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Assessment of anti-Mullerian hormone level in reproductive age group women with diabetes mellitus type one

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ABSTRACT

Objective: To assess the levels of anti-Mullerian hormone in women with type I diabetes mellitus during their reproductive age period.

Background: Reproductive impairment in poorly controlled type one diabetes mellitus results from perturbations at different levels of the gonadotropic axis, including the hypothalamus/pituitary and the ovary.

Methods: This study was designed as a case-control study. We evaluated anti-Mullerian hormone serum level in a female with type I diabetes mellitus (N = 60) who attended the Diabetes and Endocrine Center in Merjan Medical city in Babylon, from November 2015 to April 2016. These patients were compared with a healthy fertile female (N = 80) as a control group. The female's age ranges from 13 to 40 years for the two groups. Body mass index was calculated and serum samples for anti-Mullerian hormone serum levels were estimated.

Results: There was a significant difference between patients and control group regarding body mass index, residence, educational level, fertility, and menarche. Anti-Mullerian hormone level is significantly lower in patient group when compared with the control group (p = 0.000*). HbA1c level is significantly higher in a patient group when compared with the control group (p = 0.000*).

Conclusion: The results suggest that type I diabetes is an independent risk factor for decrease of anti-Mullerian hormone level in reproductive age group women.

1. Introduction

Diabetes mellitus (DM) is a syndrome of impaired carbohydrate, fat and protein metabolism caused by either lack of insulin secretion or decreased sensitivity of tissues to insulin [1]. Diabetes mellitus type 1 (also known as type 1 diabetes) is a form of diabetes mellitus in which not enough insulin is produced and the lack of insulin results in high blood sugar levels [2–4]. The cause of TIDM is unknown; however, it is believed to involve a combination of genetic and environmental factors [5,6]. TIDM is associated with an increased risk of microvascular and macrovascular complications [7].

Several studies have shown an increased prevalence of menstrual cycle abnormalities in adult women with TIDM [8,9]; these have shown that menstrual cycle irregularities are especially prevalent in young women and that these abnormalities decrease with advancing age [8,10].

Anti-Mullerian hormone (AMH), also known as Mullerian-inhibiting substance, is a member of the transforming growth factor-β (TGFβ) superfamily and it is very important biomarkers in ovarian reserves [10,11]. A decrease in AMH levels above the age of 33 compared to healthy controls was found to be associated with poorly controlled TIDM [12,13]. The real cause of this association still remains unexplored [14,15]. The negative effects of diabetes on kidneys, nerves, and vessels are well established; however, the effect of diabetes on reproductive function is less well understood, but it is important to characterize, given the increasing numbers of young women with diabetes [16].

2. Aim of the study

The aim of the study was to assess serum levels of AMH in women with TI DM during their reproductive age period.

3. Subjects and methods

This study was designed as a case-control manner. Approved by the Medical Ethical Committee of the College of Medicine/University of Babylon, informed written consent has been signed by the participant before enrollment in this study. Anti-Mullerian hormone serum levels were evaluated in female with TIDM (N = 60), and they were selected from 220 diabetic females who attended the Diabetes and Endocrine Center in Merjan Medical city in Babylon, from November 2015 to April 2016.

3.1. Exclusion criteria

1- Woman who took any hormone therapy within previous three months of hormonal assays.
2- Women age less than 13 years or more than 40 years.
3- Menopause state.
4- Hysterectomy or oophorectomy.
5- Other endocrine disorders.

Selected female was compared with healthy fertile female (N = 80) as a control group. A standard questionnaire was used for collecting demographic data (age, menarche, residence, educational level, fertility, menstrual cycle history (regularity, duration), assessment of Anthropometric data such as height and weight) to calculate body mass index (BMI).

3.2. Hormonal and biochemical analysis with sample collection

Blood samples were collected between 8:30 and 10:00 a.m. from the two groups for Anti Mullerian Hormone (AMH) serum level. These women should be fasting to estimate the fasting blood sugar, HbA1c. Samples were collected by venipuncture into 2 ml (ml) glass tubes. These samples were left to stand at least for 15 min at room temperature which then were centrifuged at 3000 rpm (rpm) for 3 min to separate the serum. Serum aliquots were obtained, and stored at −20 °C for later measurement (AMH). Serum samples for AMH were examined by sensitive Enzyme Linked Immuno Sorbant Assay method (ELISA) and the kit used was from Beckman coulter; USA in one run within about four months of collection. The lower limit of AMH (ng/ml) is 1 and the upper limit 4. Blood for HbA1c was collected in Vacuum blood collection tube glass (2 ml) and Jordan kit (Bio-rad; France) was used for HbA1c analyses. Lower limit of HbA1c (mmol/l) is <36 and upper limit is 48.

3.3. Statistical analysis

Statistical analysis of the data was performed using SPSS version 17 for Windows (Statistical Package for Social Science; SPSS, Inc., Chicago, IL). Continuous variables were expressed as the mean ± standard deviation (SD) and range; categorical variables as percentages. Between-group differences were tested by comparing means–independent samples t-test for continuous parameters, and Chi–square test was used for categorical variables; Pearson's correlation was used to examine the relation between continuous variables (AMH and HbA1c). A p value of <0.05 was considered significant for all analyses.

4. Results

4.1. Comparison between patients and control groups

There were significant differences between patients and control group regarding BMI, residence, educational level, fertility, and menarche (Table 4.1).

Table 4.1
Comparison of demographic data of patient and control group (values are mean ± SD or percentages).

Parameter	Patient group N = 60	Control group N = 80	P value
Age (years)	24.87 ± 8.47	25.91 ± 8.29	0.659
BMI (kg/m^2)	25.17 ± 5.43	22.94 ± 2.38	0.001*
Residence (N)			
Rural	(35) 58.3%	(59) 73.8%	0.000*
Urban	(25) 41.3%	(21) 26.3%	
Educational level (N)			
Illiterate	(18) 30.0%	(32) 35.5%	0.000*
School	(10) 16.7%	(30) 30%	
Higher degree	(32) 53.3%	(18) 34.5%	
Fertility			
Fertile	(31) 51.7%	(80) 100.0	0.000*
Infertile	(29) 48.3%	0	
Menstrual cycle regularity (N)			
Regular	(58) 96.7%	(80) 100%	0.10
Irregular	(2) 3.3%	0	
Menarche (year)	12.82 ± 0.75	12.16 ± 0.58	0.001*

BMI - Body Mass Index.
* Significant different from the corresponding value.

Table 4.2
Hormonal level and biochemical test of control and patient group (values are mean ± SD).

Parameter	Patient group	Control group	P value
AMH (ng/ml)	(2.82 ± 1.27)	(3.79 ± 1.91)	0.000*
HbA1c (%)	(8.73 ± 2.80)	(4.82 ± 0.39)	0.000*

AMH: Anti-Mullerian Hormone, HbA1c: Hemoglobin A1C Test.
* Significant difference from the corresponding value.

4.2. Comparison between patients and control group regarding AMH level and HbA1c

Table 4.2 shows AMH level of patients and control group regarding AMH and HbA1c. AMH serum level is significantly lower in patient group when compared with control group (p = 0.000*). HbA1c level is significantly higher in patient group than control group (p = 0.000*).

4.3. Correlation of anti-Mullerian hormone with HbA1c in patient and control group

In patient group, there was insignificant negative correlation between AMH and HbA1c (r = −0.931, P = 0.20). In control group there was insignificant negative correlation between AMH and HbA1c (r = −0.076, P = 0.50), Fig. 4.1.

4.4. Binary logistic regression analysis for patients as the dependent variable

To examine the relationship of measured factors with diabetes in women, a binary logistic regression analysis was performed. In this analysis, AMH, HbA1c, residence, BMI and education level were significantly associated with diabetes. AMH, HbA1c, residence, BMI and low education were associated with increased odds ratio in diabetic patients, see Table 4.3.

5. Discussion

There was a higher significant difference in BMI of patient vs control groups (25.17 ± 5.43 vs 22.94 ± 2.38) kg/m^2, as shown in Table 4.1. This result is similar to many research works which