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CPR/albumin and Monocyte/HDL Ratio in Gestational Diabetes Mellitus

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ABSTRACT

Objective: *The aim of this study was to determine the ratio of CRP/albumin (CRP/Alb) and the monocyte/HDL ratio (MHR), new inflammatory markers, in women with gestational diabetes mellitus (GDM) and normal glucose tolerance test (NGT).*

Methods: *Thirty pregnant women who underwent 50 gram glucose challenge test (GCT) between 24-28 gestational weeks were included the study. If the serum glucose level was above 140 mg/dl on the 50 gram GCT, 100 gram oral glucose tolerance test (OGTT) was applied. Diagnosis of GDM in 20 patients was confirmed if two of the blood glucose test results were above the following levels: fasting serum glucose ≥92 mg/dL and/or 1hour glycemia ≥180 mg/dL and/or 2 hour glycemia ≥153 mg/dL. Ten patients with a result below this value were accepted as NGT. The CRP/Alb and MHR were determined. Correlation between biochemical, demographic parameters, CRP/Alb ratio and MHR in GDM and NGT groups were analyzed.*

Results: *No significant difference was found between GDM and NGT groups interms of maternal CRP/Alb ratio and MHR. Fasting insulin, fasting glucose, and 2 hour glucose levels as well as HOMA-IR of patients with GDM were higher than those in the NGT group. Maternal CRP/Alb ratio was positively and significantly correlated with HOMA-IR (r:0.52, p<.001), fasting insulin (r:0.71, p<.002) and BMI (r:0.76, p<.01). We found insignificant correlation between MHR, BMI and HOMA-IR. Any association was not found between HOMA-IR, fasting insulin levels, BMI and CRP/Alb, and MHR in NGT group.*

Conclusion: *Maternal CRP/Alb ratio correlates with HOMA-IR and BMI of women with GDM.*

Keywords

GDM, NGT, HOMA-IR, MHR, CRP/Alb ratio.

Introduction

Inflammation is a complex process that is considered responsible for the emergence of many systemic diseases. We can examine inflammation in two parts, acute and chronic. In acute inflammation, the host organism initiates a chain of reactions in response to tissue damage. The inflammatory process involves the emergence of humoral products and leukocytes to the site of inflammation and sytemic circulation [1,2]. In the field of inflammation, neutrophils and macrophages begin to accumulate first and secrete the area in their own granules as well as reactive oxygen species. Neutrophils also cause accumulation of monocytes and dendritic cells in the environment. In comparison to a classical acute inflammatory response to a exogenous chemicals or microorgansisms, diabetes-related inflammation described as sub-acute or low grade chronic inflammattion [3]. Diabetes-associated inflammation affects dipose tissue, skeletal muscle, liver, pancreas, and brain [4]. Adipose tissue inflammation contributes to the development of insulin resistance and type 2 diabetes mellitus [1-4]. Placenta is now known to be a significant source of proinflammatory cytokines during pregnancy. Studies suggested that the inflammation in placenta and adipose tissue may be a major factor in the development of metabolic disease such as gestational diabetes mellitus (GDM).

Gestational diabetes mellitus is a metabolic disease that negatively affects the health of the mother and fetus. It is the most frequent complication of pregnancy. For this reason, follow-up and treatment is required with a multidisciplinary approach. If necessary attention

is not paid to the diagnosis and follow-up, GDM may negatively affect the future health stiuation of the mother and fetus [5]. Indeed, offsprings from mothers with GDM are at risk for obesity, diabetes mellitus and other metabolic diseases [6]. Inflammatory markers derived from hematological parameters have been used to predict the severity and prognosis of metabolic diseases such as PCOS, metabolic syndrome and type 2 DM. Leukocytes play a critical role in mediating inflammation. Since the CRP is a positive acute phase protein and albumin is a negative acute phase protein the ratio of CRP/albumin (CRP/Alb) has been suggested as a new inflammatory marker in metabolic and inflammatory diseases. Monocyte/HDL ratio (MHR) is an other inflammatory marker of chronic inflammation [7].

HDL ameliorates transformation of monocyte to macrophages, inhibits the inflammatory response, and blocks the inflammatory process. When the literature is reviewed, it appears that many inflammatory markers are studied in GDM. However, studies investigating CRP/Alb and MHR indices in GDM are not available. This study was, therefore, planned to compare CRP/Alb and MHR in women with GDM and NGT to identify their role in the etioolgy of GDM.

Materials and Methods

This retrospective case-controlled study was conducted at the Medicalpark Goztepe IVF-center. The data were obtained from the files of patients who applied to our IVF-center between December 2018 and November 2019 and who met the inclusions criteria. Thirty pregnant women who underwent 50 gram glucose challenge test (GCT) between 24-28 gestational weeks were included the study. If the serum glucose level was above 140 mg/dl on the 50 gram GCT, 100 gram oral glucose tolerance test (OGTT) was applied. Diagnosis of GDM in 20 patients was confirmed if two of the blood glucose test results were above the following levels: fasting serum glucose ≥92 mg/dL and/or 1hour glycemia ≥180 mg/dL and/or 2 hour glycemia ≥153 mg/dL [8]. Ten patients with a result below this value were accepted as NGT. The CRP/Alb ratio and MHR were determined. Possible correlation between biochemical, demographic parameters, CRP/Alb ratio and MHR in GDM and NGT groups were analyzed. Participants with multiple pregnancy, pre-existing glucose intolerance or DM and smokers, were excluded. Serum glucose levels were measured in autoanalyzer by using hexokinase/G6PD method. The fasting serum insulin levels were also measured in autoanalyzer by using electrochemiluminescence immunoassay. Homeostatic model assessment [HOMA-IR] Formula was used for calculating insulin resistance [9]. The body mass index (BMI) was calculated using the following formula: weight [kg]/square meter height [m2] at the birth. The present study conforms to the principles outlined in the Declaration of Helsinki. All patients provided verbal informed consent prior to participation in the study protocol.

Analysis of MHR and CRP/Alb ratio

Peripheral blood samples were obtained from all GDM and NG patients on admission to determine complete blood count and biochemical parameters. HDL-C levels were measured using an automated analyzer. Serum CRP levels were measured on autoanalyzer with detection range 0 to 0.5 mg/L. The MHR and CRP to albumin ratio (CRP/Alb) were calculated from parameters that were obtained from the blood samples. CRP/albumin ratio was defined as (albumin g/dL cleavage of CRP mg/ (Triglyceride mg/dL divided by HDL mg/dL).

Statistical analysis

The Statistical Package for Social Sciences, Windows version 21 was used for statistical analysis (SPSS, Chicago, IL, USA). Normality of data was analysed with Kolmogorov–Smirnov Z test. Mann Whitney U test was used for comparisons between GDM and NGT. Associations between maternal CRP/Alb, MHR biochemical, hormonal and demographic parameters were analysed with Pearson correlation method. Data are presented as mean±standard deviation (SD). $p<.05$ was accepted as statistically significant.

Results

The GDM group had higher C-reactive protein, neutrophil and monocyte count, and lower HDL-C, and lymphocyte count compared to NGT group. No significant difference was found between GDM and NGT groups interms of maternal CRP/Alb ratio and MHR. The median MHR value was 9.4 in the GDM group and 10.1 in the NGT group ($p < 0.34$). Fasting insulin, fasting glucose, and 2 hour glucose levels as well as HOMA-IR of patients with GDM were higher than those in the NGT group. Maternal CRP/Alb ratio was positively and significantly correlated with HOMA-IR (r:0.52, $p<.001$), fasting insulin (r:0.71, $p<.002$) and BMI (r:0.76, $p<.01$). We found insignificant correlation between MHR, BMI and HOMA-IR of women with GDM. Any association was not found between HOMA-IR, fasting insulin levels, BMI and CRP/Alb, and MHR in NGT group.

Discussion

In the present study, CRP/Alb ratio was significantly associated with HOMA-IR and BMI of women with GDM. Furthermore, CRP/Alb ratio was significantly correlated with fasting insulin levels in GDM group. In terms of MHR there were no significant correlation between HOMA-IR and BMI of subjects with the diagnosis of GDM. Similarly, neither MHR nor CRP/Alb ratios were correlated with other parameters in the NGT group. All these data make us think that the inflammatory process of GDM is different compared to other metabolic diseases. Among the possible causes of this difference, physiological changes due to pregnancy take the first place. While the placenta increases cholesterol intake from the mother to meet the increased steroid synthesis of the fetus, it itself stimulates cholesterol synthesis, which may cause MHR rates to remain unchanged. The positive correlation between CRP/alb ratio and HOMA-IR and BMI suggests that the inflammatory process is more intense in GDM cases than healthy pregnant women. The fact that CRP/alb ratio does not have any correlation with other parameters in patients in NGT group supports this suggestion. Previous studies have demonstrated that inflammatory responses

play an important role in the progression of GDM [1,2]. Together, in patients with GDM, positive correlation between CRP/alb ratio and HOMA-IR can be used to predict obstetrics outcome of GDM cases with and without follow-up. Although monocytes and HDL-C are important keystones [10] in the aging placenta monitarisation their levels can not used a predictor of clinical outcome of fetus and mother in women with GDM.

The MHR and CRP/alb ratio are a newly developed inflammatory markers that are calculated as the ratio of monocyte count to HDL-C level and the ratio of CRP levels to albumin level. CRP/alb ratio may be superior to monocyte count or HDL-C level alone in predicting the development and progression of GDM (10). In the present study CRP/alb ratio was associated positively with the fasting insulin levels and BMI of women with GDM. There were no correlation between hormonal and demographic parameters and MHR in both GDM and NGT subjects. Although the MHR has been suggested as a good indicator of inflammatory events in metabolic disorders it can not be used as an inflammatory index for screening GDM. On th contrary, serum albumin concentration and CRP levels can be used for monitorisation of women with GDM taking diet or insulin treatment.

When recent literature was analysed in detail, many investigations found a wide range of inflammatory indices in diabetic subjects [1,4]. Most of them reported that inflammatory markers such as CRP and albumin were lower in women with GDM compared to pregnant women with normal glucose levels [10]. In the present study we clearly showed that CRP/alb and MHR of women with GDM were similar to the results of pregnant women with NGT. Unlike other GDM studies, in the present study blood samples for measurement of inflammator markers were taken at the delivery. Taking the blood samples at the birth may be the most important reason why MHR and CRP/alb ratio are the similar in both groups. Other possible causes of similarity between two groups in terms of inflammatory indices can be listed as follows. In our study blood samples were taken only once for the measurement of inflammatory indices, so the inter-trimester change is unknown. Also, we did not consider whether insulin treatment was given in patients diagnosed with GDM.

Conclusion

In the present study we did not find a clear relationship between serum glucose, MHR, CRP and albumin levels in GDM and NGT subjects. However, we found a significant correlation between CRP/alb ratio, HOMA-IR and BMI in GDM subjects. We can, therefore, suggest that inflammatory markers have a critical role on insulin homeostasis in GDM patients.

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