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Research Article

PILOT STUDY TO FIND OUT THE ASSOCIATION OF TOTAL TESTOSTERONE LEVELS WITH METABOLIC SYNDROME

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Abstract

BACKGROUND: Metabolic syndrome (MS) is a constellation of insulin resistance, hypertension, dyslipidemia and visceral obesity. The alarming increase of MS among Indian population and its close association with CAD (Coronary Artery Disease) allure scientist to do more research in this field. Meanwhile recent scientific papers show that there is a decrease in the testosterone levels among men in India. Hence this pilot study was designed to find out testosterone levels in metabolic syndrome patients. MATERIALS AND METHODS: It was a case control study done among the people who attended Master Health Check up programme in Chettinad Hospital and Research Institute(CHRI). The study group was divided into two based on the WHO classification as MS subjects and control subjects. RESULTS: The discrete variables were compared using the chi square test. Almost 80% of the subjects were found to be diabetic. The continuous variables like HDL, TGL. BMI and total testosterone levels were measured using the Independent T test and HDL, BMI and total testosterone levels showed a significant'' p'' value. CONCLUSION: This study showed a strong inverse association between metabolic syndrome and testosterone levels. Hence we can consider to include it under the armamentorium for assessing the risk of vascular complications in metabolic syndrome after the study has been proven in a large population.
KEY WORDS: Metabolic syndrome; Testosterone; CAD.

INTRODUCTION

India is disrobed by westernisation. Changes in lifestyle made Indians more prone for non communicable diseases. Ethnicity and epigenetics too play a role here. The prevalence of MS is increasing at an alarming rate in South India due to the above mentioned reasons and according to WHO criteria the prevalence was found to be about 46.4% [1,2].MS is considered to be a major threat for public health in the 21st century because it is one of the major risk factor for CAD.

The earliest sign of MS is obesity especially visceral obesity the main factor leading to the complications of MS. Obesity is the abnormal accumulation of adipose tissue in the body. It results in the release of cytokines, adipokines, free fatty acids and estrogens and the secretion of pro inflammatory markers like IL- 6, IL- 1β, plasminogen activator inhibitor - 1,TNFα,angiotensinogen and vascular endothelial growth factor(VEGF)which leads to inflammation, the basic pathophysiologial reason to develop atherosclerosis , insulin resistance and dyslipidemia.

Recent studies are showing a decrease in the testosterone levels among Indian men. The prevalence of low testosterone levels in an urban population of South India was found to be 26.1%[4].Low testosterone is once again the life threatening condition since it again increases the risk for CAD[5,6].

Due to rapid increase in MS and testosterone deficiency, and their association with CAD, we thought of designing a project to find out the link between the two among south Indian men who are genetically vulnerable for the disease.

MATERIALS:

Study was conducted during the time period of November 2013 to June 2014 on 40 male subjects who attended the MHC programme at CHRI. These subjects were divided into two groups as metabolic syndrome and control based on the WHO criteria. Approval was got from the Chettinad ethical committee. After taking consent, anthropometric measurements were taken and 5ml of blood was drawn from each patient using vacutainers and the tests were done on the same day. Total testosterone , High density lipoprotein(HDL),low density lipoprotein(LDL), Triglycerides(TGL),Fasting plasma glucose(FPG) were measured in the samples. Men with major organ failure (heart kidney, liver), h/o hypogonadism, with h/o castration, prostatectomy, and those with active infection and autoimmune diseases were excluded from the study.

METHODS:

Patient's height was measured in centimetres with shoes off and weights was measured in kilograms in indoor clothing .Body mass index (BMI) was calculated using the formula BMI=weight (kg) / height² (m). Fasting plasma glucose was estimated using the Hexokinase method in Dade Behring with a sensitivity of 1mgdl and CV of 0.9%. HDL was estimated using auto analyser (Siemens Dimension) by PEG methods with Interassay CV's of 1% and sensitivity of 3.4ng/dl. TGL was estimated using the enzymatic method in Seimens
Dimension with a sensitivity of 0 and CV of 0.8mgdl respectively. Testosterone is estimated using Beckman Coulter auto analyser by competitive binding immune enzymatic assay. The sensitivity of the assay was 0.1ng/ml. Inter assay CV being 1%

The subjects were classified as metabolic syndrome with the help of the WHO criteria. This criteria is based on five basic conditions such as fasting plasma glucose, HDL, TGL, BMI, and blood pressure. Metabolic syndrome subjects have to satisfy 3 among 5 criteria: FPG>110MG/DL,HDL<40MG/DL,TGL.150MG/DL, BLOOD PRESSURE >120/80mmHg.For BMI we followed ICMR guidelines released in 2012. According to ICMR the Asians with BMI >23 are coming under overweight group and >25 are obesity.

RESULTS :The results were analysed using the SPSS version 21. The data was represented as mean and standard deviation .Continuous variables such as HDL, TGL, BMI and total testosterone among the two groups were compared using the Independent sample T test.BMI was found to be higher among the subjects with MS than among controls and HDL levels were found to be lower among the subjects with MS than among controls. Total testosterone

levels were found to be lower among the subjects with MS than among controls. Discrete variables like diabetes mellitus was compared using the chi square test. Among the subjects with MS 80% were found to be diabetic.

TABLE 1: Showing the mean of all the variables among the MS subjects and controls

	Mean	SD	Mean	SD	t-Value	P value
	Group				Independent Samples t-test	
HDL	42.7	9.73	34.20	4.48	4.104	.000
TGL	184.00	50.69	166.00	75.03	1.014	.316
BMI	28.28	2.78	26	2.13	2.945	.05
TESTOSTERONE	5.16	1.35	3.56	1.30	4.154	.000

Figure2: Shows the mean value of testosterone among the MS subjects and controls. The mean levels of testosterone among the MS subjects is lower than controls.

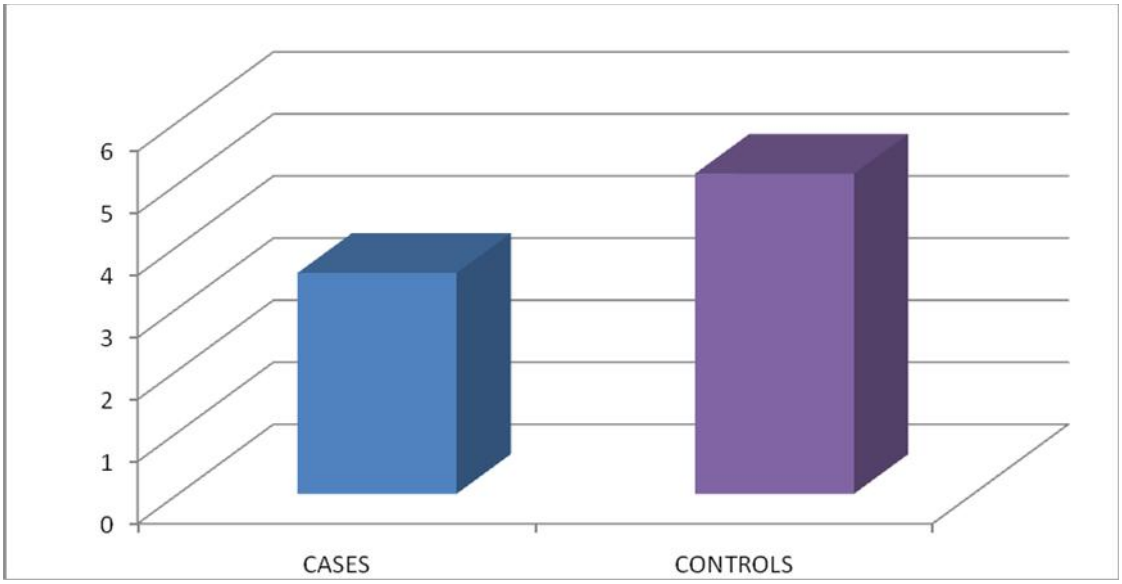

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FIGURE 2: Showing the proportion of diabetics among the MS sub

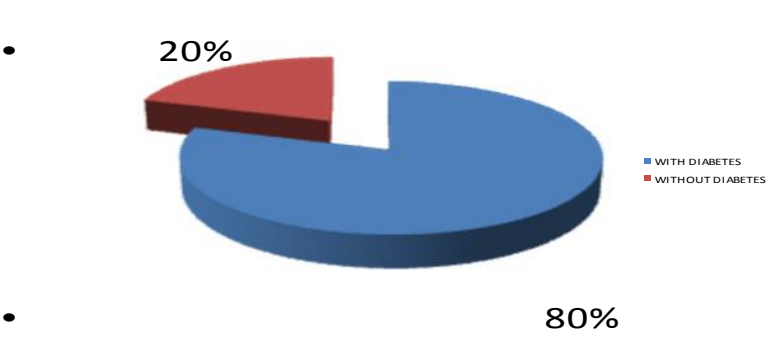

TABLE 2 : Showing the Pearson's correlation between the different variables in the MS subjects.

		HDLmg	TGLmg	BMI	T.S T.Sng	SBP	DBP
HDLmg	Pearson Correlation	1	-.204	-.175	.039	-.048	.117
	Sig. (2-tailed)		.208	.280	.810	.771	.471
TGLmg	Pearson Correlation	-.204	1	.292	-.034	-.037	.046
	Sig. (2-tailed)	.208		.067	.835	.822	.778
BMI	Pearson Correlation	-.175	.292	1	-.143	-.082	-.173
	Sig. (2-tailed)	.280	.067		.380	.617	.285
T.S T.Sng	Pearson Correlation	.039	-.034	-.143	1	-.153	-.160
	Sig. (2-tailed)	.810	.835	.380		.346	.323
SBP	Pearson Correlation	-.048	-.037	-.082	-.153	1	.744**
	Sig. (2-tailed)	.771	.822	.617	.346		.000
DBP	Pearson Correlation	.117	.046	-.173	-.160	.744**	1
	Sig. (2-tailed)	.471	.778	.285	.323	.000	

**. Correlation is significant at the 0.01 level (2-tailed).

DISCUSSION:

We have included 80 subjects in this study. This study group was divided into two using the WHO criteria as patients with MS and without MS. The criteria for defining obesity is based on ethnicity and it differs from one region to another. Hence we have taken the reference range of BMI released by ICMR dated 2012 based on Indian population. According to this criteria, in our study 22 men in the MS group were found to be obese. Rest were all within normal limits. [6] According to WHO 3/5 criteria is enough to define MS. So the rest may satisfy other criteria like hypertension, dyslipidemia and diabetes. In this study BMI is found to be highly significant.(''p'' value<0.05). Recently instead of BMI waist circumference is taken as the criteria for defining visceral obesity which unfortunately lagging in our study.

Among the lipid profile, HDL is found to be lower among subjects with metabolic syndrome than among the controls(Table 1) This has been proved by various studies for example the one done by Gerd Assmann, MD; Antonio M. Gotto Jr, MD, DPhilon showing that low HDL levels is associated with greater complications of MS[7].

Triglyceride values were found to be higher among the controls may be because of the greater indulgence for rice intake by this part of the country [8], and the smaller sample size of the study.

Among the cases about 80% of the persons were diabetics (fig 2). This has been proven by studies such as the one done in Taiwan by Chung-Hua Hsu that insulin resistance is strongly associated with MS [9].

BMI among subjects with MS showed a negative correlation with testosterone levels but not statistically significant. Studies done by Ballester J, Muñoz MC, Domínguez J et al supports this study(10)(table2). Visceral fat deposits have higher aromatase activity. They convert the testosterone present in our body to oestradiol [11,12).Obesity is found to increase the secretion of inflammatory cytokines which inhibit the pituitary gonadotrophins leading to decreased synthesis of testosterone. In turn some studies have also proved that administration of testosterone to patients will reduce their fat mass (13).

A cohort study done on a population of Uppasala showed that obesity as such can also lead to the development of complications of metabolic syndrome [14]. This shows that obesity alone can also be a causative factor for low testosterone.

The Massachussetes Male aging Study has demonstrated that low testosterone levels in a non obese population people predicts the future development of metabolic syndrome[15].So it remains to be proved whether low testosterone leads to obesity or obesity inturn leads to the development of metabolic syndrome.

HDL levels were found to have a positive correlation with testosterone even though not statistically significant. This is in par with the TELECOM study done by Halina grosman, Monica Rosales[16] which shows that as the levels of testosterone decreases, HDL levels also decreases.Studies done by Corona G, Monami M, Rastrelli G, et al also shows that increased incidence of diabetes mellitus is associated with low testosterone levels [17] .In diabetes, leydig cell function particularly steroidogenesis may be impaired by the changes in the production of hormones and cytokines leading to low testosterone levels. Other modes of reduction of testosterone in diabetes include increased leptin levels in diabetes causing Leydig cell dysfunction, increased TNF levels in diabetes inhibiting steroid biosynthesis in Leydig cells [18].Our study shows that testosterone levels are less in patients with metabolic syndrome than in normal healthy controls('p' value of <0.05)(fig 1).The study of health in

Pomeranians(SHIP) study was a prospective study done on adults of age 20-79 years, found that as the incidence of metabolic syndrome increased among the subjects , the testosterone levels started decreasing[19].Data from the third national health and nutrition examination survey also showed an inverse relationship between testosterone levels and metabolic syndrome[20]. An European study done by Laaksonen,D.E,Niskanen Salonen,R.et al, has shown that low testosterone is associated with each components of metabolic syndrome and also with metabolic syndrome as a whole[21].Testosterone values are influenced by the levels of SHBG. We could not estimate it due to the problem of cost.

CONCLUSION:

This study has proved that metabolic syndrome is associated with low testosterone levels and since both these factors independently lead to the development of CAD [22, 23] testosterone can be included under the armamentarium for assessing the vascular complications in metabolic syndrome after the study has been done on a large population.

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