ISSN Print: 2394-7500
ISSN Online: 2394-5869
Impact Factor: 5.2
IJAR 2015; 1(9): 550-554
www.allresearchjournal.com
Received: 07-06-2015
Accepted: 10-07-2015

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Original Article - Level of serum free testosterone in male patients presenting with acute coronary syndrome

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Abstract
Aims and objectives- To study clinical profile of acute coronary syndrome and to study the the role of testosterone in patients of acute coronary syndrome.
Material and methods-50 cases of ACS and 25 healthy controll males were included in the study done in in J.A. Group of Hospitals Gwalior. Detail history, clinical examination, laboratory investigations as required and Ecg was done after written concent. Data Was Filled in Preformed Proforma and then statistical analysis is as per results shown here.
Results- The present study included 50 patients who presented with acute coronary syndrome and 25 patients of age matched controls without evidence of CAD. In the study group, the mean age of presentation was 53.3 yrs. The commonest presenting symptom was chest pain followed by palpitation. Hypertension present in 34% of cases and 28% of controls. Smoking incidence was 46% in cases and 20% in controls. Higher levels of total cholesterol, triglyceride and LDL cholesterol and lower level of HDL cholesterol were seen in cases. They significantly differ in comparison to controls. Of the cases studied, about 86% had STEMI and 14% had NSTEMI. The mean serum free testosterone was significantly lower in patients with ACS. Serum free testosterone level was also significantly lower in patients with hypertension and smokers. Mean serum free testosterone level did not relate to the number of cardiovascular risk factors. Most of the patients (48%) presented with AWMI followed by IWMI (32%). Mean serum free testosterone level was lowest in patient who had IWMI+AWMI as compared with other patterns of ACS. Of the 50 cases studied, 2 patients died (percentage of mortality - 4%).Mean serum free testosterone level was inversely related to hypertension, dyslipidemia, smokers and BMI. Conclusion- The serum free testosterone was found to be lower in patients with acute coronary syndrome as compared to controls. The difference between cases and controls was statistically significant. The serum free testosterone level was lowest in patients who presented with AWMI+IWMI as compared with other patterns of ACS. The serum free testosterone level was found to be lower in cases with traditional risk factors like smoking, hypertension, dyslipidemia and BMI.

Keyword: acute coronary syndrome (ACS), testosterone level, males.

Introduction

Acute coronary syndrome most often represents acute atherosclerotic plaque rupture with exposure of throm bogenic sub-endothelial matrix. Inflammation plays a central pathogenic role in the initiation and progression of coronary atheroma and its clinical consequences. Testosterone has been shown to have immuno-modulating effects, and appears to suppress activation of pro-inflammatory cytokines. Men with low testosterone levels are at increase risk of developing acute coronary syndrome. An anti-inflammatory effect of normal physiological levels of sex hormones may therefore, be important in athero-protection [1] In males, the increasing incidence of CAD with age is associated with a decline in testosterone levels [2] Low rather than high testosterone levels are associated with CAD [3] and that low serum testosterone is associated with increased aortic atheroma [4]. Testosterone has been shown to suppress pro-inflammatory cytokine activity, inhibit apoptosis and enhance vascular smooth muscle cell proliferation. These action may be responsible for this atheroprotective effects Testosterone could, therefore, potentially be involved in maintaining fibrous cap of the atherosclerotic plaque by promoting smooth muscle cell stability. Various studies have shown that 3 months of physiological testosterone treatment leads to symptomatic improvement in men with angina [5]. The acute and chronic anti-ischaemic

properties of testosterone have also been reported 6 (Rosano *et al.*, 1999) and this effect is most likely mediated by coronary artery vasodilation7 (Webb *et al.*, 1999), which appears to involve calcium channel antagonism. This study is undertaken in order to correlate the role of serum free testosterone level in patients with Acute Coronary Syndrome.

Aims and Objectives-To study clinical profile of acute coronary syndrome and to study the the role of testosterone in patients of acute coronary syndrome.

Materials and Methods-For the study, 50 male subjects presenting with acute coronary syndrome in J.A. Group of Hospitals and those patients who have recovered from a recent acute coronary event attending Medicine OPD were taken as cases. 25 Age & sex matched healthy control were taken from the medical ward. Study was done between September 2008 and October 2009. patients with acute coronary syndrome were studied based on the history, ECG changes, estimation of serum free testosterone and estimation of cardiac markers wherever required. Informed consent were obtained from all patients. Each patient was subjected to a detailed history and clinical examination. Clinical examination include blood pressure measurement, general physical examination, anthropometric measurement, body mass index and systemic examination. Biochemical parameter included fasting and random blood sugar, blood urea, s. creatinine and lipid profile. History of hypertension, diabetes mellitus, chronic kidney disease and dyslipidemia were noted.

Statistical analysis: In the present study, values are expressed as mean±2SD. Variables are compared by 't' test for 2 sample mean. Attributes are compared by odds ratio and standard error of difference between two proportions by Chi-square test. p values < 0.05 were considered significant.

Inclusion criteria: All male patients presenting with acute coronary syndrome between the age group of 35-74 years.

Exclusion criteria: Patient with liver disease, Patient with renal parenchymal disease, Patient with diabetes mellitus

Results -In this study, 50 patients who presented with acute coronary syndrome were studied, along with 25 age and sex matched controls, who did not have any evidence of coronary artery disease.

Table 1: Distribution of patients according to age

Age	Cases	Controls
35-44	12	10
45-54	14	11
55-64	15	4
65-74	9	0
Total	50	25

Majority of the case belonged to age group 55-64 (n=15). Mean age of the cases was 53.36 yrs.

Table 2: Incidence of Different symptoms (n=50)

Symptoms	No. of cases	Percentage
Chest Pain	45	90%
Breathlessness	4	8%
Palpitation	28	56%
Syncope	3	6%

In the case group, most common presenting symptoms was chest pain (n=45) in 90%, followed by palpitation (n=28) in 56% breathlessness and syncope were found in 8% and 6% respectively.

Table 3: Distribution of risk factor in cases (n=50) & controls (n=25)

Risk Factor	Cases	Controls
Hypertension	17	7
Dyslipidemia	20	4
Smoking	23	5
Alcohol	2	2
Family History	3	2

(a) Dysplipidemia is defined by any or all of the below: T. cholesterol > 240 mg/dl, HDL-C < 40 or > 60 mg/dl, LDL-C > 130 mg/dl, Triglycerides > 160 mg/dl, Dyslipidemia was seen in 20 cases and 4 control patients.
(b) In case group (n=50), 17 patients had history of hypertension (34%) whereas in control group 7 patients had hypertension (28%)(c) In case group, 23 (46%) were chronic smokers, and among controls groups, 5(20%) were chronic smokers. (d) In case group, 3(6%) had family history of coronary artery disease and in control group 2(8%) had family history

Table 4: BMI in Cases & controls

BMI	Cases	Controls
18.5-24.9	37	25
25-29.9	13	0
>30	0	0

In the case group 13 patients (26%) were overweight. In the case group, 37 patients (74%) had normal BMI while 25 patients (100%) had normal BMI in control group.

Table 5: Mean BMI in cases and controls

Cases	Controls	p value
23.40±2.35	20.64±1.52	< 0.05 (p value = 0.000001)

BMI in cases were higher than control group and the difference was statistically highly significant.

Table 6: Mean BP in cases and controls

BP	Cases (mmHg)	Controls (mmHg)	p value
SBP	129.36±24.79	118.8±9.27	p < 0.05 (p value = 0.04)
DBP	82.2±15.02	74.4±5.83	p < 0.05 (p value = 0.014)

Mean SBP and mean DBP were higher in cases than in controls and the difference was statistically significant.

Table 7: Total cholesterol in case and controls

Total cholesterol (mg/dl)	Cases	Controls
< 200	19	20
201-239	8	1
> 240	23	4

In the case group, 23 patients (46%) had high levels of total cholesterol. In the control, 4 patients (16%) had high total cholesterol.

Table 8: Mean total cholesterol (mg/dl) in cases and controls

Cases	Controls	p value
221.4±50.10	190.2±34.05	< 0.05 (p value = 0.006)

Mean total cholesterol level was higher in cases than in control group and the difference was statistically significant.

Table 9: HDL-C level in cases and controls

HDL-C (mg/dl)	Cases	Controls
< 40	18	4
40-60	32	21
> 60	0	0

In the case group, 18 patients (36%) had HDL-cholesterol (HDL-C) level less than 40 mg/dl and 32 (64%) had in the normal range, whereas in control group, 4 (16%) had less than 40 mg/dl and 21 (84%) subjects had in the normal range.

Table 10: Mean HDL-C (mg/dl) in cases and controls

Cases	Controls	p value
40.34±9.91	45.16±5.96	< 0.05 (p value = 0.02)

Mean total cholesterol level was less than control group and the difference was statistically significant.

Table 11: LDL-cholesterol level in cases and controls

HDL-C (mg/dl)	Cases	Controls
< 100	7	19
100-129	26	6
130-159	12	0
160-189	5	0
> 190	0	0

In the case group, 7 (14%) had LDL-C levels in optimal range while 19 (76%) in the control group had LDL-C levels in optimal range. 26 (52%) and 6 (24%) respectively in case and control groups had LDL-C levels in high normal range. In case group, 5 patients (10%) had high LDL-C levels while none in control group had high LDL-C level.

Table 12: Mean LDL-C (mg/dl) in cases sand control

Cases	Controls	p value
124.14±26.0	74.94±26.39	< 0.05 (p value = 0.0001)

In the case group, LDL-C was higher than the control group and the difference was statistically significant.

Table 13: TG level in cases and controls

HDL-C (mg/dl)	Cases	Controls
< 160	42	21
> 160	8	4

In the case group 42 (84%) had TG levels in normal range and 8 (16%) above normal.
In the control group, apparently 21(84%) had TG level in normal range.

Table 14: Mean TG (mg/dl) level in cases and controls

Cases	Controls	p value
136.9±34.8	101.2±33.07	< 0.05 (p value = 0.00006)

The difference in TG level in case and control group was statistically significant.

Table 15: Serum free testosterone level and coronary artery disease (ACS) cross tabulation

S. free testosterone	Cases (ACS)	Controls (without ACS)
< 9 ng/dl	40	1
> 9 ng/dl	10	24

Yates corrected Chi-square test: 35.84, Risk ratio (95% CI): 3.32, Odds ratio (75% CI): 96.00, p value = 0.000001 significant. In the present study group, the normal level of serum free testosterone was 9-30 ng/dl. In the case group, 40 patients (80%) had serum free testosterone level lesser than 9 ng/dl while in control group only 1 subjects had lesser than 9 ng/dl. Serum free testosterone level was significantly decreased in patients who had acute coronary syndrome.

Table 16: Mean serum free testosterone level (ng/dl) in cases and controls

Cases	Controls	p value
8.36±1.80	12.94±3.06	< 0.05 (p value = 0.000001)

Mean serum free testosterone level was significantly decreased in the cases than the controls and the difference was statistically significant.

Table 17: Mean serum free testosterone level (ng/dl) cross tabulation according to number of cardiovascular risk factors in cases (n=50)

	Cases with 0-2 risk factors	Cases with ≥ 3 risk factors	p value
Mean serum free testosterone	8.02±1.23	8.58±2.08	0.33

Mean serum free testosterone level with cardiovascular risk factor did not show statistically significant difference in the present study.

Table 18: Mean serum free testosterone (ng/dl) in hypertensive cases and hypertensive controls

Cases	Controls	p value
8.38±1.56	11.27±1.85	< 0.05 (p value = 0. 0001)

Mean serum free testosterone in hypertensive cases was found to be lesser than in hypertensive control and the study was statistically significant.

Table 19: Mean serum free testosterone level (ng/dl) in smokers (cases and controls)

Cases	Controls	p value
8.72±1.96	11.1±2.21	< 0.05 (p value = 0. 00001)

Mean serum free testosterone in smokers cases was found to be lesser than in smoker control and the study was statistically significant.

Table 20: Correlation of mean serum free testosterone level with pattern of ACS

ACS	Cases	Mean serum free testosterone (ng/dl)	Percentage
AWMI	24	8.67±2.16	48%
IWMI	16	8.24±1.37	32%
UA	7	8.03±1.30	14%
AWMI+IWMI	3	7.31±1.83	6%

In the present study, most patients presented with AWMI (48%) followed by IWMI (32%).
The mean serum free testosterone level in AWMI and IWMI were 8.67±2.16 ng/dl and 8.24±1.37 ng/dl respectively.
The mean serum free testosterone level was lowest (7.31±1.83 ng/dl) in patients presented with both AWMI and IWMI.

Table 21: Correlation of mean serum free testosterone with mortality in acute coronary syndrome

	No. of cases	Mean Serum free testosterone (ng/dl)	Percentage
Mortality	2	10.1±4.6	4%
Survivors	48	8.28±1.66	96%

In the present study, most of the patient (96%) survived the attack while 2 patients (4%) succumbed to the illness. The mean serum free testosterone in survivors and death were 8.28±1.66 ng/dl and 10.1±4.6 ng/dl respectively. There was no correlation found between the serum free testosterone and mortality in patients with acute coronary syndrome.

Discussion- The present study was undertaken in order to correlate the role of serum free testosterone in patients with ACS. The mean age was 53.36±10.57 yrs in the present study group. Majority of the cases were in the age groups of 55-64 yrs (30%). The present study group was comparable to that seen in George et al. [8] 2005 study (52.4 yrs).In the present study, most common presenting symptoms was chest pain (90%) followed by palpitation (56%). In the present study, 34% patients had hypertension while only 28% of controls had hypertension. The mean systolic blood pressure (SBP) in cases was 129.36±24.79 mmHg and mean diastolic blood pressure (DBP) was 82.2±15.02 mmHg. In the present study, 46% of cases and 20% of control were smokers. The mean BMI in the present study was 23.40±2.35 in cases and 20.64±1.52 in controls. In the present study, the mean total cholesterol in cases was 221.4±50.10 mg/dl and in controls 190.2±34.05 mg/dl. The total cholesterol was higher in cases than controls and the difference was statistically significant. In the present study, serum free testosterone in patients with ACS was studied and compared with controls who had cardiovascular risk factors but no evidence of CAD. Of the 50 cases, 40 patients had serum free testosterone < 9 ng/dl which was taken as significant based on other studies done. Among 25 controls, only 1 had serum free testosterone < 9 ng/dl and 24 had serum free testosterone > 9 ng/dl.On applying chi-square test, the odd's ratio (95% CI) is 96 and risk ratio (95% CI) is 3.32 and p value is highly significant (p<0.001). The means that serum free testosterone was significantly decreased in patients who had ACS. The mean serum free testosterone in cases was 8.36±1.80 ng/dl and control was 12.94±3.06 ng/dl. The difference was statistically significant (p value < 0.001).GB Phillips *et al.* [9] 1994 in their study fond out that free testosterone correlated negatively with the degree of coronary artery disease. GMC Rosano *et al.* [6] 2007 study found out that their patients had significantly lower levels of testosterone than controls (9.8±6.5 mmol/l, p<0.01). KM English *et al.* 2000 [3] in their study concluded that men with coronary artery disease had significantly lower level of free testosterone 47.95±13.77 pmol (p value = 0.027). In the present study, we found that the mean serum free testosterone in patients with 0-2 cardiovascular risk factors was 8.02±1.23 ng/dl. Mean serum free testosterone level in patients with $\geq$ 3 cardiovascular risk factors was 8.58±2.08 ng/dl. The difference between these 2 subgroups of ACS patients was not statistically significant which means that the level of serum free testosterone level decreases irrespective of the number of cardiovascular risk factors. The inverse relationship between testosterone levels and coronary atherosclerosis found in the present study suggests a possible protective role of the hormone on the progression of atherosclerosis. The mean serum free testosterone level in hypertensive cases was 8.38±1.56 ng/dl and hypertensive control was 11.5±1.85. The difference was statistically significant.GB Phillips *et al.* [9] 1994 study demonstrated that testosterone is lower in populations of men with hypertension than in normal men. The mean serum free testosterone in smokers with ACS was 8.72±1.96 ng/dl and serum free testosterone of smokers in control group was 11.1±2.21 ng/dl. The difference was statistically significant. In the present study, most patients had AWMI (48%) and IWMI (32%). Mean serum free testosterone was highest in AWMI (8.67±2.16 ng/dl) and lowest in AWMI+IWMI (7.31±1.83 ng/dl). In the present study, most of the patients (96%) survived the illness while 2 patients died due to ACS. KT Khaw *et al.* [10] 2007 study concluded that testosterone concentrations are inversely related to mortality due to cardiovascular disease.

Conclusion-The serum free testosterone was found to be lower in patients with acute coronary syndrome as compared to controls. The difference between cases and controls was statistically significant. The serum free testosterone level was lowest in patients who presented with AWMI+IWMI as compared with other patterns of ACS. There was no correlation found between serum free testosterone level and mortality and morbidity in patients with acute coronary syndrome. The serum free testosterone level was found to be lower in cases with traditional risk factors like smoking, hypertension, dyslipidemia and BMI.

Acknowledgement-None

Conflicts of Authors –None

Source of Fund – None

Ethical Approval- Yes.

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