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## **TESTOSTERONE AND CORONARY ARTERY DISEASE IN POST-MENOPAUSAL WOMEN**

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### **ABSTRACT**

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**Objective** - There are conflicting data concerning the roles of androgens on cardiovascular function in postmenopausal women. Further investigation on the role of androgens on cardiovascular disease and their possible mechanisms of action is needed. Hence, a comparison was made between testosterone levels of coronary artery disease-positive samples and that of coronary artery disease-negative samples, to assess the relation of testosterone level with the extent of coronary artery disease.

**Materials and Methods** - A total of 58 serum samples were collected from post-menopausal women, aged above 49 years, who underwent coronary angiogram, of which 29 women were diagnosed to suffer from coronary artery disease and the remaining 29 women were free from coronary artery disease. Serum testosterone levels of all 58 patients under study were measured by adopting a highly sensitive method called Enzyme-Linked Immunosorbent Assay.

**Result and Conclusion** - The present study revealed that decreased levels of testosterone were associated as a risk factor for coronary artery disease in post-menopausal women. However, further prospective studies are needed to examine the relation between the physiological levels of circulating sex hormones and cardiovascular disease risk in post-menopausal women.

## INTRODUCTION

### **Testosterone And Coronary Artery Disease: Is There Any Link In Postmenopausal Women?**

There are conflicting data concerning the roles of androgens on cardiovascular function in postmenopausal women. It has been suggested that the relative androgen excess, which occurs as estrogen levels decline during menopause, may be more predictive of the increased risk of cardiovascular disease after menopause. However, recent studies have demonstrated a beneficial effect of testosterone on myocardial ischemia in men with coronary artery disease.

Some studies revealed that increased levels of testosterone and androstenedione positively associate with coronary artery disease in post-menopausal women (Phillips, *et al*). In contrast, Kaczmarek *et al*. reported an independent, inverse association of testosterone with coronary artery disease or extent of coronary artery disease. Contradictory results from the studies concerning androgens and coronary artery disease in post-menopausal women may be explained by samples from different cohorts. Further investigation on the role of androgens on cardiovascular disease and their possible mechanisms of action is needed.

Recent evidence points to the beneficial effects of normal levels of testosterone. There is some indication that restoring normal healthy levels of testosterone may be helpful in preventing heart disease<sup>1</sup>.

### **The Present Study**

The present study included the assessment of association between testosterone level and coronary artery disease in post-menopausal women.

In this attempt to determine whether any testosterone abnormality might be a factor in the development of coronary artery disease in post-menopausal women, serum testosterone levels were measured in relation to the degree of coronary artery disease in 58 post-menopausal women undergoing coronary angiography.

The measurement of serum testosterone levels were made by performing one of the most sensitive techniques called Enzyme-Linked Immunosorbent Assay (ELISA).

### **Study Limitations**

Hormones were measured once only. We do not exclude the effect of intra-individual and inter-individual variations of hormone levels in the study population. Only total hormone levels were measured and bio-available hormone levels were not estimated in our study.

## MATERIALS AND METHODS

### Collection of Samples

The Serum samples were collected from a highly reputed but private cardiology based hospital, Chennai. Fifty eight post-menopausal women, aged above 49 years, who were subjected to coronary angiography, were assessed in the present study. Among the 58 post-menopausal women, 29 women were diagnosed to suffer from coronary artery disease by coronary angiogram and the remaining 29 women were found free from coronary artery disease.

### Materials

The “Enzyme–Linked Immunosorbent Assay” method as described by Widsdom G.B. et al., (1976) <sup>2</sup> was adopted.

The only material required is ELISA kit, meant for direct immuno-enzymatic assay for the quantitative determination of testosterone in serum. The content of the ELISA kit includes Pre-coated microtitre plate, Enzyme conjugate, TMB substrate, Stop solution, Standards (0,1,2,3,4) and Cardboard sealers. And, of course, ELISA reader, ELISA washer, micropipettes and specimens are must requirement.

### Methods

Testosterone was detected and measured by a sandwich ELISA technique, in which the antibody (anti-testosterone) is immobilized on a microtitre well. Serum sample containing testosterone was added and allowed to react with the immobilized anti-testosterone antibody. After the well was washed, a second enzyme-linked antibody (enzyme conjugate) specific for a different epitope on the antigen and allowed to react with the bound antigen. After the removal of any free second antibody by washing, TMB substrate was added and the colored reaction product was measured using ELISA reader.

## RESULTS

The absorbance values and the concentration of testosterone of all standards as well as of 58 patients, as obtained from ELISA reader was enclosed and presented in Table-I, Table-II and Table-III respectively.

A scatter diagram of standards as well as samples (Figure 1) clearly suggests that the absorbance values and the concentration of testosterone are negatively correlated. Also, the correlation coefficient of testosterone levels in coronary artery disease-positive samples and coronary artery disease-negative samples was found to be  $-0.0871$ , hence negatively correlated.

The comparison of testosterone levels of standards, coronary artery disease-positive cases and coronary artery disease-negative cases were made easy by preparing a 3-D column type of bar diagram (Figure 2), which clearly reveals that the level of serum testosterone concentration is low in coronary artery disease-positive post-menopausal women patient's serum samples, when compared with that of coronary artery disease-negative post-menopausal women patient's serum samples.

**TABLE – I**

**ABSORBANCE VALUES AND TESTOSTERONE CONCENTRATIONS OF STANDARDS USED**

S.No:	SAMPLES	ABSORBANCE VALUES	TESTOSTERONE CONCENTRATION (ng/ml)
1.	Standard 0	2.352	0
2.	Standard 1	2.095	0.2
3.	Standard 2	1.831	1
4.	Standard 3	1.589	4
5.	Standard 4	1.098	16

**TABLE – II**

**OBSERVATION OF CAD-POSITIVE PATIENT'S SAMPLES**

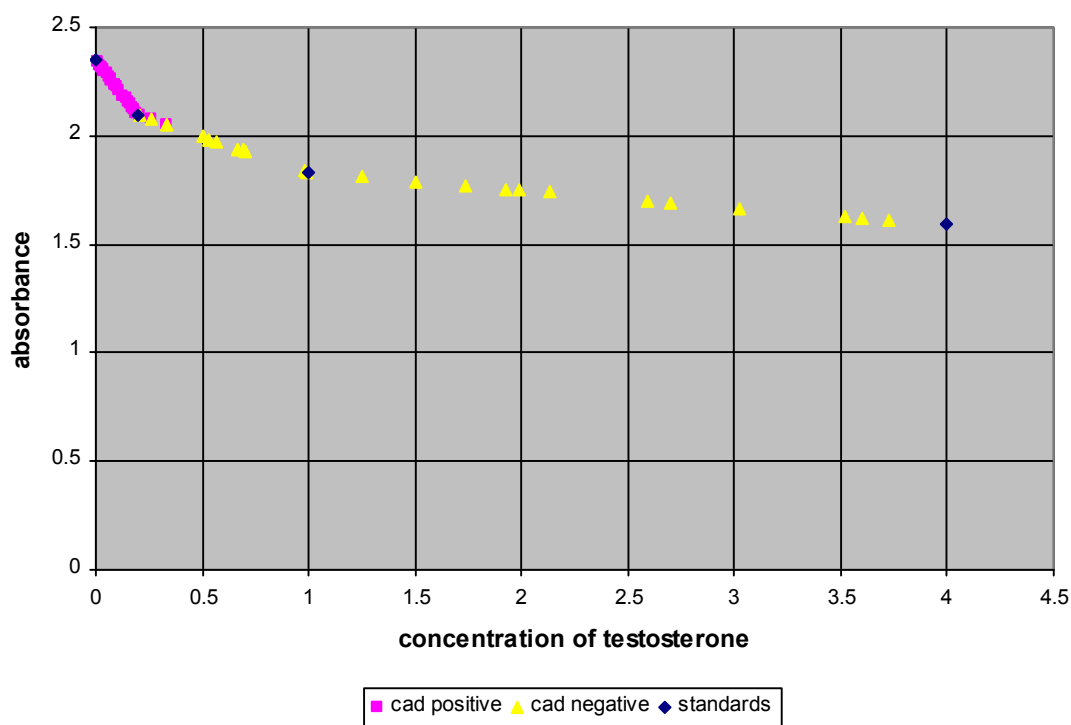
S.No:	DETAILS	ABSORBANCE VALUES	TESTOSTERONE CONCENTRATION
1.	Sample no:1	2.213	0.18
2.	Sample no:3	2.239	0.09
3.	Sample no:6	2.311	0.03
4.	Sample no:7	2.234	0.09
5.	Sample no:10	2.257	0.07
6.	Sample no:11	2.306	0.04
7.	Sample no:13	2.343	0.01
8.	Sample no:15	2.343	0.01
9.	Sample no:16	2.234	0.09
10.	Sample no:19	2.184	0.13

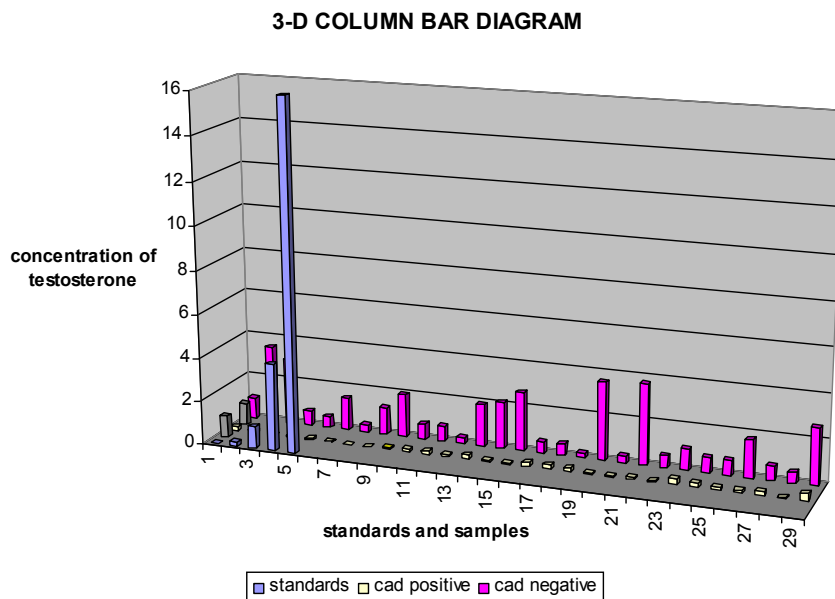
11.	Sample no:20	2.158	0.15
12.	Sample no:22	2.236	0.09
13.	Sample no:23	2.106	0.19
14.	Sample no:24	2.262	0.075
15.	Sample no:25	2.288	0.05
16.	Sample no:27	2.106	0.19
17.	Sample no:35	2.108	0.19
18.	Sample no:36	2.132	0.17
19.	Sample no:37	2.301	0.04
20.	Sample no:38	2.314	0.03
21.	Sample no:39	2.21	0.11
22.	Sample no:41	2.275	0.06
23.	Sample no:45	2.075	0.26
24.	Sample no:46	2.093	0.21
25.	Sample no:47	2.171	0.14
26.	Sample no:50	2.223	0.1
27.	Sample no:52	2.145	0.16
28.	Sample no:54	2.327	0.02
29.	Sample no:55	2.053	0.33

**TABLE – III**  
**OBSERVATION OF CAD-NEGATIVE PATIENT'S SAMPLES**

S.No:	DETAILS	ABSORBANCE VALUES	TESTOSTERONE CONCENTRATION
1.	Sample no:2	1.833	0.99
2.	Sample no:4	1.628	3.523
3.	Sample no:5	1.668	3.02
4.	Sample no:8	1.941	0.67
5.	Sample no:9	1.995	0.5
6.	Sample no:12	1.791	1.5
7.	Sample no:14	2.053	0.33
8.	Sample no:17	1.811	1.25
9.	Sample no:18	1.751	1.99
10.	Sample no:21	1.934	0.69
11.	Sample no:26	1.934	0.69
12.	Sample no:28	2.075	0.26
13.	Sample no:29	1.756	1.93
14.	Sample no:30	1.740	2.13

15.	Sample no:31	1.694	2.7
16.	Sample no:32	1.985	0.53
17.	Sample no:33	1.985	0.53
18.	Sample no:34	2.093	0.21
19.	Sample no:40	1.621	3.6
20.	Sample no:42	2.053	0.33
21.	Sample no:43	1.611	3.73
22.	Sample no:44	1.974	0.57
23.	Sample no:48	1.836	0.98
24.	Sample no:49	1.930	0.7
25.	Sample no:51	1.930	0.7
26.	Sample no:53	1.771	1.74
27.	Sample no:56	1.941	0.67
28.	Sample no:57	1.995	0.5
29.	Sample no:58	1.703	2.59

**Figure 1****SCATTER DIAGRAM FOR STANDARDS AND SAMPLES- zoomed**

**Figure 2**

## DISCUSSION

Maturana *et al.*,(2002) <sup>3</sup> noticed that there is a relation between serum testosterone level and coronary artery disease in some way that the androgen level can be considered to be an important risk factor for cardiovascular disease in post-menopausal women. In the present study, the linear difference in testosterone levels among coronary artery disease-positive and coronary artery disease-negative post-menopausal women showed that there is a potential role of testosterone in coronary artery disease in post-menopausal women and concurs with the observation of Maturana *et al.*,(2002).

In the present study, coronary artery disease-positive post-menopausal women were found to contain a lesser degree of testosterone concentration when compared with that of coronary artery disease-negative post-menopausal women. Hence, the level of testosterone was assessed for its relationship with coronary artery disease and the outcome was that the decreased testosterone might be a risk factor for coronary artery disease. This result of observation have been found to be in accordance with Kaczmarek A *et al.*,(2003) <sup>4</sup>, Gail A. Laughlin *et al.*,(2006) <sup>5</sup> and also with that of Montalcini T *et al.*,(2007) <sup>6</sup>.

However, some studies revealed that increased levels of testosterone and androstenedione positively associate with coronary artery disease in post-menopausal women (Phillips *et al.* 1997,<sup>7</sup> and Irene Lambrinoudaki *et al.*, 2006<sup>8</sup>). Also, few other studies revealed that there is no relation between the testosterone or androstenedione levels and the extent of

coronary artery disease (Barrett-Connor E *et al.*, 1995<sup>9</sup> and Odgerel Tumor et al., 2007<sup>10</sup>). Such contradictory results from the studies concerning androgens and coronary artery disease in post-menopausal women may be explained by samples from different cohorts. Further investigation on the role of androgens on cardiovascular disease and their possible mechanisms of action is needed.

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