

## ORIGINAL RESEARCH

## Serum Testosterone Levels in Heart Failure

Rakesh Kumar<sup>1</sup>, P. Nigam<sup>2</sup>

## ABSTRACT

**Introduction:** Chronic heart failure (CHF) is one of the serious health care problem which is linked with increased hospitalization and poor prognosis as well as poor quality of life of patients. Objective of this study is to compare serum testosterone levels in heart failure patients based on different age group and body weight.

**Material and Methods:** A case control study was done on 80 patients of Out Patients and Emergency Department of Nehru Chikitsalaya of B.R.D Medical College, Gorakhpur from December 2010 to August 2012. A detailed clinical history with special focus on symptoms of low testosterone level and physical examination was performed. Patients were analysed on the basis of hypertension, BP  $\geq 130/85$  mm of Hg, high fasting blood sugar ( $\geq 100$  mg/dL), HDL level  $< 40$  and mean testosterone levels (MTL).

**Results:** A total 80 subjects (40 cases of CHF and 40 age matched subject grouped as control) were studied. MTL among control group was  $444 \pm 52.4$  and in heart failure patients was  $162 \pm 48.9$  with t-score of 24. Relationship between cases grouped as per NYHA for MTL showed that 10 patients in NYHA II had MTL of  $428 \pm 28.2$  with t value of 12.9, 12 patients in NYHA III had MTL of  $165 \pm 20.2$  with t value of 21 and 18 patients in NYHA IV had MTL of  $154 \pm 16.8$  with t value of 8.3.

**Conclusion:** Heart failure is more prevalent in elderly population and most hypertensive among heart failure patients were having uncontrolled hypertension. Testosterone levels significantly decreased among patients with heart failure. In addition inverse relation between age of patients and testosterone levels were also found.

**Keywords:** Heart failure, Hypertension, Testosterone, Congestive heart failure

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<sup>1</sup>Professor of Medicine, <sup>2</sup>Ret Professor and Head, Department of Medicine, B.R.D Medical College, Gorakhpur, Uttar Pradesh, India

**Corresponding author:** Dr Rakeshkumar Shahi, I-83 Rapti Nagar Phase-IV Near BPCI, Gorakhpur, Uttar Pradesh, India

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## INTRODUCTION

Testosterone in men reaches maximum levels at approximately age 30, after which levels steadily decline at a rate of 1% to 2% annually.<sup>1,2</sup> Controversy exists regarding whether the decline in testosterone with increasing age is a normal physiologic process or whether it is a result of chronic comorbidities and lifestyle choices.<sup>2</sup> Testosterone levels are lower in patients with chronic illnesses such as end-stage renal disease, human immunodeficiency virus, chronic obstructive pulmonary disease, type 2 diabetes mellitus (T2DM), obesity, and several genetic conditions such as Klinefelter syndrome.<sup>1-6</sup>

On the other hand Hypogonadism is not considered a traditional risk factor for coronary artery disease (CAD). However, it is widely accepted that men experience a gradual decline in their testosterone levels with increasing age,<sup>1-6</sup> and male sex has long been considered a strong risk factor for CAD. Together, these 2 facts have prompted numerous investigators to search for a possible relationship between endogenous testosterone levels and CAD. The volume of evidence that links low testosterone levels with CAD has been steadily growing during the past decade. A growing body of evidence suggests that men with lower levels of endogenous testosterone are more prone to develop CAD during their lifetimes.<sup>7-12</sup> However, this is in direct contrast to findings from earlier studies that failed to find any significant association between baseline testosterone levels and the development of CAD.<sup>12-19</sup>

In addition, a key pathologic feature of CHF is a metabolic shift toward catabolism, which results from the activation of neuroendocrine and inflammatory pathways.<sup>13-14</sup> This imbalance, in turn, causes progressively worsening exercise intolerance, as well as cardiac cachexia.<sup>13-14</sup> Emerging evidence indicates that there might be a significant association between testosterone deficiency, CHF, and exercise capacity. Jankowska et al demonstrated a statistically significant prevalence of testosterone deficiency among men with CHF who were either  $\leq 45$  or  $\geq 66$  years old.<sup>15</sup> Levels of estimated free testosterone were also shown to be significantly reduced among CHF patients. Association between circulating testosterone levels and aerobic exercise capacity in CHF patients is most likely independent of heart failure severity, beta-blocker use, and chronotropic response to exercise.<sup>15</sup>

Emerging evidence indicates that CHF is more than just a syndrome affecting a failing heart. It is becoming evident that the pathophysiology of CHF involves other pathways as well, including the skeletal muscles and the endocrine sys-

tem. Studies have shown that men with CHF suffer from reduced levels of total and free testosterone.<sup>15</sup> It has also been shown that reduced testosterone levels in men with CHF portends a poor prognosis and is associated with increased CHF mortality.<sup>16</sup> Reduced testosterone has also been shown to correlate negatively with exercise capacity in CHF patients.<sup>17</sup> Those with more severe CHF, as indicated by higher New York Heart Association class, have been shown to have lower levels of testosterone, and the decline in testosterone levels has been shown to be the only predictor of the magnitude of deterioration in exercise capacity.<sup>17</sup> Testosterone replacement therapy has been shown to significantly improve exercise capacity, without affecting LVEF.<sup>18-22</sup>

These results require further confirmation in Indian population to find out the association between variables like age, body weight and heart failure and testosterone levels. No study in Indian population has been done till now to find this association, so this study is conducted to find out the association between these factors in Indian population.

## MATERIALS AND METHODS

A case control study was done on 80 patients of OPD and emergency department of Nehru Chikitsalay of B.R.D Medical College, Gorakhpur from December 2010 to August 2012.

Patients with heart failure as per Framingham criteria for CHF which include major criteria as paroxysmal nocturnal dyspnea or orthopnea, neck-vein distention, rales, cardiomegaly, acute pulmonary edema, S3 gallop, increased venous pressure >16 cm of water, circulation time >25 sec and hepatjugular reflux; minor criteria as ankle edema, night cough, dyspnea on exertion, hepatomegaly, pleural effusion, vital capacity decreased 1/3 from maximum and tachycardia (rate of >120/min); major or minor criterion as weight loss

>4.5 kg in 5 days in response to treatment were included in the study. For establishing a definite diagnosis of CHF in present study, two major or one major and two minor criteria had to be present at the same time. Patients with known case of hypogonadism before diagnosis of heart failure, patients not willing to participate, patients having prolactinoma, acute illness or infection, taking exogenous testosterone, hyperthyroidism, age <30 years and > 70 years and all females were excluded from the study.

A detailed clinical history with special focus on symptoms of low testosterone level like depressed mood, loss of libido, sexual dysfunction, fatigue, mood swing and listlessness was recorded. In physical examination diminished sexual desire, increased spontaneous erectile dysfunction, loss of strength & muscle mass, infertility, incomplete development of secondary sexual character were noted. Laboratory investigation like complete blood count, serum creatinine, serum bilirubin total, echocardiography and total serum testosterone were also done.

Hypertension was graded as M (K/C/O hypertension on medication, G1 as Mild (Diastolic blood pressure (DBP) 90-99 mm of Hg), G2 as moderate (DBP 100-109 mm of Hg) and G3 as severe (DBP >110 mm of Hg) hypertension.

As all clinical variables are not present in all patients of heart failure, patients were analysed on the basis of hypertension, BP  $\geq$ 130/85 mm of Hg or on medication, high fasting blood sugar ( $\geq$  100 mg/dL), HDL level < 40 and mean testosterone levels.

All case (40) and control (40) patients were divided into 21-30, 31-40, 41-50, 51-60 and 61-70 age groups. The mean level of serum testosterone in each group was compared and evaluated with other factors.

## RESULTS

Class	Patient Symptoms
I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea (shortness of breath).
II	Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea (shortness of breath).
III	Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, or dyspnea.
IV	Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases.

**Table-1:** New York Heart Association (NYHA) Functional Classification heart failure according to the severity of their symptoms

Parameter		Total Patients*		Mean Testosterone Level#			
		Control	Case	Control	Case	T value	P value
Age	21-30	2 (5)	1 (2.5)	555±2	305	NA	NA
	31-40	4 (10)	2 (5)	525±19.3	318±28.2	4.3	<0.01
	41-50	12 (30)	11 (27.5)	464±43.6	170±20.2	3.2	<0.01
	51-60	18 (45)	14 (35)	455±28.3	144±16.8	3	<0.01
	61-70	4 (10)	12 (30)	379±21.3	138±18.5	3.3	<0.01

\*Data are expressed as no of patients (%), #Mean Testosterone Level in ng/dl

**Table-2:** Distribution of patient according to different age groups and means testosterone level

Symptoms	Control	Case
Gynaecomastia	11 (27.5)	0 (0)
Decreased shaving	4 (10)	0 (0)
Fatiguability, tiredness	20 (50)	0 (0)
Decreased libido	11 (27.5)	5 (9)
Depression, irritability, nervousness	21 (52.5)	0 (0)
Decreased physical stamina and muscle strength	5 (12.5)	6 (13.6)
No Symptoms	15 (37.5)	29 (72.5)
*Data are expressed as no of patients (%)		
<b>Table-3:</b> Distribution of different symptoms among study patients		

In present study a total 80 subjects (40 cases of CHF and 40 age matched subject grouped as control) were included. New York Heart Association (NYHA) Grade of Health failure distribution showed that 18 (45%) patients belong to NYHA IV, 12 (30%) to NYHA III and 10 (25%) NYHA grade II.

Out of 40 CHF patients, 10 (25%) had valvular heart disease, 15 (37.5%) had hypertension, 10 (25%) had CAD and 5 (12.5%) had cardiomyopathy.

Out of 15 hypertensive patients, 12 (30%) had severe hypertension, 2 (5%) had moderate, 1 (2.5%) patients had mild hypertension and 1 (2.5%) was controlled on medication.

Distribution of fasting blood sugar (FPG) level among CHF patients showed that 5 (20.8%) patients had FPG between 130-160 mg/dL and had mild heart failure, 7 (29.2%) had FPG between 160-190 mg/dL and had moderate health failure and 12 (50%) had FPG >190 mg/dL and had severe heart failure.

Out of 40 heart failure patients, 10 (25%) had HDL > 40, 16 (40%) patients had HDL between 40- 30, 12 (30%) had between 30-20 and 2 (5%) patients had HDL <20.

For evaluation of symptoms an arbitrary level of 200 ng/dl of testosterone was taken. Out of 40 patients, 26 (65%) had level below 200 ng/dl, among control, 2 (9%) had low level of testosterone.

MTL among control group was  $444 \pm 52.4$  and in heart failure patients was  $162 \pm 48.9$  with t score of 24.

Association of hypertension with MTL showed that 3 (20%), 7 (46.66%) and 5 (33.33%) patients had mean testosterone level of  $464 \pm 43.6$  in Control and  $183.15.7$  in Case with t-value of 8.5,  $455 \pm 28.3$  in control and  $140 \pm 29.8$  in Case with t-value of 10.8 and  $379 \pm 21$  in control and  $129 \pm 14.7$  in Case with t-value of 13.

Comparison between severity of hypertension and MTL revealed that 7 Patients were on hypertensive medications with MTL of  $318 \pm 28.2$  among cases with t-value of 25, 2 patients with DBP between 90-99 mm of Hg had MTL of  $180 \pm 20.2$  in heart failure patients with t-value of 8.3, 5 patients with DBP between 100-109 had MTL of  $148 \pm 16.8$  with t-value of 13 and 12 patients with DBP >110 mm of Hg had MTL of  $140 \pm 12.2$  among cases with t-value of 21.

Relationship of low HDL level with MTL according to age group showed that 1 patients with age between 21-30 had HDL and MTL value of  $22 \pm 2.1$  and  $170 \pm 22$  respectively, 2

patients with age between 31-40 had HDL and MTL value of  $26.6 \pm 2.4$  and  $122 \pm 17.4$  respectively with t-value of 9.4, 11 patients with age between 41-50 had HDL and MTL value of  $28.1 \pm 3.6$  and  $134 \pm 12.5$  respectively with t-value of 7.6, 14 patients with age between 51-60 had HDL and MTL value of  $24.3 \pm 3$  and  $123 \pm 15.7$  respectively with t-value of 11.5 and 12 patients with age between 61-70 had HDL and MTL value of  $19 \pm 1.9$  and  $130 \pm 29.8$  respectively with t-value of 8.7.

Comparison between different grades of hypertension with MTL showed that between G1 and G2, MTL was  $134 \pm 13.6$  and  $123 \pm 11$  respectively with t-value of 0.88, between G2 and G3 MTL was  $123 \pm 11$  and  $146 \pm 12$  respectively with t-value of 1.99 and between G1 and G3 MTL was  $134 \pm 13.6$  and  $146 \pm 12$  respectively with t-value of 0.93.

Comparison between diabetic patients and their MTL showed that 4 diabetic patients with age between 31-40 had MTL of  $142 \pm 17.4$  with t-value 21, 7 patients with age between 41-50 had MTL of  $134 \pm 12.5$  with t-value 3.2, 11 patients with age between 51-60 had MTL of  $126 \pm 15.7$  with t-value 2.5 and 2 patients with age between 61-70 had MTL of  $130 \pm 19.8$  with t-value 12.2.

The present study also showed that MTL is more decreased in cases of systolic heart failure compared to patients with relatively preserved ejection fraction. Ejection fraction was <40 in 18 (45%) cases with MTL of  $123 \pm 15.7$  and >40 in 22 (55%) cases MTL of  $134 \pm 12.5$ .

Relationship between cases grouped as per NYHA for MTL showed that 10 patients in NYHA II had MTL of  $428 \pm 28.2$  with t value of 12.9, 12 patients in NYHA III had MTL of  $165 \pm 20.2$  with t value of 21 and 18 patients in NYHA IV had MTL of  $154 \pm 16.8$  with t-value of 8.3.

## DISCUSSION

A total of 40 male patients of heart failure aged 20-70 years were studied for hypertension, diabetes, severity of heart failure, systolic and diastolic types and obesity and their testosterone levels compared with 40 control subjects of respective age groups. Majority of the patients were in 4th, 5th and 6th decades of their life. In the study majority of patients with uncontrolled hypertension land up in heart failure, it may be the result of poor compliance or due to iceberg phenomenon of a disease entity in which it remains undiagnosed.<sup>19-21</sup>

Results indicated that patient with even mildly elevated glucose levels have tendency to develop cardiovascular complications and landing in CHF. Hypertriglyceridemia is also found to be prevalent among the patients in the study.

Study reported statically significant inverse correlation between age and testosterone levels and found age related decline testosterone levels among the patients. MTL were also decreased in cases of systolic heart failure compared to the patients with relatively preserved EF and the difference is significant between the two. Similar results were found in hypertensive patients where testosterone levels were found to be low compared to control across all groups. In cases of

heart failure, progressive decline in cardiac output and cardiac index is largely associated with depression in the level of circulating testosterone and other hormones.<sup>16</sup>

## CONCLUSION

This study is conducted to find out the association between variables like age, body weight and heart failure and testosterone levels in Indian population. No study in Indian population has been done till now to find this association. Study concludes that heart failure is more prevalent in elderly population and most hypertensive among heart failure patients were having uncontrolled hypertension. Testosterone levels significantly decreased among patients with heart failure. In addition inverse relation between age of patients and testosterone levels were also found. Study concludes significant association of testosterone levels with age, body weight and heart failure among Indian population.

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