

Study of Testosterone Levels in Coronary Artery Disease with Poorly Controlled Diabetes Mellitus in Males

Pradnya Phalak¹, Abhijit Pratap²^{1,2}Associate Professor, Department of Biochemistry, Dr. D. Y. Patil Medical College, Pimpri, Pune

Received: 20-03-2023 / Revised: 21-04-2023 / Accepted: 25-05-2023

Corresponding author: Dr. Abhijit Pratap

Conflict of interest: Nil

Abstract:

Introduction: Coronary artery disease including myocardial infarction is a growing pandemic worldwide and is an important cause of morbidity and mortality. Millions of lives are lost to coronary artery disease every year and is a significant medical problem. The disease is multifactorial, and an important risk factor is diabetes mellitus and patients having poor glycemic control. Testosterone is a steroid hormone which also has cardio metabolic benefits apart for reproductive functions. It is believed to cause vasodilatation of coronary vessels and thus protects or is beneficial against coronary artery diseases. Low testosterone is seen both in diabetes mellitus and as we age from adulthood to elderly. The study aims to compare the testosterone levels between diabetes mellitus patients and non-diabetes mellitus patients who have been diagnosed or suffered from acute coronary syndrome.

Materials and Method: A total of 50 patients were included in the study, patients' sample was tested for total testosterone, fasting blood sugar levels, glycosylated hemoglobin levels (HbA1c) and BMI was measured.

Results: 42 out of 50 were diabetic and having a mean age of around 63 years. Testosterone levels were low in diabetic patients as compared to non-diabetic, which was statistically significant and the decrease in testosterone levels were proportional to the increase in fasting blood sugar and HbA1c levels, which was also significant however the relationship could not be statistically assessed due to insufficient data.

Discussion: All cases of acute coronary syndrome are associated with low testosterone levels. This finding is supported by numerous studies which highlight the cardiometabolic role of testosterone. Poorer the glycemic control as shown by increasing HbA1c levels lower the serum testosterone levels, which was a novel finding requiring further studies in this area.

Keywords: Acute coronary syndrome, hypotestosteronemia, diabetes mellitus, coronary artery disease.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Coronary artery disease is an important cardiovascular cause of morbidity and mortality. It refers to cardiac disease due to the obstruction of coronary artery, which is the blood supplying artery of the heart. In the United States coronary artery disease alone is responsible for the mortality of 382,820 in 2020, and every year 805000 people suffer from heart attack [1]. As per WHO fact sheet cardiovascular diseases (CVDs) are the leading cause of death globally, taking an estimated 17.9 million lives each year. [2]

Diabetes Mellitus is a metabolic disorder in which almost all organs are affected. It is a major risk factor for coronary artery disease considering the prevalence of people suffering from diabetes mellitus. The pathophysiology of coronary artery disease in diabetes mellitus involves interaction of epigenetic, genetic and post translational changes with effects the blood vessel. [3] A 10 year systematic review from around the world revealed the prevalence

of cardiovascular disease in diabetes mellitus to be 32.2%. [4]

Testosterone is an androgen produced from testes, apart from growth and maturation of secondary sexual characters in males, it also has cardioprotective effect and decreased levels of testosterone is seen in coronary artery disease as compared with healthy controls. [5,6,7,8,9,10]

Testosterone levels are found to be low in male patients of diabetes mellitus as compared to normal. [11] Low testosterone is believed to increase insulin resistance through change in muscle / fat body composition. [12,13]

The study aims to compare the testosterone levels between diabetes mellitus patients and non-diabetes mellitus patients who have been diagnosed or suffered from acute coronary syndrome.

Materials and Methods

The study was conducted in Pune, Maharashtra, India. 50 men diagnosed with coronary artery disease were studied. The following were recorded.

1. Total testosterone in plain vacutainer and analysed by chemiluminescence method on Abbott immune analyser.
2. Fasting blood glucose in fluoride vacutainer and analysed by photometry on Siemens dimension analyser.
3. HbA1c in EDTA vacutainer and analysed by cation exchange chromatography method on Biorad D10 HPLC analyser.
4. BMI was recorded as ratio of weight over height squared (kg/m^2).
5. Data was analysed using SPSS software.

Results

A total of 50 male patients diagnosed with coronary artery disease in last 6 months were included in the study (Table no. 1). 42 patients out of 50 were diabetic and on treatment, 8 were non-diabetic but had

suffered a coronary event. The mean age of diabetic participants was 63 years, having mean BMI of $30.16 \text{ kg}/\text{m}^2$, whereas mean age of non-diabetic participants were 59 years and had a mean BMI of $27.12 \text{ kg}/\text{m}^2$.

The total testosterone levels measured in both groups showed highly significant differences, the mean testosterone levels in diabetic group were 298 ng/dl which was significantly lower than non-diabetic group mean of 339 ng/dl, a similar finding was also observed in fasting blood sugar levels and HbA1c levels between the two groups.

Mean fasting blood sugar and HbA1c was 211.8 mg/dl and 9.8% in diabetic group and 106.1 mg/dl and 5.9% in non-diabetic group, both findings were highly significant. An interesting finding observed was that the decrease in testosterone levels were proportional to the increase in fasting blood sugar and HbA1c levels, however the relationship could not be statistically assessed due to insufficient data.

Table 1: Coronary Artery Disease Patients' Profile

	Coronary artery disease (50)		P value
	Diabetic (42)	Non-Diabetic (8)	
Age in years (mean)	63	59	<0.05
BMI (kg/m^2)	30.16 ± 0.22	27.12 ± 0.19	<0.05
Testosterone (NR: 350-890 ng/dl)	298 ± 2.1	339 ± 1.4	<0.001
Fasting blood sugar (NR: <100 mg/dl)	211.8 ± 2.3	106.1 ± 2.5	<0.001
HbA1c (NR: <5.7%)	9.7 ± 0.7	5.9 ± 1.5	<0.001

Discussion

In the present study we studied the levels of testosterone in male patients diagnosed with coronary artery disease and having poor glycemic control. Our data showed 2 significant findings.

1. All cases of acute coronary syndrome are associated with low testosterone levels.
2. Poorer the glycemic control as shown by increasing HbA1c levels lower the serum testosterone levels.

Similar findings of low testosterone levels in patients of acute coronary syndrome were seen in elderly men and post-menopausal women due to maladaptive vascular changes and atherosclerosis brought about due to hypotestosteronemia. [14]

English et al [15] and Rosano et al [16] both have shown that patients of catheterization coronary artery disease have significantly low bioavailable testosterone as compared with controls with normal coronary artery.

Numerous studies have found an inverse relationship between severity of coronary artery disease and testosterone deficiency, the lower the testosterone levels more profound the severity of coronary artery disease. [16,17,18,19]

Testosterone levels are lower in patients of diabetes mellitus as compared to control and this has been supported by 2 meta-analysis done by Ding et al [20] who showed type 2 diabetes mellitus is significantly associated with low testosterone levels and Corona et al [21] demonstrated that along with total testosterone, free testosterone and sex hormone binding globulin are lower amongst patients of type 2 diabetes mellitus.

Our study correlates with various other studies in showing that testosterone deficiency is associated with acute coronary syndrome events, it also not only demonstrates testosterone deficiency in patients of type 2 diabetes mellitus but also shows an inverse relationship between them testosterone deficiency and glycemic control, hence a good glycemic control is essential to correct testosterone deficiency.

Conclusion

The study concludes that in patients of acute coronary syndrome there is significant testosterone deficiency, and which has an inverse relationship with glycemic status of patients of type 2 diabetes mellitus.

Limitation of the study: It is a pilot study to explore the relationship between testosterone and

glycemic status in coronary artery syndrome patients, however due to small sample size and inadequate data, the inverse proportional relationship between testosterone and glycemic status could not be statistically studied.

References

1. Tsao CW, Aday AW, Almarzooq ZI, Beaton AZ, Bittencourt MS, Boehme AK, et al. heart disease and Stroke Statistics—2022 Update: A Report from the American Heart Association. *Circulation*. 2022;145(8): e153–e639.
2. Cardiovascular diseases (CVDs) Fact sheet. Available at: [http://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](http://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)). Accessed 15 Mar 2023.
3. Rodriguez-Araujo G, Nakagami H. Pathophysiology of cardiovascular disease in diabetes mellitus. *Cardiovasc Endocrinol Metab*. 2018 Feb 14;7(1):4-9.
4. Einarson T.R., Acs A., Ludwig C. et al. Prevalence of cardiovascular disease in type 2 diabetes: a systematic literature review of scientific evidence from across the world in 2007–2017. *Cardiovasc Diabetol*. 2018; 17: 83.
5. Zhao SP, Li XP. The association of low plasma testosterone level with coronary artery disease in Chinese men. *Int J Cardiol*. 1998; 63:161–164.
6. English KM, Mandour O, Steeds RP, Diver MJ, Jones TH, Channer KS. Men with coronary artery disease have lower levels of androgens than men with normal coronary angiograms. *Eur Heart J*. 2000; 21:890–894.
7. Dobrzycki S, Serwatka W, Nadlewski S, Korcecki J, Jackowski R, Paruk J, Ladny J, Hirnle T. An assessment of correlations between endogenous sex hormone levels and the extensiveness of coronary heart disease and the ejection fraction of the left ventricle in males. *J Med Invest*. 2003; 50:162–169.
8. Akishita M, Hashimoto M, Ohike Y, Ogawa S, Iijima K, Eto M, Ouchi Y. Low testosterone level as a predictor of cardiovascular events in Japanese men with coronary risk factors. *Atherosclerosis*. 2010; 210:232–236.
9. Rosano G, Sheiban I, Massaro R, Pgnotta P, Marazzi G, Vitale C, Mercurio G, Volterrani M, Aversa A, Fini M. Low testosterone levels are associated with coronary artery disease in male patients with angina. *Int J Impot Res*. 2007; 19:176–182.
10. Hu X, Rui L, Zhu T, Xia H, Yang X, Wang X, Liu H, Lu Z, Jiang H. Low testosterone level in middle-aged male patients with coronary artery disease. *Eur J Intern Med*. 2011; 22:133–136.
11. Grossmann M. Low testosterone in men with type 2 diabetes: significance and treatment. *J Clin Endocrinol Metab*. 2011 Aug;96(8):2341–53.
12. Lin HY, Xu Q, Yeh S, Wang RS, Sparks JD, Chang C. Insulin and leptin resistance with hyperleptinemia in mice lacking androgen receptor. *Diabetes*. 2005 Jun 1;54(6):1717–25.
13. Singh R, Artaza JN, Taylor WE, Gonzalez-Cadavid NF, Bhasin S. Androgens stimulate myogenic differentiation and inhibit adipogenesis in C3H 10T1/2 pluripotent cells through an androgen receptor-mediated pathway. *Endocrinology*. 2003 Nov 1;144(11):5081–8.
14. Moreau KL, Babcock MC, Hildreth KL. Sex differences in vascular aging in response to testosterone. *Biology of sex Differences*. 2020 Dec;11(1):1–4.
15. English KM, Mandour O, Steeds RP, Diver MJ, Jones TH, Channer KS. Men with coronary artery disease have lower levels of androgens than men with normal coronary angiograms. *Eur Heart J*. 2000; 21:890–894.
16. Rosano G, Sheiban I, Massaro R, Pgnotta P, Marazzi G, Vitale C, Mercurio G, Volterrani M, Aversa A, Fini M. Low testosterone levels are associated with coronary artery disease in male patients with angina. *Int J Impot Res*. 2007; 19:176–182.
17. Dobrzycki S, Serwatka W, Nadlewski S, Korcecki J, Jackowski R, Paruk J, Ladny J, Hirnle T. An assessment of correlations between endogenous sex hormone levels and the extensiveness of coronary heart disease and the ejection fraction of the left ventricle in males. *J Med Invest*. 2003; 50:162–169.
18. Li L, Guo CY, Jia EZ, Zhu TB, Wang LS, Cao KJ, Ma WZ, Yang ZJ. Testosterone is negatively associated with the severity of coronary atherosclerosis in men. *Asian J Androl*. 2012; 14:875–878.
19. Phillips GB, Pinkernell BH, Jing TY. The association of hypotestosteronemia with coronary artery disease in men. *Arterioscler Thromb Vasc Biol*. 1994; 14:701–706.
20. Ding EL, Song Y, Malik VS, Liu S. Sex differences of endogenous sex hormones and risk of type 2 diabetes. *JAMA*. 2006; 295:1288–1299.
21. Corona G, Monami M, Rastrelli G, Aversa A, Sforza A, Lenzi A, Forti G, Mannucci E, Maggi M. Type 2 diabetes mellitus and testosterone: a meta-analysis study. *Int J Androl*. 2010; 34:528–540.