Semen parameters in Egyptian diabetic patients and its correlation with glycosylated hemoglobin level: A case - control study

Original Article

Emad E. Kamal[1], Aya Y. Badran[1], Walaa A. Khalifa[2], Angham H. Mahgoob[1], Mohammed Zakaria[3], Reham M. Abdel Gaber[1]

Departments of [1]Dermatology, Venereology and Andrology, [2]Internal Medicine, [3]Clinical Pathology, Faculty of Medicine, Assuit University, Assiut, Egypt.

ABSTRACT

Background: Diabetes mellitus (DM) is a well-known metabolic disorder affecting a large population worldwide. Both types of DM could have detrimental effects on semen parameters as well as the hormonal profile of the affected males.

Objective: On designing the current study, we sought to evaluate the effect of long-term control of DM by measuring glycosylated hemoglobin (HbA1c) level and detect its possible correlation with semen parameters and hormonal profile of male patients with DM.

Patients and Methods: A prospective case–control study was conducted on 60 males with DM and 40 matched controls. All participants were subjected to conventional semen analysis and measurement of free and total testosterone, follicle-stimulating hormone, luteinizing hormone, and prolactin levels by enzyme-linked immunosorbent assay technique. Measurement of HbA1c level was made for all participants.

Results: A significant negative correlation was found between HbA1c and free testosterone levels, whereas a significant positive correlation between HbA1c and prolactin levels in patients with DM. No significant correlation was reported between HbA1c and semen parameters in patients with DM.

Conclusion: Patients with DM have significantly lower semen parameters and reproductive hormone levels than matched healthy controls which might impair their fecundity and reproductive capacity. We do recommend that all males with abnormal semen analysis should undergo screening for DM.

Key Words: Diabetes mellitus, glycosylated hemoglobin, semen parameters.

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Corresponding Author: Aya Y. Badran, Department of Dermatology and Venereology, Assiut University Hospital, Faculty of Medicine, Assiut, Egypt, **Tel.:** +20101 324 4819, **E-mail:** Ayabadran@aun.edu.eg

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INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic illness with a global incidence of ~0.5-2%[1]. In 2011, the total number of patients with DM was 328 million, and this number is expected to reach 592 million by the year 2035[2].

Two types of DM are known: type 1 DM is considered an autoimmune disorder in which autoantibodies against the insulin-producing beta cells of the islets of Langerhans is produced leading to insulin deficiency[3], whereas type 2 DM is characterized mainly by insulin resistance, which may or may not be accompanied with relative decrease in insulin production[4]. Occurrence of type 2 DM is closely linked to lifestyle factors such as obesity, lack of exercises, psychological stresses, and urbanization[5,6].

It is well known that DM is closely linked to male sexual dysfunction, in addition it has a great effect on the endocrinal control of spermatogenesis and subsequently the fertility[7,8].

Formation of a covalent bond between glucose molecule and the N-terminal valine of the β-chain of hemoglobin leads to production of the glycosylated hemoglobin (HbA1c), which acts as an excellent indicator of the time-averaged blood glucose concentration in the preceding 3–12 weeks[9].

Measurement of HbA1c is a key diagnostic criterion and a key parameter for the follow-up of the treatment of DM[10].

In the current study, we sought to evaluate the difference between diabetics and nondiabetics regarding semen parameters and reproductive hormones levels, also to evaluate the effect of long-term control of DM by measuring HbA1c level, and to detect its possible

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correlation with semen parameters and hormonal profile of male patients with DM.

PATIENTS AND METHODS

A prospective case–control study was conducted at the Department of Dermatology, Venerology, and Andrology, in collaboration with the Internal Medicine Department, Assiut, Egypt. The study protocol was approved by the Assiut Medical School Ethical Review Board. The idea and the whole procedure were explained to all participants, and a written informed consent was obtained from all participants.

We included 60 male patients with DM and 40 age-matched healthy participants as a control. However, we excluded patients with varicocele, primary and secondary hypogonadism, cryptorchidism, genital tract infection, or patients with other systemic diseases (chronic liver and kidney diseases).

After complete medical history and clinical examination (general and genital), all participants were subjected to the following:

(1) Conventional semen analysis using WHO guidelines 2010 as a reference[11].

(2) Venous blood samples at early morning for measurement of total and free testosterone levels, follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, and HbA1c levels. Reproductive hormones were tested using a Thermo Scientific Multiskan FC kits (Vantaa, Finland) and measured by enzyme-linked immunosorbent assay. Normal value of free testosterone ranges from 2.50 to 11.00 ng/ml, normal value of total testosterone ranges from 15 to 50 pg/ml, normal value ranges of prolactin ranges from 4.04 to 15.20 ng/ml, normal value of FSH ranges from 1.4 to 18 mIU/ml, and normal value of LH ranges from 1.5 to 14.4 mIU/ml. HbA1c was measured by Direct Enzymatic HbA1c Assay from Diazyme Laboratories (Poway, California, USA) according to the manufacturer's protocol.

Glycemic control was detected according to HbA1c analysis dating not more than 1 month before the interview. It was graded as follows: good, 6.2–6.8%; fair, 6.9–8.3%; and poor, greater than 8.4%.

Statistical analysis

Analysis of the data was performed using the Statistical Program for Social Science (SPSS.18.0; SPSS Inc., Chicago, Illinois, USA) software program. Quantitative data were expressed as mean±SD. Qualitative data were expressed as frequency and percentage. Independent samples *t* test of significance was used when comparing between two means. Pearson's correlation coefficient (*r*) test was used for correlating data, and one-way analysis of variance when comparing between more than two means. A *P* value less than 0.05 was considered statistically significant, whereas *P* value more than 0.05 was considered insignificant.

RESULTS

The current study included 60 males with DM and 40 matched controls. Patients were classified according to disease duration into three groups: patients with DM duration less than 5 years (31.7%), patients with DM duration 5–10 years (35%), and patients with DM duration more than 10 years (Fig. 1). Most patients (78.3%) were affected with type II DM (Fig. 2).

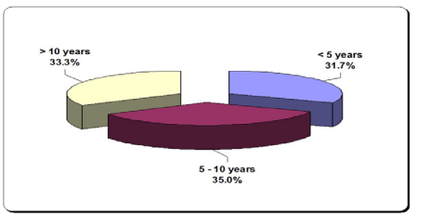

Fig. 1: Distribution of patients according to duration of DM. DM, diabetes mellitus.

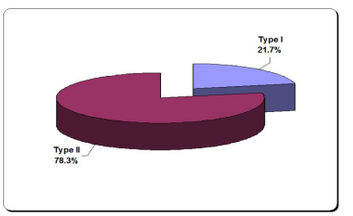

Fig. 2: Distribution of patients according to type of DM. DM, diabetes mellitus.

Patients with DM have significantly lower semen parameters than controls. We found a significant difference between patients and controls regarding semen parameters in; semen volume, sperm count, sperm motility as well as abnormal forms (*P*=0.000, 0.010, 0.000, and 0.023, respectively) (Table 1).

On assessment of serum levels of reproductive hormones, we found that patients with DM have significantly lower hormonal level than controls. A significant difference between patients and control group was found regarding free and total testosterone, FSH, LH, and prolactin levels (*P*=0.000, 0.000, 0.000, 0.002, and 0.000, respectively) (Table 2).

Regarding the serum level of HbA1c in patients and controls, a significant difference (*P*=0.000) was present

between them (Table 3). Moreover, a significant difference (P=0.005) was found in the serum level of HbA1c in type I DM and type II DM (higher in type I DM than type II) (Table 4). On studying the relationship between the level of HbA1c and reproductive hormones in patients with DM, we obtained a significant negative correlation between HbA1c and free testosterone levels (P=0.018 and r=0.304) and a significant positive correlation between HbA1c and prolactin hormone levels (P=0.002 and r=0.385) (Table 5). Lastly, we failed to find any correlation between HbA1c level and semen parameters in patients with DM (Table 6) or controls.

Table 1: Semen parameters in patients and control groups

Semen parameters	Patients (N=60)	Control (N=40)	P value
Volume			
Mean±SD	2.19±1.43	3.37±1.68	0.000*
Median (range)	1.5 (0.5–7.0)	2.9 (1.0–8.4)	
Count			
Mean±SD	36.20±32.28	78.27±70.51	0.010*
Median (range)	21.0 (2.2–132.0)	51.5 (0.0–208.3)	
Motility			
Mean±SD	20.35±11.08	32.36±15.84	0.000*
Median (range)	21.7 (0.0–68.5)	35.0 (0.0–53.7)	
Abnormal forms			
Mean±SD	59.22±19.88	50.29±21.25	0.023*
Median (range)	60.8 (11.1–100.0)	53.1 (0.0–100.0)	

This means a significant difference between patients and control groups as regards the semen parameters

Table 2: Reproductive hormone levels in patients with diabetes mellitus and controls

Reproductive hormones	Patients (N=60)	Control (N=40)	P value
Free testosterone			
Mean±SD	12.23±2.21	24.27±10.48	0.000*
Median (range)	12.5 (7.0–15.3)	20.7 (10.9–47.9)	
Total testosterone			
Mean±SD	1.87±0.82	4.72±2.14	0.000*
Median (range)	2.0 (0.2–3.7)	4.2 (1.4–9.0)	
FSH			
Mean±SD	23.58±6.40	7.27±4.81	0.000*
Median (range)	22.6 (5.7–39.7)	5.4 (1.5–19.0)	
LH			
Mean±SD	13.48±9.54	6.11±3.88	0.002*
Median (range)	15.0 (0.4–32.5)	5.1 (1.5–19.0)	
Prolactin			
Mean±SD	26.02±6.54	13.19±9.45	0.000*
Median (range)	24.9 (17.9–43.0)	10.0 (3.0–37.0)	

FSH, follicle-stimulating hormone; LH, luteinizing hormone

Table 3: Glycosylated hemoglobin level in patients with diabetes mellitus and controls

HbA1c	Patients (N=60)	Control (N=40)	P value
Mean±SD	7.31±0.68	4.83±0.85	0.000*
Median (range)	7.2 (6.0–8.9)	4.9 (3.8–6.7)	

HbA1c, glycosylated hemoglobin.

Table 4: Glycosylated hemoglobin level in patients with diabetes mellitus

	Type of DM		
HbA1c	Type I (*N*=13)	Type II (*N*=47)	*P* value
Mean±SD	7.81±0.77	7.17±0.60	0.005*
Median (range)	8.0 (6.2–8.9)	7.1 (6.0–8.3)	

DM, diabetes mellitus; HbA1c, glycosylated hemoglobin.

Table 5: Correlations between glycosylated hemoglobin and reproductive hormone levels in patients with diabetes mellitus

	HbA1c	
Reproductive hormones	*r* value	*P* value
Free testosterone	-0.304	0.018*
Total testosterone	-0.131	0.319
FSH	0.193	0.140
LH	-0.088	0.502
Prolactin	0.385	0.002*

FSH, follicle-stimulating hormone; HbA1c, glycosylated hemoglobin; LH, luteinizing hormone.

Table 6: Correlations between glycosylated hemoglobin and semen parameters in patients with diabetes mellitus

	HbA1c	
Semen parameters	*r* value	*P* value
Volume	-0.131	0.317
Count	-0.139	0.289
Motility	-0.129	0.327
Abnormal forms	0.104	0.430

HbA1c, glycosylated hemoglobin.

DISCUSSION

DM is a common metabolic disorder that has a detrimental effect on the reproductive system of males through various mechanisms[12].

A total of 60 adult males with DM and 40 matched controls were included in the current study. Most patients (78.3%) were affected by type II DM.

In the current study, we found that patients with DM have significantly lower semen parameters than controls, with a significant difference regarding semen volume, sperm count, sperm motility, as well as abnormal forms.

Since the study performed by Bartak *et al*.[13] which proved that patients with type 1 DM have lower sperm parameters, many studies have been performed regarding that issue. In 1984, Padron *et al*.[14] claimed that semen volume and sperm motility and morphology were significantly lower in patients with type 1 DM.

In 2007, Delfino *et al*.[15] reported significantly lower results of the percent of normal sperm morphology and motility in patients with DM compared with the nondiabetic healthy group.

On the contrary, Ali *et al*.[16] found a significant increase in total sperm count and sperm concentration in patients with type 1 and type 2 DM. However, sperm motility and semen volume were lower than controls.

This reduction in semen quality which occurs in patients with DM can be explained on the basis of hormonal alterations, as well as the morphological changes, which occur in the testis as a result of poor circulation to the testis induced by DM. These morphological changes include thickness of the seminiferous tubules, increase in the interstitial collagen, and peritubular or intertubular fibrosis[17,18].

It has been claimed that oxidative stress and DNA damage in diabetic vasculature which leads to endothelial dysfunction and vasculopathy are among other factors that lead to various complications of DM. As sperm cells are rapidly proliferating cells, they can be easily damaged by this oxidative stress[19].

Oxidative stress has been claimed to be an important factor in the pathogenesis of many chronic complications of diabetes[20].

In the current study, we observed that serum level of free and total testosterone was significantly lower in patients with DM. Moreover, this was in accordance with Agbecha and Usoro[21], Svartberg *et al*.[22], Grossmann *et al*.[23], and Stanworth and Jones[24], who also found low testosterone levels in male patients with DM when compared with the nondiabetic male controls.

The precise mechanism that leads to the decrease of testosterone level by DM remains poorly understood; however, the proinflammatory cytokines, estradiol, leptin, and insulin which become elevated in DM have a role in the inhibition of the hypothalamic pituitary gonadal axis at multiple levels[25].

On studying the relation between of HbA1c and reproductive hormones levels, there was a significant negative correlation between HbA1c and free testosterone level, which means that as the level of HbA1c increases (which reflects the diabetes control), the level of free testosterone decreases. This result was in accordance with the results obtained by Svartberg *et al*.[22] in their study, as they found an inverse correlation between HbA1c and total testosterone (P<0.01) level.

Niven *et al*.[26] failed to find a correlation between HbA1c level and sperm parameters in patients with DM, and this result was in accordance with the result of the current study, as we did not find any correlation between HbA1c level and semen parameters in either patients with DM or controls.

CONCLUSION

From the results of the current study, we conclude that patients with DM have significantly lower semen parameters and reproductive hormone levels than matched healthy controls, which might impair their fecundity and reproductive capacity. HbA1c level negatively correlated with free testosterone level and positively correlated with serum prolactin level. We do recommend that all males with abnormal semen analysis should undergo screening for DM.

CONFLICT OF INTEREST

There are no conflicts of interest.

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