On the pathogenesis of preeclampsia: a new pre-pregnancy risk factor for preterm and term preeclampsia and evidence from recurrences supporting their common origin

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Objective. A fundamental characteristic of any disease is the heterogeneity of its manifestation since general processes are modified through individual responses. A common pathogenesis for preeclampsia regardless of gestation is entirely plausible, as no single feature, including placental changes of varying severity and timing, is unique to preterm or term-onset cases.

This study aimed to discover any distinctive pre-pregnancy signs that may have gone unnoticed and to analyze preeclampsia onset in recurrences.

Materials and Methods. Ukrainian study comprised 103 women who had been diagnosed with preeclampsia including 15 recurrent cases and 408 women with uncomplicated pregnancies. In addition to a questionnaire addressing known risk factors, participants were interviewed in meticulous detail to document any disorders or conditions that they or their first-degree relatives had ever experienced.

Results. A notably high frequency of cholelithiasis, a previously unreported risk factor, was found: a 17-fold prevalence in women with preeclampsia (29.1% *versus* 1.7%, $p < 0.0001$) and an 8.8-fold increase among their mothers (45.6% *versus* 5.2%, $p<0.0001$). There was no difference in the rate of gallstones in patients with preterm or term preeclampsia using gestation at onset or birth. And there was no correlation between gestational age at diagnosis or delivery in recurrent cases of preeclampsia.

Conclusions. Cholelithiasis emerges as a novel risk factor for preeclampsia, warranting confirmation in diverse populations. The lack of association of the disease onset in recurrences, consistent with findings we revealed in analogous cases in the literature, reinforces the concept of a singular pathogenesis for preeclampsia.