

Association of BMI with Testosterone in Infertile Males among Local Population

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ABSTRACT

Objective: To ascertain association of raised BMI with Testosterone levels among infertile males.

Methods: A cross sectional study was conducted from April 2010 to March 2011. Sample size was 300 males (147 infertile and 153 healthy fertile control subjects) aged 30 and 60 years, selected from the Jinnah Postgraduate Medical Center (JPMC), Aziz Medical Center and Abbasi Shaheed Hospital, Karachi. All the subjects were grouped to BMI criteria (Asian pacific region for WHO). They were selected by purposive sampling after a detailed medical history and physical examination. Semen analysis was done and blood samples were collected for serum Testosterone levels. Data was analyzed via SPSS 16.0 by using Analysis of Variances (ANOVA) and independent t test to compare the means and to observe sensitivity of tests and to evaluate the significant association with in the group.

Results: A significant negative correlation existed between Testosterone and BMI .Raised BMI appear to have an association with male infertility with the reduction in Testosterone levels.

Conclusion: Obesity is confirmed as risk factor for male infertility in local population.

Key words: BMI, Male Infertility, Testosterone, Azoospermia, Oligospermia.

INTRODUCTION

Infertility is an important medical and social problem in the world and male factor is responsible for about 8% to 15% of couples.¹⁻³ A couple is said to be infertile if a female does not conceive after having unprotected sexual intercourse for one year.⁴ Variations have been observed in rates and etiology of infertility in terms of gender, sexual history, lifestyle, society, and cultural background.⁵ Male, female or both can contribute towards infertility. Almost 30% of infertile males failed to show any causes of the dysfunction, however defective spermatogenesis was found to be responsible for 2-4% infertility cases. It is attributed to chronic infections, anti-sperm anti-bodies and anatomical malformation as well as to socio-environmental and genetic factors.⁶ An association between obesity and infertility has also been suggested.⁷

Studies have shown that the association of various metabolic derangements are not only associated with excessive body weight but also are hazardous for reproductive health. Studies to confirm a direct link between obesity and male infertility disorders are sparse. This is due to major focus of research on female infertility and its possible causes while attention has not been paid to male infertility.⁸ Significant increase in occurrence of overweight people remains to be linked directly to infertility. Current studies have also shown increased risk of erectile dysfunction, gall bladder diseases and disorders of bone in obese men.⁹⁻¹¹ Increased weight and obesity are the key factors that can lead to an altered reproductive hormonal profile which is characterized by decreased Testosterone and sex hormone-binding globulin (SHBG) levels or increased estradiol levels in infertile males.¹²⁻¹⁴ Recent published data has proved that defective spermatogenesis by Sertoli cells is related to overweight and obesity which can be observed by lower inhibin levels in infertile males. The extent of effects caused by hormonal changes on male reproductive potential is still not clearly determined.¹⁵

METHODOLOGY

A cross sectional study was conducted on the patients attending outpatient department (OPD) of Aziz Medical Hospital and Jinnah Post Graduate Medical Center

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(JPMC) from June 2010 to May 2011. Total no 147infertile study group were included in the study and 153 healthy fertile male were also included for better comparison and categorized as control fertile group.

The inclusion criteria for the study was Idiopathic infertile male patients having age between 20 -50 years and the exclusion criteria included secondary infertility which includes infertility due to:

Obstructive Azoospermia, testicular insults (torsion, trauma), Cryptorchidism, Infections (mumps, orchitis, epididymitis), Pelvic surgery or hernia repair, Patients with diabetic neuropathy and Patients taking anabolic steroids, non-steroidal anti inflammatory drugs (NSAIDS), cimetidine and spironolactone (which may affect spermatogenesis); sulfasalazine and nitrofurantion that affect sperm motility therapy for at least 74 days and Patients with psychiatric disorder were also excluded.

Statistical Package for the Social Sciences (SPSS version 17.0) was used to analyze the data using descriptive statistics to evaluate the frequency distribution and percentages. The mean significant differences and p values were calculated. A detailed informed consent was taken before participation of individual & confidentiality of study subjects was maintained and this research did not include factors which can harm any human being. Semen analysis was carried out on azoospermic and oligospermic men with an abstinence of 5 days according to WHO criteria.¹⁶⁻¹⁷ Patients were also subjected to hormonal assessment which comprises of serum Testosterone only.

RESULTS

Table 1 shows descriptive characteristics of the 300 study subjects which included 153 control healthy fertile male and 147 primary infertile male with mean age 33.30±7.18 and 36.7±6.03 and mean BMI 26.7±4.3 and 24.3±3.7 respectively. Amongst the total infertile subjects, the mean BMI was found to be 26.7 ±4.3 kg/m². In healthy fertile subjects, the mean BMI was found to be 24.3 ±3.7 kg/m².

Table 1: Descriptive Statistics of Fertile and Infertile Study Subjects

Variables	P value	Infertile subjects			Fertile study subjects		
		Mean ± S.D	95% Confidence Interval		Mean ± S.D	95% Confidence Interval	
			Lower	Upper		Lower	Upper
Age(years)	0.448	33.35±7.18	32.18	34.53	36.7±6.03	35.7	37.68
Weight(kg)	< 0.01	75.4±12.6	73.4	77.5	70.5±12.5	68.05	72.0
Height(m ²)	0.962	1.67±0.07	1.66	1.68	1.7±0.7	1.68	1.71
BMI	< 0.01	26.7±4.3	26.0	27.5	24.3±3.7	23.6	25.1
T (ng/ml)	< 0.01	3.6±3.6	3.0	4.2	15.9±5.9	15.0	16.9

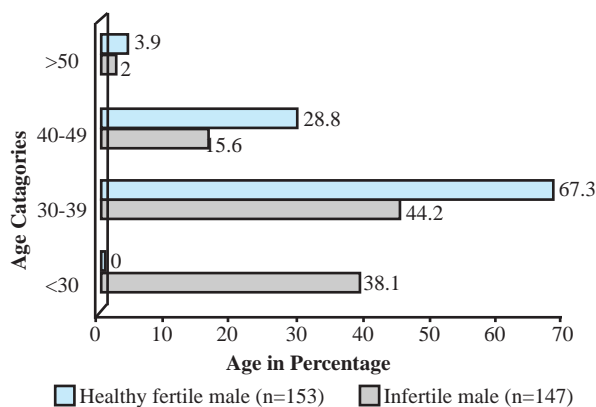


Figure 1 Shows distribution of study subjects (Infertile and fertile group) according to their age.

Among study group 38.1% of infertile has < 30 year of age, 44.2% were between 30-39 and 15.6% were 40-49 and 2% were > 50 years of age. Where as seen in healthy fertile group 67.3% were between 30-39, 28.8% were 40-49, and 4.6% were > 50 years of age.

DISCUSSION

Various studies has included BMI, as marker of body fat¹⁸ although waist hip ratio is a better predictor of reproductive outcome¹⁹ as BMI does not distinguish between android body fat distribution and gynaecoid fatty distribution. BMI is not a perfect measure of body fat and can be reliable as surrogate predictor of body fat, its validity and thresholds for excessive body fat or obesity have been questioned²⁰ but it has been recently used to measure or estimate body fat and obesity. Deurenberg in Netherlands concluded BMI as a sensitive body fat predictor by using a age and gender specific formula.²¹ In France, Wittemer et al, used BMI to measure an outcome of IVF procedure in female and concluded mean that ratio of follicle-stimulating hormone–luteinizing hormone increased significantly in accordance to BMI levels.²²

Another study conducted by Jorge et al in Boston, Massachusetts determined the relationship of BMI with DNA integrity and semen quality.²³ In 2007 by systematic review Maheshwari et al concluded that obesity is a major reproductive health problem and raised BMI were associated with decline in conception rate.¹⁸ Various physiological and psychological factors, healthy life style, diet and age, marital status and chronic diseases all has effect on individual reproductive hormonal level. Similarly effects of excessive body weight on male reproductive hormone levels can not be neglected. On reducing body weight T level can be corrected to normal, studies show that obesity has great influence on reproductive hormone.¹⁶ Pasquali in 2006 reported similar association between raised BMI and serum T levels as we have carried out in resident of Karachi but his study also shows association of high BMI with raised estrogen levels as well as sex hormone binding globulin which we have not included due to limited budget constraint¹⁶ Obese males showing decrease level of T suggest defective Leydig cell function. Studies show inverse relationship between reproductive hormones and obesity azoospermic and oligospermic males. It is also concluded by various studies that raised BMI play crucial role on regulation of Hypothalamic Pituitary axis, this probably suggests that impaired sperm production is due to unopposed feed back by hypothalamus on Leydig cells. Data also show no link between BMI and steroid hormones but our present study show decreased T levels in males with increased BMI.

Young R A et al conducted a study, to find out levels of FSH and LH and T in genetically obese Zucker rat, they found lower levels of T in obese rat as compare to lean rats although serum FSH and LH levels were in normal range. Leydig cells of genetically obese rat were hypertrophied and contain numerous fat globules.²⁴

The concentration of T and sex hormone binding globulin were measured by Kelly et al in obese individuals. He noticed downward trend in androstenedione serum concentration from 0.94 to 0.72 ng/ml in massive obese individuals, serum estradiol level were also raised while there was reduction in T levels.²⁵

In Canada Osuna²⁶ et al worked on relationship between BMI, total T and insulin resistance of obese individual. Results showed downward trend in total testosterone and SHBG levels in obese men. Their study also concluded negative correlation between BMI with T ($r=-0.447$; $p<.01$) and with SHBG $r=-0.334$; $p<0.01$). Results also show that serum total T levels are inversely related with raised BMI. These results are in accordance with our study, a little variation in serum levels are due to ethnic and geographical variations A strong inverse relation between was also found BMI and inhibin B levels and a lower T:LH ratio among men with a BMI =35 kg/m².²³

In Canada Tchernof et al²⁷ evaluated 80 infertile obese male and found negative correlation between sex hormone binding globulin (SHBG) levels with visceral body fat while estrone shows positive correlation. Computed tomography (CT) were used for detection of correlation between distribution of body fat and adipose tissue and hormonal profile were measured by radioimmunoassay.

In 2009 Macdonald et al wrote a systematic review with meta analysis²⁸ review included 31 studies. Conclusion of this literature review showed inverse relationship between BMI and free T levels although evidence were not enough to support association between semen parameters and raised BMI which are in accordance of our study results.

Kley et al²⁹ follow metropolitan life insurance company tables and has studied the relationship of ideal body weight with T and estradiol, substantial ($p < 0.001$) correlational statistics were found between excess body weight and estrone ($r = 0.80$) and estradiol ($r = 0.75$), as well as the ratios of estradiol/T ($r = 0.86$). This indicates that in adipose tissue aromatization of androgen is responsible for raised level of estradiol.

Study proves that obesity is main culprit for receptor resistance for insulin responsible for high level of serum insulin and low level of steroid hormone binding globulin in hepatocytes and as a consequence T levels are also decrease in obese male with excessive body fat has derange function of hypothalamus pituitary testicular axis possibly as a consequence of increase estrogen level which inhibit gonadotropin secretion.

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