

Effect of Diabetes mellitus Type 2 on Pituitary Gland Hormones (FSH, LH) in Men and Women in Iraq

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Abstract

The objective of this cross sectional study was to assess the effect of diabetes mellitus (DM) type2 on pituitary gland hormones (FSH and LH) in both men and women. This study comprised a total of (108) subjects out of which (50) were normal and the rest (58) were diabetic since more than 5 years. Fasting blood sugar, HbA1c, LH and FSH were measured in blood samples. The results obtained indicated a significant reduction of serum LH, FSH in women with DM comparison to non diabetics and a significant reduction of serum LH and FSH in men with DM comparison to non diabetics. Conclusion: the data from this study show reduction in serum FSH and LH of diabetic patients of both sex compared to healthy individuals.

Keywords: diabetes mellitus, HbA1c, LH, FSH.

Introduction

Diabetes Mellitus (DM) is continuing to become a health problem since the prevalence of DM has increased dramatically over the past two decades^(1,2).

Diabetes mellitus (DM) is the one of the most prevalent endocrine disorders in the world, type 2 DM is more common than type1⁽³⁾. Diabetes mellitus (DM) type2 is one of the most common endocrine disorders affecting more than 135 million in world⁽⁴⁾. The occurrence of diabetes mellitus (DM) is due to chronic hyperglycemia and disorder in carbohydrate, fat and protein metabolism⁽⁵⁾.

Diabetes mellitus type 2 formerly non insulin dependent diabetes (NIDDM) adult onset diabetes is metabolic disorder that is characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency⁽⁶⁾. Insulin resistance patients are at an increased risk of developing metabolic syndrome, a major cause of heart disease and dyslipidaemia^(7,8). The pathogenesis is still unclear, although environmental factors such as diet and physical activity, coupled with still largely unknown genetic factors, clearly interact to produce this syndrome⁽⁹⁾.

Pituitary gland is one of endocrine glands consist of posterior and anterior lobes⁽¹⁰⁾. Luteinizing hormone (LH) and follicle stimulating hormone (FSH) secreted by

anterior pituitary basophile cell. And called gonadotrophins because they stimulate the gonads in male the testes and in female the ovaries. LH and FSH are essential for reproduction. physiological effect of these two hormones are known only in the ovaries and testes, together they regulate many aspect of gonadal function in both males and females⁽¹¹⁾. In both sex FSH stimulates gamete (sperm or egg) production, while LH promotes production of gonadal hormones⁽¹²⁾.

Materials and Methods

This study was carried out in a group of diabetic patients who had been referred to AL-Kindy Hospital (specialized center of endocrinology and diabetes) during the period Nov-2010 to Jan-2011, and normal control group.

All patients with Type 2 DM for more than 5 years who had been referred to this clinic were enrolled in this study.

Subjects

The clinical material for present study comprised of total 108 subjects. Four groups were formed, on the basis of sex and with or without diabetes mellitus. Our criteria for DM were based on fasting blood sugar, HbA1c and what was obtained by structural questionnaires and by clinical and laboratory assessments. The control group consisted of individuals

who had been referred to the laboratory center for routine check up with no history of any medical disorder and they were matched with diabetic groups regarding age and sex. They had fasting blood sugar levels of less than 110 mg/dL. Serum LH, FSH measured for all groups.

1. Male Diabetic patients (Group 1)

This group composed of (30) male who had been diagnosed with diabetes for more than 5 years. And their age (50 -70) years old.

2. Female diabetic patients (Group 2)

This group consist of (28) female were diagnosed with diabetes for more than 5 years and their age (45 -70) years old.

3. Normal male subjects (Group 3)

These individuals were 25 healthy male control of comparable age and sex with group one.

4. Normal female subject (Group 4)

These individuals were 25 healthy female controls of comparable age and sex with group tow

Blood Samples

Whole blood was collected in the fasting state. (1.0 ml) whole bloods are mixed with EDTA reagent (anticoagulant) and keep for HbA1c estimation. The remaining blood is kept in tubes without EDTA at room temperature for 1 hr after which the supernatant clear fluid is pipette out to another tube. This tube is then centrifuged for 10 min the clear serum is pipette into clear dry test tube and then we taken 10 micro liter to estimate fasting blood sugar and the rest used to estimation LH and FSH.

Results and Discussion

Biochemical parameters of patients and healthy control.

Table (1)

Shows FBG, HbA1c percentage, LH and FSH in male and female of control and diabetic groups.

Variables	male			females		
	DM >5yr (n=30)	Healthy (n=25)	p-value	DM>5 yr (n=28)	Healthy (n=25)	p- value
Age (years)	57.4±10.6	60.6±11.2		55.8±13	58.1±8.2	
FBG(mg/dL)	200±18.2	85±12.8	P < 0.001	164±20.8	81.5±18.1	P < 0.001
HbA1c%	7.8±1.7	2.75±0.82	P < 0.001	6.15±1.2	2.2±7.2	P < 0.001
LH(miu/ml)	8.21±1.3	10.35±2.7	P < 0.001	35.68±8.92	44.012±10.01	P < 0.001
FSH(miu/ml)	11.04±1.85	13.03±2.4	P < 0.001	49.06±11.27	56.18±15.05	P < 0.001

Clinical method: estimation of HbA1c, LH and FSH

HbA1c estimation:

The Bio-Rad Variant Hemoglobin A1C program utilizes principles of ion exchange high performance liquid chromatography (HPLC) for automatic and accurate separation of HbA1c. preceding analysis, a simple preparation of patient sample is required to hemolyze the blood and remove labile A1c, Sample are first diluted with hemolytic reagent and then incubated at 18-28c° for minimum of 30 min. the variant's tow dual piston pumps deliver a programmed buffer gradient of increasing ionic strength to analytical cartage. Prepared sample are automatically injected interactions with material. The separated Hb then passes through the flow cell of filter photometer, where changes in absorbance (415 nm) are measured. A calibrator is analyzed with each run for adjustment of the calculation parameters for determination of HbA1c .the value recorded is in percent .This procedure was performed using a read kit from Bio-Rad, France ⁽¹³⁾.

LH and FSH estimation:

The LH and FSH biotic kit diagnostic Automation, INC. is based on the principle of a solid phase enzyme- linked immunosorbent assay which is the classical sandwich ELISA technique. Using spectrophotometrically technology to measured intensity of color at 450 nm. The concentration of LH or FSH is directly proportional to color intensity of test sample ^(14, 15).

n = number of subjects.

The biochemical findings of this study showed a significant elevation of FBG in diabetic groups compare to normal groups in both sexes, also a significant elevation of HbA1c in both diabetic male and female compared to healthy groups, it show also a significant decrease of LH in diabetic patients of both sexes compared to healthy groups, and a significant increase of FSH in diabetic male and female compared to healthy groups.

NIDDM is chronic degenerative disease of epidemic proportion and is one of the major challenges to public health ⁽¹⁶⁾.

This cross sectional study was designed to assess the correlation of LH, FSH and HbA1c levels in patients with and without DM in both sexes of (45-70 years) olds, using the available data that we collected.

The HbA1c values showed significant increase with increasing in duration of DM .male had a higher mean value of HbA1c as compared to the female.

The serum glucose is unstable in patients with DM and one effective way to monitor it by measured HbA1c, which give the average blood glucose level of preceding 2-3 months. In a study of 178 Libyan men it was found that the patients having poorly controlled diabetes showed a significant correlation between HbA1c and duration of diabetes ⁽¹⁷⁾.

HbA1c will be a valuable adjunct to blood glucose determinations in epidemiological studies .Another study of 500 diabetic patients it was found that in the group of patients with HbA1c greater than 8%, there was significant relation to the duration of diabetes ⁽¹⁸⁾.

It was found that females suffer from diabetes at an older age as compared to males. Various other studies also prove that the disease shows a little gender preference, although diabetes becomes slightly more frequent in women with advancing age ⁽¹⁹⁾. Females have estrogen hormone, which protective for developing diabetes ⁽²⁰⁾. Estrogen makes the body cell more receptive or sensitive to insulin .estrogen seen to contribute to glucose homeostasis in women ⁽²¹⁾.

The data of the present study shows that the commonest form of gonadal dysfunction

in diabetic patients are hypogonadotropic (LH, FSH).

The mean age of patients in this study was 57 years, this much lower that associated with a decline in gonadal function with age ⁽²²⁾.

There are two previous studies, one reports normal gonadotrophin (LH, FSH) ⁽²³⁾.and the other one showing elevated LH and FSH from Pakistan and may represent some distinct underlying pathological process ⁽²⁴⁾.

Since type 2 diabetes and obesity are associated with hypogonadism and since they are both established syndrome of insulin resistance ⁽²⁵⁻²⁷⁾, it possible that insulin resistance itself or the mechanisms underlying it may contribute to this defect. It has recently been suggested that insulin resistance and obesity may be pro-inflammatory states, since obesity is associated with increasing in the expression of TNF α in adipose tissue and an increase in plasma TNF α and IL-6 concentrations; furthermore, they have an increasing in oxidative damage to lipids, protein and amino acid ⁽²⁸⁻³⁰⁾.

There are experimental data to show that TNF α can reduce gonadotrophin secretion ^(31, 32).both generalized obesity and /or centrally deposited fat affect insulin function and testosterone production ⁽³³⁻³⁵⁾.due to the presence of aromatase in fatty tissue, the ability of the aged men to convert testosterone to estradiol result increase on steroidal level which increase suppress serum LH and FSH levels ^(36, 37).

There are also recent data to show the importance of insulin receptor and insulin action in the secretion of insulin by the pancreatic β - cell ⁽³⁸⁾.it is possible that there is a secretory defect at the hypothalamo-hypophyseal level in cases of insulin resistance, which is related to defective insulin receptor/insulin action. Indeed, in mice with a selective knockout of the insulin receptor in neurons, a selective defect of hypogonadotropic hypogonadism is observed ⁽³⁹⁾.

In conclusion, could be drawn that LH and FSH decrease in diabetes mellitus type2 in both sexes.

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الخلاصة

ان هذه الدراسة النوعية لتقييم تأثير مرض السكر من النوع الثاني على هرموني الغدة النخامية (FSH, LH) عند كلا الجنسين الرجال والنساء. اجريت الدراسة على مجموعة من الاشخاص يبلغ عددهم (108) وكان منهم (50) شخص من الاصحاء، لا يعانون من الامراض، و(58) مصاب بمرض السكر من النوع الثاني لاكثر من (5) سنوات. سحبت عينات من الدم من هؤلاء الاشخاص وقيست مستويات كل من (LH، FSH، HbA^{1c}، FBG). ودلت النتائج التي تم التوصل اليها الى نقصان معنوي في مستوى هرموني الـ (LH، FSH) عند النساء المصابات بمرض السكر من النوع الثاني مقارنة بالاصحاء، وكذلك نقصان معنوي في هرموني الـ (FSH، LH) عند الرجال المصابين بمرض السكر من النوع الثاني مقارنة بالاصحاء.