Study the Comparison of Gonadotropin Levels in Diabetes Mellitus Females.

Rawnaq J. Kadhim and Salman A Ahmed Department of Chemistry, College of Sciences, Al-Nahrain University, Baghdad-Iraq.

Abstract

A cross sectional study was designed to assess the correlation of LH, FSH and HbA1c levels in patients with and without DM in premenopausal women, and the correlation of age with LH and FSH hormones in diabetic women, using the data that collected. It was conducted in the specialized centre for Endocrinology and Diabetes (SCED) in Baghdad city from December 2013 to September 2014. Hundred women with type II diabetes (30-49) and hundred healthy women in the same age and BMI as control during the luteal phase of menstrual cycle were enrolled. Patients assessed for HbA1C, FSH and LH levels. Results showed that HbA1c, LH and FSH were higher in diabetic premenopausal women compared with control individuals.

Keywords: Diabetes mellitus, Gonadotropin hormones, Glycated hemoglobin.

Introduction

Diabetes mellitus is an endocrine disorder in which human body suffers a lack of insulin or resistance to insulin. Currently, 150 million people in the world suffer from diabetes. Diabetes causes varieties of complications and usually its chronic complications develop 5 to 10 years after the diagnosis of both types of the diabetes [1]. Type II is characterized by decreased sensitivity to the effect of insulin, in other word relative lack of insulin. Worldwide 246 million people are affected by DM [2]. Among them One hundred million persons have a history of diabetes (DM) worldwide [3]. Complications of diabetes are uniquely and often more severely, affect Women [4].

Prevention of diabetes include Lifestyle modifications, dietary modification, regular physical activity and weight reduction are indicated [5,6]. Long-term glycemic control routinely uses Glycated hemoglobin (HbA1c) as a marker. In accordance with its function as an indicator for the mean blood glucose level, in diabetes patients HbA1c predicts the risk for the development of diabetic complications [7]. According to American Diabetes Association (ADA) criteria HbA1C value of (≥ 6.5%) or FPG≥126 mg/dl (7.0 mmol/l) or 2-hour plasma glucose \ge 200 mg/dl(11.1 mmol/l) or in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis a random glucose ≥200 mg/dl (11.1mmol/l), is strongly predicted as pharmacotherapy for diabetes[8].

The gonadotrophin hormones LH and FSH from the interior pituitary gland controlled the

growth and the reproductive activities of the gonadal tissue. LH and FSH are called gonadotrophins because they regulate the function of the gonads (ovaries and testes), in both (male, female, FSH stimulates gametes (sperm or egg) production, while LH promotes hormones production of gonadal Gonadotrophin releasing hormone from the hypothalamus stimulates the secretion of both LH and FSH, which are subjected to feed back loops regulation by the ovarian hormones [10]. Part of the workup of infertility in women, LH along with FSH are ordered, also its useful in the investigation of menstrual irregularities, and to aid in the diagnosis delayed and precocious puberty[11].

Patients and Methods

A total of 100 type II diabetic premenopausal women (30-49) year and 100 healthy women in the same age and BMI visiting the specialized center for Endocrinology and Diabetes (SCED) from December 2013 to September 2014 during luteal phase menstrual cycle were included in this study. Venous blood samples were collected from all the subjects. The serum was later used for analyzing HbA1C, LH and FSH. HbA1c was measured using immunoturbidimetric according DCCT/NSGP protocol by Biolyzer (Turbitex/Germany Kit), LH and FSH using enzyme linked fluorescent assay technique by vidas (Biomerieux /FranceKit). Diabetes was defined according to American Diabetes Association (ADA) criteria. We excluded from this study pregnant women, menopausal women, lactating, Patients on hormonal therapy, single women, Infertile women, poly cystic ovarian syndrome, smokers, Patients with endocrine disease e.g. Cushing's syndrome and family history of diabetes.

Statistical Analysis

Minitab (version 16) was used to analyse the collected data. These data analysed using the following measure:

- 1. Descriptive statistics: frequency, percentages, mean and standard deviation.
- Inferential statistics: student t-test was used to define the difference between the means of two groups in quantitative variables. P value less than 0.05 considered statistically significant.

Results and Discussion

From hundred diabetic premenopausal women and hundred healthy premenopausal

women, the result in Table (1) showed that the Mean± SD value of age was 38.31±4.08 in diabetic women and 37.45±4.97 in healthy women with p value of ≥ 0.1839 (not significant), the level of BMI in diabetic and control was 27.42 ± 2.20 , 27.18±1.38 respectively and $p \ge 0.362$ (not significant), while the Mean± SD of HbA1c was 9.42±2.33 in diabetic women and 4.657±0.447 in control with $p \le 0.05$ (significant), the mean levels of LH and FSH in diabetic women was 5.37±0.87 and 5.66±1.25 respectively compared the levels in the control 0.576±0.092 1.855±0.353 respectively and difference is significant due to the p value of ≤0.05, this comparison shows that there is a significant increase in the level of these hormones in diabetic patients.

Table (1)
Biochemical parameters for the diabetic and control.

Parameters	DIABETIC No=100 Mean± SD	CONTROL No=100 Mean± SD	P value
Age (years)	38.31±4.08	37.45±4.97	0.183
BMI(Kg/m ²)	27.42±2.20	27.18±1.38	0.362
LH(mIu/ml)	5.37±0.87	0.576±0.092	0.000
FSH(mIu/ml)	5.66±1.25	1.855±0.353	0.000
HbA1C (%)	9.42±2.33	4.657±0.447	0.000

P value is significant ≤ 0.05 level.

The biochemical findings of this study showed a significant elevation of HbA1c in diabetic female compared to control Fig.(1) and this is similar to the findings in a group of patients studied by other researchers [12-16]. When the groups were investigated, the mean HbA1C were higher in diabetic premenopausal women.

Also it was found Fig.(1) a significant increase of LH and FSH in diabetic premenopausal women compared to control. When corpus leutum starts lysing during the last period of leuteal phase (in cases no pregnancy) the progesterone and estrogen levels will decrease while LH, FSH levels increase regularly, also the decrease of

progesterone and estrogen may cause a positive feedback mechanism at the pituitary gland level [17].

And result of this, an increment of gonadotropin (LH, FSH) will be occurring. On the other hand, LH hormone is considered as a principle factor in stimulating theca interna, causing an elevating production of pregnenolone compound which is converted by granulose cells to progesterone during leuteal phase [18].

The results of the present study are consistent with other results [19, 20].

Which showed that higher (LH, FSH) levels in diabetic premenopausal women compared with the control.

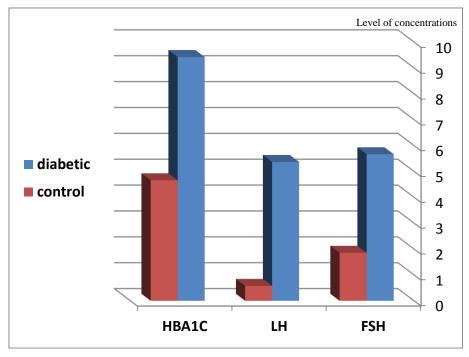


Fig.(1) Comparison of mean value of gonadotropins and HbA1C in diabetic and control group.

Table (2)
Variation of LH, FSH and HbA1C with Age.

Parameters	Group I Diabetic women Age(30-38) years No=(48) Mean± SD	Group II Diabetic women Age(38-48) years No=(52) Mean± SD	P Value
HbA1C%	7.490 ± 0.968	11.20 ± 1.72	0.00
LH(mIu/ml)	3.88 ± 0.36	6.73 ± 0.69	0.077
FSH(mIu/ml)	4.85±1.14	6.414 ± 0.799	0.00

P value is significant ≤ 0.05 level.

Table (2) shows that the mean HbA1C was 7.490 ± 0.968 in group I and 11.206 ± 1.72 in group II, while the Mean \pm SD of both LH, FSH were 3.883 ± 0.36 , 4.8517 ± 1.14 respectively in group I and 6.73 ± 0.694 ,6.4140 ±0.799 respectively in group II with p value of ≥0.081 (not significant) for LH and ≤0.05 (significant) for FSH.

It was found in the present study that there were changes in sex hormones in patients according to their age group. As shown in Table (2) and Fig.(2) that the changes in FSH hormone between age groups were significant except for LH where the changes between age groups were not significant.

The age of women is one of factors which restricted the ovarian steroid secretion

capacity, these hormones was decline around the age of 30 years old, so that gonadotropin (LH, FSH) will be increase [21, 22].

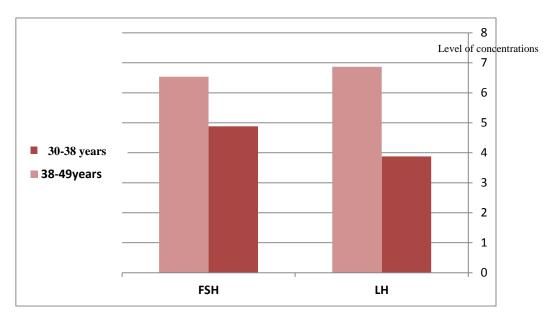


Fig.(2) Variation of LH, FSH and HbA1C with Age.

Conclusion

A significant elevation of HbA1c in diabetic female compared to control. Also a significant increase of LH and FSH in diabetic premenopausal women compared to control. According to the age of women a significant elevated in FSH level and not significant elevated level of LH in diabetic women. In conclusion could be drawn that LH and FSH increase in diabetes mellitus type II premenopausal women.

References

- [1] Shabnam O., Maryam T., Niaki, Fatemeh N., Farzan K., Sexual Dysfunction Among Women With Diabetes Mellitus in a Diabetic Center in Amol, J. Nat. Sci. Biol Med., 4(2), 321–324, 2013.
- [2] Annamaria G., Ellids D., Sexual Dysfunction in Women with Diabetes Mellitus, journal of sex research, 47, 199-211, 2010.
- [3] Golden SH., Dobs AS., Vaidya D., Endogenous Sex Hormones and Glucose Tolerance Status in Postmenopausal Women, J. Clin. Endocrinol Metab., 92, 1289–1295, 2007.
- [4] Saudek C., Herman W., Sacks D., Bergenstal R., Edelman D., Davidson MB., Diabetes Atlas 3rd Edition, International Diabetes Federation. A New Look at Screening and Diagnosing Diabetes

- Mellitus, J.Clin. Endocrinol Metab, 93, 2447–69, 2008.
- [5] Marshall S., Barth J., Standardization of HbA1c measurements a consensus statement, Diabetic Medicine, 17, 5-176, 2000.
- [6] Wexler D., Grant R., Meigs J., Nathan D., Cagliero E., Sex disparities in treatment of cardiac risk factors in patients with type 2 diabetes, Diabetes Care, 28, 514-520, 2005.
- [7] Andersen G., Christiansen J., Mortensen H., Christiansen K., Predersen-Bjerguard L., Kastrup K., Plasma lipid and lipoprotein in type 1 diabetic children and adolescent in relation to metabolic regulation, obesity and genetic hyperlipoprotenimia, Actupaediator Scand, 72, 361-365, 1983.
- [8] American Diabetes Association, Standards of Medical Care in Diabetes, Diabetes Care, 35 (1), 2012.
- [9] Elaine T., Marieb R., The Endocrine System in Anatomy and physiology, Benjamin Cummings, San Francisco, 512, 518, 2000.
- [10] Zilva F., Mayne D., Pannel P., The hypothalamus and pituitary gland. In: Clinical chemistry in Diagnosis and Treatment, 6th ed. Hodder Headline group PLC London, 106 115, 1999.
- [11] McDonough P., Molecular abnormalities of FSH and LH action, Ann. N. Y. Acad. Sci., 997, 22 34, 2003

- [12] Su C., Caballero E., Arora S., Smakowski P., Bashoff E., Florence M., Logerfo B., Horton E., Veves A., The Effect of Hormonal Replacement Therapy on the Vascular Reactivity and Endothelial Function of Healthy Individuals and Individuals with Type 2 Diabetes, The Journal of Clinical Endocrinology & Metabolism, 84(4), 343-349, 2009.
- [13] Fatemi S., Taghavi S., Evaluation of sexual function in women with type 2 diabetes mellitus, Diabetes Vasc. Dis. Res., 6, 38-39, 2009.
- [14] Rosato M., Schneider S., Shapses S., Bone Turnover and Insulin-like Growth Factor I Levels Increase After Improved Glycemic Control in Noninsulin-dependent Diabetes Mellitus, Calcified Tissue International August, 63, 107-111, 1998.
- [15] Erol B., Tefekli A., Sanli O., Ziylan O., Armagan A., Kendirci M., Eryasar D., Kadioglu A., Does sexual dysfunction correlate with deterioration of somatic sensory system in diabetic women?, International Journal of Impotence Research, 15, 198–202, 2013.
- [16] Nakhjavani M., Imani M., Larry M., Nargesi A., Morteza A., Esteghamati A., Metabolic syndrome in premenopausal and postmenopausal women with type 2 diabetes: loss of protective effects of premenopausal status, J. Diabetes Metab Disord, 13(1), 102, 2014.
- [17] Ganong's W., Review of Medical Physiology.22th edition. Lange medical book, McGraw-Hill Boston, Toronto, Newtersy, 424-340, (2005).
- [18] Salvi R., Castillo E., Voirol M., Gonadotropin-releasing hormone expressing neurons immortalized conditionally are activated by insulin, implication of the mitogen activated protein kinase pathway, *Endocrinology*, 147, 816–826, 2006.
- [19] Natah T., Wtwt M., Al-Saadi H., Al-Saadi A., Farhood H., Study the levels of adiponectin, FSH, LH and Sex hormones in Type 2diabetes (NIDDM), Journal of

- Biology Agriculture and Healthcare, 3(2), 2224-3208, 2013.
- [20] Hussein Z., Jawad Al-Qaisi J., Effect of Diabetes mellitus Type 2 on Pituitary Gland Hormones (FSH, LH) in Men and Women in Iraq, Journal of Al-Nahrain University Science, 15 (3), 57-79, 2012.
- [21] Broekman F., Soules J., Fauser B., Ovarian Aging, Mechanisms and Clinical Consequences. R, Endocrinol, Aug. 30(5), 465–493, 2009.
- [22] Broekmans F., Knauff J. Veld E., and Macklon N., Female reproductive ageing: current knowledge and future trends, Trends Endocrinol. Metab, Mar.18(2),58-65, 2007.

الخلاصة

صممت هذه الدراسة المقطعية لايجاد علاقة هرمونات اله FSH,LH و HbA1C عند النساء قبل سن اليأس المصابات وغير المصابات بمرض السكري من النوع الثاني وايجاد علاقة العمر مع هرمونات LH,FSH لدى مريضات السكري باستخدام البيانات التي جمعت. اجريت هذه الدراسة في مركز امراض الغدد الصم والسكري في مدينة بغداد للفترة ما بين شهر كانون الأول 2013 الى شهر ايلول 2014. أخذت مئة امرأة مصابة بمرض السكري من النوع الثاني أخذت مئة امرأة مصابة بمرض السكري من النوع الثاني العمر وكتلة الجسم خلال النصف الأخير من الدورة الشهرية. العمر وكتلة الجسم خلال النصف الأخير من الدورة الشهرية. وتم قياس مستويات الـ ,LH,FSH والـ Jha1C والـ LH,HbA1C و LH,HbA1C و FSH