Zika virus (ZIKV) is an arthropod-borne flavivirus that can trigger mild to severe disease in humans and is associated with a cluster of congenital and neurological malformations, characterizing the congenital Zika syndrome (CZS), however, the mechanisms that lead it are still unclear. CZS occurs only in a small percent of infections during pregnancy, suggesting that host genetics might be a risk factor to this outcome. This study investigated the association of Single Nucleotide Polymorphisms (SNP) in ZIKV pathogenesis. We worked with SNPs on the candidate genes CD209, TNFa, CXCL8, IL-6, CCL-2, TLR3, TLR4 and MICB to investigate their association in the ZIKV pathogenesis leading to SCZ, in mothers who had delivered CZS babies, their babies and healthy donors. DNA samples from seventy children with CZS and his mothers and twenty-three fathers were genotyped by gPCR using TagMan[™] genotyping assays. Other infections that might induce neurological injury were discarded by serological tests. The control group was composed of forty-three mothers who live in the same endemic areas and their healthy babies who were born in the same period of ZIKV outbreak. All associations were assessed comparing groups by Fisher's exact test. We show that the presence of the T allele in SNP rs3775291 at TLR3, that trigger to type I interferons antiviral responses, in mothers infected by ZIKV during pregnancy is associated with CZS occurrence. Furthermore, the T allele in SNP rs1799964 at TNFa gene, a relevant cytokine to antiviral mechanisms of both innate and adaptive immune system, in the CZS babies is associated with severe microcephaly. These findings suggest that genes associated with innate immune responses in pregnant mothers infected with ZIKV and their CZS babies may influence the risk of occurrence and severity of microcephaly.