

## Study the Relationship Between Obesity and Fertility in Diabetic Iraqi Men دراسة العلاقة بين السمنة والإخصاب عند الرجال العراقيين المصابين بداء السكري

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### Abstract

The aim of the present study is to investigate the relationship between obesity and fertility in Iraqi diabetic men whose body mass index (BMI) more than  $25\text{Kg/m}^2$ , and compare the results with control group corresponding age and BMI. Forty samples of men semen's were divided into two groups with and without diabetes and each group subdivided into two subgroups according to BMI. The parameters that measured in this study are (glucose, insulin and lipid profile in fasting state) also (testosterone, prolactin, alkaline phosphatase) were measured for each of four subgroups [controls(I, II) and diabetes(III, IV)]. Semen's analysis included (sperm concentration in ml, total count per ejaculate and viability). In diabetic subgroup (III) the mean levels of fasting blood glucose, insulin, cholesterol and triglycerides were significantly elevated, while significantly decrease in testosterone, prolactin, high density lipoproteins-cholesterol, alkaline phosphatase and total sperm count but there were no significant difference in total cholesterol, the sperm concentration and viability as compared with control subgroup(I). In diabetic subgroup (IV) the mean levels of fasting blood (glucose, insulin, cholesterol and triglycerides) were significantly elevated, while significantly decrease in (testosterone, prolactin, high density lipoproteins-cholesterol, alkaline phosphatase, sperm concentration, viability and total sperm count) but there were no significant difference in fasting (insulin and high density lipoproteins- cholesterol) as compared with control subgroup(II). In diabetic subgroup(III) the mean of BMI and the mean levels of fasting blood (glucose, total cholesterol and triglycerides) significantly elevated, while there were significantly decrease in(testosterone, alkaline phosphatase, sperm concentration, viability and total sperm count but there were no significant difference in fasting (insulin, high density lipoproteins- cholesterol) and prolactin, as compared with diabetic subgroup(IV). For all the above biochemical parameters investigated we can conclude that there is inverse- relationship between obesity and fertility which increase in the presence of diabetes.

Key words: BMI, obesity, diabetes mellitus, fertility, hormones, semen analysis, alkaline phosphatase enzyme

### المخلص

إن الهدف من الدراسة الحالية هو التحري عن العلاقة بين السمنة والإخصاب عند الرجال العراقيين المصابين بالسكري والذين يملكون مقياس كتلة الجسم أكبر من  $25\text{كجم/م}^2$  ومقارنة النتائج مع مجموعة السيطرة المرادفة في العمر ومقياس كتلة الجسم. حيث تم أخذ أربعين عينة من السائل المنوي للرجال وقد قسمت إلى مجموعتين مصابين وغير مصابين بالسكر وكل من هاتين المجموعتين تم تقسيمهما إلى مجموعتين فرعيتين وفقاً لمقياس كتلة الجسم. إن العوامل التي تم قياسها في هذه الدراسة في حالة الصيام هي (الكلوكوز، الأنسولين، الشكلة الشحمية) وقد تم قياس (التستوستيرون، هرمون الحليب، إنزيم الالكالين فوسفاتيز) لكل من المجموعتين الفرعيتين الأربعة مجموعتي السيطرة (I, II)، والمجموعتين المصابتين بداء السكري (III, IV). وقد اجري تحليل المنى المتضمن (تركيز الحيامن بالمل، العدد الكلي لكل قذفة و حركتها). أظهرت النتائج إن هناك زيادة في معدلات المجموعة الفرعية المصابة بداء السكري (III) في حالة الصيام لمستوى (الكلوكوز بالدم، الأنسولين، الكولسترول، التراي كليسايد). بينما هناك انخفاض معنوي في مستوى (التستوستيرون، البرولاكتين، كوليستيرول البروتينات الشحمية عالية الكثافة، والعدد الكلي للحيامن، الالكالين فوسفاتيز). لكن لا يوجد فرق معنوي بـ (الشكلة الشحمية، تركيز وحركة الحيامن بالمقارنة مع مجموعة السيطرة الفرعية (I). بينت النتائج إن هناك زيادة في معدلات المجموعة الفرعية المصابة بداء السكري (IV) لمستوى مقياس كتلة الجسم و مستوى (الكلوكوز بالدم، الكوليستيرول، التراي كليسايد) في حالة الصيام. بينما هناك انخفاض معنوي في مستوى (التستوستيرون، الالكالين فوسفاتيز، تركيز الحيامن، حركتها وعددها الكلي). لكن لا يوجد فرق معنوي بـ (الأنسولين، كوليستيرول البروتينات الشحمية عالية الكثافة، والبرولاكتين) بالمقارنة مع مجموعة السيطرة الفرعية (II) كذلك هناك زيادة في معدلات المجموعة الفرعية المصابة بداء السكري (III) لمستوى (الكلوكوز بالدم، الأنسولين، الكوليستيرول، التراي كليسايد). بينما هناك انخفاض معنوي في مستوى (التستوستيرون، البرولاكتين، كوليستيرول البروتينات الشحمية عالية الكثافة، الالكالين فوسفاتيز والعدد الكلي للحيامن) لكن لا يوجد فرق معنوي بـ (الشكلة الشحمية، تركيز وحركة الحيامن) بالمقارنة مع المجموعة الفرعية المصابة بداء السكري (IV). يمكن الاستنتاج من كل المؤشرات البيوكيميائية والتي تم التحري عنها، إن هناك علاقة عكسية بين السمنة والإخصاب تزداد بوجود مرض السكري.

الكلمات المفتاحية :- مقياس كتلة الجسم، السمنة، مرض السكري، الخصوبة، الهرمونات، تحليل المنى، إنزيم الالكالين فوسفاتيز

### Introduction

Diabetes mellitus (DM) is a chronic condition caused by inherited and / or acquired deficiency in production of insulin from beta cells of pancreas, or ineffectiveness of the insulin. It is an extremely common metabolic disorder affecting

carbohydrate, fat and protein metabolism. characterized by hyperglycemia, glucose urea and negative nitrogen balance . There are two types of diabetes, type I (insulin-dependent), type II (non insulin-dependent) [1]. Diabetic patients generally experience sexual abnormalities like sexual dysfunction, impotence and infertility [2]. Because of the paucity of studies and inconsistencies regarding the impact of DM on semen quality, this disease is seldom looked for in the infertile patient. Recently, this view has been challenged by findings showing that DM induces subtle molecular changes that are important for sperm quality and function. In addition, DM causes histological damage of the epididymis, with a negative impact on sperm transit. Various mechanisms may explain the sperm damage observed in diabetic patients. These include endocrine disorders, neuropathy, and increased oxidative stress. Many authors suggest that DM decreases serum testosterone levels. This is associated with a steroidogenic defect in Leydig cells. In addition, diabetic neuropathy seems to cause atonia of seminal vesicles, bladder, and urethra. Furthermore, DM is associated with an increased oxidative stress, which damages sperm nuclear and mitochondrial DNA [3]. Various experiments conducted on streptozotocin (STZ) induced diabetic rats supported the relation between male infertility and diabetes mellitus [2]. Diabetes is a serious condition associated with overweight and obesity. In obesity excess fat, or white adipose tissue, accumulates in the body to the extent adversely affect health, potentially reducing life expectancy. An individual can be defined as being overweight if their BMI ranged between 25–30 kg/m<sup>2</sup>, and being obese if their BMI exceeds 30 kg/m<sup>2</sup> [4] Obesity is considered now as an epidemic disease that is rapidly progressing in developed and under developed countries [5]. The effects of obesity not only related to chronic medical conditions but also have been strongly related to reproductive problems. Obesity has been proposed to affect male fertility by induce changes in and sexual behavior, sex hormones, scrotal temperatures, libido and semen parameters [4]. This spectrum of expression of hypogonadism among obese men originates from multiple interacting factors including reduced levels of gonadotropins and testosterone, altered androgen-to-estrogen ratios, insulin resistance, and sleep apnea [6]. The continuing rising the prevalence of obesity and declining male sperm count all over the world call for additional research and a greater awareness to obesity as a potential etiology of male infertility [7]. The present work aimed to study the correlation between obesity and infertility in Iraqi diabetic men.

## Material and methods

### Experimental design

In the present study, forty individual were divided into two groups [Without DM (controls) and With DM]. Each one were divided into two subgroups as follow: Subgroup(I) BMI  $\leq$  25kg/m<sup>2</sup> without DM, Subgroup ( II) BMI  $\geq$  25kg/m<sup>2</sup> without DM, Subgroup( III) BMI  $\leq$  25kg/m<sup>2</sup> with DM and Subgroup( IV) BMI  $>$  25kg/m<sup>2</sup> with DM.

Subjects:

- Diabetic group

Twenty voluntaries individuals with DM were recruited from diabetic center. All these patients were previously diagnosed by physician and they were also evaluated by physical and full medical history.

- Control group

Two subgroups were recruited by volunteers through advertisement among laboratory and hospital staff .For comparison twenty apparently healthy men who were matched for age and BMI.

Data collected included patient demographics, past medical and surgical history, all men reported their weight and height, smoking, alcohol, any drugs abuse.

### Collections of the samples

#### A. Blood samples

Blood were obtained from the patients & healthy controls after an overnight fasting, venous blood samples were aspirated at (08:00 – 10:00) Am. Blood samples were collected into disposable plain plastic tubes, each sample volume was 10cc; and centrifuged at 3000 rpm, within 30 minutes of collection. Serum was used for measuring glucose, ALP and lipid profile at the same day, using the enzyme colorimetric methods. The rest of the serum was stored at -20 °c until the time of hormonal assay.

#### B. Semen's samples

Semen was collected by self-masturbation from all men under study. sperm concentration, viability and total sperm count were measured within one hour of collection.

### Chemicals

All chemicals and standard solutions in this work was of the highest analytical grade obtained from commercial sources and used without further purification. These chemicals are:

- Glucose kit  
Linear chemicals, S.L- Spain, this kit used for measured serum.
- Insulin ELISA kit.
- Testosterone and Prolactin kits biomerieux France .  
Estimated (by MiNi VIDAS device).
- Alkaline phosphatase kit.  
Human Gesolischaft for Biochemica and Diagnostica mbH Max. Planck. Ring 21. D- 66205  
wiesbaden. Germany.
- Cholesterol, triglycerides, HDL-ch. Kits.  
Biomerieux, France.

## Methods

- Biochemical parameters measurements

Measurements of glucose, lipid profile and ALP have been done in laboratory by spectrophotometric device. While (insulin, testosterone and prolactin) hormones have been done by mene vidase device. The procedures estimating hormones and other biochemical parameters were followed the instruction administrated in the kits.

- Measurements of BMI

BMI obtained from Measuring the weight in (kilograms unit) and height in (meters unit) by using suitable scales and applied the following equation [8]. {BMI = weight / Height <sup>2</sup>}

- Semen's parameters calculations

Sperm parameters analyzed included sperm concentration (10<sup>6</sup> sperm /ml), viability(%) and total count (10<sup>6</sup>/ejaculate). Samples were assessed as described in WHO laboratory manual for the examination of human semen-cervical mucus interaction (World Health Organization, 1999).

- Statistical analysis:

Data were analyzed by one-way analysis of variance (ANOVA), data were presented as means ± SE. The level of significance was P ≤ 0.5 (analysis of data was performed by using statistical package for SPSS version 13).

## Results and Discussion

In the present study:-

1) In diabetic subgroup (III) the mean levels of fasting blood glucose, insulin, cholesterol and triglycerides were significantly elevated, in addition to presence of insulin resistance .while there were significantly decrease in testosterone, prolactin, high density lipoproteins- cholesterol, alkaline phosphatase and total sperm count but there were no significant difference in BMI, total cholesterol, the sperm concentration and viability as compared with control subgroup (I), and these data demonstrated in Tables (1,2,3 and 4).

2) In diabetic subgroup (IV) the means of fasting blood glucose, insulin, cholesterol and triglycerides were significantly elevated, in addition to presence of insulin resistance while there were significantly decrease in testosterone, prolactin, high density lipoproteins- cholesterol, alkaline phosphatase, sperm concentration, viability and total sperm count but there were no significant deference in BMI fasting insulin and high density lipoproteins- cholesterol as compared with control group(II), and these data demonstrated in Tables Tables (1,2,3 and 4).

3) In diabetic subgroup(III) the means of BMI fasting blood glucose, total cholesterol and triglycerides significantly elevated, in addition to presence of insulin resistance, while there were significantly decrease in testosterone, alkaline phosphatase, sperm concentration, viability and total sperm count but there were no significant difference in fasting (insulin, high density lipoproteins- cholesterol) and prolactin, as compared with diabetic subgroup(IV), and these data demonstrated in Tables (1,2,3 and 4) too.

**Table(1): The difference in mean of (BMI, blood glucose, serum insulin level and insulin resistance) among 4 subgroups.**

Parameters	(I) BMI ≤ 25 without DM	(II) BMI ≥ 25 without DM	(III) BMI ≤ 25 with DM	(IV) BMI ≥ 25 with DM
BMI Kg / m <sup>3</sup>	A	B	A	B
Mean ± SE	23.81 ± 3.42	35.26 ± 6.81	24.04 ± 6.22	37.95 ± 7.12
Glucose mmol / L	A	B	B	C
Mean ± SE	6.22 ± 1.64	7.97 ± 1.84	9.61 ± 2.07	12.27 ± 3.49
Insulin mIU / ml	A	B	B	B
Mean ± SE	5.38 ± 1.08	8.03 ± 2.44	7.72 ± 2.36	10.41 ± 3.63

Differences letters A,B,C are significant at (P ≤ 0.05) to compression columns.

**Table(2): The difference in mean of (lipid profile and alkaline phosphatase) among 4 subgroups.**

Parameters	(I) BMI ≤ 25 without DM	(II) BMI ≥ 25 without DM	(III) BMI ≤ 25 with DM	(IV) BMI ≥ 25 with DM
Lipid profile	TG	A	B	C
	Mean ± SE	82.43 ± 11.53	106.02 ± 20.33	113.46 ± 19.05
T. chol.		A	B	C
	Mean ± SE	162.78 ± 28.65	188.78 ± 40.21	184.71 ± 33.12
HDL		A	B	B
	Mean ± SE	43.82 ± 8.69	35.04 ± 9.01	37.22 ± 7.40
ALP U / I Mean ± SE		A	B	C
		133.26 ± 11.46	129.64 ± 6.33	127.52 ± 7.41
				118.62 ± 10.52

Differences letters A,B,C are significant at (P ≤ 0.05) to compression columns.

**Table(3): The difference in mean of (testosterone and prolactin) among 4 subgroups.**

Parameters	(I) BMI ≤ 25 without DM	(II) BMI ≥ 25 without DM	(III) BMI ≤ 25 with DM	(IV) BMI ≥ 25 with DM
Testosterone mmol / L	A	B	B	C
Mean ± SE	4.31 ± 0.94	3.68 ± 0.68	3.02 ± 0.61	2.43 ± 0.60
Prolactin ng / ml	A	B	B	B
Mean ± SE	11.24 ± 1.64	10.63 ± 1.92	10.21 ± 2.03	9.53 ± 1.84

Differences letters A,B,C are significant at (P ≤ 0.05) to compression columns.

**Table(4): The difference in mean of (concentration, viability and total count of sperm) among 4 subgroups.**

Parameters	(I) BMI ≤ 25 without DM	(II) BMI ≥ 25 without DM	(III) BMI ≤ 25 with DM	(IV) BMI ≥ 25 with DM
Concentration 10 <sup>6</sup> / ml	A	A	A	B
Mean ± SE	52.64 ± 8.73	50.33 ± 6.69	47.30 ± 7.02	20.66 ± 3.48
Viability %	A	A	A	B
Mean ± SE	72.34 ± 6.84	69.66 ± 10.35	63.28 ± 9.41	32.21 ± 7.62
Total count 10 <sup>6</sup> / ejaculate	A	A	B	C
Mean ± SE	91.68 ± 10.89	90.36 ± 8.47	74.26 ± 10.36	40.62 ± 9.74

Differences letters A,B,C are significant at (P ≤ 0.05) to compression columns.

In this study the patients grouped as normal weight and obese as in the subgroups(I,III) and (II,IV) respectively, according to the standard ranges of BMI [4]. BMI has some role in female fertility; however, little information is available on the impact of BMI on male fertility. An inverse relationship between BMI and the values of total sperm count, sperm concentration, normal sperm morphology, and motility [9]. Hakonsen *et.al* [10] reported that there is a causal inverse association between BMI and semen quality. Kort *et.al* [9] found that BMI correlated negatively with the total number of normal spermatozoa, both hormone irregularities and body mass index is associated with alteration in sperm parameters. Men with high BMIs typically are found to have an abnormal semen analysis represented by decrease in sperm count (~ - 30.42%). This change were statistically significant as compared with the normal subjects [9]. These results were in agreement with the results of the present study, which illustrated in Table (4).

In the present study, the patients in the subgroups (III and IV) were suffer from DM, their results of fasting blood glucose levels were very high as demonstrated in Table (1). These results were in agreement with the criteria for the diagnosis of diabetes in which {FBG  $\geq$ 126 mg/dl (7.0 mmol/l)}[11].

Bener *et.al* [12] confirmed a strong association between type 2 DM and infertility in Qatari men. Also show that the prevalence of infertility in type 2 DM men was 35.1%, the prevalence of primary and secondary were 16% and 19.1%, infertility was significantly higher in patients with diabetes compared with patients without diabetes [12]. In addition, secondary infertility was higher than primary infertility. About half of the infertile men with diabetes were overweight, and 29.1% of them were obese [3].

Cavaliere, *et.al* [13]reported that in previous study, insulin levels for group of diabetic men, have been shown to influence the levels of sex hormone binding globulin (sHBG), a glycoprotein that binds to sex hormones, specifically testosterone and estradiol, thereby inhibiting their biologic activity as a carrier. High circulating insulin levels inhibit sHBG synthesis in the liver, where as weight loss has been shown to increase sHBG levels. While Jensen, *et.al* [14] reported that in obese males the decrease in sHBG means that less estrogen will be bound, resulting in more biologically active, free estrogen. In addition to the conversion of testosterone to estrogen in obese patients, the decreased ability of sHBG to sustain homeostatic levels of free testosterone also contributes to abnormal testosterone levels. Tsai, *et.al* [15] reported that the failure to maintain homeostatic levels might magnify the negative feedback effect of elevated total estrogen levels. These results were in agreement with the results of the present study in which increased of obesity and elevated in the insulin level in diabetic men lead to decreased in testosterone level, as the results reported in Table (1and3).

La Vignera *et.al* [3] suggest that DM decreases serum testosterone levels. This is associated with a steroidogenetic defect in Leydig cells.

Obesity is a major risk factor for diabetes Mellitus; obesity is permanently associated with unhealthy lipid profile characterized by high triglycerides and LDL-ch, and low HDL-ch [16]. Also it is well known that in uncontrolled diabetes mellitus, there will be an increase in total cholesterol, Triglycerides and LDL- ch associated with decrease in HDL- ch and contribute to coronary artery disease, which is related with significant changes in lipid metabolism and structure. Although abnormalities in cellular cholesterol level in diabetes, the precise mechanisms underlying these enzymatic changes not been elucidated. Such a significant increase in TG may be due to the lack of insulin under diabetic condition, while insulin activates the enzyme lipoprotein lipase and hydrolysis TG under normal condition [17]. These results were in agreement with the results of the present study, Table (2).

Arora *et.al* [18] reported that in previous study it conclude a proportional correlation between serum triglyceride level and BMI, with the highest triglyceride levels observed in overweight and obese patients. Many studies have shown an association between BMI and triglycerides, and the association between lipid profile and body fat distribution had been much discussed during the past decades. Both lipid profile and body fat have been shown to be the important predictors for metabolic disturbances including dyslipidemia, hypertension, diabetes, cardiovascular diseases, hyperinsulinaemia etc.

Obesity is associated with IR mainly via decreased number of insulin receptors. There is well known effect of obesity that amplified the IR state and increased insulin secretion to overcome the resistance, this might be due to fat excess that had an influence on sex hormone metabolism directly or indirectly by impairing insulin action [19]. Also resistin (adipose tissue specific factor) ,which is reported to induce insulin resistance. An increase in resistin secretion owing to a higher number of adipo cytes links obesity to type II diabetes. as a consequence of insulin resistance in patients with type II diabetes, high circulating levels of insulin are present in the blood stream. Hyperinsulinemia, which often occurs in obese men, has an inhibitory effect on normal spermatogenesis

and can be linked to decreased male fertility [4]. These results were in agreement with the results of the present study, which illustrated in Table (1 and 4).

The relationship between obesity and male infertility is multi factorial [20]. Obesity has significant negative effects on reproductive physiology and may interfere with many testicular functions. Also, it associated with alteration in semen parameters and serum sex hormones [16]. Over recent decade, several authors published that overweight and obesity are considered factors induced decreasing sperm counts [4]. Hammoud *et.al* reported that obese male are three times more than male of normal weight to have a sperm count less than 20 million/ml, known as oligospermia [21]. Chavarro. *et.al* they were found that men with a BMI greater than 25 kg/m<sup>2</sup> had a lower total sperm count than men of normal weight, and the measured volume of ejaculate decreased steadily with an increasing BMI [22]. These results were in agreement with the results of the present study, Table (4).

A decrease in the testosterone:estrogen ratio is consistently displayed in obese infertile men [4]. in a study by Aggerholm *et.al* they were conclude that obese men had 6% higher levels of estradiol and 25–32% lower levels of testosterone than normal men. The severity of obesity determines the degree to which levels of estradiol are increased and testosterone decreased. The increased conversion of androgens into estrogens, which is characteristic of obesity, depresses the function of the pituitary gland by disturbing normal feedback in the testis [23].

Du plessis *et.al* reported that the results of several studies point to an increased likelihood of abnormal semen parameters among overweight men, and an elevated risk for infertility among couples. also reported that, there are Several mechanisms might account for the effect of obesity on male infertility, both directly and indirectly associated poor sexual action, alteration in sex hormone (reduced inhibin B and androgen levels accompanied by elevated estrogen levels) and increased scrotal temperatures, ultimately manifesting as impaired semen parameters (decreased total sperm count, concentration and motility; increased DNA fragmentation index) [4].

Palmer *et.al* concluded that, There is emerging evidence that male obesity negatively impacts fertility through changes to hormone levels, as well as direct changes to sperm function and sperm molecular composition [24].

Obese, infertile men exhibit endocrine changes that are not observed in men with either obesity or infertility alone. this defective response to hormonal changes might be explained by partial or complete dysregulation of the hypothalamic–pituitary–gonadal axis HPG axis in which the increase in estrogen and decrease in testosterone levels negatively affects spermatogenesis and regular testicular function. Inhibin B levels are directly related to normal spermatogenesis and thus the low levels of this protein observed in obese males result in abnormal spermatogenesis. The dysregulation of the axis is shown because, despite the low inhibin B levels observed in obese males, there is no compensatory increase in follicle-stimulating hormone; FSH levels as expected. Increased estrogen levels further contribute to the negative feedback effect on the hypothalamus and lead to decreased gonadotropin-releasing hormone GnRH [4].

The results of the present work meet with some researchers result's from several recent studies, which they are reporting the relationship between semen quality and obesity.

PRL plays a diverse role in men's reproduction and health. The previous study show that there was an inverse correlation between serum testosterone, prolactin level and BMI. Also, there was a strongly negative and significant association between serum testosterone, prolactin level and total cholesterol. Furthermore, the associations between serum testosterone, prolactin concentrations were found to be significantly positive with HDL-cholesterol [25]. These findings have been corroborated by the results in present study, Table (2,3).

Faris *et.al* concluded that in the previous study they were show that, the level of ALP in the seminal plasma and sperms correlated with the concentration of the sperms [26]. There is another study by Bell *et.al* conducted on one of the cattle breeds showed an inverse relationship between the ALP concentration and sperm concentration. The significant differences of ALP concentration refer to sperm number only not for the sperm motility percent or grade activity [27]. This result agree with the result of Lewist *et.al* in which they are revealed to the existence of a positive relationship between sperm counts and concentration of this enzyme in the semen samples [28]. The levels of ALP enzyme increased in the first split ejaculate compared to the second split is because the largest amount of the first split of ejaculate secreted from prostate [29]. Low and Saltie revealed, that the ALP enzyme linked to the sperm cell membrane by Phosphatidy linositolglycan located on the outer surface of the sperm [30]. The site of ALP enzyme is in the plasma membrane in addition to cytoplasmic droplet and acrosome body of the sperm[31]. The ALP enzyme act through hydrolysis of phosphate ester of the nucleotide , sugars and ATP and has a potential role in removing phosphorus from Adenosine Monophosphate (AMP), also works to prevent the addition carbohydrates groups to glycoproteins in the surface of sperm [32]. Becq *et.al*

reported that the ALP enzyme present in the chloride channels in the sperm, and that have a role in the acrosome reaction, and thus there is a positive linear relationship between the level of this enzyme and sperm concentration in the semen samples [33].

In recent years, the incidences of obesity, diabetes mellitus and male factor infertility have increased in the general population. The importance of insulin has been demonstrated in male rat reproduction by using streptozotocin to deplete the  $\beta$ -cells of the pancreas, thereby inducing insulin dependent diabetes mellitus IDDM. Insulin deficiency in these rats led to a decrease in Leydig cell number as well as an impairment in Leydig cell function. This consequently translated to a decrease in androgen biosynthesis and serum testosterone levels. The impaired Leydig cell function and subsequent decrease in testosterone in IDDM could be explained by the absence of the direct stimulatory effects of insulin on Leydig cells, as well as by an insulin-dependent decrease in FSH and LH levels. It also has been reported that insulin plays a central role in regulation of the hypothalamic-pituitary-testicular axis by the reduction in secretion of LH and FSH in diabetic men, as well as in knockout mice lacking the insulin receptor in the hypothalamus. Both the diabetic men and the knockout mice had notably impaired spermatogenesis, increased germ cell depletion, and Sertoli cell vacuolization. Diabetes mellitus is thought to affect male reproductive function at multiple levels due to its effects on the endocrine control of the spermatogenesis process and spermatogenesis itself, as well as impairing penile erection and ejaculation [26].

### Conclusion

From this study, we can conclude that there is inverse- relationship between obesity and fertility which increase in the presence of diabetes.

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