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Original Article

Profiling Glycated Hemoglobin Level, Lactate Dehydrogenase and Alkaline Phosphatase Activity in Gestational Diabetes Mellitus Obese Women and Compare Them with Each Other

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A B S T R A C T

Background and Aims: The aim of this study was profiling glycated hemoglobin (HbA1c) level, lactate dehydrogenase (LDH) and alkaline phosphatase (ALP) activity in obese women with gestational diabetes mellitus (GDM) and evaluating the correlation between them.

Materials and Methods: Sample size was 90 subjects admitted to the clinical laboratory, who were divided into three groups, in each group (n=30). Subjects glycemic control was checked by HbA1c; ALP, LDH activity and serum glucose were determined with commercial kit. Age and body mass index (BMI) was recorded for each subject. The correlation analysis between blood activity of ALP, LDH activity, HbA1c, glucose, BMI and age in diabetic and normal pregnant women was carried out.

Results: The mean of HbA1c level was significantly higher in the GDM obese women than in women with normal pregnancy (p=0.01). In contrast, the means of ALP and LDH activity were lower in the GDM obese women than in women with normal pregnancy (p=0.09, and p=0.15, respectively). Also, an increase from the first to the third trimester of pregnancy in Hb-A1c levels was occurred from 3.6±0.016 to 4.0±0.15 mmol/L, from the first to the third trimester of pregnancy an increase in ALP activity was occurred from 174.4±12.2 to 177.5±16.3 U/L and there is an increase towards the third trimester.

Conclusions: Analysis of HbA1c level, LDH and ALP activity provides the evidence about health during the pregnancy. Using the HbA1c, LDH and ALP as a biomarker for monitoring GDM will be useful.

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Introduction

Previous studies have shown that the gestational diabetes mellitus (GDM) has significant implications for the health of mothers [1]. Earlier studies have shown that circulating chemokine is not different between women with GDM and the control subjects [2]. Previous studies demonstrated that the prediction of gestational diabetes in obese women using biomarkers are related to insulin resistance patients in the early second trimester [3]. Based on some studies, reference intervals have reported for plasma alkaline phosphatase (ALP), calcium, lactate dehydrogenase (LDH), phosphate, during pregnancy periods [4]. It is clear that women with normal glucose tolerance pre-gravid and developing gestational diabetes in the late gestation have subclinical metabolic dysfunction prior to conception compared with women with normal glucose tolerance [5]. It is interesting that continuous glucose monitoring can diagnose high postprandial blood glucose levels [6]. Researchers reported that subclinical hypothyroidism in pregnancy have been associated with an increased risk of gestational diabetes [7]. Also, researchers reported that alterations in the insulin-signaling pathway and subsequent glucose disposal are the underlying cause of insulin resistance in the patients with GDM [8]. Furthermore, researchers reported that increased glycated hemoglobin (HbA1c) in obese GDM-negative women at delivery indicated gestational dys-glycemia [9]. It should be noted that the effect of prior GDM on glucose according to the weight status reported by researchers [10]. Additionally, researchers reported that urine albumin-to-creatinine ratio is associated with glycaemic status in women with GDM [11]. Importantly, investigators found that original concerns regarding the use of drug have meant that diet control and insulin has been the mainstay of treatment for hyperglycaemia during pregnancy [12]. It has been suggested that maternal gestational weight gain is an independent predictor of total adiposity [13]. Several studies have examined the association between gestational weight gain and offspring birth weight in singleton term pregnancies of women with type 1 diabetes [14]. A number of recent studies have suggested that women having GDM are at the threat of early postpartum metabolic syndrome [15]. It is becoming more apparent than fetal growth in relation to gestational weight gain in women with type 2 diabetes [16].

The aim of this study was evaluation of blood HbA1c level, LDH, ALP activity in women with GDM and obesity.

Materials and Methods

Materials

LDH (685477-01) kit was purchased from Roch, Germany; ALP (140219) kit was prepared from Bionik, Iran; HbA1c (696552-01) kit was purchased from Roch, Germany.

Instruments

Instruments used were Cobas Integra, 500252, Germany and Bt3000, 41100146, Iran.

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Methods

This study included 90 women who were divided into three groups: (I) Pregnant with GDM (n=30), (II) pregnant women with obesity and GDM (n=30) and (III) normal pregnant women as referent (n=30). Also, normal women with obesity were considered as another control group. Whole blood samples were obtained in the first (12 weeks), second (27 weeks) and third trimester (33 weeks) of gestation and demographic, clinical history and anthropometric measures were recorded in Pars laboratory, Babol, Iran. The age group was 18-35 years old. A 4 ml fasting blood sample was collected from all subjects in sterile tubes. Serum samples were separated. To analyze the HbA1c level, the whole blood and serum was used for LDH and ALP activity. The analysis of biomarkers, including HbA1c level, LDH and ALP activity in obese women with gestational diabetes mellitus, in normal weight women with gestational diabetes mellitus and in women with normal pregnancy were carried out according to manufacturer's instructions. For all the participants, medical history was recorded through a structured questionnaire and an informed consent was obtained. The inclusion criteria included the subjects with body mass indexes of at least 30 kg/m^2 and history of gestational diabetes. The subjects excluded from the study were those diagnosed with type 1 and type 2 diabetes mellitus, but the age below 18 years or above 35 years, and those who were diagnosed with diabetes before pregnancy.

Blood samples were collected in Ethylenediaminetetraacetic acid, whole blood samples were used for analysis of HbA1c by using ion exchange resin method with Roch kit according to the manufactures' instructions. ALP activity was measured by enzymatic method; glucose by GOD-POD method; and LDH activity by enzymatic IFCC-UV assay method. The correlation analysis between blood activity of ALP, LDH activity, HbA1c, glucose, body mass Index (BMI), and age in diabetic and normal pregnant women was carried out. The assay and the outcomes of assaying biochemical markers employed here have been typically validated against other methods and had good inter- and intra-assay coefficients of variation [16-18]. This study was conducted based on the guidelines in the declaration of Helsinki, and all procedures involving human patients were approved by the Ethics Committee of Islamic Azad University, Damghan, Iran. Written informed consent was obtained from all subjects after a full explanation of the purpose and nature of all procedures was provided.

Statistical analysis

The statistical package SPSS 18.0 software was used to analyze the data. Data were expressed in mean±SD. The difference between variables with normal distribution was analyzed using ANOVA test and for between groups nonparametric Kruskal-Waalis test. Pearson's correlation coefficient was used for parametric and Spearman's is used for non-parametric. $P \leq 0.05$ was considered statistically significant.

Results

The mean HbA1c levels were significantly elevated in obese women with GDM compared to those with normal pregnant controls

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(p=0.01). In contrast, the mean ALP and LDH activity were lower in the obese women with GDM than in the normal pregnant controls (p=0.09, p=0.15, respectively) (Table1).

The increase in the level of HbA1c occurred during the first to the third trimester of pregnancy, from 3.6±0.016 to 4.0±0.15 mmol/L, and an increase towards the third trimester. Also, from the first to the third trimester of pregnancy, an increase in ALP activity occurred from 174.4±12.2 to177.5±16.3 U/L, towards the third trimester there is an increase, but from the first to the third trimester of pregnancy, a drop in LDH activity occurred from 177.2±6.8 to 174.1±8.0 U/L, and another drop towards the third trimester (Table 2). The correlation plot between blood concentration of ALP, LDH activity, HbA1c, glucose, BMI, and age level in diabetic and normal pregnant women has shown in figure 1. Correlation coefficient between LDH and ALP was different (r=-0.065). Also, correlation coefficient between HbA1c and age, BMI and glucose levels were different (r=-0.055, r=0.003 and -0.214, respectively).

Table 1. HbA1c level, LDH, ALP activity in studied groups

Variables	Group I	Group II	Group III	P-value
HbA1c (mmol/L)	3.2 ±0.05	4.3 ± 0.22	4.2 ± 0.15	0.01
ALP (U/L)	195.3±7.6	164.7 ± 19.8	158.5 ± 18.1	0.09
LDH (U/L)	184.0± 7.3	179.3± 7.0	163.4± 7.2	0.15

All values are expressed as mean±SD. Group I= Healthy pregnant women; Group II= women with gestational diabetes and non-obese; Group III= women with gestational diabetes and obese; HbA1c= Glycated hemoglobin; ALP= Alkaline phosphatase; LDH= Lactate dehydrogenase

Table 2. HbA1c level, LDH, ALP activity in the first, second and the third trimester in GDM obese women

Variables	First trimester	Second trimester	Third trimester	p-value
HbA1c (mmol/L)	3.6 ± 0.16	3.7 ± 0.18	4.0 ±0.15	0.25
ALP (U/L)	174.4 ± 12.2	184.9 ± 11.5	177.5±16.3	0.87
LDH (U/L)	177.2 ± 6.8	181.1± 9.8	174.1± 8.0	0.84

All values were expressed as mean±SD. HbA1c= Glycated hemoglobin; ALP= Alkaline phosphatase; LDH= Lactate dehydrogenase

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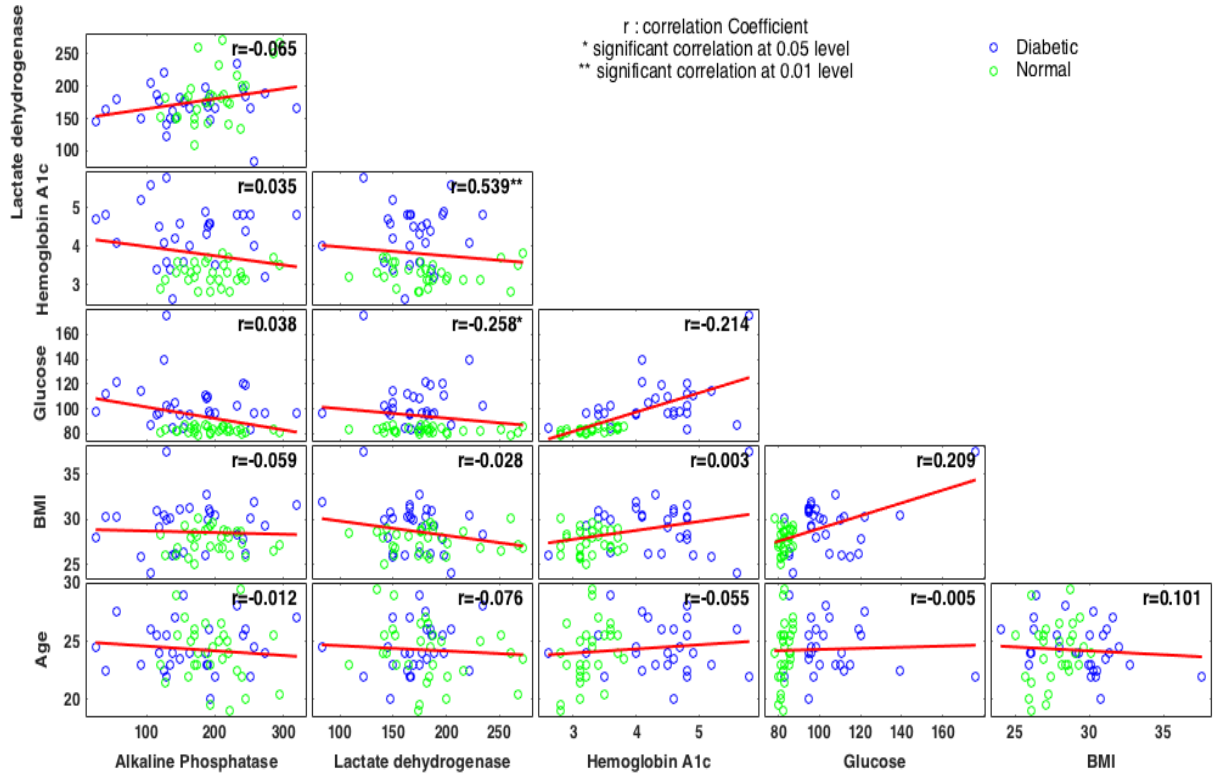


Fig 1. The correlation analysis between blood activity of alkaline phosphatase, lactate. dehydrogenase activity, glycated hemoglobin, glucose, body mass index and age level in diabetic and normal pregnant women. Pearson's correlation test and matrix scatter plot were performed to evaluate the correlation between parameters.

Discussion

One of the important findings in the current study is that the mean of HbA1c levels were higher in GDM obese women compared to the normal pregnant group. This result is in concordance with the reports done by other investigators. Knight et al. [7] and Ensenauer et al. reported that HbA1c levels increased in GDM [9]. In contrast, the mean of ALP and LDH activity was lower in obese women diagnosed with GDM than in normal pregnant women. In addition, from the first to the third trimester of pregnancy, an increase in HbA1c levels was seen. Elevated HbA1c value and changes in ALP activity in GDM obese in comparison to normal healthy group demonstrate that biochemical markers involved in GDM obese women. This result is in agreement with the reports done by other investigators [7, 10]. A possible cause of this phenomenon may be due to the changes in some of enzyme activity and carbohydrate metabolism during the pregnancy, which leads to a change in glucose tolerance and thus it leads to changes in the HbA1c levels. The increased ALP activity of the serum during the first to third trimester leads to changes in phosphate concentration. In this study, increased ALP activity can be detected during the first to third trimester of pregnancy.

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From the first to the third trimester of pregnancy, a drop in LDH activity occurs in conditions of this study, we observed various alterations in biochemical marker in GDM obese women that may be related to the metabolic capacities compared to normal pregnant controls. The results obtained from subjects with obese pregnancy suggested that LDH and ALP activities have not elevated significantly above in women with normal pregnancy. Despite minor differences, the activity of LDH and ALP was almost the same as in GDM obese women compared to the GDM women. It is difficult to determine whether this reflects enzyme activity related to obesity status. Analysis of HbA1c level, LDH and ALP activity provides evidence about health during the pregnancy. Using the HbA1c, LDH and ALP as a biomarker for monitoring GDM will be useful. In the current study, we found that the levels of ALP and LDH were closely related to age, BMI, glucose and HbA1c levels in the GDM obese women. However, the molecular mechanisms underlying the relationship between these enzyme activity, BMI, glucose and HbA1c levels in GDM obese women are not clear. Further studies are needed to explore the roles of these biochemical markers. Therefore, in our laboratory, new procedures will be conducted for exploration in a further study of the underlying mechanism.

Limiting the clinical usefulness of this study beyond all these positive results and suggestions, some limitations and methodological flaws of our study should be mentioned. The small sample size might have led to the loss of the power of statistical analysis. Our present data showed that there is a relationship between these enzymes (ALP and LDH) and BMI, glucose and HbA1c levels in GDM obese women and they may provide further information in elucidating the correlation between these enzyme and BMI, glucose and HbA1c levels in GDM obese women.

Conclusions

Our findings revealed the pattern of changes in blood HbA1c level, LDH, ALP activity in GDM obese women. Thus, the metabolic distress occurring in pregnancy may affect on HbA1c level, LDH, and ALP activity. Therefore in the future, it will be important to examine the possible role of more biochemical markers involved in GDM obese women.

Conflict of Interest

Authors do not have any commercial affiliations, or potential conflicts of interest associated with this work submitted for publication.

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