



“STUDY OF HORMONAL AND CLINICAL EVALUATION OF HYPOGONADISM IN DIABETES MELLITUS PATIENTS,,

Dr. Sunil Kumar* Senior Resident, Department Of General Medicine PMCH Patna. *Corresponding Author

Dr. Pragati Prabhat Senior Resident, Department Of General Medicine PMCH Patna

Dr. Amrita Kumari Senior Resident, Department Of General Medicine PMCH Patna

(ABSTRACT) **BACKGROUND:** To determine the 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.

MATERIALS 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) at department of General medicine Patna medical college and hospital Patna Bihar. . 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.

CONCLUSION: Hypogonadism was higher in the patients with diabetes than in the control subject, there was no correlation of hypogonadism with components of the metabolic syndrome or microvascular complications of diabetes mellitus. 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.

KEYWORDS : diabetes mellitus, hypogonadism, testosterone, coronary artery disease.

INTRODUCTION

Hypogonadism is a clinical condition comprising both clinical and biochemical evidence of testosterone deficiency, Hypogonadism in male is defined as a condition in which there is a characterization of both sign and symptom, there are multiple causes of low testosterone level in diabetes mellitus patients. Male hypogonadism is one kind of recognized medical condition in which these remains underdiagnosed by clinicians. Testosterone deficiency has proven to be a risk factor for CAD, this received scant attention in the medical literature, we conducted this study with the objective to determine the frequency of hypogonadism in diabetes mellitus and its variation with regard to CAD.

Hypogonadism was defined on the basis of erectile dysfunction clinically and total testosterone levels biochemically. CAD was diagnosed on the basis of finding of coronary angiography. Many studies shoed that in one third of diabetic.

A clinical syndrome which consists of with or without signs and associated with biochemical evidence of testosterone deficiency in called Hypogonadism. 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. 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. 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^x. Many studies showed that over few years, prevalence of low testosterone levels in men (hypogonadism) with DM were observed many studies showed that in one third of diabetic men there are low fre testosterone levels, due to deficiency of testosterone in men is associated with negative consequences. Many research showed that in Dm patients there is increasing evidence of few years' prevalence of low testosterone levels in 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. 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 General medicine at Patna medical college and Hospital patna Bihar. 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 No statically significant correlation was observed between hypogonadism and age, duration of diabetes, glycemc control, 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

The 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. 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^{svii}. According to the study Juan J. Tarin 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. 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. Another studied done by Olabinri B.M et.al 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. Another study which was carried out by Dhindsa et al 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 study and also study of Kapoor et al 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:

HH is found in 25% of men an additional 4% have hypergonadotropic

hypogonadism. Low testosterone concentrations in men, very high CRP concentrations, mild anemia, and decreased BMD. 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. Testosterone deficiency is a significant problem of males with DM, patients with CAD have markedly low levels of testosterone as compared with patients without any CAD.

REFERENCES:

- Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, et al. Testosterone therapy in adult men with androgen deficiency syndromes: An endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* 2006;91:1995-2010.
- Jones TH. Testosterone Deficiency in Men. Oxford, United Kingdom: Oxford University Press; 2008a
- Jones TH. Clinical awareness and diagnosis of male hypogonadism. *J Mens Health* 2008b;5:S26-34.
- Matsumoto AM. Andropause: Clinical implications of the decline in serum testosterone levels with aging in men. *J Gerontol Med Sci.* 2002;57A(2):M76-M99
- AACE Hypogonadism Task Force. *Endocr Pract.* 2002;8:439-456.
- Jones TH. Clinical awareness and diagnosis of male hypogonadism. *J Mens Health* 2008b;5:S26-34.
- Barrett-Connor E, Khaw KT, Yen SS. Endogenous sex hormone levels in older adult men with diabetes mellitus. *Am J Epidemiol.* 1990;132:895-901.
- Haffner SM, Valdez RA, Stern MP, Katz MS. Obesity, body fat distribution and sex hormones in men. *Int J Obes Relat Metab Disord* 1993;17:643-9.
- Hoffman AR, Crowley WF. Introduction of puberty in men by long-term pulsatile administration of low-dose gonadotropin releasing hormone. *N Engl J Med.* 1982; 307:1237-41.
- Grumbach MM. A window of opportunity: the diagnosis of gonadotropin deficiency in the male infant. *J Clin Endocrinol Metab.* 2005;90:3122-7.
- Dhindsa S, Miller MG, McWhirter CL, Mager DE, Ghanim H, Chaudhuri A, et al. Testosterone concentrations in diabetic and nondiabetic obese men. *Diabetes Care* 2010;33:1186-92.
- Haffner SM, Valdez RA, Stern MP, Katz MS. Obesity, body fat distribution and sex hormones in men. *Int J Obes Relat Metab Disord* 1993;17:643-9.
- English KM, Mandour O, Steeds RP, Diver MJ, Jones TH, Channer KS. Men with coronary artery disease have lower levels of androgens than men with normal coronary angiograms. *Eur Heart J.* 2000;21:890-4.
- Nieschlag E, Swerdloff R, Behre HM, Gooren LJ, Kaufman JM, Legros JJ, et al. Investigation, treatment and monitoring of late-onset hypogonadism in males: ISA, ISSAM, and EAU recommendations. *Int J Androl.* 2005;28:125-7.
- Kapoor D, Aldred H, Clark S, Channer KS, Jones TH. Clinical and biochemical assessment of hypogonadism in men with type 2 diabetes: Correlations with bioavailable testosterone and visceral adiposity. *Diabetes Care.* 2007;30:911-7.
- Nachtigall LB, Boepple PA, Pralong FP, Crowley WF Jr. Adult-onset idiopathic hypogonadotropic hypogonadism--a treatable form of male infertility. *N Engl J Med.* 1997;336:410-5.
- Seminara SB, Jameson JL, Geyer A, Nachtigall LB, Boepple PA, Holmes LB, Crowley WF Jr. The genetic and clinical heterogeneity of gonadotropin-releasing hormone deficiency in the human. *J Clin Endocrinol Metab.* 1996;81:4388-95.
- Juan J. Tarin et al., Delayed Motherhood Increases the Probability of Sons to be Infertile. *Journal of Assisted Reproduction and Genetics Issue Volume 18, Number 12 / December, 2001 Pages 650-654*
- Lise Aksglaede, Niels E. Skakkebaek and Anders Juul. Abnormal Sex Chromosome Constitution and Longitudinal Growth: Serum Levels of Insulin-Like Growth Factor (IGF)-I, IGF Binding Protein-3, Luteinizing Hormone, and Testosterone in 109 Males with 47,XXY, 47,XYY, or Sex-Determining Region of the Y Chromosome (SRY)-Positive 46,XX Karyotypes. *J. Clin. Endocrinol. Metab., Jan 2008; 93: 169-176.*
- Olabinri B. M; Olawoye T. L et al., The Relationships between Percent Body Fat and Other Anthropometric Nutritional Predictors among Male and Female Children in Nigeria. *African Journal of Biomedical Research, Vol. 9, Vol. 1, 2006, pp. 45-52*
- Ganesh HK, Vijaya Sarathi HA, George J, Shivane VK, Bandgar T, Menon PS, et al. Prevalence of hypogonadism in patients with type 2 diabetes mellitus in an Asian Indian study group. *Endocr Pract* 2009;15:513-20.
- Dhindsa S, Miller MG, McWhirter CL, Mager DE, Ghanim H, Chaudhuri A, et al. Testosterone concentrations in diabetic and nondiabetic obese men. *Diabetes Care* 2010;33:1186-92.
- Gray A, Feldman HA, McKinlay JB, Longcope C. Age, disease, and changing sex hormone levels in middle-aged men: Results of the Massachusetts male aging study. *J Clin Endocrinol Metab* 1991;73:1016-25.
- Kapoor D, Aldred H, Clark S, Channer KS, Jones TH. Clinical and biochemical assessment of hypogonadism in men with type 2 diabetes: Correlations with bioavailable testosterone and visceral adiposity. *Diabetes Care* 2007;30:911-7.