Correlation between Obesity and Semen Interleukin-6 with Sperm Concentration and Motility in Iraqi infertile Men

Rehab Al Maliki[1] ;M.Sc. , Mohammad O. Selman[1] FIBMS , Thaer M. Farhan[2] FIBMS and Anam Al Salihi[2] ;Ph.D.

1- High Institute for Infertility Diagnosis and ART/ Al-Nahrain University,Baghdad,Iraq
2- College of Medicine ,AL-Nahrain University

Abstract:

Background

Obesity has been defined as abnormal or excessive fat accumulation that may impair health while the Body mass index (BMI) is a simple index of the weight-to-height ratio that is commonly used in classifying overweight and obesity in adult populations. Many semen parameters alteration can be ascribed to obesity like decreased sperm concentration, abnormal morphology, compromised chromatin integrity and abnormal motility. Many evidences showed an adverse effect of excess body fat on spermatogenesis.

Methods

A total sample size composed of (70)infertile men were grouped into three groups according to published BMI ranges as follows: normal weight, overweight and obese .A single semen sample was collected for each infertile men.Heightin (m) and weight in (kg) were recorded on day of semen collection .BMI was calculated as BMI= Kg\m2. Sperm parameters evaluated according to World Health Organization guidelines.Quantitation of the IL-6 in seminal plasma were accomplished using commercially available ELISA kit.

Results

In the current study, a positive correlation was found between body mass index and IL-6, on the contrary, a significant negative correlation was found among IL-6 level and progressive sperm motility and sperm concentration as well.

Conclusion

There is an increase of IL-6 from the adipose tissue with increasing BMI. The IL-6 cause reduction of the sperm motility by increasing the level of ROS. The obesity reduces the spermatogenesis by androgenic deficiency results in low sperm concentration and motilitywhich it may be the main reason of their infertility.

The aim of the study: to evaluate the correlation between the obesity and IL-6 and their effects on sperm concentration and motility.

Introduction

Obesity has been defined by the World Health Organization (WHO) as "abnormal or excessive fat accumulation that may impair health, (1)
Body mass index (BMI) is a simple index of the weight-to-height ratio that is commonly used in classifying overweight and obesity in adult populations. (2)

Adipose tissue secretes two main classes of molecules known as adipocytokines and adipose-derived hormones. These substances are especially significant because they have been implicated in creating a chronic state of inflammation and hyperinsulinemia in obese individuals, both of which have been associated with abnormal reproductive function (3). Obesity is also associated with immunological abnormalities which are probably result from intricate adipose-immune interactions (4,5)

The state of chronic low-grade inflammation has long been thought to be primarily due to an accumulation of proinflammatory macrophages within the adipose tissue and the production of proinflammatory cytokines by adipocytes and macrophages, such as tumor necrosis factor- alpha (TNF-?) and interleukin-6 (IL-6) (6).

Both IL-6 and TNF-a promote leucocyte production of Reactive Oxygen Species (ROS) (7).Altered semen parameters ascribed to obesity include decreased sperm concentration, abnormal morphology, compromised chromatin integrity and abnormal motility. Although there is a convincing amount of evidence to show an adverse effect of excess body fat on spermatogenesis, not all studies have come to the same conclusions (2, 8,9,10,11and 12)
The aim of the study: to evaluate the relationship between obesity and IL6 and their effects on sperm concentration and motility.

Material and methods

Semen was collected by self-masturbation from (70) healthy infertile males attended to High Institute of Infertility Diagnosis and ART. Their age between (26-45) years presenting for routine semen analysis testing. A single semen sample was collected for each infertile male. Samples were then diluted with an equal volume of sterile phosphate-buffer saline ,mixed thoroughly and centrifuge for 10 min. at 400×g .Diluted seminal plasma was removed aliquotted and frozen at -40C? (13) The men should not have previous surgery (e.g. vasectomy reversal or varicocele removal. Infertile males were grouped according to published BMI ranges as follows : 20-24.99 kg/m2 is classified as normal weight, 25-30 kg/m2 as overweight, greater than 30 kg/m2 as obese .
Infertile male height (m)and weight (Kg) were recorded on day of semen collection .BMI was calculated for each patient according to the following equation, BMI= Kg/m2. Semen specimens permitted to liquefy for 60 minutes at 37??. Sperm parameters evaluated according to World Health Organization guidelines 1999. (14)
Detection and quantitation of the IL-6 in aliquots of thawed seminal plasma were accomplished using commercially available Enzyme -Linked Immunosorbent Assay (ELISA) kit.. (15)

Statistical analyses:

The data were statistically analyzed using SPSS/PC version 19 software (SPSS, Chicago). Sperm parameters (concentration, progressive motility and total motility) were analyzed using one way ANOVA complete randomized design (CRD). Differences among means (BMI groups) were computed using the Duncan multiple ranges test (Duncan, 1955). The correlation between IL6, BMI and sperm parameters were carried out by Person correlation. (16)

Results:

Figure(1) demonstrate the correlation between body mass index and IL-6 level in seminal plasma of infertile men.There was highly significant (P<0.01) positive correlation between body mass index and IL-6 level Correlation coefficient and probability level were 0.890 and 0.0007 respectively.

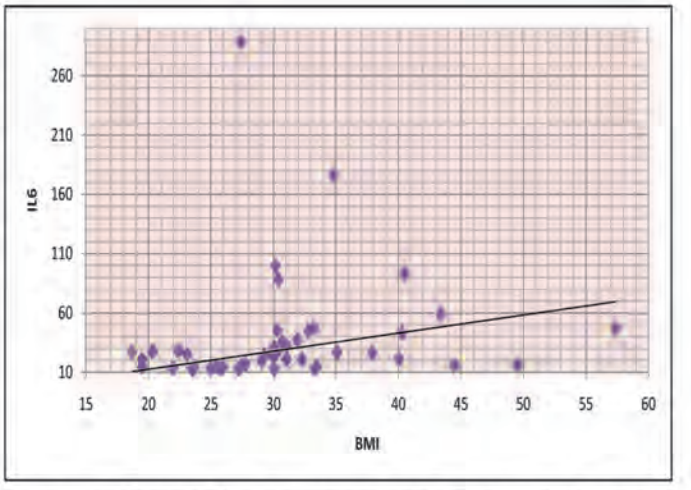

Figure1: Correlation between body mass index and IL-6 level in seminal plasma of infertilemen.
R=0.890
p.v.=0.0007**

Highly significant (P<0.01) negative correlation was appeared among IL-6 level and progressive sperm motility (%), non-progressive sperm motility (%) and normal sperm morphology (%). So, significant (P<0.05) negative correlation was observed between IL-6level and sperm concentration. (Table 1)

Table 1: Correlation between sperm parameters IL-6level in seminal plasma of infertile men.

Pearson Correlation of IL6	Immotile sperm	Non-prog.motile sperm	Prog.motile sperm	Concent.
	-0.294	-0.329	-0.335	-0.276
Sig.	0.012 *	0.005 **	0.004 **	0.019 *

**: Highly significant (P<0.01)
*: significant (P<0.05)
NS: non-significant (P>0.05)

The results of sperm parameters when compared between normal, over weight and obese groups are showed in Table (2) Non significant differences for all groups were noted in the results of non-progressive sperm motility (%) and immotile sperm (%). However, a significant decrease (P<0.05) in the sperm concentration, non-progressive sperm motility (%) and normal sperm motility was showed in obese group when compare with other groups.

Table 2: sperm parameters in infertile men when comparing between normal, over weight and obese groups.

Sperm Parameters	BMI		
	Normal	Over weight	Obese
Concent.	41.458 a ±5.85	51.217 a ±6.54	27.160 b ±5.83
Prog.motile sperm	32.000 a ±3.57	34.087 a ±4.16	23.880 b ±4.11
Non-prog.motile sperm	18.708 a ±2.16	19.348 a ±2.24	15.040 a ±2.39
Immotile sperm	32.708 a ±3.83	33.609 a ±3.63	29.440 a ±5.18
Normal sperm morpho%	25.458 a ±2.82	27.130 a ±2.79	18.160 b ±3.28

* Means with different superscripts within each row are significantly different (P<0.05).
* Means with similar superscripts within each row are non-significantly different (P>0.05).

Discussion

Similar to the present results, different studies have documented that IL-6 showed a significant positive correlation with BMI which reported that there was a tendency for increase in IL-6 secretion from adipose tissue with increasing BMI and increasing body fat.(17,18)
Highly significant (P? 001) negative correlation was detected among IL-6 level and progressive sperm motility, this is in agreement with other studies who demonstrated that the IL-6 significantly reduced sperm progressive motility (10,18,19) on the other hand there was significant positive correlation between IL-6 and reactive oxygen species (ROS) (20). High concentration of ROS cause sperm pathology (ATP depletion) leading to insufficient axonemal phosphorylation, lipid peroxidation and loss of motility and viability (21,22,23). We can conclude that IL-6 cause reduction of sperm motility by increased level of ROS which cause sperm pathology (ATP depletion) and loss progressive motility.
In current study, a significant (P? 0.05) negative correlation between IL-6 level and sperm concentration was found, this result agreed with (Furuya,Y.andNandipati, K.C.et al) who demonstrated that there is inverse correlation between IL-6 and sperm concentration in infertile patients (20.24).the cause of this result was explained by (huijuan,Z. et al) who demonstrated that the over expression of IL-6 could disrupt the integrity of sertoli cells, blood testis barrier and ultimately impair spermatogenesis(20,22,25,26,27).
Many studies have examined the correlation between obesity and sperm parameters, in the present study there was a significant decrease (P? 0.05)in sperm concentration and normal sperm motility in obese group when compare with other groups this results agreed with other studies which reported that BMI has direct negative correlation to sperm parameters and that BMI is associated with low motile sperm count and low sperm concentration (14,20,28,29). this may be due to the fact that the visceral obesity can serve as a major endocrine disrupter and can also influence the endocrine interaction by reducing the level of luteinizing hormone and testosterone ,moreover androgen deficiency or hypogonadism found in males who are obese or have metabolic syndrome can account for problems with spermatogenesis and erectile dysfunction (30,31), Thus, one can conclude that the obesity reduces spermatogenesis by androgen deficiency result in low sperm concentration and low normal sperm motility which it may be the main reason of their infertility.

References:

1- World Health Organization. Office of Health Communications and Public Relations. Obesity and overweight .Geneva: World Health Organization:2006
2- Booth ML.HunteC.,GoreC.J.,BaumanA.,Owen N. The relationship between body mass index and waist circumference:implications for estimates of the population prevalence of overweight.
Int.J.Obes.Relat.Meta.Disord.2000:24:1058-61
3- Pitas AG.NA Joseph. Adipocytokines and insulin resistance J Clin. Endocrinol metab.2004: 89(2) :447-452
4- Moulin CM , Marguti L , Peron j P et al. Impact of adiposity on immunological parameters. Arq. Bras. Endocrinol.Metabol.2006: 53: 183-189.
5- Dixit VD. Adipose-immune interactions during obesity and caloric restriction: reciprocal mechanisms regulating immunity and health span. J Leukoc.Biol. 2008: 84: 882-892.
6- Sell H, Eckel J. Adipose tissue inflammation: novel insight into the role of macrophages and lymphocytes. Curr. Opin. Clin. Nutr. Metab.Care. 2010: 13:366-370.
7- Tune O, Bakos HW. Impact of body mass index on seminal oxidative stress. Andrologia. 2011: 43(2): 121-128.

8- Swan SH, Elkin EP,andFenster L., The question of declining sperm density revisited an analysis of 101 studies published 1934-1996.Environ. Health Perspect. 2000:108:961-966.
9- Jensen TK,Andersson AM, Jorgensen N,et al. Body mass index in relation to semen quality and reproductive hormones among 1.558 danish men. FertilSteril. 2004:82:863-70.
10- Martini AC, tissera A, Estofan D, et al. Overweight and seminal quality: a study of 794 patients. Fertil. Steril. 2010: 94(5):1739-1743.
11- Hammoud AO, Wilde N, Gibson M, et al. Male obesity and alteration in sperm parameters. Fertil. Steril. 2008: 90:2222-2225 12- Smit M, Romijn JC, Wildhagen MF, et al, Sperm chromatin structure is associated with the quality of spermatogensis in infertile patients. Fertil .Steril. 2009{ Epub ahead of print}
13- Joseph A.P, Lynne T, Frederick P,B et al.Concentrations and significance of cytokines and other immunologic factors in semen of healthy fertile men. Human Reproduction.2007: 22(11):2928-2935.
14- Hilton I K, Joe B M, Carlene W E, et al. Impact of body mass index values on sperm quantity and quality. J. Andro.2006: 27(3): 450-452.
15- Quantikine: Human IL-6 Immunoassay, Tools for cell biology research, Catalog No. D6050, 560, 50, PD6050. R&D Systems.www.RnDSystems.com at 1/6/2014
16- Duncan, D B., Multiple range and multiple F tests. Biometrics ,1955:11:1-42
17- Riham GM, Azza M AA, Seham A K,et al. frequency of distribution of interleukin-6 gene 174G C polymorphism in obese Egyptian cohort. J. Am. Science 2011:7(8): 788-794.
18- Philip A K, Subramanian R, ChunlingLI,et al. Adipose tissue tumor necrosis factor and interleukin-6 expressionin human obesity and insulin resistance .Am. J. PhysiolEndocrinnol. Metab. 2001:280: 745-751.
19- Lampiao F, du Plessis SS.TNF-alpha and IL-6 affect human sperm function by elevating nitric oxide production.Reprod. Biomed Online. 2008:17(5): 628-631
20- Nandipati K C,Pasqualotto F F,Thomas AJ Jr and Agarwal A. Relationship of interleukin-6 with semen characteristics and oxidative stress in vasectomy reversal patients. Andrologia. 2005:37(4): 131-134
21- Amrit K B, and Bilaspuri G S. Impacts of oxidative stress and antioxidants on semen function. Veterinary Medicine International .2011: 2011: 686137-686148.
22- Eve D L, Hong J, Armand Z,et al . Reactive oxygen species and sperm physiology. Reviews Reproduction. 1997: 2:48-54.
23- Guthrie HD,and Welch G R. Effects of reactive oxygen species on sperm function. International J. Animal Reproduction.2012:78(8): 1700-1708.
24- Furuya Y, Akashi T and Fuse H. Soluble fas and interleukin-6 and interleukin-8 levels in seminal plasma of infertile men.Arch. Androl. 2003:49(6): 449-452.
25- Rival C,Theas, M.S., Guazzone, V.A.andLustig, L. interleukin-6 and IL-6 receptor cell expression in testis of rats with autoimmune orchitis. JReprodImmunol. 2006:70:43-58.
26- Boockfor, F. R.and Schwarz, L. K. Effects of interleukin-6, interleukin-2 and tumor necrosis factor alpha on transferring release from Sertoli cells in culture. Endocrinology. 1991:129:256-262.
27- Okuma, Y.et al. Regulation of activin A and inhibin B secretion by inflammatory mediators in adult rat Sertoli cell cultures. J Endocrinol. 2005:187:125-134
28- Sallmen, M and Sandler D. P. Reduced fertility among overweight and obese men. Epidemiology. 2006: 17(5): 520-523
29- Hammoud, A.O. and Gibson. Impact of male obesity on infertility: a critical review of the current literature. FertilSteril. 2008: 90(4): 897-904.
30- Strain, G. W. Zumoff, B. Kream, J. et al. Mild hypogonadotropic hypogonadism in obese men. Metabolism. 1982:31: 871-875
31- Tsai, E.C. Matsumoto, A. M. Fujimoto, W. Y. Boyko, E.J. Association of bioavailable , free and total testosterone with insulin resistance influence of sex hormone-binding globulin and body fat. Dabetes Care. 2004:27:861-868.