

Salt and Pregnancy Complications: A Proposal for Future Research

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Introduction

Salt (sodium chloride, NaCl) is a major mineral element that plays a pivotal role in health and disease [1]. According to the world hypertension league (WHL) and the international society of hypertension (ISH), the daily levels of dietary salt intake should be less than 5 g (sodium 2000 mg) for adults [2,3]. Excessive dietary salt intake is one of the important causes of cardiovascular diseases, hypertension and stroke [4,5].

Recently, different investigations demonstrated that excessive salt intake has a pivotal role in the development of inflammatory reactions [6-8]. On the other hand, different studies indicated the role of inflammation in the pathophysiology of pregnancy complications, such as miscarriage and preeclampsia [9,10]. Hence, an important question arises about this condition: may excessive dietary salt intake increases risk of pregnancy complications?

Immune Regulation during Normal Pregnancy

Pregnancy has a number of profound immunological and hormonal alterations [11]. Pregnancy hormones affect the immunological balance during the three trimesters of pregnancy [11]. It is very well documented that immunological shift toward anti-inflammatory responses are essential for a successful pregnancy [11-13].

Common examples of this phenomenon are:

1. Decrease the activities of inflammatory cells; including T-helper 1 cells (Th1) and T-helper 17 cells (Th17) associated with their inflammatory cytokines (e.g., interferon gamma (IFN- γ), Tumor necrosis factor alpha (TNF- α), interleukin-1 (IL-1), IL-6, IL-17 and IL-23).
2. Increase the activities of anti-inflammatory cells; including T helper cell type 2 (Th2) and regulatory T cells (Treg) associated with their anti-inflammatory cytokines (e.g., IL-4, IL-5, IL-9, IL-10, IL-13 and Transforming growth factor- β (TGF- β)) [11,12,14].

Inflammation and Pregnancy Complications

Numerous studies have been demonstrated the role of inflammatory reactions in the pathophysiology of pregnancy complications; including miscarriage and preeclampsia [9,10,15]. It is observed that increased concentration of IFN- γ and TNF- α can damage the fetoplacental tissues [13]. By contrast, increase an anti-inflammatory cytokine IL-10 can prevent fetoplacental damages and spontaneous abortions in murine models [16].

Different investigations indicated the roles of increased Th1/Th17 and decreased Th2/Treg patterns and their cytokines in recurrent miscarriages and preeclampsia [9,15,17,18]. For example, Wang et al. [19,20] reported an increased number of Th17 cells in placental tissues and a high level of IL-17 cytokine in peripheral blood of women with recurrent miscarriage.

Calleja-Agius et al. [17] found increased levels of TNF- α /IL-10 and IFN γ /IL-10 ratios in pregnant women who had a high risk of miscarriage. Inflammatory cytokines TNF- α and IL-6 also involve in the pathophysiology of hypertension during preeclampsia [21].

Salt-derived Inflammation

In 2013, two studies that published in Nature uncovered that excessive dietary salt intake induced severe inflammatory reactions through augmentation of Th17 cells and their highly inflammatory cytokines [6,7]. The results showed that a high salt treatment promotes the severity of experimental autoimmune encephalomyelitis (EAE) (a mouse model of multiple sclerosis) and increased inflammatory cytokines (IL-17, IL-23, TNF- α and IL-2) in murine model [6,7].

Conversely, a high salt treatment inhibits activities of regulatory T cells and anti-inflammatory cytokines IL-4 and IL-13 [22,23]. High salt treatment also decreases anti-inflammatory cytokines and increases inflammatory cytokines by mouse and human macrophages in vitro [24,25].

Yi et al. [26] found a higher number of monocytes in the blood of healthy individuals with high dietary salt intake (12 g/d) than the individuals with normal dietary salt intake. It is of interest that reducing salt intake led to increased production IL-10 and decreased production of IL-23 and IL-6 by lymphocytes [26].

Possible Role of High Salt Intake in the Pathophysiology of Pregnancy Complications

There are a few studies about the involvement of high salt intake and pregnancy complications. For example, it is reported that high dietary salt intake increased risk of gestational hypertension and preeclampsia [27-29]. Although, Abdoli [30] and Rakova et al. [31] proposed that high salt intake can involve in the pathophysiology of miscarriage and preeclampsia through involvement of Th17 cells and their associated inflammatory reactions.

Nevertheless, the link between high salt intake and pregnancy complications is seem to be logical, because high salt intake has a pivotal role in the induction of severe inflammatory reactions [6,7] and inflammatory reactions are involved in the pathophysiology of pregnancy complications [9,10] (Figure 1).

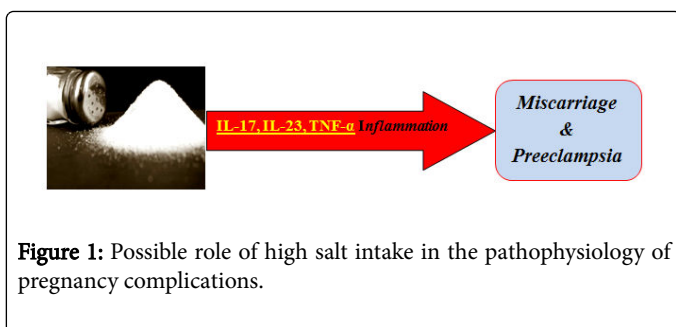


Figure 1: Possible role of high salt intake in the pathophysiology of pregnancy complications.

Therefore, an increase risk of pregnancy complications is plausible for pregnant women with high dietary salt intake. However, further researches should be conducted to elucidate the role of high salt intake in the pathophysiology of pregnancy complications.

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