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Correlation between Seminal Fructosamine and Glycosylation Gap and Some Sex Hormones in the Young Infertile Male in Mosul City

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Abstract

Infertility represents a growing health problem in Mosul city and worldwide. Infertility defined as a failure to induce pregnancy after unprotected sexual intercourse for more than 12 months. Infertility in male is a multifactorial complex pathology that leads to different types of problems. This work try to explore the correlation between glycosylation gap and seminal Fructosamine and another parameter in the young male patient in Mosul city. The study included 50 subjects with age range 19-29 years with BMI 18-26 Kg/m^2, from October 2019 to July 2020. The infertility group include 25 patients newly diagnosed with infertility before starting any treatment; have no infection and no structural abnormality. The control group included 25 healthy subjects. Hemoglobin A1c, serum Fructosamine, Serum and seminal testosterone, estradiol and testosterone: estradiol ratio.in addition to some plasma trace element as K, Mg and Zn also measured. There was a significant elevation in the glycosylation profile in the infertile male in compare to control ($p<0.05$). The results of this work showed that there was a significant elevation in glycosylation gap in the infertile group ($p<0.01$). Testosterone and Testosterone/ Estradiol ratio significantly reduced in the infertile group in comparison to control group ($p< 0.0004$ and 0.0002 respectively). Serum and Seminal plasma Testosterone/ Estradiol ratio showed no significant changes between the two groups ($p>0.05$). In conclusion, there was a significant positive correlation seminal plasma fructosamine and glycosylation gap in infertile male group.

Keywords: Seminal plasma, Fructosamine, Glycosylation

الارتباط بين فركتوزامين السائل المنوي و فجوة الجليكوزيل وبعض الهرمونات الجنسية لدى الشاب المصاب بالعقم في مدينة الموصل

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الخلاصة

يمثل العقم مشكلة صحية متنامية في مدينة الموصل وفي جميع أنحاء العالم. يُعرَّف العقم بأنه الفشل في إحداث الحمل بعد الجماع غير المحمي لأكثر من ١٢ شهرًا. العقم عند الذكور هو أمراض معقد متعدد العوامل يؤدي إلى أنواع مختلفة من المشاكل. يحاول هذا العمل استكشاف العلاقة بين فجوة الارتباط بال كلايكوزيلاشن والفركتوزامين المنوي وعوامل آخرى في المرضى من الشاب في مدينة الموصل. اشتملت الدراسة على ٥٠ شخصًا تتراوح أعمارهم بين ١٩-٢٩ عامًا بمؤشر كتلة الجسم ١٨-٢٦ كلغ/م٢. للفترة من اكتوبر٢٠١٩ الى تموز٢٠٢٠. تضم مجموعة العقم ٢٥ مريضًا تم تشخيصهم حديثًا بالعقم قبل البدء في أي علاج ؛ ليس لديهم عدوى ولا شذوذ هيكلي. ضمت المجموعة الضابطة ٢٥ من الأشخاص الأصح HbA1c في الدم اما الفركتوزامين ، والتستوستيرون ، استراديول والتستوستيرون / استراديول. كما تم قياس بعض العناصر مثل البوتاسيوم و المغنيسيوم و الزنك في بلازما السائل المنوي. كان هناك ارتفاع كبير في معامل الارتباط بالجليكوزيل في المصابين بالعقم مقارنة بمجموعة السيطرة .(P <0.05) كان هناك ارتفاع كبير في فجوة الارتباط بالجليكوزيل في مجموعة العقم .(p <0.01) انخفضت نسبة التستوستيرون والتستوستيرون / استراديول بشكل كبير في مجموعة العقم مقارنة بمجموعة السيطرة (P <0.0004)و ٠,٠٠٠٢ على التوالي. أظهرت نسبة التستوستيرون / استراديول في المصل والبلازما المنوية عدم وجود تغيرات معنوية بين المجموعتين.

في الختام ، كان هناك ارتباط إيجابي معنوي بالفركتوزامين في البلازما المنوية وفجوة الارتباط الجليكوزيل في مجموعة الذكور المصابين بالعقم.

الكلمات المفتاحية : بلازما السائل المنوي، الفركتوزامين، كلايكوزيلاشن.

Introduction

Infertility represents a growing health problem in Mosul city and worldwide. Infertility defined as a failure to induce pregnancy after unprotected sexual intercourse for more than 12 months. Infertility in male is a multifactorial complex pathology that leads to different types of problems(1). The seminal analysis is the main and the primary procedure for the diagnosis of the possible underlying cause of infertility(2). Semen is testicular fluid consist of sperms (5%) and seminal plasma that produces by accessory sex glands (95%)(3,4).Semen consists of proteins, lipid, inorganic ions, sugars and hormones that play a crucial role in the fertilization process(3,4).

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Glycosylation process is a non-enzymatic binding of glucose or fructose to different types of proteins as haemoglobin and albumin[5]. Glycosylation leads to a significant impact on protein function that reflects as changes in the cell-cell adhesion that affect sperm and oocyte cells due to changes in protein-carbohydrate interaction that guide specific cell surface recognition[6]. Fructosylation i.e. adding seminal plasma fructose to albumin- one of the major glycoprotein in seminal plasma that presents due to high fructose level that inhibits sperm oocyte fusion due to conformational changes as described by Olejnik et al and Johnson et al [7,8].

Many works study the effect of changes in serum and seminal level of hormones on male fertility especially serum testosterone, estradiol and testosterone/ estradiol ratio that reflects as changes in spermatogenesis process[9]. Testosterone/ estradiol ratio guide the prepare spermatogenesis and maintain sperm viability before and after intercourse [10]. Serum and seminal plasma trace element as K, Mg and Zn also play a vital role in spermatogenesis[11]. Changes in serum glucose and fructose lead to a significant change in glycosylation process that reflected as elevate HbA1c and serum fructosamine level in seminal plasma. The aim of this study: to explore the correlation between glycosylation gap and seminal fructosamine and another parameter in the young infertile male in Mosul city.

Patients and Methods

The study included 50 subjects with age range 19-29 year with BMI 18-26 Kg/ m^2. The infertility group include 25 patients newly diagnosed by Infertility specialist with infertility before starting any treatment; have no infection and no structural abnormality. The control group included 25 healthy subjects. This study carried out under ethical approval No. 45 that issued by ethical committee of Ninevah college of medicine. All seminal plasma and serum samples collected from patients after follow the physician's direction the assay was carryout in Orkida-private Laboratory in Mosul. After abstinence for 2 to 4 days, semen samples collected by masturbation. Seminal samples allowed to liquefy at room temperature for 30 minutes then centrifuged at 2500 g for 10 minutes supernatant collected according to the World Health Organization (1999) criteria[2]. Seminal plasma immediately separated and divided into 2 aliquots, then stored at -20°C until assayed. Serum samples collection fasting venous blood was drawn. 2.5 ml of serum was collected in five Eppendorf 0.5 ml tubes with 1 ml of the supernatant of seminal fluids. HbA1c measured by Chromatographic–spectrophotometric method [12]. Mean blood glucose (MBG); predicted HbA1c and Glycosylation gap (GG) calculated using equations[13].

MBG =1.76*(HbA1c) -3.67mmol/L

P-HbA1c = 0.017*FA + 1.61

GG = M-HbA1c – P-HbA1c

Serum and Plasma of semen fructosamine by NBT-spectrophotometric method [14]. The concentrations of K, Mg, and Zn in serum and seminal plasma detected with Electrolyte Analyzer-PSD [14] and the hormones assayed using multi-parametric immune analyzer MINI VIDAS® automated immunoassay system by Biomerix (France) [15]. Data will represent as Mean ± SD and analyze using SPSS software. Person s correlation use to show the correlation between the measured parameters.

Results

The results of this work showed that there was a significant elevation in the glycosylation profile in the infertile male in compare to control ($p<0.05$). There was a significant elevation in glycosylation gap in the infertile group ($p<0.001$) Table 1.

Table 1. Glycosylation profile in young infertile male in compare to healthy controls

Parameter	Control	Infertile group	P-Value
m-HbA1c	5.16± 0.45	6.32±0.6	< 0.0001
S. Fructosamine µmol/L	211±39	240±31	< 0.005
MBG	5.41±0.8	7.5±1.06	< 0.0001
p-HbA1c	5.19±0.66	5.7±0.53	< 0.004
GG	-0.026±0.01	0.63±0.13	< 0.0001

MBG=Mean blood glucose, P-HbA1c= predicted HbA1c and GG= Glycosylation gap

Serum (S.) Estradiol showed a significant reduction in the infertile group ($p<0.0001$) while Testosterone/ Estradiol ratio showed a significant increase in comparison to the control group ($p<0.03$). Serum Testosterone showed no significant change between the control and infertile group ($p<0.3$). Seminal plasma (Se.) hormones showed Testosterone and Testosterone/ Estradiol ratio significantly reduced in the infertile group in comparison to control group ($p< 0.0004$ and 0.0002 respectively). In contrast seminal plasma estradiol significantly elevated in the infertile group ($p<0.05$) Table 2.

Table 2. Serum and seminal plasma testosterone, estradiol and testosterone/ estradiol ratio in young infertile male in compare to healthy controls

Parameter	Control	Case	P-Value
S. Testosterone nmol/L	15.3± 2.12	14.3±5.13	0.3722
S. Estradiol pmol/L	92.44±14.3	71±5.1	0.0001
S.T/E2 ratio	0.17±0.04	0.205±0.07	0.0349
Se. Testosterone nmol/L	4.62±0.75	3.78±0.82	0.0004
Se. Estradiol pmol/L	266±35	292±42	0.0214
Se. T/E2 ratio	0.017±0.004	0.013±0.003	0.0002

Serum Testosterone/ Estradiol ratio (S.T/E2) significantly increase in infertile group in comparison to control ($p<0.05$). Seminal plasma Testosterone/ Estradiol ratio (Se.T/E2) showed significant reduction in infertile group in comparison to control ($p<0.001$).

In the control group, both serum and seminal plasma Mg and Zn significantly reduced in the infertile group ($p<0.05$, $p<0.0001$ respectively). Serum K showed no significant change between both groups ($p<0.91$). Seminal plasma Mg and Zn significantly reduced in the infertile group in comparison to control group ($p<0.0001$, $p<0.0001$ respectively). In contrast, seminal plasma K significantly elevated in the infertile group in comparison to control ($p<0.0001$) as shown in Table 3.

Table 3. Serum and seminal plasma potassium, magnesium and zinc levels in young infertile male in compare to healthy controls.

Parameter	Control	Case	P-Value
Serum K mEq/L	4.22± 0.64	4.24±0.62	0.9111
Serum Mg mEq/L	2.1±0.3	1.93±0.28	0.0437
Serum Zn µg/dL	94.44±6.41	54.92±6.3	< 0.0001
Se. K mEq/L	10±1.31	23±3.45	< 0.0001
Se. Mg mEq/L	11.12±1.01	8.74±1.46	< 0.0001
Se. Zn µg/dL	128.5±9.43	25.15±5	< 0.0001

Seminal plasma/serum ratio showed significant elevation in K level ($p<0.001$) with no significant change seen in Mg ($p>0.05$) while Zn showed significant reduction ($p<0.001$) in infertile group when compare with control as shown in Figure 1.

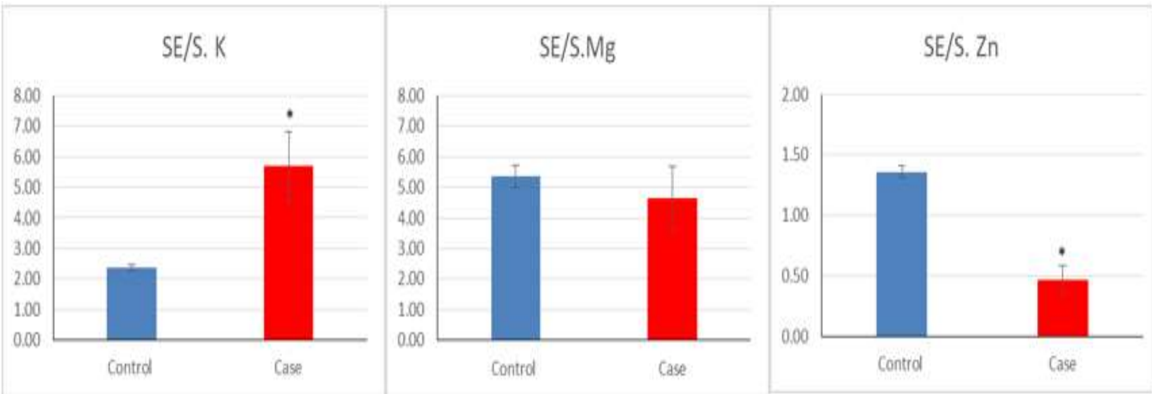

Figure 1. Seminal plasma/serum levels of K, Mg and Zn. Blue represent control group and Red represent infertile male group.*=p<0.01.

In both groups, there was a significant positive correlation between serum/Seminal plasma Fructosamine ratio and glycosylation gap ($r= 0.81$, $p<0.001$) Figure 2.

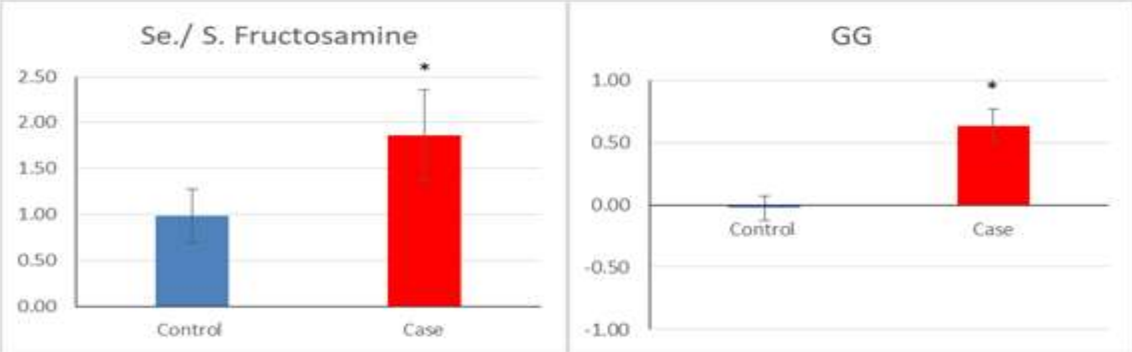

Figure 2. Seminal plasma/ serum fructosamine (left) and Glycosylation gap (Right). Blue represent control group and Red represent infertile male group.*=p<0.01.

Discussion

Glycosylation of proteins play role in the male infertility that represent major health problem. Seminal plasma proteins and other components determine the successfulness of fertilization process. In addition to the changes in seminal plasma-hormones that guide spermatogenesis and sperm fit after ejaculation. In this work, glycosylation profile showed elevation in all parameters and this agree with results obtained by Janiszewska & Maria Kratz[(4)], Cheon et al[(5)], and Kratz et al[(17)]. Testosterone and estradiol play vital role in spermatogenesis[(10, 18, 19)]and this work study both serum and seminal plasma changes of these two hormones. Many studies agree with the results obtained in this work that showed reduction in Estradiol in the infertile group with significant elevation Testosterone/ Estradiol ratio [(20, 21)].

Seminal plasma Testosterone and Testosterone/ Estradiol ratio significantly reduced in the infertile male and this agree with results obtained by Chen et al[22]. Seminal plasma estradiol elevated in the infertile male and this agree with Chen et al. and Collodel et al.[22, 23]. Serum and Seminal plasma Testosterone/ Estradiol ratio showed no significant changes between the two groups and this agree with results discussed by Kratz et al [17].

The results showed significant reduction in both serum and seminal Mg and Zn in the infertile male and this agree with both [24], [25], [26]. Seminal plasma K elevated in the infertile males and this also agree with Gusani et al, [27]. Serum/seminal plasma fructosamine significantly elevated in infertile male Janiszewska etal., and Olejnik et al [4,7].

To sum up, There was a significant positive correlation between glycosylation gap in blood seminal plasma fructosamine, some sex hormones and trace elements, which reflect that the elevation in glycosylation process may lead to increase susceptibility to develop infertility in young adult.

Recommendation

This study recommended further study to the other components of seminal fluid with larger size sample.

Ethical approval

This study carried out under ethical approval No. 45 that issued by ethical committee of Ninevah college of medicine.

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