



## **HYPERMETHYLATION IN THE PROMOTER OF THE MTHFR GENE IS ASSOCIATED WITH DIABETIC RETINOPATHY**

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**Background:** DNA methylation is an epigenetic mechanism for regulating the transcription of many genes and has been linked to the development of various diseases. Methylenetetrahydrofolate reductase (*MTHFR*) is a promising gene since the enzyme promotes methyl radical synthesis in the homocysteine cycle and can provide methyl groups for DNA methylation. In addition, several studies have correlated gene polymorphisms of this enzyme with a greater risk of diabetes, but little is known regarding the relationship between epigenetic changes in this gene and diabetes and its complications. The aim of this study was to investigate the relationship between methylation profile in the *MTHFR* gene promoter and biochemical, inflammatory and oxidative stress markers in individuals with type 2 diabetes (DM2) with or without diabetic retinopathy (DR). **Methods:** Specific PCR for methylation was used to analyze *MTHFR* methylation profile in leucocytes DNA. Biochemical markers (glycemia, glycated hemoglobin, total cholesterol, LDL, HDL, triglycerides, serum creatinine), inflammatory markers (C-reactive protein and alpha-1 acid glycoprotein) and oxidative stress (total antioxidant capacity and malonaldehyde) were determined in peripheric blood samples and microalbuminuria in 24h urine samples. The X<sup>2</sup> and Mann-Whitney statistical tests were performed and p values <0,05 were considered significant. **Results:** The hypermethylated profile was most frequently observed in individuals with retinopathy (p <0.01) and was associated with higher total cholesterol and LDL levels (p=0.0046, 0.0267, respectively) in this group. In the control group the



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hypermethylated profile affected the total antioxidant capacity. **Conclusion:** hypermethylation in the promoter of the *MTHFR* gene is associated with the occurrence of DR and with lipidic and oxidative stress parameters.

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