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A Study of Serum Testosterone Levels in Young Patients with Coronary Artery Disease in Western Rajasthan

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Abstract: ***Background: There are few data regarding acute coronary syndrome (ACS) in young adults. ACS in young adults may have some characteristics that are different from those in older populations. Objective: To study the epidemiologic profile and serum testosterone levels of patients suffering from Acute Coronary Syndrome in Western Rajasthan. Methods: It was a cross sectional study conducted at Dept of medicine, MDM Hospital, Jodhpur. A Total of 64 patients were evaluated having age less than 40yrs and presenting with ACS. Patients above 40yrs and with chronic diseases were excluded. Results: Total 64 pts were evaluated. All were males. Of them 50 were having ACS and 14 had Non Cardiac complaints. Out of 50 ACS pts 38% each were in the age group of 31-35 and 36-40 yrs and 8% pts were in the age group of 21-25 yrs. Out of 50 ACS 25% pts had AWMI and 18.8% had IWMI and 18% had NSTEMI. Out of 50 ACS pts 76% had Low S.Testosterone and 24% had normal S.Testosterone level. Conclusions: 76% cases had low serum Testosterone level at the time of ACS and 24% had normal testosterone level. 64.3% controls had normal testosterone level and 35.7% controls had low testosterone level. The effect of low testosterone on ACS is statistically significant. The maximum number of patients in this study who had Acute coronary Syndrome were in the age group between 31-40 years. 25% of study population had Anterior wall MI. Young patients are more likely to have ST elevated MI.***

Keyword: ACS, S. Testosterone, AWMI, IWMI, NSTEMI

1. Introduction

Atherosclerotic coronary artery disease (CAD) is a leading cause of mortality and morbidity in the western world. It is a chronic progressive condition, and treatment is required indefinitely. Men are more than twice as likely as women to develop CAD. In India, CAD manifests almost a decade earlier than in Western countries.

As men age, their testosterone levels decline and fat mass increases. Serum testosterone levels are correlated inversely with fat mass, particularly visceral fat area. Testosterone replacement in young and older hypogonadal men is associated with a reduction in overall fat mass and inhibition of uptake of labelled triglycerides and enhanced lipid mobilization in visceral fat .The induction of androgen deficiency in young men is associated with a decrease in lipid oxidation rates and an increase in total fat mass. Marin[(1)]et al. have reported that testosterone supplementation of middle-aged men with truncal obesity and low-normal testosterone levels is associated with a reduction in visceral fat volume, serum glucose concentration, blood pressure, and an improvement in insulin sensitivity, suggesting that testosterone is an important regulator of regional fat metabolism. The knowledge that the incidence of cardiovascular disease in women rise as estrogen level fall after menopause has fuelled interest in its potential cardioprotective effects[(2)]. What is less well appreciated is the testosterone level also decline with advancing age, not just in men but in women too[(3-6)]. This suggests that low testosterone level may contribute to the pathogenesis of cardiovascular disease

There is a widespread perception that the gender differences in the prevalence of coronary artery disease (CAD) are due to higher testosterone concentrations in men and that testosterone supplementation in men would adversely affect the plasma lipoprotein profile, therefore increasing the risk of atherosclerotic heart disease. The case reports of cardiovascular accidents among athletes who had abused androgenic steroids have strengthened this notion; however, there are no data substantiating a cause-and-effect relationship between androgens and cardiovascular disease. Little attention has been paid to the role of testosterone in the pathogenesis of CAD. Males do not have a menopause equivalent, but sex hormones do fall with advancing age. The more elderly population, in which the prevalence of CAD is highest, has relatively low testosterone levels. A low level of free testosterone has been shown to be related to development of premature CAD, defined as the development of CAD before the age of 40 years. However, current evidence is still inconclusive and the role of testosterone in premature CAD is yet to be understood, highlighting the serious need of research on ageing process. As testosterone supplementation in the elderly and middle aged males with hypogonadism conferred a better cardiovascular state and even deceleration of atherosclerosis process, it is beneficial to clarify this relationship in this age group. Furthermore testosterone replacement therapy which is used to treat testosterone deficiency secondary to ageing may have beneficial effect in the setting of heart failure and ischaemic heart disease [(7-9)].

2. Material and Method

The study was conducted at Department of Medicine, MDM Hospital, Dr. S. N. Medical College Jodhpur. A Cross sectional study was conducted to study the serum Testosterone levels in young patients with acute coronary syndome. Total 64 patients were evaluated.

Inclusion Criteria
Patients who have suffered from acute coronary syndrome [ACS; ST-segment elevation myocardial infarction (STEMI), non–ST-segment elevation myocardial infarction (NSTEMI) or unstable angina (UA)] and Age < 40 years.

The diagnosis of myocardial infarction was based on the European Society of Cardiology criteria 2012 for Universal definition of Myocardial Infarction.

Exclusion Criteria:
1) Patients age > 40years.
2) Previous known case of diabetes, hypertension, ischemic heart disease, chronic kidney disease, hepatic dysfunction, prior history of peripheral vascular disease, chronic obstructive pulmonary diseases, HIV etc
3) Any past history of malignancy, sarcoidosis, tuberculosis, any chronic inflammatory diseases

An informed consent was taken from the patients regarding participation in the study. For the selected candidates a detailed history regarding the risk factors for coronary artery disease, quantitative assessment of serum testosterone levels by chemiluminescence assay will be done.

3. Methodology

After written informed consent from subjects comprehensive clinic-epidemiological data were collected. Diabetes, hypertension, hypercholesterolemia will be defined as ADA guidelines, JNC 8, and Adult Treatment Panel 4 respectively. Acute coronary Syndrome (ACS) was defined by European Society of Cardiology 2012. Relevant laboratory investigations were done. The data collected was analysed for statistical association between the incidence of ACS and serum testosterone levels.

4. Observations and Results

1) In the present study out of 64 patients 50 had acute coronary events. Maximum ACS cases were in the age group of 31-35 and 36-40 i.e. 38% in each group. 8% cases were in the age group of 21-25 which is too early for ACS to begin with causing significant morbidity in early years of productive life.
2) In the present study 25% of cases had Anterior wall MI, 18.8 % cases had Inferior wall MI and equally 18.8 % cases had NSTEMI. Lateral wall and Posterior wall MI was present in 3.1 % cases. Anterolateral MI was present in 6.3% cases and Anteroseptal MI was present in 3.1% cases. The crux is that 78.1 % patients in present study had ACS and 21.9% patients had no Acute coronary events.
3) In the present study out 50 cases 76% had low serum Testosterone level at the time of ACS and 24% had normal testosterone level. 64.3% controls had normal testosterone level and 35.7% controls had low testosterone level at the time of ACS. The effect of testosterone level on ACS was statistically significant (P=0.005).
4) In the present study mean testosterone level in cases was 166.68 ng/ml with standard deviation being 62.91. Mean Testosterone level in controls was 248.79 ng/ml with standard deviation being 63.89. The effect of mean Testosterone level on ACS is statistically significant (p<0.001).

[1] Age Wise Distribution of ACS

Age in years	Cases	Controls	Total
20-25	4	2	6
	8.0%	14.3%	9.4%
26-30	8	5	13
	16.0%	35.7%	20.3%
31-35	19	3	22
	38.0%	21.4%	34.4%
36-40	19	4	23
	38.0%	28.6%	35.9%
Total	50	14	64
	100.0%	100.0%	100.0%

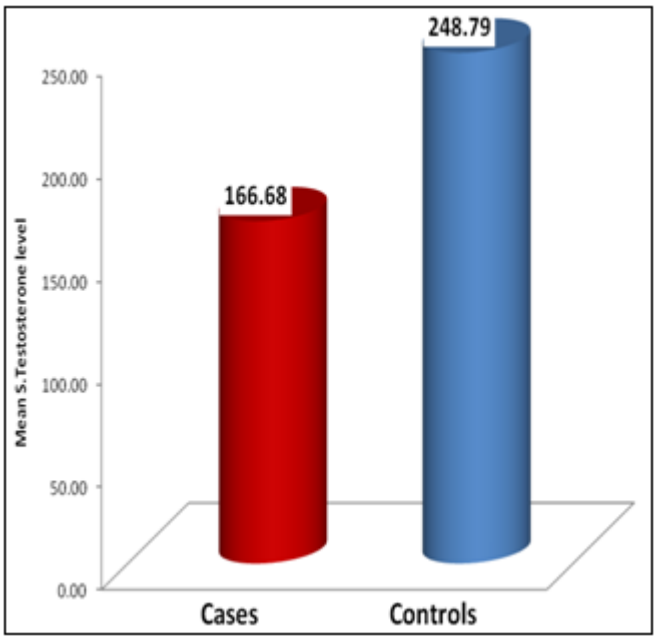
[2] Distribution of Type of ACS

Acute Coronary Syndrome	*No of cases*	*Percent*
Anterior wall MI	16	25.0
Anterolateral MI	4	6.3
Anteroseptal MI	2	3.1
Inferior wall MI	12	18.8
Lateral wall MI	2	3.1
Posterior wall MI	2	3.1
NSTEMI	12	18.8
NAD	14	21.9
Total	64	100.0

[3].Distribution of Testosterone Level in Cases and Controls

Participants	Testosterone level		Total
	Normal	Low	
Cases	12	38	50
	24.0%	76.0%	100.0%
Controls	9	5	14
	64.3%	35.7%	100.0%
Total	21	43	64
	32.8%	67.2%	100.0%

[4].Bar chart showing distribution of serum Testosterone level in cases and controls



5. Discussion

In the study population, all 64 patients were males aged less than or equal to 40 years. Out of 64 subjects, 50 subjects had acute coronary event and 14 had minor illness unrelated to cardiovascular system. Maximum ACS cases were in the age group of 31-35 and 36-40 i.e. 38% in each group. 60.3% of study population had ST elevated MI and 18.8 % of study population had NSTEMI. 25% of study population had Anterior wall MI. In[(10)] a similar study conducted at U.N. Mehta Cardiology centre Ahmedabad between January 2008 to December 2012, 109 young patients (≤ 40 years) with ACS with age ranged from 30 to 40 years.

In a study done at Bangkok general hospital[(11)] from august 2002 to October 2005 Younger patients were more likely to have an STEMI. The incidence of STEMI in patients< 45 years, 45-54 years and > 54 years old were 67.3%, 54.9% and 36.0% respectively. Among young patients,rates of STEMI, NSTEMI and UA were 67.3%, 19.3% and 13.4% respectively. These results confirm our results that young patients are more likely to have ST elevated MI.

In the present study out of 76% cases had low serum Testosterone level at the time of ACS and 24% had normal testosterone level. 64.3% controls had normal testosterone level and 35.7% controls had low testosterone level at the time of ACS. The effect of testosterone level on ACS was statistically significant (P=0.005).

In a similar study conducted by CM Wickramatilake[(12)] ,MR Mohideen[(12)] titled Premature coronary artery disease and testosterone in Sri Lankan men Total testosterone levels of cases were significantly lower than those of controls (11.1 ± 3.2 nmol/L vs. 27.1 ± 4.3 nmol/L, p = 0.001), which remained significant, following adjustment for the clinical covariates (age, BMI, smoking, diabetes mellitus). Also in a study conducted at Medicana International Ankara Hospital, Turkey[(13)] by Ahmet Baris Durukan, The association between serum testosterone levels and coronary artery disease in middle-aged men showed that the mean level of serum testosterone was 3.97 ±1.46 in the non-CAD group, whereas in patients with CAD it was 3.37 ±1.34. There was a statistically significant difference between the two groups (p = 0.043), and the serum Testosterone levels were lower in the CAD group . These results are similar to our study that young CAD patients have low testosterone level confirming that low testosterone is a risk factor for Acute coronary events.. Akishita [(14)] et al, in their respective studies concluded that low androgen level are risk factor for acute coronary syndrome.

6. Conclusion

76% cases had low serum Testosterone level at the time of ACS and 24%had normal testosterone level. 64.3% controls had normal testosterone level and 35.7% controls had low testosterone level. The effect of low testosterone on ACS is statistically significant. The maximum number of patients in this study who had Acute coronary Syndrome were in the age group between 31-40 years.25% of study population had Anterior wall MI.Young patients are more likely to have ST elevated MI.

7. Study Limitations

Our study was cross-sectional, observational design which precludes definitive conclusions regarding the causal relationship between Testosterone level and Acute coronary syndrome. It should be also highlighted that the magnitude of contribution of low serum testosterone status to increased ACS events might be variable and modest. A limitation of this study was that information on important determinants of serum testosterone concentration, were not collected. In addition, we did not explore the putative mediating effect of alcohol consumption. Moderate, regular alcohol consumption by apparently healthy people is associated with lower cardiovascular morbidity and mortality than in abstainers. Finally, in this study we did not explore the putative mediating effect of inflammatory status. Despite the aforementioned limitations, our study has several unique strengths. First, this study measured the increased incidence of acute coronary syndrome in young Indian population (< 40 years) opening opportunity for evaluating novel risk factors for ACS in young individuals. Secondly showing low testosterone is associated with increased ACS.

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