

# Abstract

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## Possible interplay between vitamin C deficiency and prolactin in pregnant women with premature rupture of membranes: facts and hypothesis.

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**BACKGROUND:** The precise etiologic mechanisms involved in the premature rupture of membranes (PROM) during pregnancy, the main cause of preterm delivery worldwide, are unknown. Previous studies have shown that: (a) the rupture of chorioamniotic membranes is related to an imbalance between synthesis and degradation of collagen induced by the overexpression/activity of various matrix metalloproteinases (MMP); (b) during human labor and delivery the expression of prolactin receptors (PRL-R) increases in chorioamniotic membranes, decidua and placenta; (c) prolactin (PRL) can influence the synthesis of prostaglandins, the expression of some MMP (MMP-2, MMP-9 and decysin) and tissue inhibitors of MMP in general; (d) vitamin C deficiency induces the expression/activity of extracellular MMP and is considered a risk factor for PROM; and (e) vitamin C potentiates the dopamine-mediated inhibition of PRL in rats.

**DISCUSSION:** The present hypothesis proposes that a decreased hypothalamic dopaminergic tone-and thus an increased synthesis/release of pituitary PRL - is induced by vitamin C deficiency below a critical threshold (<18 microg/10<sup>8</sup> leukocytes) and that both factors, in turn, would cause upregulation of the expression/activity of several MMP. The increased PRL concentrations (acting like a Th1-type cytokine) along with the overexpression of other proinflammatory cytokines would induce a premature switch from a favorable Th2-type immune response to a noxious Th1-type immune response in the intrauterine environment.

**CONCLUSION:** This change, in conjunction with the upregulation of MMP-2 and MMP-9, would cause a premature imbalance between synthesis/degradation of collagen in chorioamniotic membranes (an "anticipation" of the normal parturition cascade?), which favors extracellular matrix degradation, proposed as the most relevant event in the genesis of PROM. This hypothesis represents a new dimension in the study of the etiology of PROM.

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