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HORMONAL AND CLINICAL PROFILE OF HYPOGONADISM IN DIABETES PATIENTS

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ABSTRACT

Introduction: *Hypogonadism in male is defined as a condition in which there is a clinical characterization of both sign and symptom and biochemical evidence of testosterone deficiency. Male hypogonadism is one kind of recognized medical condition in which these remains under diagnosed by clinicians. A clinical syndrome which consists of with or without signs and associated with biochemical evidence of testosterone deficiency in called Hypogonadism. Over two decades ago, association between the diabetes mellitus (DM) and hypogonadism came to limelight when a high prevalence of low testosterone levels was observed in men with diabetes. Many studies showed that in one-third of diabetic men there are low free testosterone levels, which are independent of sex hormone-binding globulin (SHBG). Due to deficiency of testosterone in men is associated with negative consequences. Many research showed that in DM patients there is increasing evidence of hypogonadism is a risk factor for coronary artery disease, the leading cause of mortality. Other adverse effects are also been reported associated with hypogonadism which included as poor quality of life, sexual dysfunction, increased fracture risk, increasing fat mass, cognitive decline, and mortality.* ***Aim:*** *The main aim of this study is to find out the type of hypogonadism as either hypogonadotropic or hypergonadotropic in DM patients.* ***Material and methods:*** *Total 70 patients were include in this study in which patients visiting out patients department (OPD) of medicine and in patients department (IPD). Individuals with chronic systemic illness, abuse drugs or alcohol and undergone cancer chemotherapy or radiotherapy were excluded in this study. Detailed history of the patients was taken from the patients like height, weight and arm span with general and systemic examination to rule out any systemic illness were noted. Estimation of hormonal levels was noted from all patients.* ***Result:*** *Total 80 DM male patients were included in this study. Out of 70 patients 49 (70%) were below 35 years old and remaining 21(30%) were above 36 years old. Out of 70 patients 55 had hypogonadotropic hypogonadism and 15 had hypergonadotropic hypogonadism in male respectively. Out of total patients 55 had hypogonadotropic hypogonadism. Most common etiology was idiopathic hypogonadotropic hypogonadism. Patient with bilateral anorchia or vanishing testis syndrome, two patients had kallmann syndrome, five of them had hypopituitarism and interestingly three patients had features of gigantism and hypogonadism. 15 patients had hypergonadotropic hypogonadism in which 11 had Klinefelter syndrome and 4 had Turner's syndrome.* ***Conclusion:*** *The most common cause is Idiopathic hypogonadotropic hypogonadism is shown in male. Height, weight and Arm span varied significantly between Males of hypogonadotropic hypogonadism and hypergonadotropic hypogonadism. Maximum number of patients of DM in India, the incidence of hypogonadism is more in diabetic patients as compared to the general population. Hence, implementation of screening programs in diabetic patients is necessary to understand and detect individuals with low serum total testosterone at any early stage and to supplement testosterone accordingly.*

Keywords: *diabetes mellitus, hypogonadism, testosterone, Hypogonadotropic hypogonadism*

Introduction

Hypogonadism in male is defined as a condition in which there is a clinical characterization of both sign and symptom and biochemical evidence of testosterone deficiency[i]. Male hypogonadism is one kind of recognized medical condition in which these remains underdiagnosed by clinicians[ii]. A clinical syndrome which consists of with or without signs and associated with biochemical evidence of testosterone deficiency in called Hypogonadism[iii]. Lack of

testosterone in male individuals is known as Hypogonadism that can be hypothalamic or pituitary or testicular origin, or a combination of both. Hypogonadism is testicular failure which is due to genetic disorders (eg, Klinefelter's syndrome), trauma, radiation, orchitis, chemotherapy, or undescended testes, is known as hypergonadotropic hypogonadism or primary hypogonadism. gonadotropin deficiency or dysfunction in male individuals results a disease or damage to the hypothalamic-pituitary axis is known as hypogonadotropic hypogonadism, central hypogonadism, or secondary hypogonadism. Men especially which is older than 50 years might have low testosterone levels with functional abnormalities at multiple levels of the hypothalamic-pituitary-testicular axis[iv,v,vi]. Over two decades ago, association between the diabetes mellitus (DM) and hypogonadism came to limelight when a high prevalence of low testosterone levels was observed in men with diabetes[vii]. Free testosterone levels in male; independent of sex hormone-binding globulin (SHBG) has been low in one-third of diabetic men[viii]. Gonadotropin releasing hormone (GnRH) deficiency is caused by impaired gonadotropin release in the setting of otherwise normal anterior pituitary anatomy and function and in the absence of secondary causes of hypogonadotropic hypogonadism. Individuals with normal GnRH have normal pituitary function tests and their hypogonadism typically responds to a physiologic regimen of exogenous[ix]. In a male at the time of birth also there may be present of signs of gonadotropin deficiency in which typically the significance of these findings is not recognized until puberty. Cryptochidism and micropenis can be a manifestation of an early impairment in the reproductive axis which is associated with abnormally low serum concentrations of gonadotropins and testosterone in the first month of life. Most individuals have a eunuchoid body habitus though the rate of linear growth is normal[x]. Many studies showed that over few years' prevalence of low testosterone levels in men (hypogonadism) with DM were observed[xi]. Many studies showed that in one-third of diabetic men there are low free testosterone levels, which are independent of sex hormone-binding globulin (SHBG)[xii]. Due to deficiency of testosterone in men is associated with negative consequences. Many research showed that in DM patients there is increasing evidence of hypogonadism is a risk factor for coronary artery disease, the leading cause of mortality[xiii]. Other adverse effects are also been reported associated with hypogonadism which included as poor quality of life, sexual dysfunction, increased fracture risk, increasing fat mass, cognitive decline, and mortality[xiv,xv]. The main aim of this study is to find out the type of hypogonadism as either hypogonadotropic or hypergonadotropic in DM patients.

Material and methods:

This study is conducted in the department of medicine at Vedanta Institute of Medical Sciences Dahanu Palghar, Maharashtra and hospital during the period of 1 year. Total 70 patients were include in this study in which patients visiting out patients department (OPD) of medicine and in patients department (IPD). Patients with the age above 20 years with underdeveloped secondary sexual characters were included in this study. Individuals with hronic systemic illness, abuse drugs or alcohol and undergone cancer chemotherapy or radiotherapy were excluded in this study. Detailed history of the patients was taken from the patients like height, weight and arm span with general and systemic examination to rule out any systemic illness were noted. Estimation of hormonal levels was noted from all patients. Thyroid hormone, cortisol, growth hormone levels, prolactin, testosterone and estradiol levels were recorded for data. Radiological examination like X-ray Cone View Sella, X-ray left forearm and X-ray left wrist was done for asses the bone age and epiphyseal fusion. MRI Brain (Sella) was also done to rule out structural causes of pituitary dysfunction.

Result:

Total 70 DM male patients were included in this study. Out of 70 patients 49 (70%) were below 35 years old and remaining 21(30%) were above 36 years old as shown in table no 1 below.

TABLE 1: Study population characteristics

Age	Total no of patients	Percentage
<35 years (12-18yrs)	49	70
>36 years	21	30
	70	100

Table 2: distribution of study population

Sex	Hypogonadotropic hypogonadism	Hypergonadotropic hypogonadism
Males	55	15

Out of 70 patients 55 had hypogonadotropic hypogonadism and 15 had hypergonadotropic hypogonadism in male respectively as shown in above table no 2.

Table 3: Etiology wise distribution of hypogonadotropic hypogonadism

Hypogonadotropic hypogonadism	No. of patients
Idiopathic	42
Vanishing testis syndrome	1
Kallmann syndrome	2
Hypopituitarism	5
Gigantism and hypogonadism	3
Craniopharyngioma	2
Total	55

In this study out of total patients, 55 patients had hypogonadotropic hypogonadism. Most common etiology was idiopathic hypogonadotropic hypogonadism. Patient with bilateral anorchia or vanishing testis syndrome, two patients had kallmann syndrome, five of them had hypopituitarism and interestingly three patients had features of gigantism and hypogonadism as shown in above table no 3.

Table 4: Etiology wise distribution of hypergonadotropic hypogonadism

Hypergonadotropic hypogonadism	No.of patients
Klinefelter syndrome	11
Turner's syndrome	4
Total	15

15 patients had hypergonadotropic hypogonadism in which 11 had Klinefelter syndrome and 4 had Turner's syndrome as shown in above table no 4.

Discussion:

Based on the pituitary hormones and the gonadal hormones Individuals who present with hypogonadism can be classified either into hypogonadotropic or hypergonadotropic. In this study most of the individuals were in the age group of 30-40 years, majority below 35 years. IHH present almost in all individuals and 5 patients were presenting above the age of 47 years with IHH which is similar to study of Nachtigall et al[xvi]. Idiopathic hypogonadotropic hypogonadism (IHH) is the most common cause and most of them were a male which is correlated to the study done 74 by Seminara et al 1998 who showed a male-to-female ratio of nearly 4:1[xvii]. According to the study Juan J. Tarín et al as the birth order increased the probability of having hypogonadism decreases. The probability of a man being infertile would be greater if he comes from a small family than from a large family[xviii]. Arm span, height and weight were significantly higher in hypergonadotropic males than hypogonadotropic a male which is shows by similar studies done by Niels E. Skakkebaek and Lise Aksglaede in which they found accelerated growth in early childhood in boys with 47XXY and 47 XYY karyotype[xix]. Another studied done by Olabinri B.M et.al[xx] there is highly significant of Height has correlation with arm span in both males and females. It is found that height showed a high positive correlation with body's armspan in males and also a high positive significant correlation exist between height. In this study the prevalence of hypogonadism was around 78.6% which is quite opposite to study of Ganesh et al[xxi]. Another study which was carried out by Dhindsa et al[xxii] showed low testosterone involving 103 patients in the United States of America; the prevalence was around 33% which is lower than this study. The findings of this study was not consistent with the findings revealed in a Jordanian et al[xxiii] study and also study of Kapoor et al[xxiv] who found that 7% had hypogonadotropic hypogonadism and lower prevalence of primary hypogonadism (high LH and FSH) levels which was seen in 26% of patients with DM compared to 16.9% of those who were hypogonadal.

Conclusion:

Hypogonadism diagnosis, at times, might not be validated with the help of androgen deficiency questionnaire or symptoms only. The most common cause is Idiopathic hypogonadotropic hypogonadism is shown in male. Height, weight and Arm span varied significantly between Males of hypogonadotropic hypogonadism and hypergonadotropic hypogonadism. Maximum number of patients of DM in India, the incidence of hypogonadism is more in diabetic patients as compared to the general population. Hence, implementation of screening programs in diabetic patients is necessary to understand and detect individuals with low serum total testosterone at any early stage and to supplement testosterone accordingly.

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