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Total and allergen-specific IgE levels during and after pregnancy in relation to maternal allergy

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Abstract

Type 2 T-helper cell (Th2)-skewed immunity is associated with successful pregnancy and the ability to easily direct immune responses to a Th2-polarised profile may be an evolutionary benefit. The Th2-like immunity associated with allergic disease might generate favourable effects for the maintenance of pregnancy, but could also promote development of Th2-like immune responses and allergic disease in the offspring. The aim of this study was to explore, by using IgE as a stable proxy for Th2, the Th1/Th2 balance in allergic and non-allergic women by measuring allergen-specific and total IgE antibody levels in plasma during pregnancy and after delivery. Specific and total IgE antibody levels were determined by ImmunoCAP technology at five occasions during pregnancy (gestational weeks 10–12, 15–16, 25, 35 and 39), as well as at 2 and 12 months after delivery. Thirty-six women without and 20 women with allergic symptoms were included, of whom 13 were sensitised with allergic symptoms and 30 were non-sensitised without allergic symptoms. The levels of total IgE, but not allergen-specific IgE, were increased during early pregnancy when compared to 12 months after delivery in the sensitised women with allergic symptoms, but not in the non-sensitised women without allergic symptoms ($p < 0.01$). This increase in total IgE levels during early pregnancy only in the sensitised women with allergic symptoms indicates that allergy is associated with an enhanced Th2 deviation during pregnancy.

Keywords: Allergy; IgE; Phadiatop; Pregnancy; Th2

1. Introduction

The human fetus expresses paternal alloantigens and is therefore regarded as foreign by the maternal immune system. The fetus is normally not rejected, probably due to multiple protective mechanisms, but the current understanding of the establishment and maintenance of the immunological tolerance in human pregnancy is not complete. During the last 15 years, pregnancy has been described as a type 2 T-helper cell (Th2)-like phenomenon, with high levels of type 2 (Th2)-like cytokines at the feto–maternal interface (Wegmann et al., 1993),

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probably in order to divert the maternal immune response away from damaging type 1 T-helper (Th1)-mediated immune responses (Piccinni et al., 1998). Pregnant women show an increased number of interferon-γ (IFN-γ) and *interleukin-4* (IL-4) secreting peripheral blood mononuclear cells (PBMC) cells as compared to after delivery (Matthiesen et al., 1998, 2003; Persson et al., 2008). Furthermore, stimulation with paternal leukocytes increases the secretion of IL-4 by maternal PBMC during normal pregnancy (Ekerfelt et al., 1997). Previous studies have reported a high secretion of Th2-like cytokines at the time of delivery of normal pregnancies and increased Th1-like cytokines at the time of a spontaneous abortion (Marzi et al., 1996; Makhseed et al., 2001). Taken together, local as well as systemic Th2 deviation during pregnancy may be associated with successful pregnancy and the ability to easily direct immune responses to a Th2-polarised profile may be an evolutionary benefit.

Allergic diseases are associated with high IgE antibody levels and expression of the allergen-induced Th2-like cytokines IL-4, IL-5 and IL-13 (Robinson et al., 1992; Mazzarella et al., 2000; Gould et al., 2003). IL-4 and IL-13 induce IgE synthesis (Punnonen et al., 1993) and IL-5 causes allergic inflammation by promoting eosinophil maturation (Egan et al., 1996).

Regulatory T cells (Treg) are able to suppress Th1 as well as Th2 activity, and impaired Treg function has been suggested to contribute to the disease (Ling et al., 2004). Th17 cells and their inflammatory mediators attract and promote neutrophil development, and are not known to drive Th2 responses, implying a role for Th17 cells in non-allergic asthma (reviewed in Oboki et al., 2008). The role of Th17 cells in allergy is not clear, and needs further investigation.

Allergic disease is associated with shorter waiting time to pregnancy (Westergaard et al., 2003), longer gestational age, higher birth weight (Somoskovi et al., 2007) and less pre-term births (Savilahti et al., 2004). Thus, the Th2-like immunity associated with allergic disease might generate favourable effects on the likelihood of becoming pregnant and the maintenance of pregnancy.

The higher cord blood IgE levels seen in newborns of allergic mothers, as compared to newborns with a paternal or no allergic history (Magnusson, 1988; Johnson et al., 1996; Liu et al., 2003), may result from a stronger Th2 shift at the feto–maternal interface of allergic mothers, although this has not been investigated. The Th2 polarisation during pregnancy may influence the offspring for variable periods postnatally. As the cytokine milieu at the priming of T cells directs Th1/Th2 differentiation (Demeure et al., 1994), the gestational environment could be very important for shaping immune responses in the offspring. In support of this, a murine allergy model demonstrated that enhanced Th2-like immunity during pregnancy strongly influenced the Th1/Th2 profile in the neonate (Herz et al., 2000). Newborn mice from ovalbumin-sensitised mothers showed a decreased ability to produce the Th1 cytokine IFN-γ, higher frequency and higher titers of IgG_1 antibodies to β-lactoglobulin after β-lactoglobulin immunisation (Herz et al., 2000). These results indicate that prenatal exposure to a Th2-like environment favours the development of Th2-like immune responses in the offspring. Also, in humans maternal sensitisation to allergens is associated with reduced maternal production of the Th2 antagonist IFN-γ and elevated production of the Th2-like cytokine IL-13 in the newborn baby (Kopp et al., 2001).

To further explore the Th1/Th2 balance in allergic and non-allergic women during pregnancy, we used IgE as a stable proxy for Th2 and examined changes in total IgE and allergen-specific IgE antibodies during pregnancy in a group of 20 pregnant women with allergic symptoms and 36 pregnant women without allergic symptoms. We hypothesised that immune responses would be biased towards a Th2-like profile during pregnancy in both groups, with a more pronounced deviation in the allergic group.

2. Materials and methods

2.1. Study group

The study comprised 20 pregnant women with allergic symptoms and 36 pregnant women without allergic symptoms from the Linköping area, County of Östergötland, Sweden. The study was approved by the Regional Ethics Committee for Human Research at the University Hospital of Linköping. For technical and practical reasons, it was not possible to perform this study with a larger number of participants. The allergic status was established by a typical clinical history, *i.e.* symptoms of allergic rhinoconjuntivitis (ARC, $n = 17$), asthma ($n = 4$ of whom 1 also had ARC) or eczema ($n = 2$, both also had ARC). An experienced allergy research nurse interviewed the women using structured questionnaires. The allergic status of the women were further determined using the Phadiatop® test (see below) and the women were divided into two groups; 13 women who were sensitised with allergic symptoms (sensitised according to Phadiatop testing combined with a history of allergic symptoms) and 30 women who were non-sensitised without allergic symptoms. The pregnant women were recruited from among women attending the maternity