the serum testosterone level in males and response to ADAM questionnaire with chronic kidney disease (CKD).

For this purpose, a total of 90 diagnosed cases of adult male with different stages of CKD (CKD stage 3, 4, 5 and 5D) patients along with age matched 88 healthy individuals were included as per inclusion and exclusion criteria.

In this present study it was observed that 90 patients having chronic kidney disease among them majority 37(41.1%) patients belonged to age 41-50 years. The mean age was found 42.74±10.2 years. Similarly, Zainab et al. (2014) showed the mean age was 46.66±10.36 years in CKD patients. Blumel et al. (2009) mentioned that the prevalence of CKD significantly increased with age, where they found 17.9% belonging to 40–54 years age group, 29.2% in 55–69 years age group, and 66.7% of 70 years or more. In another study, Colak et al. (2014) found that the mean age was 45.0±7.5 years in CKD patients. Blumel et al. (2009) observed that the mean age of their studied population was 55.1±12.0 years and varied from 40–85 years, which were higher than the current study. This was probably due to geographical variations, racial and ethnic differences, genetic causes, and different lifestyle influences, which may all have had significant impacts on the development of CKD in their study population.

More than two third (66.7%) patients had normal (3.2-14.6 ng/ml) S. testosterone and their mean S. testosterone were found 4.29±1.9 ng/ml. Positive ADAM questionnaire was found 62(68.9%) patients.

In this present study it was observed that a total of 88 healthy subjects were include in this study out of them majority 36(40.9%) subjects belonged to age 41-50 years. The mean age was found 42.8±9.8 years. Similarly, Zainab et al. (2014) showed the mean age was 44.6±8.17 years in healthy subjects. All healthy subjects had normal (3.2-14.6 ng/ml) S. testosterone and their mean S. testosterone was found 9.15±1.2 ng/ml. Positive ADAM questionnaire was found 10(11.4%) healthy subjects.

In this present study it was observed that 22.2% patients had CKD stage 3, 24.4% had stage 4, 25.4% had stage 5 and 27.8% had stage 5D. As many as 40 to 60% of CKD stage-5 men have been reported to be hypogonadal on the basis of low concentrations of total and free testosterone (Carrero 2011).

In this series it was observed that in group A (CKD), 60(66.7%) patients had normal (3.2-14.6 ng/ml) S. testosterone and their mean S. testosterone was found 4.29±1.9 ng/ml. In group B (Healthy), all subjects had normal (3.2-14.6 ng/ml) S. testosterone and their mean S. testosterone were found 9.15±1.2 ng/ml. The mean S. testosterone was statistically significant ($p<0.05$) between two groups. Similarly, (Zainab et al. 2014) showed that the mean serum total testosterone was 8.81±3.43 nmol/l in CKD patients and 15.17±5.59 in control group. The difference was statistically significant ($p<0.005$) between the two groups. (Albaaj et al. 2006) found in their study that the mean (±SD) testosterone concentration for all patients was 13.9 (±6.5) (median 13.2; range 0.5–37.0) nmol/l. Mean (±SD) testosterone concentrations were 15.5 (±5.1) (range 5.7– 27.1 nmol/l) in the transplant group; 13.0 (±6.9) (range 0.5– 35.5 nmol/l) in the dialysis group; and 14.2 (±6.4) (range 0.6–37 nmol/l) in the low-clearance group.

In this present study it was observed that positive ADAM questionnaire was found 62(68.9%) in group A (CKD) and 10(11.4%) in group B (Healthy). The difference was statistically significant ($p<0.05$) between two groups. (Chueh et al. 2012) found positive ADAM questionnaire 73.2% in CKD patients. The Androgen Deficiency in the Aging Male (ADAM) questionnaire is widely used screening tool for screening men, suspected of androgen deficiency. The ADAM questionnaire was developed by Morley et al in 2000. It is used as a screening tool to detect men at risk of androgen deficiency. This questionnaire is highly oriented towards the Western world, and high sensitivity (~81%-97%) but poor specificity (~16%-30%) to detect androgen deficiency have been reported (Morley et al, 2006; Martinez-Jabaloyas et al, 2007).

In this current study it was observed that positive response to ADAM questionnaire was found 11.4% in healthy subjects, 10.1% in CKD stage 3, 54.5% in CKD stage 4, 100% in CKD stage 5 and 5D. Among those groups only CKD stage 5 and 5D patients observed low S. testosterone and was found 39.1% and 84.0% respectively.

In this present study a negative Spearman's rank correlation ($r=-0.893$; $p=0.001$) between Stage of CKD and S. Testosterone of CKD patients was observed. Similarly, (Zainab et al. 2014) reported that there was a significant negative correlation between free testosterone in both ESRD patients and control groups with a significant difference in testosterone between these two groups. (Colak et al. 2014) showed that CKD patients had more cardiovascular risk factors (CVRF) than transplant patients and also that their concomitant testosterone levels were low.

Conclusion:

This study was undertaken to evaluate the of serum testosterone level and reponse to ADAM questionnaire in males with chronic kidney disease. Serum testosterone significantly decreased with progression of CKD stages. A significant negative correlation existed between the stages of CKD and serum testosterone. Positive ADAM questionnaire also found to be significant in CKD patients.

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