# Anti-C1q autoantibodies in pregnancy: a potential biomarker for preeclampsia onset in ART gestation?

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**Objective.** C1q protein, the classical complement pathway activator, is a crucial player in early placentation, promoting trophoblast invasion and spiral artery remodelling. C1q-deficient mice display preeclamptic symptoms. Despite being prevalent in autoimmune diseases (AIDs), anti-C1q autoantibodies (anti-C1q) are present in 2-8% of the healthy population. In our previous study, elevated anti-C1q levels were observed in the first trimester of healthy pregnancies, contrasting with lower levels in women developing preeclampsia (PE) and in oocyte donation pregnancies (OD), which have a high risk of PE. This study aims to characterize the specificity of anti-C1q in physiological pregnancy compared to those found in pathological conditions.

**Materials and Methods.** Sera from healthy spontaneous, PE, and OD pregnancies, followed at the IRCCS Burlo Garofolo (Trieste, Italy), were collected at each trimester. Pregnant women affected by autoimmune diseases were also included.

**Results.** In healthy pregnancies anti-C1q targets primarily the globular domain (g) of C1q, in contrast to AID-associated anti-C1q that recognize its collagen-like region (CLR) (P-value = 0.0291). Immunoglobulin subclass analysis revealed IgG2 prevalence in both healthy and AID pregnancies, suggesting a shared immunological response. Functional assays demonstrated that healthy pregnancy-associated anti-C1q modulated the classical complement pathway activation, potentially in a protective manner (% functionality with gh = 87.5 ± 6.1, with CLR = 101.7 ± 5.5, with no anti-C1q = 100.0 ± 6.2).

**Conclusions.** This research highlights anti-C1q functional specificity in healthy pregnancies, emphasizing a unique targeting of C1q globular domain. Observed pathogenic roles of anti-CLR autoantibodies underscore potential immunological role to pregnancy complications. Further investigations are needed to unveil mechanisms and assess their possible use as early predictive biomarkers of PE.