Alterations of global DNA methylation, DNA methyltransferase and histone deacetylase transcripts expression in fetal endothelial cells from gestational diabetes women

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Background

Gestational diabetes mellitus (GDM) is a rising public health issue worldwide. Kingdome of Saudi Arabia (KSA), ranks second in the prevalence of diabetes in the Middle East countries with 7 million diagnosed diabetic patient and 3 million pre diabetic(1). Which affect 2.7% to 18.7% of all pregnancies The condition of fetal exposure to GDM increased lifelong risk of type 2 diabetes mellitus in both mothers and their offspring and endothelial cells dysfunction(2). Hyperglycemia increase an inflammatory markers that primes to increase oxidative stress and endothelial dysfunction for per mothers and their fetuses. Research studies Proven the relationship between GDM, and epigenetic change happened on umbilical cord endothelial cells(3). DNA methylation is dynamic prosses by adding methyl group from S-adenyl methionine (SAM) to the fifth carbon of a cytosine residue to form 5mC its regulated by DNA methyltransferase DNMTs families (DNMT1, DNMT2, DNMT3a and DNMT3b) and histone deacetylation is reversible process to transfer acetyl group to the ε-amino group of lysine residues on the N-terminal tails of histones regulated by deacetyl-transferases HDATs families(4).

Objectives

Study to investigate whether alteration in global DNA methylation, DNA methyltransferase and histone deacetylation transcripts expression occur in human umbilical vein endothelial cells from pregnant with GDM (GDM-HUVEC) compared to human umbilical vein endothelial cells from nondiabetic pregnant (C-HUVEC).

Methods

HUVECs isolated from 8 GDM and 6 nondiabetics pregnancies, using collagenase enzymes. Then, DNA and RNA extracted and stored at -80C. The alteration in global DNA methylation level was measured using a 5-methylation Cytosine colorimetric assay. DNA methyltransferase and histone deacetylation transcripts expression was measured using quantitative real time PCR(qRT-PCR) for the following five enzymes: DNMT1,DNMT3a,DNMR3b,HDAC1and HDAC2

Results

Our results showed that DNA hypermethylation occurs in GDM-HUVEC compered to C-GDM by using Global DNA methylation (figure-1). Nonsignificant (NS) increase showing in DNA methylation and deacetylation for transcripts enzymes DNMT1,DNMT3a,DNMR3b and HDAC1 in GDM-HUVECs compered to C-HUVEDCs. On other hand, significantly increase shown in enzyme transcript HDAC2 (P<0.05) (figure-2)

Figure 1 Alteration in global DNA methylation level

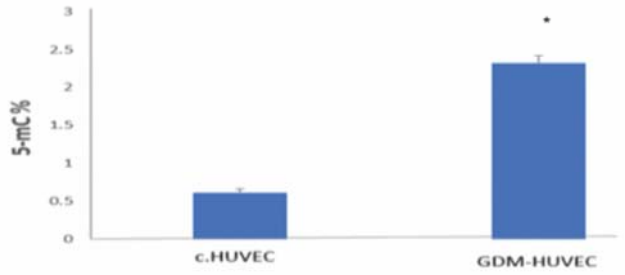
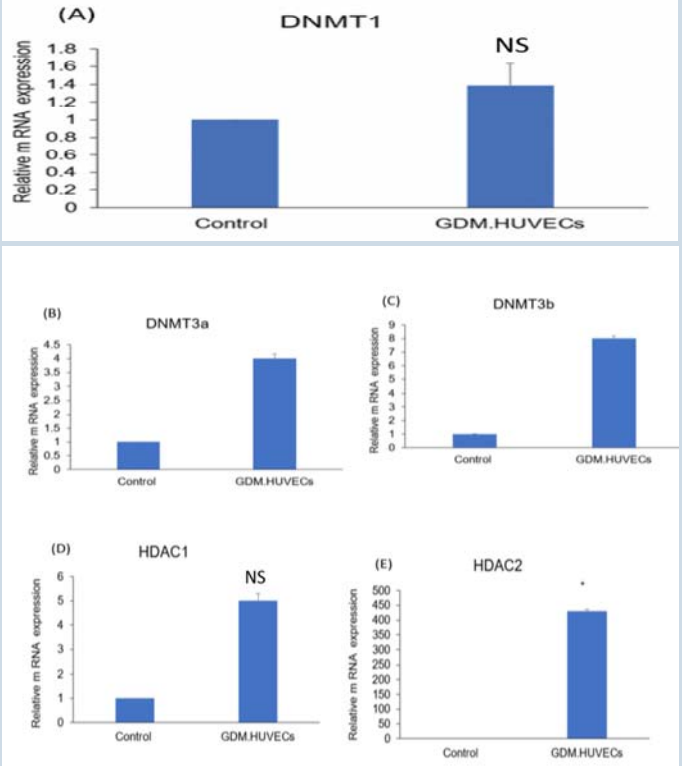


Figure 2 DNA methyltransferase and histone deacetylase mRNA expression



Discussion

our study shows that global hypermethylation (P<0.001) were induced by GDM this finding is in a good agreement with results of former studies on DNA methylation. Also, our study provides quantitative data about significantly increase methylation on HDAC2 (P<0.05), several studies have highlighted the effect of HDAC2 on endothelial cell dysfunction to offspring. Nerveless, DNA Alteration of other enzymes DNMT1, DNMT3a and DNMT3b and HDAC1 is nonsignificant change but its induced by GDM. In a different way designed studies will be needed to determine a relationship between global DNA hypermethylation and histone deacetylation with GDM to answer the question is the DNA methylation is implicated in GDM pathogenesis or its one of the consequences

Conclusions

The data presented provide evidence for the alteration in global DNA associated with hyperglycemia, and HDAC2 increase consist the important role of methylation on endothelial dysfunction

References