

# Affiliation of Serum Total Testosterone with Lipid profile in Healthy Middle Aged Males

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## ABSTRACT

**Objective:** To construct a foreseeable connection of total testosterone with lipid profile in middle aged healthy men.

**Study Design:** Analysis / cross sectional study.

**Place and Duration of Study:** This study was conducted at the Dow University of Health Sciences Karachi for duration of nine month from April 2012 to January 2013.

**Materials and Methods:** Two hundred disease free nonsmoker males of 30 to 50 years of age were enrolled for this study, total testosterone value was estimated by Chemiluminescence assay method and fasting lipid profile which includes cholesterol, triglyceride, high density lipoprotein (HDL) and low density lipoprotein (LDL) were tested in Hitachi 902 auto analyzer by photometry technique. Mean differences of all the lipid parameters in between the two groups of testosterone were computed by independent sample T test. Correlation between total testosterone and fasting lipid parameters was assessed by Pearson correlation. Multivariable linear regression was also applied to predict the change in the levels of lipid profile parameters on the basis of per unit rise in total testosterone level.

**Results:** In this study the mean ( $\pm$  SD) value of total testosterone was 15.92 ( $\pm$  6.322) nmol/L, while the mean ( $\pm$  SD) values of cholesterol, triglyceride, HDL and LDL were 182.71 ( $\pm$  40.673), 134.02 ( $\pm$  55.407), 41.37 ( $\pm$  8.018) and 118.13 ( $\pm$  33.451) mg/dl respectively. Statistically significant difference ( $P = 0.021$ ) was observed in the mean value of serum triglyceride when compared with the two testosterone groups. Significant negative ( $P = 0.000$ ) and positive ( $P = 0.001$ ) association of testosterone with triglyceride and HDL respectively were also documented. Multivariable linear regression model showed significant decrease in triglyceride level by 2.742 mg/dl and significant increase in HDL level by 0.304 mg/dl for each additional nmol/L of age adjusted testosterone.

**Conclusion:** Convincing negative and positive associations of total testosterone with triglyceride and HDL respectively in this study suggest a promising link between low total testosterone and obesity.

**Key Words:** Serum Total Testosterone, Lipid Profile, Cholesterol, Triglyceride, HDL, LDL

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## INTRODUCTION

With the inception of furtherance life in the emerging countries, decreased athletics and ferocious eating habits, (especially the fast food) were noticed, which is the root cause of obesity and overweight.<sup>1</sup> As a consequence, risk factors like increased accumulation of abdominal fat, abnormal lipids mainly high density lipoproteins (HDL) and triglycerides which later leads

to cardiovascular and many metabolic diseases.<sup>2,3</sup>

Persons having dyslipidemia leads to metabolic syndrome and are more likely to die due to cardiovascular and many metabolic diseases.<sup>2,3</sup>

Persons having dyslipidemia leads to metabolic syndrome and are more likely to die due to cardiovascular diseases and have risk of developing stroke and heart attack three times as compared to those who are not suffering from it.<sup>4</sup>

Along with the manifested effects of low levels of serum total testosterone in men <sup>5,6</sup> low testosterone levels are also associated with altered lipid profile which will lead to various metabolic disorders.<sup>7,8</sup>

The exact mechanism that how low total testosterone causes dyslipidemia remains unclear, however some possible mechanisms suggests that testosterone modifies the metabolism of proteins and fat, according to researches testosterone under normal conditions reduces fat by inhibiting lipoprotein lipase<sup>9</sup> and glyceraldehyde 3-phosphate dehydrogenase.<sup>10</sup>

Active for of testosterone also reduces lipid levels by breakdown of fats inside the cells.<sup>11</sup> Testosterone also

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inhibits adipocytes differentiation in such a way that adipogenesis is impaired.<sup>12</sup> Studies have also suggested that testosterone replacement has also favorable effects on lipid profile.<sup>13</sup>

The basic aim behind the study was to construct a foreseeable connection of total testosterone with lipid profile. However most of the previous studies on low total testosterone & lipid profile were conducted on subjects belongs to elder age group and also has cardiovascular complications. We conducted this study in disease free middle aged men.

## MATERIALS AND METHODS

This study was a cross sectional analysis which was conducted in duration of nine month April 2012 to January 2013. Dow University of Health Sciences Karachi, for which two hundred disease free nonsmoker males of 30 to 50 years of age were enrolled. Sample size estimation was done with the prevalence of androgen deficiency in Massachusetts Male Aging Study, which was 12.3%.<sup>14</sup> The study inclusion criteria was based on healthy, nonsmoker males aged between 30 to 50 years, so individuals with any systemic disease acute and chronic disease, those taking any testosterone supplementation or suffering from hypogonadism & smokers as altered levels of testosterone were reported in smokers<sup>15</sup> were excluded from the study. A total of 323 subjects were approached for sampling, out of which 123 subjects were eliminated as they were not met with the study inclusion criteria. Detailed medical history and complete general physical examination and systemic clinical examination were carried out. Blood samples were collected at early morning in a fasting state of (12-14 hours). Early morning samples were required for Serum total testosterone due to its diurnal variation<sup>16</sup> and fasting was required for Lipid profile measurements. Total testosterone was tested in Cobas e 411 by chemiluminescence assay. Fasting lipid profile which includes cholesterol, triglyceride, high density lipoprotein (HDL) and low density lipoprotein (LDL) were tested in Hitachi 902 auto analyzer by photometry technique followed by enzymatic colorimetric and homogeneous enzymatic colorimetric test principles.<sup>17</sup> Reference values taken for all bio chemical assays are according to DDRRL.<sup>18-20</sup>

Data analysis was carried out by SPSS software. Testosterone values were divided into two groups. Group I having low testosterone levels (< 9.7 nmol/L) and group II having normal or above normal testosterone levels ( $\geq$  9.7 nmol/L). Mean comparison between the two testosterone groups were analyzed by independent sample T test, whereas correlation between total testosterone and fasting lipid parameters was assessed by Pearson correlation. Multivariable linear regression model was then also applied to predict the change in the levels of serum cholesterol, triglyceride,

HDL and LDL on the basis of per unit rise in testosterone value adjusted with age.

## RESULTS

Table I shows mean values of total testosterone, cholesterol, triglyceride HDL and LDL of 200 healthy subjects having mean age of  $38.72 \pm 6.56$  years.

**Table No. 1: Descriptive Statistics.**

Variables	Mean	Standard Deviation	Minimum	Maximum	Range
Testosterone nmol/L	15.92	6.322	5.63	43.64	38.01
Age (Years)	38.72	6.563	30	50	20
Cholesterol (mg/dl)	182.71	40.673	96	305	209
Triglyceride (mg/dl)	134.02	55.407	43	297	254
HDL (mg/dl)	41.37	8.018	24	75	51
LDL (mg/dl)	118.13	33.451	44	207	163

**Table No. 2: Mean Differences.**

Variables	Low Testosterone Group (n = 27)	Normal Testosterone Group (n = 173)	P Value
Mean $\pm$ SD Cholesterol	192.81 $\pm$ 38.058	181.13 $\pm$ 40.945	0.166
Mean $\pm$ SD Triglyceride	142.19 $\pm$ 38.368	132.75 $\pm$ 57.595	*0.021
Mean $\pm$ SD HDL	40.48 $\pm$ 8.021	41.51 $\pm$ 8.032	0.537
Mean $\pm$ SD LDL	125.48 $\pm$ 32.328	116.98 $\pm$ 33.568	0.220

\*Significant (p < 0.05)

**Table No. 3: Correlation of Testosterone with Lipid Parameters.**

	Correlation Coefficient	P Value
Cholesterol	-0.112	0.114
Triglyceride	-0.314	*0.000
HDL	0.243	*0.001
LDL	-0.047	0.512

\*Significant (p < 0.05)

**Table No. 4: Multivariable Linear Regression Model of Age adjusted Testosterone with Lipid Profile.**

	Unstandardized Coefficients ( $\beta$ )	P Value
Cholesterol	-0.746	0.099
Triglyceride	-2.742	*0.000
HDL	0.304	*0.001
LDL	-0.265	0.479

\*Significant (p < 0.05)

Out of 200 study subjects 13.5% had low total testosterone and categorized into low testosterone group, whereas 86.5% had normal testosterone and categorized into normal testosterone group.

Differences of mean in between the two groups was computed by Independent Sample T Test, showed significant (P = 0.021) changes in mean values of triglyceride as shown in table 2.

Correlation between serum total testosterone and lipid profile was analyzed by Pearson correlation, showed statistical significant inverse correlation with

triglyceride ( $P = 0.000$ ) and statistical significant positive correlation ( $P = 0.001$ ) with HDL as shown in table 3.

Multivariable linear regression model was applied to find the unit change in dependent variable due to unit change in independent variable. The independent variables were testosterone and age and the dependent variables were cholesterol, triglyceride, HDL and LDL in this study.

A significant decrease in triglyceride level by 2.742 mg/dl for each additional nmol/L of age adjusted testosterone and a significant increase in HDL level by 0.304 mg/dl for each additional nmol/L of age adjusted testosterone were recorded as shown in table 4.

The interaction between testosterone and age for each study variable was also analyzed which was insignificant for each study variable, hence testosterone and age were not associated with each other for any change in cholesterol, triglyceride, HDL & LDL.

## DISCUSSION

This study was designed to record the effects of total testosterone levels on lipid profiles of disease free middle aged men.

Total testosterone deficiency has been reported throughout the world in different studies. Frequency of low testosterone recorded in this study was 13.5%. Araujo and his fellows in an observational cohort study found the crude prevalence of low androgen to be 12.3%.<sup>14</sup> Similarly Goel and his colleagues found lower testosterone frequency in 40 to 60 years old diseased free Indian men as 24.2%.<sup>21</sup> Mean value of serum total testosterone recorded in this study was  $15.92 \pm 6.322$  nmol/L, whereas Eendebak and fellows in a study recorded a mean testosterone value of  $14.0 \pm 0.4$  nmol/L in South Asian males aged between 40 to 84 years suggesting the role of ethnicity in testosterone.<sup>22</sup>

Fasting triglyceride levels  $\geq 150$  mg/dl and HDL cholesterol levels in male  $< 40$  mg/dl or on specific treatment for such an abnormal value are also included in the diagnostic criteria for metabolic syndrome by IDF.<sup>23</sup> Current study showed (according to DDRRL reference ranges)<sup>19,20</sup> overall 31.5% of the study population ( $n = 200$ ) (in both TT groups) had high triglyceride levels and 47% of all the subjects had low HDL cholesterol levels. Similarly Ray et al., in 767 healthy military adults aged between 18-50 years in India found the prevalence of high triglyceride and low HDL as 14% and 67% respectively.<sup>24</sup> Moreover 37% and 30.6% of the present study subjects belonged to low ( $n = 27$ ) and normal ( $n = 173$ ) TT groups respectively had high triglyceride levels whereas 52% and 48% of the current study population had low levels of HDL cholesterol were from low ( $n = 27$ ) and normal ( $n = 173$ ) TT groups respectively. Significant negative correlation ( $\beta = -2.742$ ) of TT with triglyceride, while significant positive correlation ( $\beta = 0.304$ ) of TT with HDL was recorded in the present study, which is consistent with the findings of Akishita and his colleagues, who also revealed that TT was significantly

related to triglyceride ( $\beta = -0.242$ ) and HDL ( $\beta = 0.228$ ).<sup>25</sup> Further Haffner et al., also determined the relationship of sex hormones to lipid profile in 178 non diabetic men and found significant negative association between total testosterone and triglyceride and significant positive association between total testosterone and HDL levels<sup>26</sup> which is again consistent with the present study findings. However Haffner also found significant correlation between TT, total cholesterol and LDL cholesterol levels, which is in contrast with the current study results as TT was not correlated significantly with total cholesterol and LDL cholesterol in the present study, though overall 33.5% and 36% of the study population ( $n = 200$ ) (in both TT groups) had high total cholesterol and LDL levels respectively, while Ray et al.<sup>24</sup> found the prevalence of high total cholesterol and LDL as 22% and 22% in 767 young healthy military adult officers respectively. Laouali and colleagues examined the correlation of low TT and mortality in older men, and found significant negative ( $P < 0.01$ ) association of total testosterone with triglyceride<sup>27</sup> which is quite analogous ( $P = 0.000$ ) with the current study findings.

## CONCLUSION

Significant negative and positive associations of total testosterone with triglyceride and HDL respectively in this study suggests a promising link between low total testosterone and obesity, as low total testosterone probably causes alteration in fat metabolism leading to dyslipidemia..

### Author's Contribution:

Concept & Design of Study:	Muhammad Omar Shamim
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**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Eisenmann JC. Secular trends in variables associated with the metabolic syndrome of North American children and adolescents. *Am J Human Biol* 2003;15:786-794.
2. Carr DB, Utzschneider KM, Hull RL, Kodama K, Retzlaff BM, Brunzell JD, et al. Intra-abdominal fat is a major determinant of the national cholesterol education program adult treatment panel III criteria for the metabolic syndrome. *Diabetes* 2004; 53:2087-2094.
3. Cassells HB, Haffner SM. The metabolic syndrome: risk factors and management. *J Cardiovascular Nursing* 2006; 2:306-313.

4. Isomaa B, Almgren P, Tuomi T, Forsén B, Lahti K, Nissén M, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care* 2001; 24:683–689.
5. Neaves WB, Johnson L, Porter JC, Parker CR, Petty CS. Leydig cell numbers, daily sperm production and serum gonadotropin levels in aging men. *J Clin Endocrinol Metabol* 1984; 59:756-763.
6. Paniagua R, Nistal M, Saez FJ, Fraile B. Ultrastructure of aging human testis. *J Electron Microscopy Technique* 1991; 19(2):241-260.
7. De Wit AE, Giltay EJ, De Boer MK, Bosker FJ, Van Der Mast RC, Comijs HC, et al. Associations between testosterone and metabolic syndrome in depressed and non-depressed older men and women. *Int J Geriatr Psychiatr* 2019;34(3):463-71.
8. Kelly DM, Jones TH. Testosterone and obesity. *Obesity Reviews* 2015;16(7):581-606.
9. Ramirez ME, McMurry MP, Wiebke GA, Felton KJ, Ren K, Meikle AW, et al. Evidence for sex steroid inhibition of lipoprotein lipase in men: comparison of abdominal and femoral adipose tissue. *Metabolism* 1997; 46:179–185.
10. Dieudonne MN, Pecquery R, Leneuve MC, Giudicelli Y. Opposite effects of androgens and estrogens on adipogenesis in rat preadipocytes: Evidence for sex and site-related specificities and possible involvement of insulin-like growth factor I receptor and peroxisome proliferator-activated receptor- $\gamma$ 2. *Endocrinol* 2000;141:649–656.
11. Gupta V, Bhasin S, Guo W, Singh R, Miki R, Chauhan P, et al. Effects of dihydrotestosterone on differentiation and proliferation of human mesenchymal stem cells and preadipocytes. *Molecular and Cellular Endocrinol* 2008;296(1-2):32–40.
12. Schiffer L, Kempegowda P, Arlt W, O'Reilly MW. Mechanisms in Endocrinology: The sexually dimorphic role of androgens in human metabolic disease. *Eur J Endocrinol* 2017;177(3):125-143.
13. Kato Y, Shigehara K, Nakashima K, Iijima M, Kawagushi S, et al. Five-year effects of testosterone replacement therapy on lipid profile and glucose tolerance among hypogonadal men in Japan: a case control study. *The Aging Male* 2019; 7:1-6.
14. Araujo AB, O'Donnell AB, Brambilla DJ, Simpson WB, Longcope C, Matsumoto AM, et al. Prevalence and incidence of androgen deficiency in middle-aged and older men: Estimates from the Massachusetts male aging study. *J Clin Endocrinol Metabol* 2004;89(12):5920–5926.
15. Jeng HA, Chen YL, Kantaria KN. Association of cigarette smoking with reproductive hormone levels and semen quality in healthy adult men in Taiwan. *J Environmental Sci Health* 2014; 49(3): 262-268.
16. Brambilla DJ, Matsumoto AM, Araujo AB, McKinlay JB. The effect of diurnal variation on clinical measurement of serum testosterone and other sex hormone levels in men. *J Clin Endocrinol Metabol* 2009; 94(3):907-913.
17. Matsuzaki Y, Kawaguchi E, Morita Y, et al. Evaluation of two kinds of reagents for direct determination of HDL cholesterol. *Int J Analytical Bio-Sci* 1996;19:419-427.
18. Roberts WI, McMillan GA, Burtis CA, Bruns DE. Reference Information for Clinical Laboratory. *Tietz Fundamental of Clinical Chemistry* 6th Edition. St. Louis. Saunders Elsevier 2008; 45:860.
19. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). NIH Publication 2001; 01-3670.
20. Stein EA, Myers GL. National cholesterol education program recommendations for triglycerides measurement. Executive Summary. *Clinical Chemistry* 1995; 4:1421–1426.
21. Goel A, Kumar S, Natu SM, Dalela D, Sinha RJ, Awasthi S. A cross-sectional pilot study to determine the prevalence of testosterone deficiency syndrome in working population of Indian men. *Ind J Urol* 2009; 25(2):190-194.
22. Eendebak RJ, Swiecicka A, Gromski PS, Pye SR, O'Neill TW, Marshall A, et al. Ethnic differences in male reproductive hormones and relationships with adiposity and insulin resistance in older men. *Clin Endocrinol* 2017; 86(5):660-668.
23. Aguilar M, Bhuket T, Torres S, Liu B, Wong RJ. Prevalence of the metabolic syndrome in the United States, 2003-2012. *J Am Med Assoc* 2015; 313(19):1973-1974.
24. Ray S, Kulkarni B, Sreenivas A. Prevalence of prehypertension in young military adults & its association with overweight & dyslipidaemia. *Ind J Med Research* 2011; 134:162-167.
25. Akishita M, Fukai S, Hashimoto M, Kameyama Y, Nomura K, Nakamura T, et al. Association of low testosterone with metabolic syndrome and its components in middle-aged Japanese men. *Hypertension Research* 2010; 33:587–591.
26. Haffner SM, Mykkanen L, Valdez RA, Katz MS. Relationship of sex hormones to lipids and lipoproteins in nondiabetic men. *J Clin Endocrinol Metabolism* 1993;77(6):1610-1615.
27. Laouali N, Brailly-Tabard S, Helmer C, Ancelin ML, Tzourio C, Singh-Manoux A, et al. Testosterone and all-cause mortality in older men: the role of metabolic syndrome. *J Endocrine Society* 2018; 2(4):322-35..