Science Journal of Medicine and Clinical Trials
ISSN: 2276-7487
http://www.sjpub.org

Published By
Science Journal Publication
International Open Access Publisher

Research Article **Volume 2013, Article ID sjmct-259, 6 Pages, 2012, doi: 0.7237/sjmct/259**

Association between BMI and Prolactin Levels in Male Patients

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Accepted 3 December, 2013

Abstract

Objective: To ascertain association of raised BMI with Prolactin levels among infertile males. Methods: A cross sectional study was conducted from june 2010 to May 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 (Ascian 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 Prolactin levels. Data was analyzed via SPSS 17.0 by using Analysis of Variances (ANOVA) and independent t test to compare the means and to evaluate the significant association with in the group. Results: No correlation existed between PRL and BMI .Raised BMI appear to have an association with male infertility due to reduction in sperm count in males. Conclusion: Adiposity is confirmed as risk factor for male infertility in local population.

Keywords: BMI, Male Infertility, Prolactin, Azoospermia, Oligospermia.

Introduction and Background:

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). Variation 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 toward 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). An intact hypothalamus-pituitary-testicular axis is required to initiate and maintain quantitative and qualitative normal spermatogenesis (8, 9).

Spermatogenesis and Steroidogenesis are two functions performed by the testis. Both of these functions are influenced by genetic, hormonal, biochemical and environmental factors (10). The endocrine control is exerted by the pituitary gland through the secretions of gonadotropins: FSH (Follicle stimulating hormone) and LH (Luteinizing hormone). Both LH and FSH are required for initiation of spermatogenesis. The pituitary itself is under the control of hypothalamus via the gonadotropin releasing hormone (GnRH). Stimulation with LH resulted in bio synthesis and secretion of T from Leydig cells (11, 12). T secretion is regulated by feedback mechanism of LH. When Leydig cells are congenitally defective the testes remain intra—abdominal and there is lack of androgen-dependent differentiation of the internal and external genitalia. Leydig cells make 95% of the total T concentration(13). Leydig cells utilize cholesterol, which is a main reservoir for T synthesis (14).
Hypogonadotropic hypogonadism, which is failure of the pituitary gland to produce adequate amounts of FSH and LH, can lead to decreased sperm counts and a state of infertility (15,16). Normal serum concentration of Prolactin (PRL) have been shown to exert permissive roles in the male reproductive tract but excessive serum PRL concentration is correlated with infertility, hypogonadism, impotence and galactorrhea (17). The changes in LH and FSH may be the reason that causes the dysfunction of spermatogenesis and sperm maturation in patients with idiopathic azoospermia and oligospermia (18).

PRL is a hormone which is produced by the pituitary gland in the absence of its controlling factor which is called dopamine. PRL, as the name suggests, is the milk-making hormone which sharply increases in pregnant women to enable them to lactate. However this hormone can be secreted excessively in women without pregnancy, and also in men. The high levels of PRL affect the normal functioning of the testes and are indirectly responsible for defective spermatogenesis (75). Hyperprolactenemia in men is responsible for lack of libido. The rise in the level of PRL may be due to several factors including the use of drugs such as anti-depressants, tranquilizers and anti-vomiting agents. Another cause of high PRL is the presence of small tumors in the pituitary gland which can be detected by CT scan or MRI. Normally, treatment with bromocriptine (dopamine antagonist) restores normal levels of PRL. In case the tumor in the pituitary gland is large, surgical removal of the growth is carried out. PRL is determined in subjects with galactorrhea, androgen deficiency and loss of libido (19,20).

High levels of PRL interfere with the production of FSH and LH, which in turn will affect the testicular function. In men, high PRL concentration causes decrease in sexual potency. Hyperprolactenemia can cause both reproductive and sexual dysfunction(19,20).Association between adiposity with sex hormone have evaluated by several prior studies and shows synergy between obesity in their association with various hormone levels like estrone, estradiol and prolactin (21,22).Raised level of body mass index (BMI) has lower the polactin and testosterone levels but no significant impact on semen parameters of sperm quantity and quality.(23,24,25), Several studies have assessedThe relationship between adiposity and physical activity with prolactin levels have observed by several studies , with varying results (23,26,27). Some (28,29,30) studies in female suggest an raised levels of

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serum Prolactin after a bout of vigorous exercise but in males the its not clear yet.Adipocytes have prolactin receptors shows a positive influence of prolactin on growth and development of adiposite in an animal model study. (31),

Study Objectives: To determine the association between BMI (body-mass index) and serum prolactin levels in male patients. To correlate the levels of serum prolactin with infertility in male patients.

Methadology:A cross sectional study was conducted on the patients attending outpatient department (OPD) of Aziz Medical Hospital and Jinnah Post Graduate Medical Center(JPMC) from June 2010 to May 2011. 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 PRL only.

Materials and Methods: Total no 147 infertile 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**.**

Study design: It was a case control study.
Study Duration: The duration of study was one year.
Sample Size:147 infertile male and 153 healthy fertile males
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Sampling Techniques: Sampling technique was non probability, purposive sampling.
Study Population: This research involves human subjects, 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.
Ethical statement: The study was approved from Institutional Review Board (IRB), the Board of Advanced studies and Research (BASR) and funding committee of DUHS.
Determination of Prolactin level: The quantity of PRL in human serum is measured by the help of "EI".
A-PRL" kit which works at the principal of micro plate immunoassay
Semen analysis: Semen analysis was used to assess the quantity and quality of spermatozoa and seminal fluid (32).After taking detailed history, the process of semen collection was verbally explained to the patients.
Statistical Analysis:
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.

Results
Table 1 shows descriptive characteristics of the 300 study subjects which included 153 control healthy fertile male and 147 primary infertile male. The common age group in infertile study group and controls were 20-40 years followed by mean age of infertile study group is 30.30± at 95%C.I (34.53,32.18) where as in control healthy males mean age is 36.7 ±6.3 at 95% C.I (37.68,35.7) years as shown in Table:1.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.The mean value of sperm count of infertile males 41.2±41.4 millions/ml with 95%C.I (48.0,34.5) and fertile group mean sperm count was 112±23.9 millions/ml with 95% C.I (116.0,108.4) and it is also shown that there is significant difference in sperm count between infertile male and healthy fertile group.

Table: 1 Descriptive statistics of fertile and infertile study subjects

VARIABLES	p value (< 0.0.5)	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< 0.01	75.4±12.6	73.4	77.5	70.5±12.5	68.05	72
Height(m^2)	0.962	1.67±0.07	1.66	1.68	1.7±0.7	1.68	1.71
FBS	< 0.01	99.7±34.3	94.1	105.3	91.8±11.3	89.6	94.1
BMI	< 0.01	26.7±4.3	26	27.5	24.3±3.7	23.6	25.1
PRL(mIU/ml)	< 0.01	16.9±2.1	13.5	20.4	9.6±3.3	9.1	10.1
Sperm Count	< 0.01	41.2±41.46	34.5	48	112±23.9	108.4	116

Table: 2 Biophysical And Endocrine Profiles Of Studied (Infertile)Group With Their Mean (SD) And 95% Confidence Interval

Parameters	Mean(SD)	95% CI
Age(years)	33.30±7.2	(32.1,34.48)
BMI kg/m^2	26.7±4.3	(26.0,27.5)
PRL hormone (mIU/ml)	16.9±2.1	(13.5,20.4)

The mean age of the studied group was 26.7±4.3 years with 32.1years as the lower limit and 34.48 years as the upper limit of 95% confidence interval. Body mass index was also calculated after height and weight measurement, which was observed as 26.7±4.3 kg/m^2 with 26.0 as the lower limit and 27.5 as the upper limit of 95% of confidence interval. 20.7± 1.0mIU/m was discovered as the mean value for follicular stimulating hormone and had 19.0 mIU/ml as the lower limit and 20.7 mIU/ml as the upper limit of 95% confidence interval. Mean PRL hormone value was illustrated as 16.9±2.1mIU/ml with 13.5as the lower limit and 20.4 as the upper limit of 95% confidence interval.(Table:2)

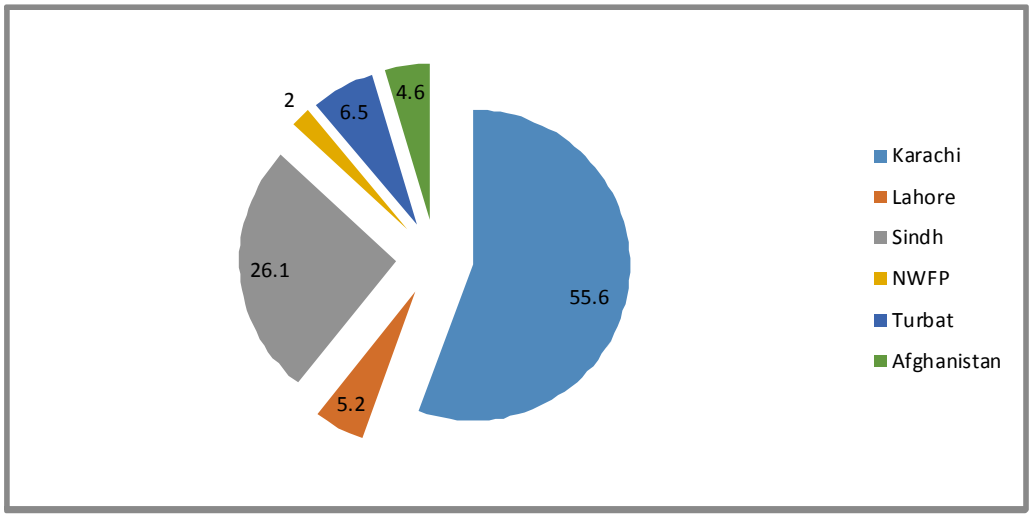

Figure: 1 (A) Shows Distribution of Infertile Group Coming From Different Areas

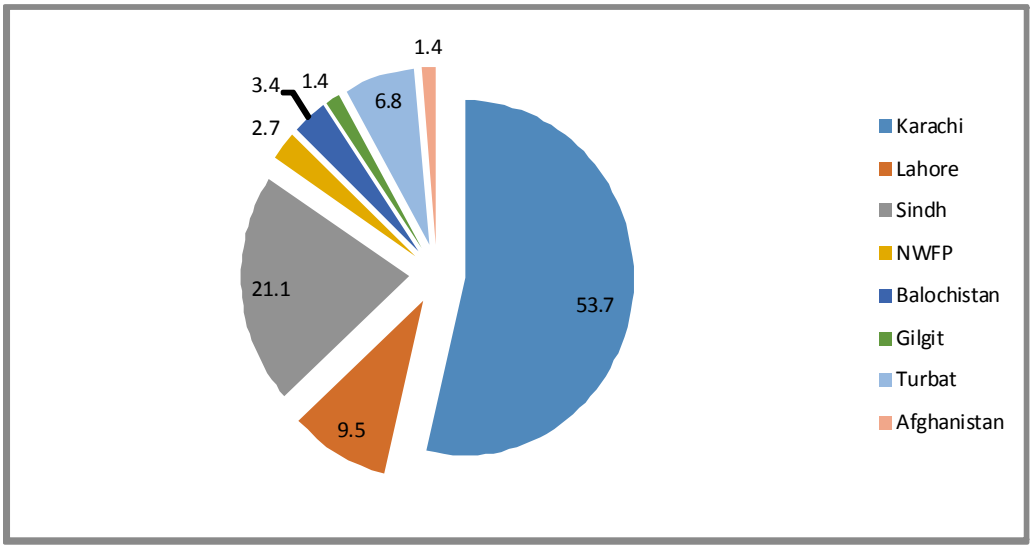

Figure.1 (b) Shows distribution of fertile group coming from different areas

It was observed in the studied infertile males that 63.9% of patients had PRL falling in the normal range that is 1.8-17mgIU/ml. Only 36.1% of patients had PRL level above 17mIU/ml.(Table :4)

Table: 4 Frequency Distribution Of PRL In infertile Male

PRL mgIU/ml	n=147	%
Normal Range 1.8-17mgIU/ml	94	63.9
Grater than 17 mgIU/ml	53	36.1

It was observed that PRL showed no correlation to BMI, (r= - 0.186, P<0.05). Sperm concentration was found to be significantly lower in men with a BMI greater than 25 as compared to men with BMI less than 25.(Table:3)

Table:3 Correlation between BMI and other variables under study

	BMI	Sperm motility	sperm count	PRL
BMI	1	0.138*	-0.250*	0.055
Sperm motility		1	-0.231*	0.122*
sperm count			1	-0.239*
PRL				1

***. Correlation is significant at the 0.05 level**

Discussion

Male infertility has become a very common problem and causes severe mental anguish and anxiety to sufferers. It is difficult to assess prevalence of infertility in developing countries. The perceptual experience of infertility in Pakistan is almost the same as in different parts of the world, except the fact that infertile males are reluctant to report for evaluation in the study's country. Demographic health surveys data provided by WHO (2004) showed that female primary infertility prevalence in Nepal was 6%, in Korea 2%, in Indonesia 7 % ,India 3%, Bangladesh 4% and Pakistan was 4%. However, the prevalence of male infertility in Pakistan is 7%. Rahim et al in Pakistan has concluded in their study (33) that 50% cases of infertility are due to male factor. The frequency of infertility was 12%, that due to male factors is 45%, while 41.64% caused by female factors, was unexplained in 7.50%, and both parties were involved in 5.70% of infertile study group.

Among various causes of male infertility, obesity was one of the leading factors (34), but the relationship of BMI with spermatogenesis and reproductive hormone is certainly not straightforward.Another study conducted by Jorge et al in Boston, Massachusetts determined the relationship of BMI with DNA integrity and semen quality (35).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 (34).

Association between Serum Prolactin and BMI:

Mean value of PRL is 9.6 (mIU/ml) in healthy control group and 16.9 (mIU/ml) in infertile males, almost in accordance with the values reported by a study in Pakistan and worldwide previous data (35).Hyperprolactinemia is associated with infertility in females (36,37) as well as in males. Extreme high PRL levels are associated with loss of libido and low serum T levels. These observations led to the evaluation of therapy with bromocriptine, which reduces PRL secretion (38).
In Israel, Laufer et al evaluated Israeli infertile men after bromocriptine treatment , and concluded positive association between raised PRL levels and impotency. Hyperprolactinemia interferes with sperm production and sperm motility. They noticed a marked increase in sperm motility in oligoasthenospermic subjects after bromocriptine therapy(39).

In Spain (40) Doknic et al in 2002 reported that obesity is associated with prolactinomas and weight reduction normalized the PRL levels.Raised serum PRL levels promote obesity by several ways: (39)

1) By stimulation of lipogenesis.
2) Reduction of dopaminergic tone.
3) By disruption of circadian neuroendocrine tone.

Greenman et al (41) conducted a retrospective study to establish the relationship between hyperprolactinemia and body weight in obese infertile males. They found that

decreased serum leptin and BMI levels after bromocriptine therapy.

Primary hyperprolactinamia leads to obesity with BMI greater than 30kg/m^2 and secondary hypogonadism (170). Increased Body mass index (BMI) is associated with androgen deficiency; an androgen deficit is thus related with reduced muscle mass, osteoporosis, and a higher incidence of bone fractures. In addition to its negative effects on body composition, the androgen deficit also causes impaired libido and sexual dysfunction and might lead to depression (42,43). A retrospective study by Creemers et al concluded no association between body weight reduction and degree of hyperprolactinemia.(44)

Conclusion

Hence we concluded that the BMI > 30 is associated with altered sperm count in obese males and no correlation between BMI and serum PRL levels.

Recommendations for further studies

We recommend that BMI can be used as an indicator for obesity and use to measure the risk not only for obesity but for reproductive health measure. Further studies for DNA damages studies for mutation and Y chromosomes deletion should be carried out to ascertain the hazardious effect of obesity and raised BMI on reproductive health.

Acknowledgements

Professor Nazrul Hasnain, Professor Masood Qureshi, ,Dr.Nadeem Alum, Muhammad Owais,

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How to Cite this Article: Fahmida khatoon, Abd-Elnaser Badawy, "Association between BMI and Prolactin Levels in Male Patients" Science Journal of Medicine and Clinical Trials, Volume 2013, Article ID sjmct-259, 6 Pages, 2012, doi: 0.7237/sjmct/259