NOD2 Gene Status in Pediatric and Adult Crohn Disease Patients in Algerian Population

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Abstract:

Background: Chronic Inflammatory Bowel Diseases (IBD), including Crohn disease (CD) and ulcerative colitis (UC) are gastrointestinal disorders under the influence of a complex genetic basis. One hundred sixty-three predisposition loci were identified by genome-wide association (GWAS) studies, refocusing the pathogenesis of IBD on immunity genes. The NOD2 gene has been widely implicated in the pathogenesis of IBD in different geographical populations. Three most common mutations within NOD2 gene were selected, namely SNP8, C/T (R702W variant), SNP12, G/C (G908R variant) and SNP13, (1007fsinsC variant). We investigated these three SNP in a pediatric Algerian cohort for the first time, since no previous association studies between pediatric IBD and the NOD2 gene were available for the Algerian population.

Methods: A case-control study was performed in the pediatric IBD population. PCR-RFLP was used to detect the three NOD2 gene mutations in 46 CD patients and 100 healthy control subjects. All samples were genotyped for the NOD2 gene Polymorphisms by the PCR-RFLP method. Statistical study was performed by the Fisher exact test or Chi-2 using the GraphPad Prism 7.0 software. Then data from the pediatric cohort were compared to our precedent published data from a case-control study performed on a cohort including 132 IBD patients and 114 healthy control subjects.

Results: In the pediatric cohort, there is no statistically differences in allelic frequencies between cases and controls respectively R702W (6.36% vs. 6.38%; p=1), G908R (2.72% vs. 1.06%; p=0.6) and 1007fsinsC mutation was found neither in the CD patients nor in control. In the adult cohort, the R702W allelic variant showed the highest frequency in CD patients (8%) (p = 0.09, OR = 3.67, 95%CI: 0.48-4.87) but its frequency was also high in controls (5%) (p = 0.4; OR = 1.4; 95%CI: 0.65-3.31). Likewise, G908R and 1007fsinsC mutations showed similar frequency in CD patients and in controls (3% vs. 2%; p=0.5; OR=1.67; 95%CI: 0.44-6.34; 2% vs.1%; p=0.4, OR=2.69; 95%CI: 0.48-14.87, respectively). The total frequency of the mutated NOD2 chromosomes was higher in adult CD patients (13%) than in pediatric CD patients.
(9%). In our precedent study on the adult cohort, we have confirmed that the NOD2 gene is significantly associated with a specific clinical sub-phenotype in CD, indicating that the NOD2 gene is involved in IBD susceptibility across Algerian adult population. However, we failed to show any association between the three variants of the NOD2 gene across Algerian pediatric CD patients.

**Conclusion:** In our precedent study, we have confirmed that the NOD2 gene is significantly associated with a specific clinical sub-phenotype in adult CD patients. Here, our results show no association of NOD2 gene variants with pediatric MC. The low penetrance of the at-risk genotypes we observed indicates that the NOD2 gene does not delineate a subgroup of simple Mendelian diseases.

**Keywords:** IBD, PCR-RFLP, SNP, NOD2, Pediatric Crohn Disease.

10. **Declaration of conflicts**

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11. **Authors’ Biography**

No biography

12. **References**

No references