

# ASSOCIATION OF BRONCHIAL ASTHMA-OBESITY PHENOTYPE WITH ER22/23EK AND TTH111I POLYMORPHISMS OF THE GLUCOCORTICOID RECEPTOR GENE

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**Abstract.** The aim of the work was to study the association between ER22/23EK and Tth111I polymorphisms of the glucocorticoid receptor (GR) gene with the body mass index (BMI) of patients with bronchial asthma (BA), considering the age of BA onset.

**Materials and methods.** 553 patients with BA and 95 practically healthy persons who previously signed an informed consent to participate in the study were examined. Patients were divided into two clinical groups according to the age of BA onset. Group I included 282 patients with late-onset of asthma (late asthma phenotype), and Group II included 271 patients with early onset (early asthma phenotype). The diagnosis of BA and the severity of the course were established according to the recommendations of GINA-2016 and subsequent versions. Diagnosis of obesity was carried out in accordance with the Order of the Ministry of Health of Ukraine dated August 5, 2009, No. 574, and the European Association for the Study of Obesity (EASO, 2016). The study was approved by the Bioethics Committee of the Medical Institute of Sumy State University. Determination of ER22/23EK (rs 6189/6190) and Tth111I (rs10052957) polymorphisms of the GR gene was performed using the polymerase chain reaction followed by the analysis of restriction fragments. Statistical analysis of the obtained results was carried out using the SPSS-17 program.

**The results.** The analysis of anthropometric parameters showed that among the examined patients with BA, there were 152 (27.5 %) patients with normal body weight (NBW), 206 (37.3 %) were overweight, and 195 (35.2 %) with obesity. Visceral type of obesity was verified among all patients. It was established that among overweight and obese BA patients, there was a higher frequency of GG genotype according to the ER22/23EK polymorphism of the GR gene compared to patients with NBW. Heterozygotes were found 5.6 and 3.5 times more often in patients with normal body weight compared to patients with obesity. Analysis of the ratio of G and A alleles depending on BMI shows a higher frequency of the G allele in obese patients compared to patients with NBW. The distribution of alleles and genotypes according to the Tth111I polymorphism in the examined patients with BA depending on the BMI shows a twice higher frequency of homozygotes for the main C allele in overweight and patients with obesity compared to patients with NBW. Carriers of homozygotes for the minor allele were detected 4.7 times and 2.1 times more often in patients with NBW compared to overweight patients and with obesity. A probable difference in the distribution of alleles and genotypes according to the Tth111I polymorphism of the GR gene was established in patients with early and late BA ( $p = 0.001$ ). Carriers of homozygotes for the main allele of CC were found more often in patients with early and late BA in the presence of obesity.

**Conclusions.** A higher frequency of the GG genotype according to the ER22/23EK polymorphism of the GR gene and homozygotes according to the main CC allele according to the Tth111I polymorphism of the GR gene in overweight BA patients and with obesity compared to patients with NBW was proven. The protective role of the ER22/23EK polymorphism of the GR gene in relation to the occurrence of obesity in the dominant, superdominant and additive models of inheritance and the Tth111I polymorphism of the GR gene in the superdominant model was established. A higher frequency of carriers of homozygotes for the main C allele in patients with early-onset and late-onset BA in the presence of obesity compared to patients with NBW, a protective role of the Tth111I polymorphism of the GR gene on the risk of developing obesity in patients with late-onset BA in superdominant and recessive models of inheritance was established.

**Key words:** bronchial asthma, obesity, onset, course, ER22/23EK, and Tth111I polymorphisms of the glucocorticoid receptor gene.