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Research Article

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Male Reproductive Function in Patients with Diabetes Mellitus

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Abstract

Introduction: Diabetes mellitus (DM) affects a growing number of men in reproductive age. Diabetes can impair male reproduction, though changes on the hypothalamus-pituitary-testicular axis, it may cause sexual dysfunction and defective function of the male accessory glands. However, clinical data regarding sperm parameters and other aspects of reproductive function in diabetic patients are limited.

Objective: To evaluate the characteristics and bio-functional differences of sperm in diabetic patients.

Materials and methods: observational, comparative cohort study of diabetic patients with a history of infertility or subfertility, collecting their main bio - functional sperm parameters, hormone levels and metabolic characteristics.

Results: A sample of 90 patients with DM, with an age of 40±10 years (mean ± SD) and range between 20 and 60 years old, the highest percentage of patients being around 30 years old, with a time of infertility of 4.7 ± 4.2 years, and an average diabetic disease time of 9.8 years. Patient's type 1 represented 36% of total and 63% had type 2 DM. Up to 62 % of patients had suffered from DM for more than 10 years. A total of 199 non-diabetic patients with infertility aged 37.7 ± 7.39 years were obtained as control group. Age and BMI were higher in the group of DM compared to controls. Patients with DM had a significantly lower percentage of sperm with progressive motility, pH, sperm concentration and total sperm count per ejaculate, as well as a lower proportion of spermatozoa with normal morphology than controls. A negative correlation was observed among the number of diabetic complications and semen volume (R=-0.277, p <0.05). Biochemical parameters, such as triglycerides, cholesterol and gonadotropins did not show any significant differences, while creatinine was higher and testosterone was lower in the group of DM compared to control group.

Conclusion: Infertile patients with DM show a significant impairment of the main sperm parameters we compared with non-diabetic infertile patients. These findings may explain why patients with DM have frequent fertility disorders.

Keywords: Diabetes mellitus; Male reproductive function

Introduction

Several risk factors are involved in the infertility pathogenesis, as failed spermatogenesis a cause of testicular cancer, germ cell aplasia, varicocele, altered sperm transport, environmental factors, as well as congenital abnormalities, infectious processes, bilateral tubal occlusion, pregnancy-related infections, alterations in functional sperm parameters, also the antisperm antibodies (AA). However, there is from 10% to 25% of idiopathic cases in which the cause of infertility cannot be identified [1,2].

Diabetes mellitus (DM) is a chronic metabolic disease characterized by hyperglycemia. DM is one of the main stressors in modern public health due to complications which include retinopathy, neuropathy, nephropathy and male infertility. Within these concerns about fertility, a decline in male fertility, specifically decreasing sperm quality, has received significant attention [3]. This capacity of spermatozoa may also be influenced by a disease associated with genetic and environmental factors such as the Metabolic Syndrome, as male overweight and/or Diabetes mellitus (DM). Despite of the direct association between the presence of DM and sperm fertilizing potential problem in contemporary whitens. Other than erectile dysfunction [4], which includes retrograde ejaculation and premature ejaculation, which are long acknowledged as sequelae of the condition, the impact of DM on male reproductive health remains controversial. Thus, DM also can affect male reproductive function at multiple levels as a result of its effects on the endocrine control of spermatogenesis and spermatogenesis itself [5]. A decrease in sperm motility and semen volume in patients with DM type 2 has been observed, and hypogonadism, always linked to the metabolic syndrome. Numerous factors can contribute to male infertility in patients with metabolic syndrome, which may be hyperglycemia, atherosclerosis and / or oxidative stress, which in turn contribute to cell damage [6]. Obesity has also been negatively related to semen quality [7].

Studies of sperm quality in diabetes have been limited to microscopic evaluation of conventional seminal parameters (semen volume, sperm count, motility and morphology). Conventional seminal analysis has limited value in determining fertility status [8] unless there are marked abnormalities, such as oligoastenoteratospermia or azoospermia. The scarcity of studies regarding the effects of DM on human male reproductive function and the conflicting nature of existing data have resulted in a clear lack of consensus in current literature regarding the magnitude of the problem [5,9]. Nevertheless, the association of DM with decreased male fertility is much clearer in the various animal models that are employed to study the condition: all show significantly decreased fecundity [10,11]. In examining the impact of hyperglycemia associated to DM in the long term to the progression of a greater vascular and endothelial alteration, besides being responsible for severe comorbidities and complications such as dyslipidemia, hyperinsulinemia and hypoglycemia [12]. Therefore, DM can have an effect on reproductive functions, such as subtle yet important changes in the metabolic profile of the testis [13,14]; the increased presence in the male reproductive tract of a group of compounds that are implicated in numerous diabetic complications as neuropathy and angiopathy, and significantly

higher percentage of both sperm nuclear and mitochondrial DNA damage [5,15,16].

The aims of our study were to evaluate the relationship between diabetes mellitus and subfertility, based on the hormonal and metabolic test and seminogram study in subfertile patients with these characteristics.

Materials and Methods

An observational, comparative study was performed in which involved manually reviewing the available charts of patients who had diabetes with a history of subfertility or infertility. Another hand, we obtained as control group, non-diabetic patients studied for presenting Subfertility or conjugal infertility. Through the historical review of the clinical records and the analytical records of the center, a database was made with the selected variables. The control group was carefully randomly selected from records of clinical records made during periods similar to diabetic patients, including men with no history of diabetes with an equivalent age, and who were consulted for evaluation of marital infertility. The control group was sized so that it was roughly composed of twice as many patients as the group of diabetic patients. We analyzed sperm parameters of both groups.

Results

A study was conducted in 90 patients with diabetes mellitus (ICD9 code) for marital infertility, aged 21 to 60 years with a mean of 40,4 (± 10.94), the highest percentage of patients were Around 30 years, with an in-fertility time from 1 to 20 years with an average of 4.71 (± 4.27), and a diabetic disease time from 2 to 23 years with an average of 9.88 ± 5.5 years; 36.7% of the patients had DM1 and 63.3% had DM type 2. There were 72.5% of patients with a mean illness time of 10 years. The mean BMI was at 29.8 kg/m^2 ± 5.2. 71.9% had a BMI greater than 25, 50% higher than 27 (Table 1).

Parameter	Mean ± SD
Age (years)	40.4 ± 10.9
BMI (Kg/cm2)	29.8 ± 5.2
Type 1 Diabetes (%)	33%
Type 2 Diabetes (%)	67%
Time-course of Disease (years)	9.8 ± 5.5
Time-course of Infertility (years)	4.7 ± 4.2

Table 1: Demographic and clinical profiles of Diabetes subfertil patients.

Mean blood glucose levels were 7.8 mmol/L, HbA1c 6.9%, LH 6.85 IU/L FSH 9.28 IU/L, Testosterone 10.9; SHBG ratio of 29.36. Cholesterol of 4.6, LDL of 2.96, Triglycerides of 1.66 was also evaluated, with 40% above 1.5. The creatinine was 114.9 mg/ml, the highest percentage being 87 mg/ml. (Table 2). The majority of Diabetes patients had nephropathy (24.4%), 30% Arterial Hypertension, 31% dyslipemia.

Parameter	Diabetes	Controls	p-Value
	Mean ± SD	Mean ± SD	
BMI (Kg/cm^2)	29.8 ± 5.2	25.9 ± 3.9	0.001
Time-course of Disease (years)	4.7 ± 4.2	3.8 ± 2.3	0.036
Cholesterol (mmol/L)	4.6 ± 1.1	4.9 ± 1.0	NS
Triglycerides (mmol/L)	1.6 ± 0.9	1.9 ± 1.2	NS
Creatinine (umol/L)	115 ± 76.2	86.6 ± 20.7	0. 003
Total Testosterone (nmol/L)	10.9 ± 5.9	14.0 ± 7.5	0.047
LH (UI/L)	6.8 ± 7.7	4.5 ± 2.6	NS
FSH (UI/L)	9.3 ± 12.5	6.5 ± 5.5	NS

Table 2: Laboratory testing of Diabetes subfertil patients.

A total of 199 patients with infertility or subfertility with an age between 22 to 62 years were obtained as control group, in the period from 2000 to 2014 of a sample of 9505 patients, with a mean of 40.4 years ± 10.9 SD. A time of infertility of 3.86 ± 2,355. LH values of 4.5 and FSH 6.5. Testosterone of 14 and SHBG 27,66. We also obtained data on cholesterol levels of 4.6 and triglycerides of 1.91 in the control groups, compared with diabetic patients with Creatinine of 115, Testosterone of 10.9 and BMI 29.8, Mean BMI was in controls was 25.9 kg/cm^2 (Table 3).

Parameter	Mean ± SD	Range
Base glucose level (mmol/L)	7.8 ± 2.9	4.3 – 17
Hemoglobin A1c (%)	6.9 ± 1.8	3.4 – 10.8
Creatinine (µmol/L)	114.9 ± 76.2	61 - 543
Glomerular Filtration (mL/min)	70.8 ± 27.3	10 - 196
Cholesterol (mmol/L)	4.60 ± 1.18	1.79 - 8.28
LDL cholesterol (mmol/L)	2.96 ± 1.08	0.75 – 6.08
HDL cholesterol (mmol/L)	1.27 ± 0.72	0.32 – 3.70
Triglycerides (mmol/L)	1.66 ± 0.94	0.50 – 4.68
Total Testosterone (nmol/L)	10.9 ± 5.9	0.7 - 27.8
LH (UI/L)	6.85 ± 7.69	0.87 – 36.2
FSH (UI/L)	9.28 ± 12.55	0.35 – 71.0

Table 3: Clinical profiles of patients with/without Diabetes.

To compare between two types of diabetes, we found significative difference in color ability and creatinine levels, percentage of inmovility and Teratozoospermia index (Table 4). There were significative difference in semen parameters between diabetics patients and controls, for Semen Volume, pH, Concentration, Sperm cells of ejaculate, progressive mobility, immobility, sperm normal shape (Table 5). Therefore, We analyzed the correlation between seminal volume and diabetes complications (R=-0,28, p<0,005) (Graphic 1). To evaluate immobility between both diabetes groups, it had correlation between Glomerular filtration vs Immobility (R=-0,26, p<0,05) (Graphic 2). Semen volume had correlation with base glucose level (R= -0.23, p<0,05) (Graphic 3).

Parameter	Diabetics Mean ± SD	Controls Mean ± SD	p-Value
Abstinence Time (days)	5.2 ± 2.3	5.4 ± 3.0	NS
Semen Volume (cc)	2.1 ± 1.4	3.3 ± 1.6	0.205
pH	7.2 ± 0.4	7.5 ± 0.2	<0.001
Concentration (mill/mL)	32.7 ± 49.3	64.8 ± 59.1	<0.001
Sperm cells of Ejaculate	69 ± 110	204 ± 183	<0.001
Sperm progressive motility (%a +b)	20.7 ± 20.2	50.6 ± 19.7	<0.001
Immobility	70 ± 24.3	41.2 ± 16.7	<0.001
Sperm Normal Shape (%)	7.4 ± 7.9	11.9 ± 12.3	0.003
Terazoospermia Index	1.54 ± 0.19	1.52 ± 0.17	NS
Antisperm antibodies (% positives)	1.1	0.5	NS

Table 4: Comparasion in clinical profiles in Diabetes patients

Parameter	Diabetics Mean ± SD	Controls Mean ± SD	p-Value
Age (years)	37.7 ± 9.1	41.8 ± 11.5	NS
BMI (Kg/cm^2)	27.7 ± 5.3	30.9 ± 4.8	NS
Σ comorbidities	1.5± 1.1	1.0± 1.0	0.029
Creatinine (µmol/L)	138 ± 108	102 ± 47	0.045
Glomerular Filtration (mL/min)	71 ± 35	70 ± 22	NS
Hemoglobin A1c (%)	7.4 ± 1.7	6.6 ± 1.9	NS
Total Testosterone (nmol/L)	11.8 ± 6.3	10.5 ± 5.7	NS
LH (UI/L)	9.4 ± 11.2	5.8 ± 5.6	NS
FSH (UI/L)	10 ± 15.3	8.8 ± 10.7	NS
Semen Volume (mL)	1.7 ± 1.0	2.3 ± 1.6	NS
Sperm cells concentration (x106/mL)	25.6 ± 44.8	36.3 ± 51.5	NS
Immobilities (%)	78.6 ± 24.9	65.8 ± 23.1	0.025
Sperm progressive motility (a+b) (%)	15.8 ± 21	23.1 ± 19.5	NS
Sperm Normal Shape (%)	5.2 ± 5.0	8.4 ± 8.9	NS
Terazoospermia Index	1.6 ± 0.18	1.51 ± 0.19	0.04
Antisperm antibodies (% positives)	0	1.6	NS

Table 5: Sperm Parameters of patients with/without Diabetes.

Discussion

The rising incidence of DM worldwide will inevitably result in a higher prevalence in males of reproductive age. Sterility is already a major health problem in developed countries and the developing world with up to one in six couples requiring specialized research or treatment to conceive [17,18]. Semen disorders are believed to be causal or contributory in 40%-50% of infertile couples [19,20]. On the other hand, the last 50 years has seen an apparent decrease in semen quality. The increased incidence of systemic diseases such as DM may further exacerbate this decline in male fertility.

When a comparison between the clinical and analytical parameters of the diabetic patients, both type I and II, a significant difference was observed with the presentation of comorbidities among patients with type I diabetes, with a 1.5 compared to 1 in Patients with type 2 diabetes. Creatinine also presents a significant difference, as well as immobility of the spermatozoa and the rate of teratozoospemia. There were differences between age and creatinine in patients with DM1 and DM2, due to disease time, pathologies associated with diabetes and cell damage. In contrast, we found no relationship between metabolic control (HbA1c) and bio functional sperm parameters and hormone concentration.

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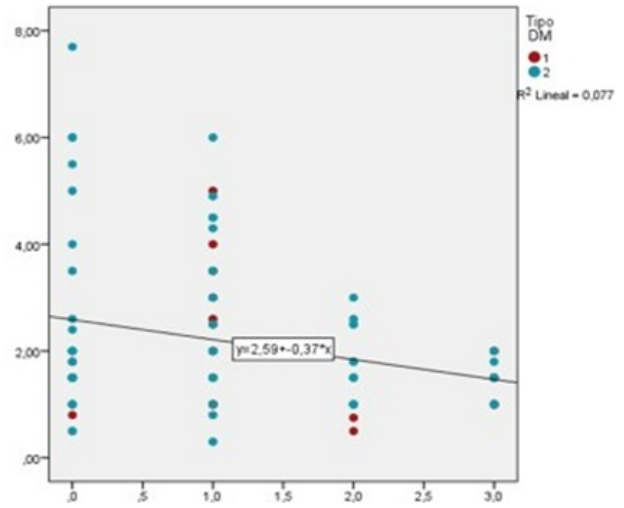

Figure 1: Correlation between of Sperm Volume (ml) vs Diabetes complications.

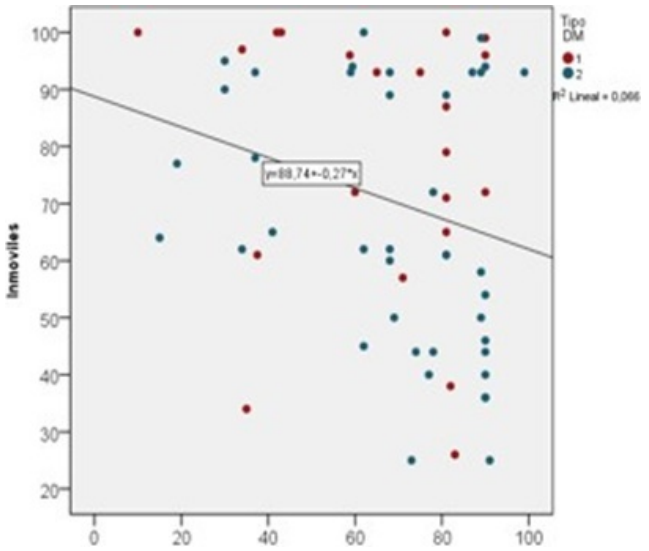

Figure 2: Correlation between of Immobility vs Glomerular Filtration.

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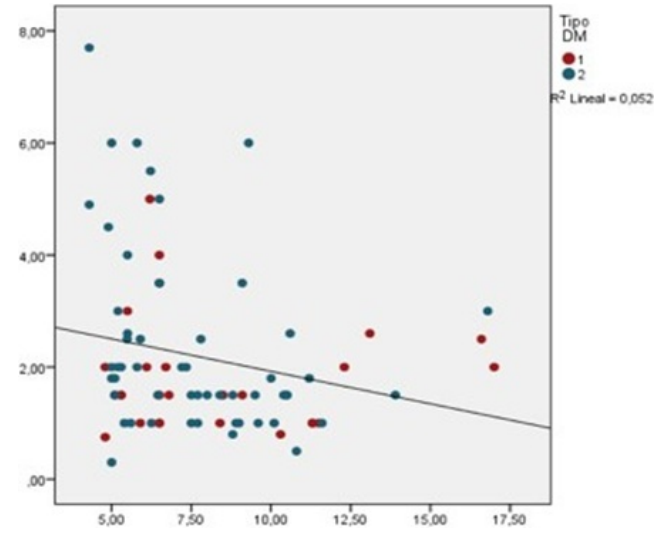

Figure 3: Correlation between of Semen Volume (mL) vs Base glucose level (mmol/L).

Our study shows that patients with DM had a low percentage of spermatozoa with progressive motility and a high percentage of spermatozoa with abnormal morphology than controls, as well as alterations in pH and concentration between groups with significant differences. Previous studies have estimated the prevalence of type 1 DM in subfertile men at 1% [4,5]. Based on the background prevalence of metabolic syndrome and male infertility in this age group, this figure is expected to be around 0.3% [4]. The highest BMI was also determined among diabetic patients and the control group, without finding significant differences among the other parameters associated with the metabolic syndrome. In studies conducted at the level of fertility clinics, DM is not currently seen as particularly relevant in the question of male fertility assessment. This would suggest the need for a large-scale epidemiological study, investigating the relationship between male fertility and DM. In previous studies, the evaluation of sperm motility and an analysis in 17 patients with DM did not present significant alterations.

In addition to higher spermatozoa immobility, patients with DM1 also had a higher percentage of terazoospermia index than DM2, associated with fasting glucose, the comorbidities and kidney failure (Creatinine) becomes more important in patients with diabetes lasting longer than 10 years. Indeed, we found a significant increase in low quality spermatozoa in patients with diabetes and kidney failure (GF) duration ranging from 5 to 10 years [5]. To the best of our knowledge, this study shown lower testosterone level in Diabetes patients than controls. That confirms previous data regarding a reduction in fertility potential mainly in DM1 patients [21]. To our knowledge, there are no studies that have evaluated simultaneously the spermatozoa parameters examined in three kinds of groups.

The overwhelming evidence that sperm DNA damage affects male fertility and reproductive health. Patients with DM have a lower percentage of sperm with progressive motility, alterations in morphology, and these findings may explain why patients with DM have greater alterations in fertility. Diabetic patients in our study had a higher BMI probably associated with a Metabolic Syndrome related to Diabetes, which could be related to the changes in the seminogram.

Oxidative stress is also recognized as an important factor in the pathogenesis of many of the chronic complications of diabetes [22,23]. In fact, DNA damage in the diabetic vascular zone is an important factor for the initiation of the mechanisms resulting in endothelial dysfunction a cause of vasculopathy.

Conclusion

Although this study demonstrates that, apart from seminal volume, pH and progressive joint motility, other conventional seminal parameters of diabetic men do not differ significantly from control subjects, there is a difference from a clinical perspective that this is important, especially given. Type 1 Diabetes patients had a lower percentage of sperm and motility and alteration in morphology.

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