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Assessment Of Serum Testosterone Hormone Level In Patients With Acute Coronary Syndrome Less Than 50 Years Old Age Male And Its Association -With Other Risk Factors

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Abstract:

Background and objectives : Testosterone has been shown to provide a protective role in the development of cardiovascular diseases in men, the low serum level of testosterone in the middle age patients may contribute to coronary artery disease (CAD),this study was applied to check serum levels of testosterone in less than 50 age group patients with CAD and it`s relation to other risk factors.

Subjects and Methods: This cross sectional coparative study was applied over 6 months from first of April 2018 to first of October 2018 ,this study was conducted in coronary care unit of al_hussein teaching hospital and outpatient on 101 middle age males ,fifty five of them presented with ACS and the other 46 apparently normal(as healthy control) ,mean age was 43.5±5.6 years ,serum testosterone was tested for both groups in addition to data that collected from them by a performed questionnaire, a man with a total testosterone level below 300 ng/dL should be diagnosed with low testosterone.

Result: serum testosterone level was low in 37 of 55 patient group (92.5%) and 3 of 46 of control group (7.5%) with a significant p.value (0.05) , 94% of patient group presented within 40_50 years age group and73% for control group.

Low testosterone significantly associated with age >40 years()and other risk factor of CAD including obesity and dyslipidemia.

Conclusion: Serum testosterone level were found to be decreased significantly in patients with ACS and this low level significantly associated with other risk factor for ACS.

Key words: Testosterone, coronary syndrome and risk factors.

Introduction

Acute coronary syndrome (ACS): Patients with acute coronary syndrome (ACS) commonly are classified into two groups to facilitate evaluation and management, namely patients with acute myocardial infarction with ST-segment elevation (STEMI) on their presenting electrocardiogram (ECG) and those with non- ST-segment elevation acute coronary syndrome (NSTE-ACS). [1]

The 2018 joint task force of the European Society of Cardiology (ESC), American College of Cardiology Foundation (ACCF), the American Heart Association (AHA), and the World Health Federation (WHF) defined MI, whether STEMI or NSTEMI, as the presence of acute myocardial injury detected by abnormal cardiac biomarkers in the setting of evidence of acute myocardial ischemia[2].

Unstable angina and NSTEMI differ from each other based on whether the ischemia that caused symptoms is severe enough to cause sufficient myocardial damage to release detectable quantities of a marker of myocardial injury, unstable angina is considered to be present in patients with ischemic symptoms suggestive of an ACS and no elevation in troponin, with or without ECG changes indicative of ischemia (ST-segment depression or transient elevation or new T wave inversion)(3).

The diagnosis of acute coronary ischemia depends upon the characteristics of the chest pain, specific associated symptoms, abnormalities on electrocardiogram (ECG), and levels of serum markers of cardiac injury.[4]

A patient with a possible ACS should be treated rapidly. Thus, initial management steps must be undertaken before or during the time the diagnosis is being established (4).

Risk factor for coronary artery disease : Many individuals in the general population have one or more risk factors for coronary heart disease (CHD), and over 90 percent of CHD events occur in individuals with at least one risk factor (5) The five leading modifiable risk factors (hypercholesterolemia, diabetes, hypertension, obesity, and smoking) are estimated to be responsible for more than half of cardiovascular mortality [6]. On the other hand, the absence of major risk factors predicts a much lower risk of CHD [7]

Testosterone and coronary artery diseases : testosterone is the principal male sex hormone whose androgenic effects are responsible for development of male sex organs and maturing characteristics including sex drive, muscle mass, strength, and bone density(8) .

The controller of the gonadal axis is gonadotropin-releasing hormone (GnRH), which is released from the hypothalamus. GnRH acts on the anterior pituitary to stimulate release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH)[]. In men’s testes, LH stimulates testosterone synthesis by Leydig cells, and FSH stimulates spermatogenesis by Sertoli cells[9].

Only a small fraction of the total circulating testosterone is in a free form, with the vast majority bound to sex hormone-binding globulin (SHBG) or albumin. Biologically active, free testosterone binds to the androgen receptor present in the cytosol of most tissues (10).

Subject and methods:

This is case control study was performed in consecutive male patient age less than 50 years over a period of fife months from 1st of may to the 1st of november 2018.

The total number of male are101dividing in to 55 patients with ACS collected from CCU of al_hussain teaching hospital and the other 46 as control sample from out patients and health care workers in the same hospital.

All patient with ACS diagnosed by clinical examination ,ECG , and cardiac biomarker and classified as having STEMI,NON-STEMI,UA.

The following patients excluding from the study;
(1) those are older rhan 50 years age group
(2) Those with major organ failure (heart, respiratory, liver, or renal failure).
(3) Patients with cancer prostate, prostatectomy, castration or those receiving androgen therapy.
(4) Patients receiving androgens or steroids medications.
(5) Patients with endocrine disorders (except DM).
(6) Those with active infection or autoimmune diseases.

Written consent was taken from all participant and Data was collected from each patient by using a performed questionnaire which include;

1.DEMOGRAPHIC CHARACTERS; age, residence, occupation and level of education.

2.CLINICAL INFORMATIONS; chief complaint, smoking history, history of ischemia heart disease, type of acute coronary syndrome, history of alcohol, dyslipidemia, history of diabetes, history of hypertension .

Statistical Analysis:

The data obtained from this study was analyzed using the Statistical Package for Social Sciences (SPSS) software version 22.0, descriptive analysis was done using (mean ± standard deviation), (frequency) and (percentage of each value) with the $\chi 2$ and (p value less than o.o5) to be considered as significant.

Result

Table1: Distribution of the total participants according to the testosterone level

- The higher extent (92.5%) of the low level testosterone was within the case-group while the higher extent (70.5%)for the of normal level testosterone was within the control-group.
- ACS patients had significant low level of TT with p.value (0.04%)

Table 1			case-control		Total	X2 P value
			Cases	Control		
Testosterone level	Low	No.	37	3	40	0.04
		%	92.5%	7.5%	100.0%	
	Normal	No.	18	43	61	0.17
		%	29.5%	70.5%	100.0%	
Total		No.	55	46	101	
		%	54.5%	45.5%	100.0%	

Table 2: sociodemographic factor

Cases older than 40 years age had significant low level of testosterone compared with control group.

Table2 Socio-demography		Cases				Control			
		Low testosterone	Normal testosterone	Total	P vale	Low testosterone	Normal testosterone	Total	P value
Age (year)									
<40	No.	1	2	3	0.398	1	11	12	1.624
	%	33.3%	66.7%	100.0%		8.3%	91.7%	100.0%	
	No.	36	16	52		2	32	34	

>40	%	69.2%	30.8%	100.0%	0.05	5.9%	94.1%	100.0%	0.876
M.S									
Single	No.	0	1	1	2.272	0	5	5	2.449
	%	0.0%	100.0%	100.0%		0.0%	100.0%	100.0%	
married	No.	37	17	54		3	38	39	
	%	68.5%	31.5%	100.0%	0.132	7.7%	92.3%	100.0%	0.999
Total	No.	37	18	55		3	43	46	
	%	67.3%	32.7%	100.0%		6.5%	93.5%	100.0%	

Table 3: Distribution of the Testosterone Level Values according to the Participants-Anthropometry. There is siginificant association between WC,BMI and TT of p value (0.024,0.05) respectively.

Table 3			**Cases**		**Total**			**Control**		
			Low TT	**Normal TT**		**P .val**	**Low TT**	**Normal TT**	**Total**	**P.val**
WC	**<102**	**No.**	**31**	**17**	**48**	**1.405**	**1**	**36**	**37**	**3.451**
		%	**64.6%**	**35.4%**	**100.0%**		**2.7%**	**97.3%**	**100.0%**	
	>102	**No.**	**6**	**1**	**7**	**0.024**	**2**	**7**	**9**	**0.063**
		%	**85.7%**	**14.3%**	**100.0%**		**22.2%**	**77.8%**	**100.0%**	
BMI	**<30**	**No.**	**22**	**18**	**40**	**0.351**	**2**	**22**	**24**	**2.605**
		%	**51.9%**	**48.1%**	**100.0%**		**8%**	**92%**	**100.0%**	
	>30	**N**	**12**	**3**	**15**		**5**	**17**	**22**	
		%	**80%**	**20%**	**100.0%**	**0.05**	**22.0%**	**78%**	**100.0%**	**0.302**
Total		**N**	**34**	**21**	**55**		**3**	**43**	**46**	
		%	**67.3%**	**32.7%**	**100%**		**6.5%**	**93.5%**	**100%**	

Table4: Distribution of the Testosterone Level Values according to the Selected Participants-Behavioral characters. There is no statistical significance between behavioral factor (smoking , alcohol) and low level of testosterone.

			Cases				**Control**			
			Low TT	**Normal TT**	**Total**	**X^2, P.val**	**Low TT**	**Normal TT**	**Total**	**X^2, P.val**
Smoker	**Yes**	**No.**	**27**	**15**	**42**	**.720**	**1**	**21**	**22**	**0.270**
		%	**64.3%**	**35.7%**	**100.0%**	**.396**	**4.5%**	**95.5%**	**100.0%**	**0.400**
	NO	**N**	**10**	**3**	**13**		**2**	**22**	**24**	

		%	76.9%	23.1%	100.0%		8.3%	91.7%	100.0%	
alcohol	Yes	N	5	1	6	.938				…….
		%	83.3%	16.7%	100%	0.333				
	NO	N	32	17	49		3	43	46	
		%	64.6%	35.4%	100%		6.5%	93.5%	100%	
		N	37	18	55		3	43	46	
Total		%	66.7%	33.3%	100%		6.5%	93.5%	100.0%	

DISCUSSION:

The term acute coronary syndrome (ACS) is applied to patients in whom there is a suspicion or confirmation of acute myocardial ischemia or infarction. Non-ST elevation myocardial infarction (NSTEMI), unstable angina, and ST-elevation myocardial infarction (STEMI) are the three types of ACS(11)

Sex hormones and gender differences have been reported to be associated with coronary artery disease (CAD) [12]. Serum testosterone level has been shown to be decreased with advancing age in men [13]. Recent studies showed that testosterone deficiency is related to cardiovascular disease and its risk factors in men, including obesity, hypertension, dyslipidemia, diabetes and atrial fibrillation [14]. Kajinami et al. [15] found that imbalance of sex hormones exists in men with CAD.

Several studies have demonstrated that testosterone levels either fall following acute myocardial infarction, (16) or are lower in patients with a new myocardial infarction (MI) than in old MI and normal controls with normal coronary angiograms (17). Some studies found a rise in TT levels during the early
days after a MI (18).

Recently, Akishita et al. [19] indicated that a low testosterone level is an independent risk factor for cardiovascular disease events in middle-aged Japanese men with coronary risk factors.

In this study s.testoster one was significantly low in patient with acute coronary syndrome (92.5%) as compared to control group(7.5%) with significant p value(0.04) and agree with the result of recent studies that mentioned above and agree with another epidemiological and observational syudies that show the low testosterone was associated with CV disease risk [20],In addition a recent study of alkamel et al. [21] described an association between low serum T levels and premature coronary artery disease in men 45 years of age and younger.

In our study the mean age of population was 43.5±5.6 with a 94.5% of case group were more than 40 years old which was in agreement with Recent data from the Massachusetts Male Aging Study (MMAS) that revealed an increasing incidence of hypogonadism within the aging US population. The Massachusetts Male Aging Study estimates indicate that ≈2.4 million men aged 40 to 69 suffer from hypogonadism in the United States (22), Testosterone in men reaches maximum levels at approximately age 30, after which levels steadily decline at a rate of 1% to 2% annually (23), 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.

It is unknown whether low testosterone in patients who are ill is the cause of their illness or whether it is caused by their disease. The exact mechanism of action that leads to lower testosterone levels with age has not been discovered, New evidence from rat models suggests that the synthesis of testosterone by testicular Leydig cells in response to luteinizing hormone may decrease with age. Reactive oxygen species (ROS), which are generated by the mitochondria of Leydig cells, are a normal byproduct of testosterone synthesis. The accumulation of ROS over time may cause damage to the Leydig cell DNA and thereby render it incapable of producing testosterone (24).

REFERENCES:

1. Authors/Task Force Members, Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, Caso P, Dudek D, Gielen S, Huber K. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). European heart journal. 2011 Aug 26;32(23):2999-3054.
2. .Thygesen K, Alpert JS, Jaffe AS, et al. Fourth Universal Definition of Myocardial Infarction (2018). J Am Coll Cardiol 2018; 72:2231
3. Authors/Task Force Members, Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, Caso P, Dudek D, Gielen S, Huber K. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation2011 Aug 26;32(23):2999-3054.;
4. Authors/Task Force Members, Hamm, C.W., Bassand, J.P., Agewall, S., Bax, J., Boersma, E., Bueno, H., Caso, P., Dudek, D., Gielen, S. and Huber, K., 2011. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). European heart journal, 32(23), pp.2999-3054.
5. Kudenchuk PJ, Maynard C, Cobb LA, et al. Utility of the prehospital electrocardiogram in diagnosing acute coronary syndromes: the Myocardial Infarction Triage and Intervention (MITI) Project. J Am Coll Cardiol 1998; 32:17.
6. Stamler J, Stamler R, Neaton JD, et al. Low risk-factor profile and long-term cardiovascular and non cardio vascular mortality and life expectancy: findings for 5 large cohorts of young adult and middle-aged men and women. JAMA 1999; 282:2012.
7. Patel SA, Winkel M, Ali MK, et al. Cardiovascular mortality associated with 5 leading risk factors: national and state preventable fractions estimated from survey data. Ann Intern Med 2015; 163:245.

8. Zhao SP & Li XP. The association of plasma testosterone level with coronary artery disease in Chinese men. International Journal of Cardiology 1988; 63: 161–164.
9. Amory JK, Bremner W. Endocrine regulation of testicular function in men: implications for contraceptive development. Molecular and cellular endocrinology. 2002 Jan 25;186(2):205-9.
10. Mooradian AD, Morley JE, Korenman SG. Biological actions of androgens. Endocrine reviews. 1987 Feb 1;8(1):1-28.
11. Ohlsson C, Barrett-Connor E, Bhasin S, Orwoll E, Labrie F, Karlsson MK, Ljunggren Ö, Vandenput L, Mellström D, Tivesten Å. High serum testosterone is associated with reduced risk of cardiovascular events in elderly men: the MrOS (Osteoporotic Fractures in Men) study in Sweden. Journal of the American College of Cardiology. 2011 Oct 11;58(16):1674-81.
12. 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. European journal of internal medicine. 2011 Dec 1;22(6):e133-6.
13. 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 journal of andrology. 2012 Nov;14(6):875.
14. Alkamel A, Shafiee A, Jalali A, Boroumand M, Nozari Y. The association between premature coronary artery disease and level of testosterone in young adult males. Archives of Iranian Medicine (AIM). 2014 Aug 1;17(8).
15. Farias JM, Tinetti M, Khoury M, Umpierrez GE. Low testosterone concentration and atherosclerotic disease markers in male patients with type 2 diabetes. The Journal of Clinical Endocrinology & Metabolism. 2014 Dec 1;99(12):4698-703.
16. . Lee WC, Kim MT, Ko KT, Lee WK, Kim SY, Kim HY, Yang DY. Relationship between serum testosterone and cardiovascular disease risk determined using the Framingham Risk Score in male patients with sexual dysfunction. The world journal of men's health. 2014 Dec 1;32(3):139-44.
17. Simons M, Alpert JS. Acute coronary syndrome: Terminology and classification.
18. Jiangtao L, Dongchen Z, Shudong X, Yunpeng S, Lihong W, Liangrong Z, Jianhua Z. Reduced testosterone levels in males with lone atrial fibrillation. Clinical Cardiology: An International Indexed and Peer-Reviewed Journal for Advances in the Treatment of Cardiovascular Disease. 2009 Jan;32(1):43-6.
19. Hu X, Zhang K, Jiang H. Is testosterone or estrogen more important for male patients with coronary artery disease?. European journal of internal medicine. 2012 Jun 1;23(4):e114-5.
20. Geisthövel W, Perschke B, Klein H. Plasma testosterone, free testosterone fraction LH and FSH in males during the early stage of acute myocardial infarction (author's transl). Zeitschrift fur Kardiologie. 1979 Nov;68(11):776-83.
21. Wickramatilake CM, Mohideen MR, Pathirana C. Fluctuations of testosterone in acute coronary syndrome. Sri Lanka Journal of Diabetes Endocrinology and Metabolism. 2013 May 7;3(1).

22. 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 May 1;210(1):232-6.
23. Araujo AB, Dixon JM, Suarez EA, Murad MH, Guey LT, Wittert GA. Endogenous testosterone and mortality in men: a systematic review and meta-analysis. The Journal of Clinical Endocrinology & Metabolism. 2011 Oct 1;96(10):3007-19.
24. Zmuda JM, Cauley JA, Kriska A, Glynn NW, Gutai JP, Kuller LH. Longitudinal relation between endogenous testosterone and cardiovascular disease risk factors in middle-aged men: a 13-year follow-up of former multiple risk factor intervention trial participants. American journal of epidemiology. 1997 Oct 15;146(8):609-17.