Insulin Resistance and Hypogonadism

Md. Ruhul Amin¹, Md. Faruque Pathan², AHM Aktaruzzaman³, Nazmul Kabir Qureshi⁴, Fahmida Akter⁵, Sabura Rahman⁶, Md. Ehsanul Huq⁷, Shahana Shermin⁸, Md. Rezwanur Rahman⁹

Abstract

Backgound: The number of hypogonads is increasing day by day. It may be due to sedentary life style with increased obesity, increased tension or stressed lifestyle among all groups of populations. Visceral obesity is associated with insulin resistance, diabetes mellitus and also with hypogonadism. **Objective:** This study was carried out to determine the proportion of insulin resistance among male subjects with hypogonadism in different age groups along with status of erectile quality among diabetics and non diabetics. Materials and method: This cross sectional study among 161 adult male subjects aged ≥ 20 to ≤ 60 years were purposively selected from Bangladesh Institute of Research and Rehabilitation in Diabetes Endocrine and Metabolic Disorders (BIRDEM), Dhaka, Bangladesh between May 2009 to September 2010. Glycemic status and insulin resistance (by HOMA-R) were done and relevant history were documented. **Results:** The highest proportion (38.9%) of hypogonadism was in \geq 50 years age group whereas highest proportion (39.6%) of the eugonads was in the age group of 40 to 49 years. More than half of the hypogonad subjects had weak erectile quality (54.0%) which were followed by absent erectile quality in 32.7% and 13.3% subjects had normal erectile quality. Among the eugonad subjects 41.7% had normal erectile quality, 41.6% subjects had weak erectile quality and 16.7% subjects had no erectile quality. More than ninety percent of the hypogonad subjects and about 60% of the eugonad subjects had insulin resistance. The average HOMA-R was more in the subjects with hypogonadism with diabetes which was highly significant (*p*-value < 0.001). Conclusion: Hypogonadism is associated with insulin resistance.

Keywords: Hypogonadism, insulin resistance.

Delta Med Col J. Jan 2013;1(1):3-7

- 1. Assistant Professor, Dept. of Endocrinology, Sir Salimullah Medical College & Mitford Hospital, Dhaka, Bangladesh.
- 2. Professor, Dept. of Endocrinology, Bangladesh Institute of Research and Rehabilitation in Diabetes Endocrine and Metabolic Disorders (BIRDEM), Dhaka, Bangladesh.
- 3. Junior Consultant (Medicine), Upazila Health Complex, Shingair, Manikganj, Bangladesh.
- 4. Specialist, Dept. of Medicine, Endocrinology & Gastroenterology, United Hospital Limited, Dhaka, Bangladesh.
- 5. Research Officer, Planning & Research Unit, DGHS, Dhaka, Bangladesh.
- 6. Course, DCP, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.
- 7. Assistant Professor, Dept. of Community Medicine, Delta Medical College, Dhaka, Bangladesh.
- 8. Senior Medical Officer, Dept. of Gynae & Obs., Bangladesh Institute of Research and Rehabilitation in Diabetes Endocrine and Metabolic Disorders (BIRDEM), Dhaka, Bangladesh.
- 9. Associate Professor, Dept. of Biochemistry, Delta Medical College, Dhaka, Bangladesh.

Correspondence: Dr. Md. Ehsanul Huq. e-mail: ehsanulhuq@yahoo.com

Introduction

Due to great advancement in the field of science and technology there is increased life expectancy all over the world. It has also increased the expectations of long sexual life. But medical advancement is not up to the expectations. So the number of hypogonads is increasing day by day. It may be due to sedentary life style with increased obesity, increased tension or stressed lifestyle among all groups of populations. It may be due to endocrine disruptors like so many chemicals, drugs and environmental pollutants which destruct different endocrine glands like gonads, pituitary, etc.¹

On the other hand hypogonadism is found more in patients with diabetes.² It may happen that hypogonadism causes fat deposition which in turn leads to insulin resistance and ultimately leads to diabetes. It is also proved by the fact that testosterone replacement in hypogonadal patients decreases insulin resistance and improves blood sugar control.³ Visceral obesity is associated with insulin resistance, diabetes mellitus and also with hypogonadism.⁴⁻⁸ So treatment of hypogonadism may increase muscle mass, improve glucose uptake and thereby can decrease insulin resistance and can decrease the number of the diabetic patients.⁹

There is no clear consensus for an accepted lower limit of normal testosterone level.¹⁰ It is established that patients with testosterone level below 12 nmol/L with signs and symptoms of hypogonadism can be benefited by replacement with testosterone.^{10,11} So testosterone level of < 12 nmol / L is taken as cut off point and these subjects are taken as patients with hypogonadism.

Insulin resistance is defined as impaired whole body insulin mediated glucose disposal. Clinically insulin resistance is the inability of a known quantity of exogenous or endogenous insulin to increase glucose uptake and utilization in an individual as much as it does in a normal population. It may be measured by Homeostasis model assessment (HOMA-R) method. In this method if the value is more than 1 (one), it is considered that the patient has got insulin resistance. Insulin resistance may cause metabolic syndrome associated with obesity, hypertension, atherosclerosis and dyslipidaemia. Although a relationship between insulin resistance and fat gain has been demonstrated it is not clear whether insulin resistance is a promoting fa ctor or simply a consequence of fat gain.¹²⁻¹⁴

Now a days patients with hypogonadism and erectile dysfunction are considered more frequent than those which were thought previously.¹⁵ Patients with type 2 diabetes have impaired sexual life which is worsened

by hypogonadism. Low testosterone in type 2 diabetes is in fact associated with more severe erectile dysfunction, hypoactive sexual desire and low intercourse frequency.³ Several studies have shown that testosterone replacement in diabetic patients with hypogonadism or without hypogonadism has improved the erectile dysfunction.^{3,10}

Among the multiple causes of erectile dysfunction hypogonadism is an important one which in most of the time is over looked in the common diseases like diabetes mellitus. But the treatment of hypogonadism is satisfactory and promising.⁹ So every rational patient should be evaluated for hypogonadism.

Materials and method

This cross sectional study was conducted to evaluate insulin resistance in hypogonad patients. The study was carried out in the department of Endocrinology of Bangladesh Institute of Research and Rehabilitation in Diabetes Endocrine and Metabolic Disorders (BIRDEM), Dhaka, Bangladesh from May 2009 to September 2010. Ethical permission was taken from BIRDEM Ethical Review Committee.

Purposively a total of 161 male subjects of 20 to 60 years without having any systemic illness that can affect testosterone level were selected in this study. Serum testosterone level was measured in all the subjects. Among them 113 subjects who had serum testosterone level of ≤ 12 nmol/L irrespective of blood glucose level were grouped as hypogonads. On the other hand 48 subjects were selected as eugonads having testosterone level of > 12 nmol/L with normal blood glucose level. Hypogonad subjects were further subdivided based on blood glucose level into diabetics and non diabetics. Status of insulin resistance was determined using HOMA-R method as described by Matthews et al.¹⁶ Detailed history and clinical findings were evaluated and documented with special emphasis on erectile status. Informed co nsent was taken from all the study subjects after explaining the purpose of the study in detail. Proportions of the studied variables and ANOVA were done by using software SPSS for windows version 11.5.

Results

In this study age distribution, erectile status, status of insulin resistance done by HOMA-R and comparison of insulin resistance among the study subjects were evaluated. Regarding age distribution the highest proportion (38.9%) of hypogonadism was in ≥ 50 years age group whereas highest proportion (39.6%) of the eugonads was in the age group of 40 to 49 years (Table I).

Table I: Age distribution	of the study subjects
---------------------------	-----------------------

Age group (years)	Study subjects		
	Hypogonads (n=113)	Eugonads (n=48)	
20-29	10 (8.6%)	10 (20.6%)	
30-39	26 (23.0%)	11 (22.9%)	
40-49	33 (29.2%)	19 (39.6%)	
≥ 50	44 (38.9%)	8 (16.7%)	

More than half of the hypogonad subjects had weak erectile quality (54.0%) which were followed by absent erectile quality in 32.7%. Rest of the subjects was normal functioning (13.3%). Among the eugonad subjects the percentage of normal erectile quality was 41.7% and weakly present erectile quality was found in 41.6% subjects and 16.7% subjects had no erectile quality (Table II).

Table II: Erectile status of the study subjects

Study subjects	Erectile status		
	Normal	Weak	Absent
Hypogonads	13.3%	54.0%	32.7%
Eugonads	41.7%	41.6%	16.7%

More than ninety percent of the hypogonad subjects had insulin resistance (91.2%). On the other hand among the eugonad subjects 60.4% had insulin resistance (Table III).

Table III: Insulin resistance of the study subjects

Study subjects Insulin resistance		No insulin resistance	
Hypogonads (n=113)	91.2%	8.8%	
Eugonads (n=48)	60.4%	39.6%	

Insulin resistance was measured by using HOMA-R among the groups. The average HOMA-R was more in the subjects with hypogonadism with diabetes. Highly significant (p-value <0.001) difference was found among the study subjects (Table IV).

Table IV: Comparison of insulin resistance amongthe study subjects

Grouping of study subjects	Insulin resistance Mean ± SD	F-value	p-value
Eugonadism (n=48)	1.56 ± 1.21		
Hypogonadism with diabetes (n=66)	5.76 ± 6.28	9.696	< 0.001
Hypogonadism without diabetes (n=47)	4.49 ± 5.57		

Discussion

This cross sectional study was carried out to determine the proportion of insulin resistance among male subjects with hypogonadism.

The study revealed that more than two third of hypogonads presented with erectile dysfunction and were in ≥ 50 years of age group. It is striking that a remarkable number of eugonads also had similar complaints and were within 40 to 49 years of age group clearly exploring the fact of vulnerability of aging for erectile dysfunction independent of gonadal status though the major proportion were hypogonads. These findings are almost similar to the study done by Rhoden et al.¹⁷ But Slag et al.¹⁸ showed that erectile dysfunction. This discrepancy might be due to advanced health facilities and awareness leading to early recognition in the western society.

Insulin resistance is the hallmark feature of type 2 diabetes and is also an important component of the metabolic syndrome. There is evidence to suggest that testosterone is an important regulator of insulin sensitivity in men and observational studies have shown that testosterone levels are low in men with diabetes.⁶ Visceral obesity is also more among hypogonads which is strongly associated with insulin resistance.^{10,19} These findings are in accordance with our results which shows more than 90% of hypogonads had insulin resistance. Moreover we found a substantial proportion of eugonads to have insulin resistance and erectile dysfunction. Grover et al.²⁰ showed that erectile dysfunction is independently associated with metabolic syndrome.

The study revealed that hypogonadism is associated with insulin resistance with or without diabetes. So every patient with metabolic syndrome or diabetes mellitus, and other related diseases should be evaluated for hypogonadism.

References

- Archambeault DR, Yao HH. Activin A, a product of fetal Leydig cells, is a unique paracrine regulator of Sertoli cell proliferation and fetal testis cord expansion. Proc Natl Acad Sci U S A. 2010;107(23):10526-31.
- Corona G, Mannucci E, Petrone L, Ricca V, Balercia G, Mansani R, Chiarini V, Giommi R, Forti G, Maggi M. Association of hypogonadism and type II diabetes in men attending an outpatient erectile dysfunction clinic. Journal of Impotence Research.2006;18:190-97.
- Corona G, Monami M, Rastrelli G, Aversa A, Sforza A, Lenzi A, Forti G, Mannucci E, Maggi M. Type 2 diabetes mellitus and testosterone: a meta-analysis study. International Journal of Andrology.2011; 34:528-40.
- Moriarty-Kelsey M, Harwood JE, Travers SH, Zeitler PS, Nadeau KJ. Testosterone, obesity and insulin resistance in young males: evidence for an association between gonadal dysfunction and insulin resistance during puberty. J Pediatr Endocrinol Metab.2010;23(12):1281-87.
- Guay A, Jacobson J. The relationship between testosterone levels, the metabolic syndrome (by two criteria), and insulin resistance in a population of men with organic erectile dysfunction. J Sex Med.2007;4:1046-55.
- Zitzmann M, Faber S, Nieschlag E. Association of specific symptoms and metabolic risks with serum testosterone in older men. Journal of Clinical Endocrinology & Metabolism.2006,91:4335-43.
- Hall SA, Esche GR, Araujo AB, Travison TG, Clark RV, Williams RE, McKinlay JB. Correlates of low testosterone and symptomatic androgen deficiency in a population-based sample. Journal of Clinical Endocrinology & Metabolism.2008;93:3870-77.
- Hossain P, Kawar B, Nahas ME. Obesity and diabetes in the developing world - A growing challenge. N Engl J Med.2007;356:213-15.

- Wang C, Alexander G, Berman N, Salehian B, Davidson T, McDonald V, Steiner B, Hull L, Callegari C, Swerdloff RS. Testosterone replacement therapy improves mood in hypogonadal men - a clinical research center study. Journal of Clinical Endocrinology and Metabolism.1996;81(10):3578-83.
- Kapoor D, Aldred H, Clark S, Channer KS, Jones TH. Clinical and biochemical assessment of hypogonadism in men with Type-2 diabetes, correlation with bioavailable testosterone and visceral adiposity. Diabetes Care.2007;30:911-17.
- Wu FCW, Tajar A, Beynon JM, Pye SR, Silman AJ, Finn JD, O'Neill TW, Bartfai G, Casanueva FF, Forti G, Giwercman A, Han TS, Kula K, Lean MEJ, Pendleton N, Punab M, Boonen S, Vanderschueren D, Labrie F, Huhtaniemi IT . Identification of late-onset hypogonadism in middle-aged and elderly men. N Engl J Med.2010;363(2):123-35.
- Kraegen EW, Clark PW, Jenkins AB, Daley EA, Chisholm DJ, LH Storlien. Development of muscle insulin resistance after liver insulin resistance in high-fat-fed rats. Diabetes.1991;40(11):1397-403.
- Storlien LH, Jenkins AB, Chisholm DJ, Pascoe WS, Khouri S, Kraegen EW. Influence of dietary fat composition on development of insulin resistance in rats. Diabetes.1991;40(2):280-89.
- Lovejoy J, Girolamo MD. Habitual dietary intake and insulin sensitivity in lean and obese adults. American Journal of Clinical Nutrition.1992;55(6):1174-79.
- Travison TG, Araujo AB, Donnell O, Kupelian V, McKinlay JB. A population-level decline in serum testosterone levels in American men. Journal of Clinical Endocrinology and Metabolism.2007; 92:196-202.
- Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Teacher DF, Turner RC. Homeostasis model assessment: insulin resistance and b cell function from fasting plasma glucose and insulin concentration in man. Diabetologia.1985;28:412-19.
- Rhoden EL, Morgentaler A. Risks of testosterone-replacement therapy and recommendations for monitoring. N Engl J Med.2004;350(5):482-92.

- Slag MF, Morley JE, Elson MK, Trence DL, Nelson CJ, Nelson AE, Kinlaw WB, Beyer HS, Nuttall FQ, Shafer RB. Impotence in medical clinic outpatients. JAMA.1983; 249:1736-40.
- 19. Marin P. Testosterone and regional fat distribution. Obesity Research.1995;3:609-12.
- 20. Grover SA, Lowensteyn I, Kaouache M, Marchand S, Coupal L, DeCarolis E, Zoccoli J, Defoy I. The prevalence of erectile dysfunction in the primary care setting: importance of risk factors for diabetes and vascular disease. Arch Intern Med. 2006;166:213-19.