



CLINICAL AND HORMONAL PROFILE OF HYPOGONADISM

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Conflicts of Interest: Nil

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Abstract:

Introduction: Hypogonadism is an important problem with which many boys and girls present to the Medicine OPD. 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. The clinical features of hypogonadism are sufficiently well recognized, the causes sufficiently well known, and the tests of the hypothalamic-pituitary-testicular axis sufficiently accurate to permit the diagnosis in most patients. Hypogonadism is one of the most common endocrine disorders in men and is characterized by low serum testosterone levels and/or low sperm counts with clinical signs and symptoms of androgen loss. Hypogonadism can be primary or secondary, congenital or acquired. The causes and management of primary and secondary hypogonadism and an overview of hypogonadism in older men are reviewed elsewhere. 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. Several studies reported a high prevalence of low testosterone levels in men (hypogonadism) with T2DM. 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.

Aim: The main aim of this study is to find out the type of hypogonadism as either hypogonadotropic or hypergonadotropic.

Material and methods: This study is conducted in the department of Biochemistry in collaboration with Dept. of Medicine at Govt. Medical College and SVBC Hospital. Total 50 patients were included in this study in which patients visiting out patients department (OPD) of medicine. Patients with the age above 12 years with underdeveloped secondary sexual characters, delayed puberty were included in this study. 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. Radiological examination like X-ray Cone View Sella, X-ray left forearm and X-ray left wrist was done for assess the bone age and epiphyseal fusion. MRI Brain (Sella) was also done to rule out structural causes of pituitary dysfunction.

Result: Total 50 patients were included in this study. Out of 50 patients 44 (88%) patients were males and remaining were female (12%). Among total patients 39 (78%) were below 18 years of age and

remaining were above 18 years were 11(22%). Most common etiology was idiopathic hypogonadotropic hypogonadism patient with bilateral anarchic or vanishing testis syndrome.

Conclusion: Most common age group below 18 years of age has presentation of hypogonadism which is more common in Males than in female. 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. Therefore, significant correlation existed between total testosterone and LH in males, whereas height and arm span correlated well in both males and females.

Keywords: Hypogonadism, Testosterone, Hypergonadotropic hypogonadism, Hypogonadotropic hypogonadism

Introduction

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 axisⁱⁱⁱ. A clinical syndrome which consists of with or without signs and associated with biochemical evidence of testosterone deficiency is called Hypogonadism^{iv}. Several studies reported a high prevalence of low testosterone levels in men (hypogonadism) with T2DM^v. Free testosterone levels in male; independent of sex hormone-binding globulin (SHBG) has been low in one-third of diabetic men^{vi}. 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^{vii}. When there is complete or partial absence of GnRH-mediated release of LH and FSH occur deficiency of GnRH. As there is

reproductive defect about two thirds of individuals with IGD have and impaired sense of smell (anosmia/hyposmia)^{viii}. 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. Cryptorchidism 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^{ix}. Low or normal serum concentration of LH and FSH in the setting of low circulating concentrations of sex steroids (testosterone and estradiol) is GnRH deficiency. Exogenous GnRH is a regimen of physiologic doses that LH secretions are apulsatile and responsiveness^x. The main aim of this study is to find out the type of hypogonadism as either hypogonadotropic or hypergonadotropic.

Material and Methods:

This study is conducted in the department of Biochemistry in collaboration with Dept. of Medicine at Govt. Medical College and SVBC Hospital. Total 50 patients were included in this study in which patients visiting out patients department (OPD) of medicine. Patients with the age above 12 years with underdeveloped secondary sexual characters, delayed puberty were included in this study. 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. Follicle stimulating hormone, luteinizing hormone, 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.

Diagnosis and Signs and symptoms of hypogonadism

1. Pre pubertal

- Delayed development of secondary sexual characteristics
- Small testes, genitalia
- Decrease in height

2. Post pubertal

- Sexual difficulties
- Erectile dysfunction
- Infertility
- Decreased muscle and/or skeletal mass
- Decreased body hair
- Low energy, fatigue
- Change in mood, sleep, or increased anger
- Decreased cognitive function

OBSERVATIONS AND RESULTS:

Total 50 patients were included in this study. Out of 50 patients 44 (88%) patients were males and remaining were female (12%). Among total patients 39 (78%) were below 18 years of age and remaining were above 18 years were 11(22%) as shown in table no 1 below.

Table 1: Study population characteristics

Age	Total no of patients	% (Males)	% Females
<18 years (12-18yrs)	39	35	4
>18 years	11	6	5

Table 2: Sex distribution of study population

Sex	Hypogonadotropic hypogonadism	Hypogonadotropic hypergonadism
Males	39	5
Females	2	4

Males were predominant with females in number as 44 and 6 respectively. 39 had hypogonadotropic hypogonadism and 5 had hypergonadotropic hypogonadism in male whereas in females 2 had hypogonadotropic hypogonadism and 4 had hypergonadotropic hypogonadism respectively as shown in above table no 2.

Table 3: Etiology wise distribution of hypogonadotropic hypogonadism

Hypogonadotropic hypogonadism	No. of patients
Idiopathic	33
Vanishing testis syndrome	1
Kallmann syndrome	1
Hypopituitarism	4
Gigantism and hypogonadism	1
Craniopharyngioma	1
Total	41

In this study out of total patients, 41 patients had hypogonadotropic hypogonadism. Most common etiology was idiopathic hypogonadotropic hypogonadism. Patient with bilateral anorchia or vanishing testis syndrome, one patient had kallmann syndrome, four of them had hypopituitarism and interestingly one patient had features of gigantism and hypogonadism as shown in above table no 3.

Table no: 4 Etiology wise distribution of hypergonadotropic hypogonadism

Hypergonadotropic hypogonadism	No. of patients
Klinefelter syndrome	5
Turner's syndrome	4
Total	9

9 patients had hypergonadotropic hypogonadism in which 5 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 adolescence in the age group of 12-15 years, majority below 18 years. IHH present in adolescence almost in all individuals and few present in adult age group. 5 patients were presenting above the age of 18 years with IHH which is similar to study of Nachtigall et al^{xi}. 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^{xii}. 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^{xiii}. 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^{xiv} in which they found accelerated growth in early childhood in boys with 47XXY and 47 XYY karyotype. According to PC Sizonenko and L Paunier et al^{xv} testosterone correlated significantly with LH in males which they found major rise of Testosterone. That was preceded by the rise of plasma LH and was accompanied by the rise of plasma FSH. Another studied done by Olabinri B.M, Olawoye T et.al^{xvi} 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 arms pan in males and also a high positive significant correlation exist between height and arms pan in female children.

CONCLUSION:

Most common age group below 18 years of age has presentation of hypogonadism which is more common in Males than in female. 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. Therefore, significant correlation existed between total testosterone and LH in males, whereas height and arm span correlated well in both males and females.

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