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# IMPACT OF AGE AT MENARCHE ON CLINICAL AND BIOCHEMICAL CHARACTERISTICS IN WOMEN WITH TYPE 2 DIABETES

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*Objectives*. Previous studies have shown that early age at menarche could be associated with higher risks of type 2 diabetes, depressive symptoms, breast cancer, reproductive and cardiovascular disease. The aim of this study was to examined the association between menarche timing and the clinical and biochemical characteristics in women with type 2 diabetes (T2DM). *Material and Methods*. We evaluated 326 women aged between 44 and 60 years with confirmed T2DM-cohort 2010-2012. Data on menarche were collected using confidential self-administered questionnaire. Anthropometric, biochemical parameters were assessed. The anthropometric measurement included body mass index (BMI). The fastind plasma glucose (FPG), glycosylated hemoglobin ($HbA_{1c}$), serum cholesterol, serum triglycerides, serum high-density lipoprotein (HDL)-cholesterol, insulinemia were measured. According to age at menarhe, the women with type 2 diabetes were included in two group: with menarche before 12 years (category 1) and after 12 years (category 2). *Results*. 77 women with T2DM reported age at menarche before 12 years and 249 women reported age at menarche after 12 years. Mean age at diagnosis of T2DM in the first group was 57.18 ± 11.50 years and in the second group 60.64 ± 10.21 years. In the first group mean BMI, FPG, $HbA_{1c}$, serum cholesterol, triglycerides, HDL-cholesterol, insulinemia was 33 kg/m$^2$, 190 mg/dl, 8%, 16 µIU/ml, 211 mg/dl, 51 mg/dl, 175 mg/dl and in the second group the mean of the same d*eterminations was* 32 kg/m$^2$, 175 mg/dl, 8%, 16 µIU/ml, 221 mg/dl, 50 mg/dl, 165 mg/dl. Mean valures of triglycerides and triglycerides to HDL-cholesterol ratio were significantly different between the groups. In our study, age at menarhe are corrrelated positive with HDL-cholesterol r = 0.271, p = 0.024 in the first group and r = 0.179, p = 0.008 in the secound group. Our data showed a negative correlation between age at menarhe and trgycerides/HDL-cholesterol ratio (r = -0.177, p = 0.009) in the secound group. *Conclusion***.** The present study indicates that women with T2DM and age at menarche before 12 years have increased cardiovascular risk.

*Key words*: age at menarche, type 2 diabetes, obesity

## INTRODUCTION

Menarche is the first menstrual bleeding, in female humans. The timing of menarche is influenced by genetic, racial and environmental factors, especially psychosocial and nutritional factors. Age at menarche has largely decreased in Europe and seems stabilised at 13 years with 0.5 years variations between countries [1]. According to the Third National Health and Nutrition Examination Survey, the average age a girl begins menstruating has declined in the last century, from 13.3 years to 12.4 years of age in United States [2]. Causes that may be contributing to the general trend include nutrition changes and exposures to pesticides with proestrogenic activity [3,4]. Age variations of menarche may be important, previous studies have shown that early age at menarche could be associated with higher risks of type 2 diabetes (T2DM), depressive symptoms, breast cancer, reproductive and cardiovascular disease [5–7]. The association between menarche timing and

diabetes remains unclear; the association between menarche timing with higher body mass index (BMI) and greater waist circumference may is causally responsible for the downward trend of menarche [8]. The aim of this study was to examined the association between menarche timing and the clinical and biochemical characteristics in women with T2DM.

## MATERIALS AND METHODS

We evaluated 326 women, aged between 44 and 60 years with confirmed T2DM (cohort 2010–2012). Data on menarche, were collected using confidential self-administered questionnaire. Anthropometric, biochemical parameters were assessed. The anthropometric measurement included body mass index (BMI). BMI was computed as a ratio of weight to the square of height (kg/m$^2$). Subjects were asked to fast for 12 h before blood sampling, which was done between 8.00 and 9.00 a.m. The fastind plasma glucose (FPG), glycosylated hemoglobin ($HbA_{1c}$), serum cholesterol, serum triglycerides, serum high-density lipoprotein (HDL)-cholesterol, insulinemia were measured. Insulin was evaluated using an Enzyme-linked Immunosorbent Assay (ELISA) kits, $HbA_{1c}$ was determined by high-performance liquid chromatography (HPLC) and plasma glucose, serum cholesterol, serum triglycerides, serum HDL-cholesterol using automatic devices. According to age at menarhe, the women with type 2 diabetes were included in two category: with menarche before (category 1) and after 12 years (category 2).

### Statistical analyies

Data are presented as mean±SD. Clinical characteristics were compared using the t Student Test. Pearson's moment-product correlation coefficients were calculated to evaluate correlations between variables. Significance was defined at the 0.05 level of confidence. All calculations were performed using the Statistical Package for Social Sciences Software (SPSS) version 15.

## RESULTS

77 women with T2DM reported age at menarche before 12 years and 249 women with T2DM reported age at menarche after 12 years. Mean age at diagnosis of T2DM in the first group was 57 years, ranging from 23 and 81 years. In the second group, mean age at diagnosis of T2DM was 60 years ranging from 43 to 84 years. In the first group mean BMI, FPG, $HbA_{1c}$, serum cholesterol, triglycerides, HDL-cholesterol, insulinemia was 33 kg/m2, 190 mg/dl, 8%, 16 µIU/ml, 211 mg/dl, 51 mg/dl, 176 mg/dl and in the second group the mean of the same determinations was 32 kg/m2, 175 mg/dl, 8%, 16 µIU/ml, 221 mg/dl, 50 mg/dl, 165 mg/dl. Tables 1 show the characteristics for the cohort by menarche age category.

In our study age at menarhe are corrrelated positive with HDL-cholesterol r=0.271, p=0.024 in the first group (Figure 1) and r=0.179, p=0.008 in the secound group (Figure 2).

Our data showed a negative correlation between age at menarhe and trgycerides/HDL-cholesterol ratio (r=-0.177, p=0.009) in the secound group. Correlation between age at menarhe and trgycerides/HDL-cholesterol ratio is shown in Figure 3.

*Table 1*

Characteristics of diabetic women that reported age at menarche before and after 12 years

| | **Category 1 (n=77)** | **Category 2 (n=249)** | **p** |
|---|---|---|---|
| Age (years) | 57.12±11.45 | 60.68±10.20 | NS |
| BMI (kg/m$^2$) | 33.20±6.94 | 32.03±8.49 | NS |
| FPG (mg/dl) | 190.62±83.72 | 175.86±80.48 | NS |
| $HbA_{1c}$(%) | 8.65±1.01 | 8.66±1.22 | NS |
| Basal insulin (µIU/ml) | 16.12±12.90 | 16.04±10.42 | NS |
| Serum cholesterol (mg/dl) | 211.09±54.95 | 221.57±55.38 | NS |
| Serum HDL cholesterol (mg/dl) | 46.97±13.79 | 48.85±16.16 | NS |
| Serum trgycerides (mg/dl) | 176.39±37.49 | 165.62±10.48 | p<0.05 |
| Trgycerides/HDL-cholesterol ratios | 4.87±1.52 | 3.87±1.06 | p<0.05 |

Comparison is signifiant at the 0.05 level: p<0.05

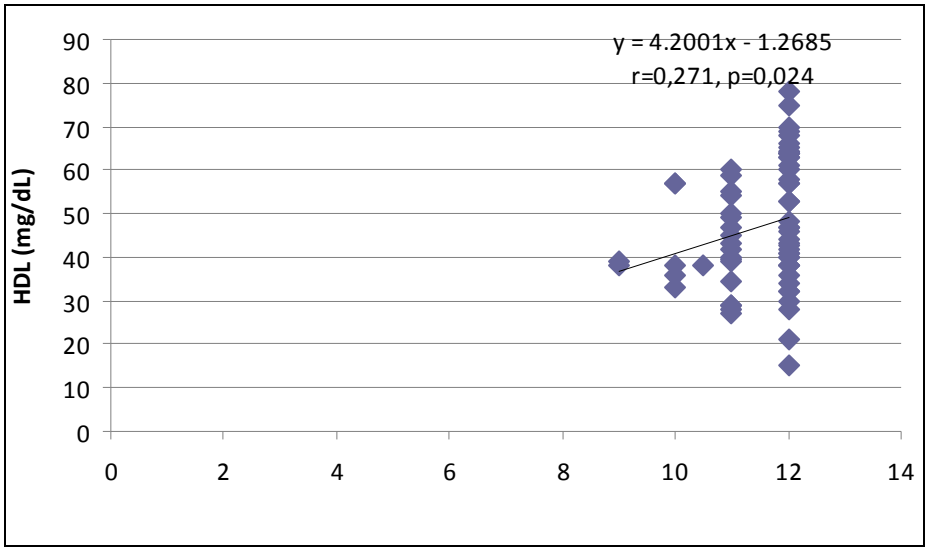


Figure 1. Correlation between age at menarhe and HDL-cholesterol in category 1 patients.

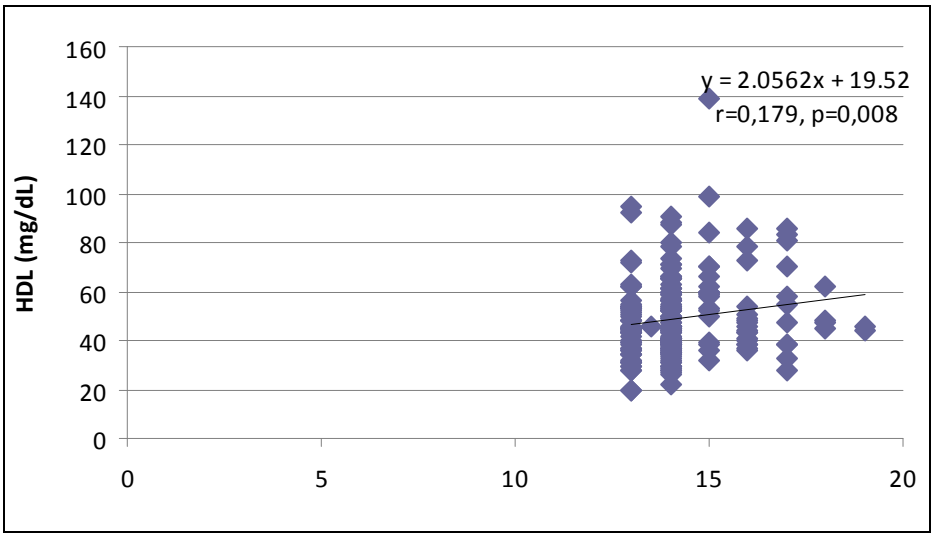


Figure 2. Correlation between age at menarhe and HDL-cholesterol in category 2 patients.

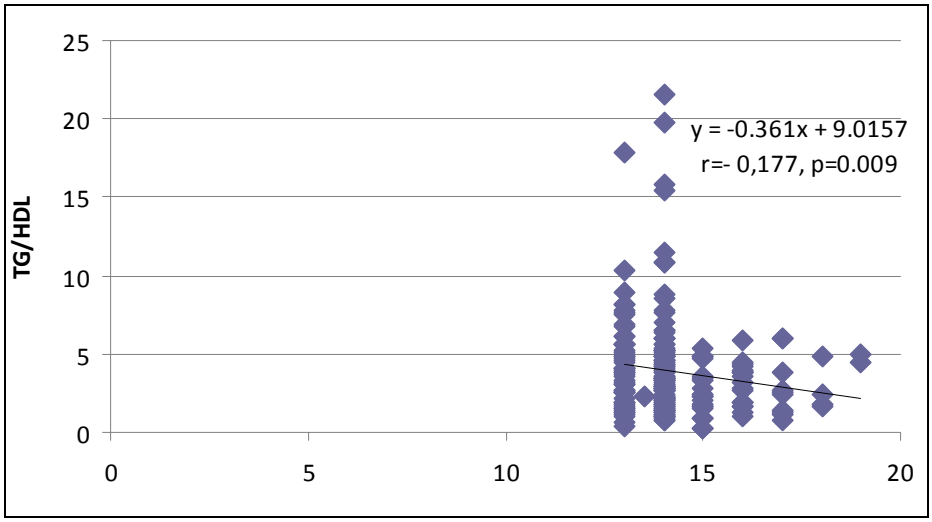


Figure 3. Correlation between age at menarhe and trgycerides/HDL-cholesterol ratios.

## DISCUSSION

Previous studies have shown that age at menarche is associated with higher risk of later T2DM. In a recent issue of *Diabetes Care*, Elks CE *et al.* published a article entitled "*Age at Menarche and Type 2 Diabetes Risk, The EPIC-InterAct study*". The autors evaluated the association between age at menarche and incident T2DM in 5.995 cases and they report that "*Women in the earliest menarche quintile (8–11 years, n=2.418) had 70% higher incidence of type 2 diabetes compared with those in the middle quintile (13 years, n =3.634)*" [9]. A study performed by Dreyfus JG *et al.* analysed the age at menarche and risk of T2DM among African-American and white women in the Atherosclerosis Risk in Communities (ARIC) study[7]. They found that early menarche was associated with T2DM in white women but associations were attenuated after adjustment for adiposity.

In our study mean valures of triglycerides and triglycerides to HDL-cholesterol ratio were significantly different between the groups. We observed a negative correlation between age at menarhe and trgycerides/HDL-cholesterol ratio in the secound group. It is known that high trgycerides values are associated with the presence of small, dense low-density lipoprotein (LDL) particles. The number of total and smaller LDL particles was in past studies significant correlated with cardiovascular risk [10–12]. The ratio triglycerides/ HDL-cholesterol proposed by Gaziano *et al*, is an atherogenic index that has proven to be a highly significant independent predictor of coronary heart disease [13].

## CONCLUSION

The present study indicates that women with T2DM and age at menarche before 12 years have increased cardiovascular risk.

## ACKNOWLEDGEMENT

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