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Full Length Research Paper

Evaluation of Testosterone and PRL in Type 2 D.M Sudanese Male patients - Khartoum state: a Cross Sectional Study

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Abstract

Background: Diabetes Mellitus Type2 (DM) incidences are increasing worldwide. It accounts for more than 90% of all diabetic patients. The association between low testosterone and DM has recently received considerable attention. Investigators have highlighted the potential metabolic consequences of testosterone decline, showing a potential role of low testosterone on age-associated metabolic changes such as abdominal obesity. Objective: The aim of this study was to evaluate testosterone and prolactin levels among Sudanese men with type 2 DM. Methods: Total testosterone, prolactin and estrogen were quantitatively measured using Automated ELIZA Enzyme Immunoassay Analyzer (AIA-2000). Results: The mean plasma levels of testosterone, prolactin were significantly lower when compared with normal reference value with p.value (0.00, 0.00), respectively, while the mean levels of both Estradiol E2 and BMI observed a statistical significantly higher levels when compared with reference value p.value was (0.000, 0.000), respectively. In this study 37/40(92%) of the patients were overweight, 11/37(29.7%) of those 92% have low testosterone, 10/37(27%) have increased E2 level , and 10/37(27 %) married with no children. Pearson's correlation study between E2 and BMI was found positively correlated as well as between age and duration of disease, r value = (0.89, 0.485), p.value was (0.000, 0.002), respectively and negative correlation findings between E2 and testosterone hormones, and between PRL and BMI, r.value = (-0.68, -0.34) p.value was (0.02, 0.031), respectively. Conclusion: There is an inverse relation between BMI and low testosterone levels, and an obvious relationship between testosterone and E2 among Type 2 diabetic patients with obesity appear to be at a greater risk of low testosterone leading to hypogonadism.

Keywords: PRL, Testosterone, DM, Sudan.

INTRODUCTION

Diabetes Mellitus Type2 (DM) incidences are increasing worldwide. It accounts for more than 90% of all diabetic patients (WHO). The World Health Organization (W.H.O) predicts that the current diabetic population of 177 million (estimate 2000) people will increase to 370 million by the year 2030 (WHO). The prevalence and incidence rates of DM in Sudan in 1992 reached 3.4% in those ≤ 25 years of age UNPD (1999). It was found to be 5.5% in the Northern State and 8% in Khartoum State. The prevalence was particularly high (10.8%) in a certain community in the Northern State. The association between low testosterone and DM has recently received considerable attention (Bate et al, 2002, Goodma, et al,

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Table 1. shows study group characteristics of (DM type2 patients, no = 40)

parameters	Range	Median	Mean ±SD	*P-value*
Testosterone no= 40	22 - 971	415.5	425.2 ± 189	0.000
Estradiol no= 11	40 - 77	60	58.2 ± 10.0	0.000
Prolactin no= 40	.36 – 15.9	7.6	7.5 ± 3.9	0.000
BMI no = 40	21 – 39	28	28.5 ± 3.6	0.000
Age no = 40	26 – 76 years	53	54.4 ± 11.9	
Duration of disease	17 – 30 years	6	8.7 ± 7.5	

2000). Investigators have highlighted the potential metabolic consequences of testosterone decline, showing a potential role of low testosterone on age-associated metabolic changes such as abdominal obesity (Derby et at, 2006), diabetes and markers of pre-diabetes (Laaksonon et al, 2004, Dhindsa et al, 2004). In population-based studies, low testosterone is commonly associated with type 2 diabetes and the metabolic syndrome, and it identifies men with an adverse metabolic profile. The difference in testosterone levels between men with diabetes compared to men without diabetes is moderate and comparable in magnitude to the effects of other chronic diseases, suggesting that low testosterone may be a marker of poor health. Although the inverse association of testosterone with diabetes is partially mediated by SHBG, low testosterone is linked to diabetes via a bidirectional relationship with visceral fat, muscle, and possibly bone. There is consistent evidence from randomized trials that testosterone therapy alters body composition in a metabolically favorable manner, but changes are modest and have not consistently translated into reductions in insulin resistance or improvements in glucose metabolism (Grossmann M, 2001). Some studies showed that high circulating prolactin was associated with lower prevalence of diabetes and impaired glucose regulation (IGR), the adjusted odds ratios (95% CI) for IGR and diabetes for the highest compared with the lowest quartile of prolactin were 0.54 (95% CI 0.33-0.89) and 0.38 (0.24-0.59) in men and 0.54 (0.36-0.81) and 0.47 (0.32-0.70) in women (Wang et al, 2013). Also a Cross-sectional study showed an inverse association between low PRL concentrations and prevalent T2DM risk in men and women after multivariable-adjustment (men: Q1 vs. Q4: relative risk (RR), 1.55; 95% confidence interval (CI), 1.13 - 2.14; women: Q1 vs. Q4: RR, 1.70; 95% CI, 1.10 - 2.62). Likewise, higher PRL concentrations were associated with significantly lower T2DM risk (RR per SD increase in log-PRL: 0.83; 95% CI, 0.72 - 0.95 in men, and 0.84; 95% CI, 0.71 - 0.98 in women, respectively). An inverse association between PRL and with metabolic syndrome (MetS) risk was not retained after multivariable adjustment. Longitudinal analyses yielded no association of PRL with incident MetS or T2DM (Balbach et al, 2013). Our purpose of this study was to evaluate testosterone and prolactin levels among men with type 2 DM in Sudan-Khartoum State, in order to minimize diabetic complications such as infertility in men.

PATIENTS AND METHODS

This is a cross-sectional study comprised a total of 40 men patients with type 2 DM who attended Jabir Abu Alizz Diabetes Center in Khartoum state, Sudan, between March 2014 and December 2014. And Noorain Diabetes Center in Omdurman December 2014 till February 2016. The study was approved by the ethical committee of Faculty of Medical Laboratory Sciences, Jabir Abu Alizz Diabetes Center and Noorain Diabetes Center and all patients gave their verbal consent to participate in the study, and answered a questionnaire which provided information about their Age,

duration of diabetes, body mass index, medication and clinical history, marriage years and number of children they have.

Blood collection

A venous random blood sample (5 ml) was drawn from each participant, using a disposable syringe, then the blood was drown into a plain container and leaved to clot. Serum was obtained after centrifugation at 3000-4000 rpm for 10 minutes, separated in new containers and stored at ¯ 20 C for hormonal measurements.
Methods: Total testosterone, prolactin and estrogen were quantitatively measured using Automated ELIZA Enzyme Immunoassay Analyzer (AIA-2000).

Statistical analysis

Data was entered and analyzed using statistical analysis software SPSS (statistical package for social sciences),t-test was used for comparison of means and standard deviation, Pearson's correlation coefficient was used for correlations between variables, p.value <0.05 was considered as significant.

RESULTS

This is cross-sectional study involved 40 male patients with DMT2. Blood samples were collected from patients to assess serum levels of testosterone, E2, and prolactin, that were compared with reference value of testosterone (270– 1070ng/dl) and E2 (10 – 40 pg/ml, PRL (2 – 18ng/ml) and BMI (18.5-24.9kg/m2) healthy subjects. Table 1: presents the distribution pattern of the quantitative parameters in DM patients, the range, median, mean, age, duration of disease, and the parameters. In this study mean plasma levels of

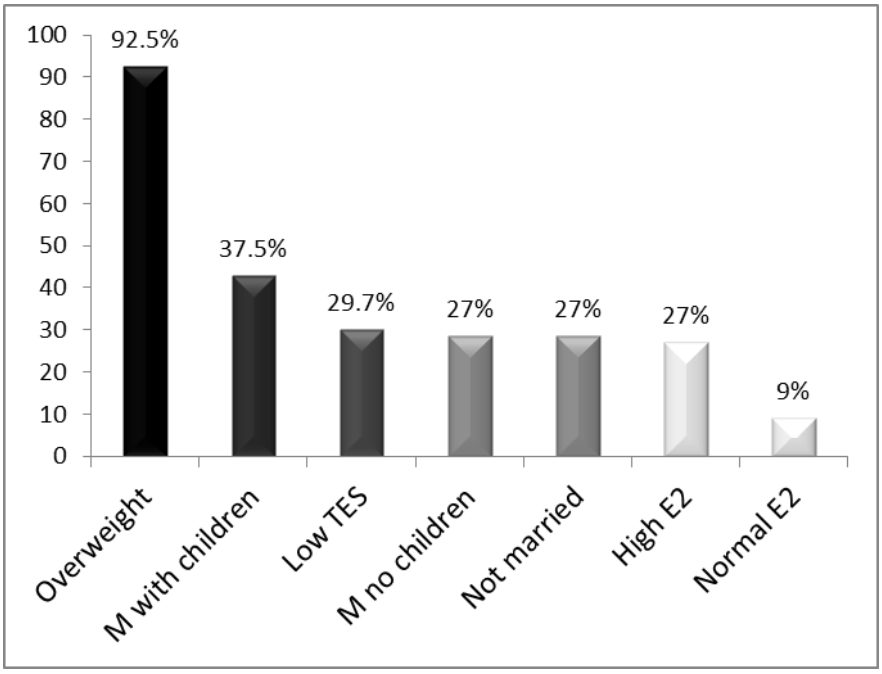

Figure 1. Shows distribution of DM patients with overweight BMI, married with children, low testosterone level, married no children, not married, increased E2 and those with normal E2.

testosterone, prolactin were significantly lower when compared with normal reference value with p.value (0.00, 0.00), respectively, while the mean levels of both Estradiol E2 and BMI observed a statistical significantly higher levels when compared with reference value p.value was (0.000, 0.000), respectively. Estradiol E2 was measured for patients with low testosterone and high BMI only to confirm the deficiency of testosterone.

Figure 1, shows distribution of DM patients with increased BMI, married with children, decreased testosterone level, married no children, not married, increased E2 and those with normal E2. In this study 37/40(92%) of the patients were overweight, 11/37(29.7%) of those 92% have low testosterone, 10/37(27%) have increased E2 level , and 10/37(27 %) married with no children.

Pearson's correlation study between E2 and BMI was found positively correlated as well as between age and duration of disease, r =(0.89, 0.485), p.value was (0.000, 0.002), respectively (figures 2,3). Figure 4, 5 demonstrated a negative correlation findings between E2 and testosterone hormones, and between PRL and BMI, r.value = (-0.68, -0.34) p.value was (0.02, 0.031), respectively.

DISCUSSION

Testosterone is the primary male sex hormone that is vital for sustaining proper erectile function and libido. It is also critically involved in building muscle, burning fat, and supporting endothelial function, energy level, mood, immune function, red blood cell production and bone density. In this study mean plasma levels of testosterone was found significantly lower when compared with the normal reference value, p.value (0.00). In the present study, 27.5% of patients with type 2 diabetes had a total testosterone level of <260 ng/dl. Our result findings were agreed with the previous (Ayman, et al, 2015, Grossmann et al, 2008), who had reported low significant difference in testosterone levels among their patients when compared with control group, and with high in percentage (36.4%, 43%), while other two cross-sectional studies, from United Kingdom and Spain (Apoor et al, 2007), reported low percentage of low testosterone (17%, 20%), respectively. Another cross-sectional study from Brazil showed that free and total testosterone levels were subnormal in 46% and 34% of diabetics, respectively. In our study 63.6% of the patients had low testosterone in the age group (50 – 70 years).The rest 36.4% aged (26 – 45 years). Some cross-sectional and longitudinal studies(18)] indicated that the testosterone levels decrease with age. In the other hand Grossmann et al, who reported that 43% of men of the age (60 – 70) had low total testosterone, also our findings were in consistent with the findings revealed by Grossmann et al (19)] and Fukui et al, who found that those with low testosterone levels were older than individuals with testosterone levels in the normal range. In this research work Estradiol E2 was measured for 11 patients with low testosterone and

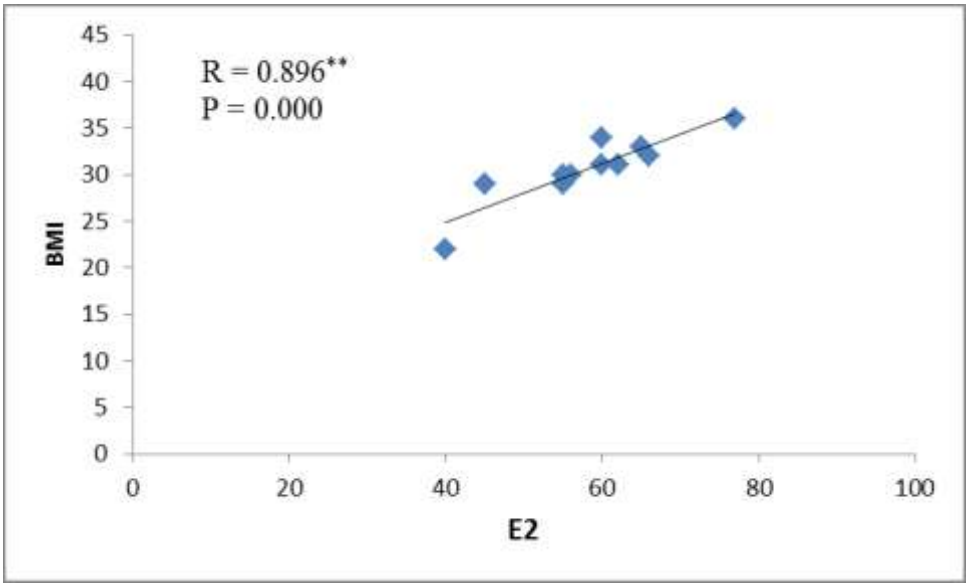

Figure 2. Shows positive correlation between estradiol E2 and BMI in patients with DM

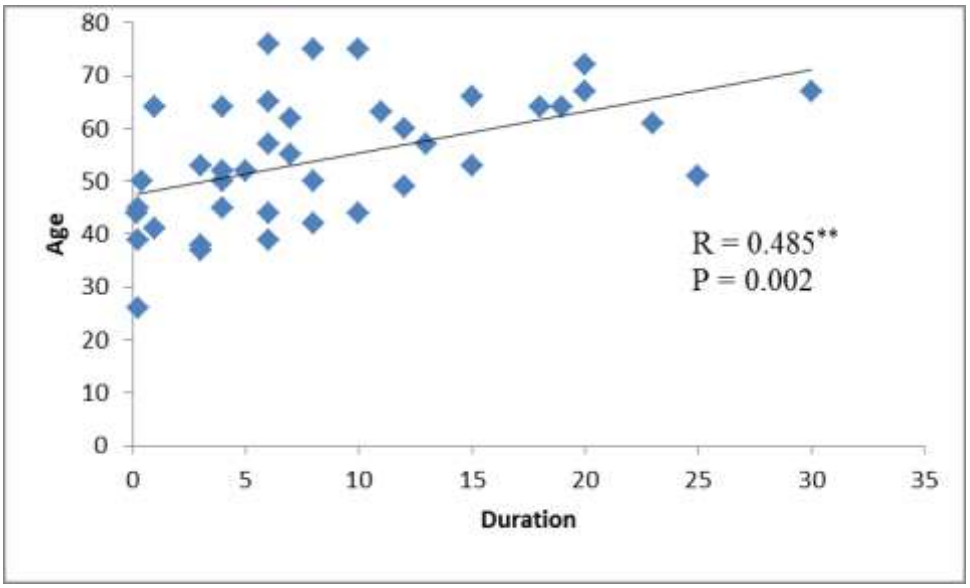

Figure 3. Demonstrates positive correlation between E2 and BMI levels among DM patients.

high BMI only, it was found high in almost 10(91%) of the patients revealing high significance difference p.value (0.000) when compared with reference value. Our result findings in this context was similar and leading to interpret the Previously ones (21,22,23), who had said that, lower total testosterone levels found in the diabetics could be as a results of increased conversion of the testosterone to estradiol (E2) in the presence of insulin resistance and obesity. In this study prolactin mean level was significantly lower (table 1) when compared with reference value with p.value (0.00) although it's level decreased in only 4 patients with age range 60-70 years. In this study 92% of the patients were overweight, and the mean BMI of the patients was (28.5 ± 3.6) (table 1), 29.7% of those 92% have low testosterone, 27% have increased E2 level , and 27 % married with no children which demonstrated in (figure 1). In this research results, correlation studies indicated that there is a positive correlation between BMI and E2 and between duration of disease and age among diabetic patients, r = (0.896, 0.485) and p.value (0.000, 0.002), respectively,(figure 2, 3), while BMI correlate negatively with the level of testosterone among diabetic patients (r=.683), p.value (0.021) (figure 4). Consistent to these findings, many

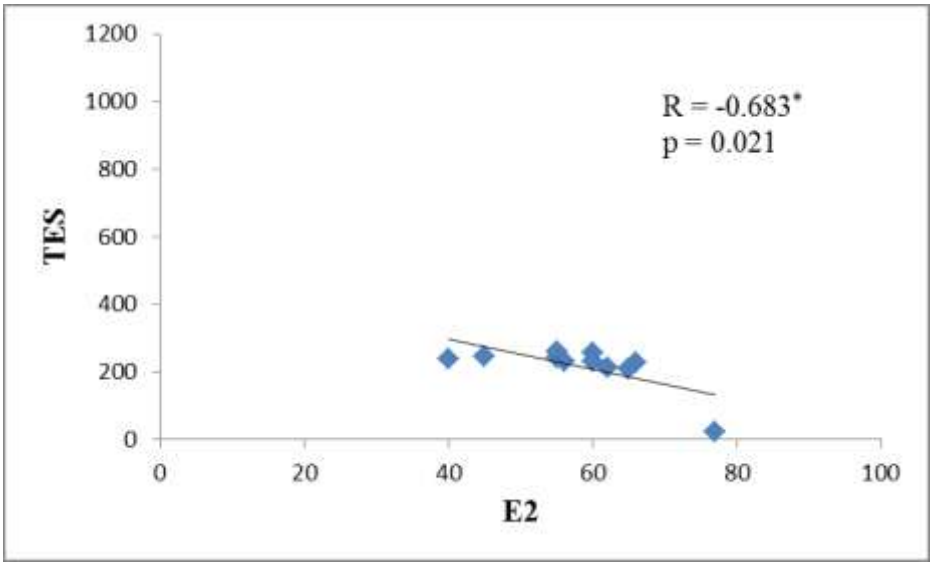

Figure 4. Shows negative correlation between Testosterone level and E2 level among DM patients.

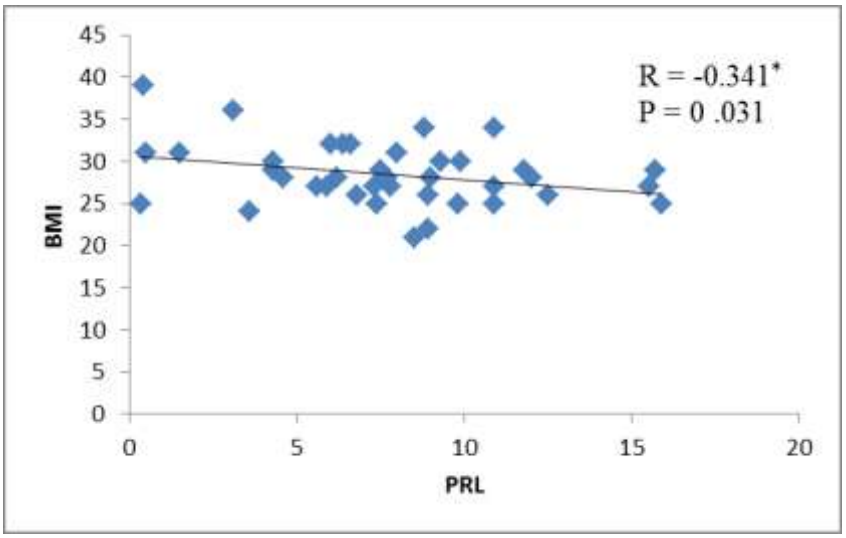

Figure 5. presents negative correlation between PRL level and BMI among DM patients.

previous studies (24,25,26) had agreed. On the other hand, contrary to our results, in other cross sectional study reported that there is no relationship between total testosterone and BMI (Tripathy et al, 2003). Also there was a significant correlation between prolactin and BMI, that presented r= 0.34), p.value (0.031), we did not found such correlation have been reported.

In conclusion, there is an inverse relation between BMI and low testosterone levels, and an inverse relationship between testosterone and E2. Type 2 diabetic patients with obesity appear to be at a greater risk of low testosterone leading to hypogonadism. the number of diabetic patients with low serum testosterone is undoubtedly enormous. This urgently calls for implementing early, universal screening programs, in order to detect those who have low serum total testosterone level at any early stage and to supplement testosterone accordingly. We recommend screening all type 2 diabetics for androgens.

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