Original Article

The correlation between Glycosylated Hemoglobin and menstrual cycle length in Type 1 diabetic adolescents

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Abstract

Introduction:
Type 1 diabetes mellitus (T1DM) is the most common endocrine problem seen in children and adolescents; it is one of the main diseases which damages the body organs such as disrupt hypothalamic pituitary-gonadal function if blood sugar is not well controlled. This study aimed to find the correlation between Glycosylated Hemoglobin and menstrual cycle length in Type 1 diabetic adolescent referred to Iran Diabetes Association.

Materials and Methods:
This is a prospective longitudinal study. The subjects consisted of 60 diabetic girls aged 11-19 years selected by easy sampling method. The research instruments included a questionnaire, HbA1c sample laboratory test, interviews on the biophysical data. Data were analyzed through descriptive and inferential statistical tests.

Results:
Our results showed that 86.6% of the patients had normal menstrual cycle.10% had oligomenorrhea and 3.33% amenorrhea. No one had primary amenorrhea. There was no statistically significant correlation between the mean HbA1c and menstrual cycle length.

Conclusion:
In this study, blood sugar rate and HbA1c in adolescents showed no significant effect on the menstrual cycle.

Keywords: Diabetes Mellitus, Glycosylated Hemoglobin, Female Adolescent, Menstruation

Introduction:

Diabetes is the most common endocrine-metabolic disorder in children and adolescents, with the prevalence of 0.6 to 5 per 1000 in Iran (1, 2). The main etiology of type 1 diabetes is still unknown. The incidence of type 1 diabetes is less common in over 20 year olds. Usually the onset of this type of diabetes is very sudden. Diabetes mellitus is a disease that damages various systems in the body (4), and type I diabetes adversely affects maturity and growth in adolescents, causing short stature due to growth abnormalities in bone physiology, according to some studies (5). A specific index for diabetes control is HbA1c. Glycosylated hemoglobin (naturally

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between 4 and 6%) is a useful indicator of mean blood glucose level in previous 8 to 12 weeks; its high value means exposure to micro-vascular complications. Therefore, long term improvement of glycemic control must be planned. This index is an international standard that is measured 3 to 4 time each year for the evaluation of blood glucose in type 1 diabetes (6).

There have been few studies conducted in connection with menstrual disorders and type I diabetes (7) with conflicting and inconsistent results related to type I diabetes effect on menstruation and menarche (8). But, one study on 24 adolescent girls with type I diabetes aged 12.5 to 20.3 years showed glycosylated hemoglobin rate of 12.8 for girls with irregular menstruation, and 10.5 for girls with regular menstruation (9). A usual reason for young girls attending health centers is menstrual disorders. Although these irregularities could be natural a few years after menarche, they may be pathological and need immediate attention (10). Menstrual disorders in the first few years after menarche must immediately be investigated to prevent future complications like infertility. These disorders are mostly temporary and recover spontaneously, but some are serious and require treatment. Amenorrhea and oligomenorrhea may be a sign of endocrine disorders (11). Most studies on adolescent girls with type I diabetes, uninformed about menstrual cycles, show that menstrual disorders are not diagnosed in time. There have been only a few studies on the effect of glycosylated hemoglobin on menstrual cycle in this age group, and even those were conducted retrospectively on adults who were asked about menstrual disorders in their youth. In addition, in most studies, random or fasting blood glucose has been investigated, which show a limited prospect of blood glucose control as compared with glycosylated hemoglobin (9, 10). The present study was conducted to investigate the relationship between glycosylated hemoglobin and regularity of menstruation in adolescent girls with type I diabetes.

Materials and Methods:

This longitudinal prospective study was conducted on adolescent girls with type I diabetes at Iran Diabetics Society in 2006. At confidence interval of 95% and test power of 80%, sample size was calculated 59, but practically 60 adolescent girls with type I diabetes who met inclusion criteria were selected by convenient sampling method. First, medical records of girls were reviewed (274 in total) and samples were selected according to study inclusion criteria, which were age of 11 to 19 years, elapse of at least two years from menarche for those with irregular cycles, no polycystic ovaries or thyroid disorders based on diagnosis of a specialist, not using hormones that affect menstruation.

Data were collected through interviews and biophysical information. Data collection tools were a questionnaire and laboratory tests for measuring glycosylated hemoglobin. The questionnaire included demographic details, glycemic control method, diabetes complications, and some menstrual features. Participants were asked to specify start and finish of the last three menstrual cycles. Menstrual cycles shorter than 21 days and longer than 35 were considered as menstruation disorders (12). Every participant was tested twice for glucosylated hemoglobin within a three month interval at a specific laboratory. The first test was done when meeting participants for the first time and they were to complete the questionnaire. Telephone contact was maintained with all participants over the next three cycles as a reminder to record bleeding start and finish times and to do the second laboratory test. At the end of the third cycle, participants were asked to hand in their completed questionnaires and test results to the Diabetics Society. For those with oligomenorrhea, the following tests were requested as well; TSH (Thyroid-Stimulating Hormone), T3 (Tri-Iodotyronine), T4 (Thyroxine), FSH (Follice-Stimulating Hormone), LH (Luteinizing Hormone), serum testosterone, DHEAS (Dehydroepiandro-sterone sulfate), prolactin, hydroxy progestrone. Also, clinical examinations were carried out for conditions such as hirsutism, acne, greasy skin, hair loss, deep voice, and acanthosis nigricans. Hirsutism was diagnosed based on Freeman-Galway classification for scores over 8. Acanthosis nigricans was also diagnosed according to pigmented velvety soft thick skin lesion in the armpit, back of the neck, under breasts, and inner thighs. According to the test and clinical examination by an endocrinologist, six patients with polycystic ovary syndrome were excluded from the study. Also, based on test results, another participant with primary amenorrhea and high testosterone level (as high as in a man), and diagnosis by a specialist whose type I diabetes had not been due to primary amenorrhea was excluded. All glycosylated hemoglobin tests were measured by High-Performance Liquid Chromatography (HPLC). According to the normal glycosylated hemoglobin rate of between 4.2 and 6.4%, participants were classified into normal group (less than 7.2%) and abnormal group (over 7.2%). Descriptive statistics were used for data analysis, and to assess the relationship between variables Fisher's exact test, simple regression test, and odds ratio were used.

This study was approved by the research ethics committee at Tehran University of Medical Sciences. The objectives of study were explained to all participants and they were assured of confidentiality and declared their consent to take part. All laboratory tests were conducted free of charge.

Results:

Of all participants, 41.7% were aged 18 to 19 and 6.7% were aged 12 to 13 years. Also, 45% were with diabetes for 6 to 10 years and 11.7% for 11 or more years. 45% used 40 to 60 insulin units per day and 0.5% used 20 units per day. In 73.3% of participants HbA1c was over 7.2 and in 26.7% it was normal (less than 7.2). Simple regression test did not reveal a significant correlation between diabetes and menstrual regularity (P=0.361, B=0.93). Also, the difference in odds ratio of diabetes to menstrual regularity and HbA1c values was insignificant (P=0.839, OR=1.125). Results showed that none of the participants had less than 21 days between menstrual cycles, and in 10.3% this interval was more than 35 days. Also, 89.5% who had normal intervals between menstrual cycles had normal HbA1c level but 15.3% did not. Fisher's exact test showed that there was no significant correlation between menstrual intervals and HbA1c level (P=0.649).

Table 1- Absolute and relative frequency distribution of participants according to mean HbA1c and menstrual cycle intervals

Mean HbA1c	Normal (less than 7.2)	Abnormal (over 7.2)
Mean menstrual interval	Number (%)	Number (%)
Normal (35 days or less)	17 (89.5)	35 (89.7)
Abnormal (over 35 days)	2 (15.5)	4 (15.3)
Total	19 (100)	39 (100)

P=0.649

Discussion:

Participants' mean age was 16.76±1.87 years with 6.19±3.71 years mean duration of illness since diagnosis. Results obtained indicated that there was no significant correlation between duration of illness and regularity of menstruation. Also, no correlation was found between menstrual intervals and HbA1c level. In a study by Schroder et al. titled ‘relationship between glycemic control and menstruation in diabetic adolescents’, none of the participants had polymenorrhea, but 15.2% had oligomenorrhea with a highly significant correlation with HbA1c (P<0.05) (9). In terms of oligomenorrhea, this study’s results were different, and this difference was due to exclusion of adolescents with polycystic ovaries that had oligomenorrhea. In Strawmayer et al. study titled ‘different menstrual cycle in type I diabetic women and non-diabetic women’, results showed that none of the subjects had polymenorrhea, and 78.7% of diabetics and 66.7% non-diabetics (over 31 days’ menstrual intervals) had oligomenrrhea, and the difference between two groups in this respect was significant (P=0.02) (7). The present study is in line with Strawmayer’s in that none of the participants had polymenorrhea, but that is not true for oligomenorrhea. The difference lies in the difference in oligomenorrhea criterion, which was an interval of 31 days in Strawmayer’s and 35 days in the present study. Another difference was the exclusion of participants with polycystic ovaries in the present study.

According to a study by Kjaer et al. titled ‘epidemiology of menarche and menstrual disorders, in non-selected type I diabetic women compared with control group’, 10.6% diabetics and 4.8% non-diabetics had oligomenrrhea, and the difference between them was significant (P<0.02) (13). Also, 7.3% diabetics and 5.2% non-diabetics had polymenorrhea (P<0.005). Due to differences in sample demographics and research method, the results of the two studies are different. In Kjaer’s study, participants were aged 18 to 49 years and those with diseases that impact menstruation like thyroid disorders and polycystic ovaries were not excluded, whereas in this study age range was 11 to 19 years and participants with these diseases were excluded.

An objective of any study is the application of results in different settings, so that a change or improvement in current situation could be achieved. The results of this study can be helpful for diabetic adolescents in determining the relationship between diabetes type I and menstruation disorders, and also educating their families for timely preventative or therapeutic intervention in menstrual disorders.

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