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THE INFLUENCE OF HMGB1 GENE (RS41369348) POLYMORPHISM ON THE SUSCEPTIBILITY AND CLINICAL FEATURES OF PATIENTS WITH IGAV

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10.1136/archdischild-2021-europaediatrics.442

IgA vasculitis (IgAV) or Henoch-Schönlein's purpura is the most prevalent systemic small vessel vasculitis in childhood, in which pathogenesis environmental and genetic factors play role. From genetic factors different studies proven that genes located inside the HLA region and gene polymorphisms located outside the HLA region contribute to the onset and different clinical features of IgAV. The aim of this study was to investigate the role of single nucleotide polymorphism (SNP)- rs41369348 (delT; chr13:30467220-30467227 (GRCh38.p12)) for high mobility group box-1 (HMGB1) gene in the susceptibility and clinical features of patients fulfilling classification criteria for IgAV.

In this study, we included 76 children with IgAV and 150 age- and sex-matched healthy controls without any history of autoimmune disease.

After extracting genomic DNA from the whole peripheral blood, genotyping was carried by real-time PCR method using TaqMan SNP genotyping assays. Clinical data and laboratory parameters were collected for all IgAV patients.

The normal T/T genotype was found in 83% of the IgAV patients and 91% of the control group. Heterozygous T/delT genotype was detected in 11% and 8% of the patient group and healthy controls, respectively. Homozygous mutant delT genotype was found in only 1 IgAV patient.

Although there was higher frequency of heterozygous T/delT genotype of this gene polymorphism in IgAV group compared to control group, no genotype difference between those two groups was observed. No statistically significant differences in genotype nor allele were disclosed when patients with different IgAV clinical features were compared.

Accordingly to our study, the HMGB1 gene polymorphism rs41369348 was not linked to increased susceptibility to childhood IgAV, its severity nor different clinical manifestations.

SUPPORT: Croatian Science Foundation project IP-2019-04-8822

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DIFFERENT HISTOLOGICAL CLASSIFICATIONS FOR IGA VASCULITIS NEPHRITIS – WHICH ONE HAS THE BEST ASSOCIATION WITH THE DISEASE OUTCOME?

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10.1136/archdischild-2021-europaediatrics.443

Introduction IgA vasculitis nephritis (IgAVN) is almost the only cause of morbidity and mortality among children suffering from this most common childhood-vasculitis. Several histological classifications are used in the analysis of renal biopsy findings in IgAVN, but it remains unknown which one is the best predictor of severity and disease outcome.

The aim was to compare the four most commonly used histologic classifications for IgAVN and to establish which variables of each histological classification have the strongest association with unfavorable outcome.

The cross-sectional study included 74 patients with IgAVN (diagnosed by EULAR/PRES/PRINTO criteria) and available renal biopsy specimens for analysis using the four histological classifications for IgAVN (the International Study of Kidney Disease in Children (ISKDC) classification, the Oxford classification, the Haas histologic classification of IgA nephropathy and the modified semi-quantitative classification (SQC), developed by Koskela et al.). The clinical outcome was defined through four categories, graded according to the modified classification of Counahan (physical examination, hematuria, proteinuria, urine albumin-to-creatinine ratio, hypertension and eGFR). The linear relationships between outcome and histological classifications were analysed using ordinal regressions using the first-order of polynomial orthogonal contrasts.

The SQC classification proved to be the best, reducing the deviation (of the model-predicted outcome value from the observed value) by 9.5% ($\chi^2=13.89$, $p<0.001$), followed by the Oxford classification with a deviation reduction of 8.0% ($\chi^2=11.76$, $p=0.001$), then the ISKDC classification with a decrease in deviation of 3.3% ($\chi^2=4.89$, $p=0.027$). The worst was the Haas classification with a decrease in deviation of 2.1% ($\chi^2=3.06$, $p=0.080$).

Analysis of individual variables of Oxford and SQC classifications showed that with increasing values in the variables of interstitial fibrosis ($t_{66}=3.23$, $p=0.002$), tubular atrophy ($t_{66}=2.94$, $p=0.005$) and tubular dilatation ($t_{66}=2.40$, $p=0.019$) in the SQC classification, and endocapillary hypercellularity ($t_{66}=3.14$, $p=0.003$) and crescents ($t_{66}=2.07$, $p=0.043$) in the Oxford classification the outcome worsens.

This study showed that the SQC classification has the strongest association with the IgAVN severity and outcome. Although crescents on renal biopsy were considered the most important outcome indicators, our study suggests that tubulointerstitial changes could be more important as predictors of poor outcome. Interstitial and renal tubules changes should be further explored in order to have better predictive values of IgAVN outcome and to be incorporated into existing or new classifications, on the basis of which guidelines for the treatment of patients would be developed.

SUPPORT: Croatian Science Foundation project IP-2019-04-8822.

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THE IMPACT OF SYSTEMIC IMMUNOMODULATORY THERAPY ON THE INTRAOCULAR INFLAMMATION AND THE NEED FOR TOPICAL GLUCOCORTICOID THERAPY IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS- ASSOCIATED UVEITIS

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10.1136/archdischild-2021-europaediatrics.444

Juvenile idiopathic arthritis associated uveitis (JIA-U) is the most common and potentially most destructive extraarticular manifestation of JIA. The aim of this research was to