

# -predictor-of-uncontrolled- asthma-in-pregnancy- 61afa8e5f418c.pdf

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## High Levels of Immunoglobulin E Plasma as a Predictor of Uncontrolled Asthma in Pregnancy



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**Abstract— Objectives:** The underlying immunological mechanisms of asthma in pregnancy are not fully understood. Pregnant women who tend to be allergic, exposure to several antigens causes activation of Th2 cells and production of Immunoglobulin E (IgE). This study aims to determine the differences of IgE levels in uncontrolled asthma, partly controlled, well controlled and women without asthma in pregnancy. **Methods:** This was a case control study conducted in Makassar Indonesia from November 2020 - June 2021. IgE levels were measured from blood samples and asthma control determined by GINA criteria. **Results:** Women with Asthma in pregnancy were 40 and 40 non asthma in pregnancy. Subject of asthma in pregnancy were 14 uncontrolled, 16 partly controlled and 10 well controlled. The mean age was not different between women with asthma in pregnancy and pregnant women without asthma ((28.025 ± 5.17 vs 28.025 ± 4.26). IgE levels were higher in pregnant women with asthma than pregnant women without asthma (529.8 ± 688.11 vs 66.77 ± 119.09 IU/mL: p=0.001). Serum IgE levels were higher in uncontrolled asthma compared with partly controlled (801.02 ± 170 vs 476.93 ± 143 IU/mL). IgE levels were higher in partly controlled asthma compared with well controlled (476.93 ± 143 vs 72.75 ± 26.47; p value = 0,001). **Conclusion:** IgE levels were higher in women with asthma pregnancy compared with pregnant women without asthma and the highest levels of serum IgE levels were found in uncontrolled asthma.

**Keywords:** asthma, pregnancy, controlled, IgE

### 1. Introduction

The prevalence of asthma in pregnancy was 3.7 - 8.4%.<sup>1</sup> Pregnant women with asthma in pregnancy represent a special challenge for asthma specialists and allergists. Asthma influences the outcome of pregnancy and also pregnancy affects asthma severity. Maternal inflammatory pathways may contribute to reduced foetal growth through alterations in placental function.<sup>2</sup> Asthma represents a risk factor for several maternal and fetal complications, such as asthma exacerbations, use of corticosteroids, hospitalizations due to asthma attacks, cesarean delivery, preterm delivery, preeclampsia, gestational hypertension, low birth weight, intrauterine growth restriction, and fetal death.<sup>3</sup> The risk of an exacerbation requiring medical intervention may be as high as 50% in females with severe asthma and this may further increase the risk of poor outcomes. Adequate management and gain asthma controlled during pregnancy will decrease perinatal risk.<sup>4</sup> The pathogenesis of asthma in pregnancy is not fully understood. The mechanism thought to play a role in the occurrence of asthma in pregnancy is associated with hormonal changes, especially due to an

increase in progesterone and cortisol.<sup>5</sup> Tan et al in asthmatic subjects who received the hormone progesterone caused a reduction in the density and response of 2-adrenoceptors, reduced response to cyclin-AMP.<sup>6</sup> Another mechanism is through an increased Th2 inflammatory response. Pregnancy is characterized by physiological immunosuppression, namely immunological tolerance that protects the fetus from the mother's immune response. Physiological pregnancy itself is a condition with a predominance of Th2. Asthma is considered an inflammatory T helper 2 cell with chronic airway inflammation leading to bronchial hyperresponsiveness and airway obstruction. This condition will lead to the emergence of gravid asthma or worsening of asthma. Pregnancy also induces an increase in the number of regulatory T cells (Treg) that play a role in the maintenance of maternal tolerance to paternal antigens expressed by the fetus during pregnancy and inhibits the activation of effector T lymphocytes and NK cells. Tregs exert an inhibitory effect on natural killer lymphocytes which are responsible for protection against viral infections.<sup>7</sup> Impaired maternal immunity with reduced cell-mediated immunity makes maternal asthma more susceptible to infection and predisposes to exacerbation<sup>17</sup> and worsens asthma control. Other physiological effects of pregnancy, namely diaphragmatic elevation and hyperventilation in pregnancy will also increase the risk of hypoxia in asthma.<sup>7,8</sup> In pregnant women who tend to be allergic, exposure to several antigens causes activation of Th2 cells and production of IgE. Normal individuals do not have a strong Th2 response to most antigens. When individuals are exposed to several antigens such as proteins in flower pollen, dust, animal hair, certain foods, the dominant T cell response is the formation of Th2 cells. Atopic individuals may be allergic to one or more of the above antigens. Hypersensitivity occurs as a result of activation of Th2 cells that respond to protein antigens or protein-bound chemicals. Antigens that cause rapid-type hypersensitivity reactions are often referred to as allergens. Interleukin 4 (IL-4) and IL-13, which are some of the cytokines secreted by Th2 cells, will stimulate B lymphocytes specific for foreign antigens to differentiate into plasma cells which then produce IgE. The allergen will bind to IgE attached to mast cells and degranulation of the mast cells occurs.<sup>2</sup> The degranulation releases preformed mediators such as histamine, proteases and newly generated mediators such as leukotrienes and prostaglandins which cause bronchoconstriction, mucus secretion and vasodilation.<sup>9,10</sup> IgE has been shown to play a fundamental role in the triggering, development, and chronicity of the inflammatory responses within the disease.<sup>11</sup> This study aims to determine the differences of IgE levels in uncontrolled asthma in pregnancy, partly controlled, well controlled compared with non-asthmatic pregnant women.

## 2. Methods

This was a case control study and conducted in Makassar Indonesia from September 2020 to June 2021. The subjects were women with asthma in pregnancy and pregnant without asthma in Makassar Indonesia. Inclusion criteria: Cases of pregnant subjects with asthma in pregnancy and controls were pregnant women without asthma. The exclusion criteria were pregnant with lung infections including Covid 19 or in labour. The subjects with asthma in pregnancy were divided into well controlled asthma, partly controlled and uncontrolled using criteria in GINA Guideline.<sup>12</sup> Screening on pregnant women performed at the polyclinic, starting with a history taking, physical examination, ultrasonography and spirometry. Subjects participated in the study by filling out an informed consent form which was approved by the Hasanuddin University Health Research decree with number 01186/H.4.8.4.5.31/PP.36- COMETICS/2020.

## 3. Results

Subjects were 40 pregnant women with asthma and 40 pregnant women without asthma. In this study there were 14 women with uncontrolled asthma in pregnancy, 16 partly controlled and 10 well controlled. The mean age was not significantly different between the two groups (table 1)

**Table 1.** Characteristic of subjects

Variabel	Asthma in pregnancy n = 40	Non-asthma in pregnancy n = 40	P
Age (year)	28.025 ± 5.17	28.025±4.26	p=0.999*
Uncontrolled	14		
Partly controlled	16		
Well controlled	10		

\* t test

In this study, we found IgE levels of subjects with asthma in pregnancy were higher compared without asthma pregnancy and statistically significant (p<0.05).

**Table 2.** Comparative analysis of IgE levels asthma in pregnancy asthma and without asthma in pregnancy

Pregnant Woman (n=80)	Mean IgE (IU/mL)	P Value *
Asthma (40)	529.827±688.11	0.001
Non-Asthma (40)	66.27±119.09	

\* t test

In this study subjects of uncontrolled asthma were 14 pregnant women, partly controlled were 16 and well controlled were 10. IgE levels of subjects with uncontrolled asthma in pregnancy were higher compared to partly controlled and well controlled, statistically significant (p<0.05) (Table 3).

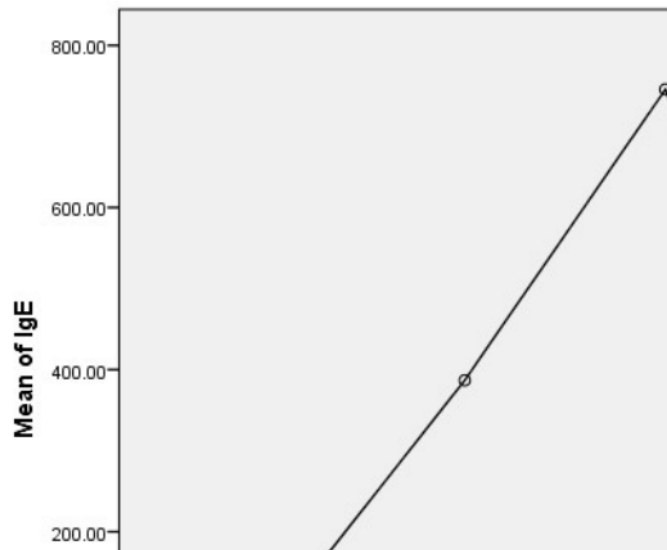
**Table 3.** Comparative Analysis of IgE Levels based on the Degree of Asthma Control

Pregnant women (n=80)	Mean IgE (IU/mL)	P Value*
uncontrolled asthma (14)	801.02± 170	0.001
partly controlled asthma (16)	476.93 ± 143	
Well controlled asthma (10)	72.75 ± 26.47	
Non-Asthma (40)	66.77 ± 119	

\*Anova test

As seen in graph 1, IgE levels were lower in well controlled asthma in pregnancy, then higher in partly controlled asthma and the highest mean levels were in uncontrolled asthma. The lowest levels were found in pregnant women without asthma.

Graph 1. Differences of IgE levels based on the degree of asthma controlled



#### 4. Discussion

This study was conducted on 40 women with asthma in pregnancy and 40 without asthma pregnancy. Asthma subjects with pregnancy were classified as asthma control degrees based on the asthma control criteria from the GINA Guideline and obtained 14 uncontrolled asthma, 16 partly controlled asthma and 10 well controlled asthma. The mean age was not significantly different between the subjects. The levels of serum IgE were higher in pregnant women with asthma than pregnant women without asthma and statistically significant (table 2). Amina et al reported that IgE level was predictive in asthma, and it may be used to differentiate between asthmatic and non-asthmatic individuals.<sup>13</sup> Pregnant women with asthma, exposure to antigens/allergens causes activation of T cells with the formation of Th2 cells. Rapid-type hypersensitivity occurs as a result of activation of Th2 cells that respond to protein antigens or protein-bound chemicals. Interleukin 4 (IL-4) and interleukin-13 (IL-13), which are some of the cytokines secreted by Th2 cells, will stimulate B lymphocytes that are specific to foreign antigens to differentiate into plasma cells which then produce IgE. Allergens will bind to IgE attached to mast cells and degranulation of these cells occurs. The acute inflammation secretes cytokines and mediators such as histamine, proteases, leukotrienes and prostaglandins that cause bronchial smooth muscle contraction, mucus secretion and vasodilation. Furthermore, various cells are involved and activated in chronic inflammation in asthma. These cells are T lymphocytes, eosinophils, macrophages, mast cells, epithelial cells, endothelium, fibroblasts and bronchial smooth muscle which will secrete various cytokines and inflammatory mediators such as IL-33, IL-4, IL-5, IL-13 and TNF-alpha, MMP, TGF-beta and various other mediators. Inflammatory cells, cytokines and mediators then cause obstruction, hyperresponsiveness, bronchoconstriction and remodeling.<sup>8</sup> The pathogenesis of asthma in pregnancy is not fully understood. One of mechanism is through and increased Th2 inflammatory response. Pregnancy is characterized by physiological immunosuppression, namely immunological tolerance that protects the fetus from the mother's immune response. Physiological pregnancy itself is a condition with a predominance of Th2 and also IgE. This study found that serum IgE levels were higher in pregnant women with uncontrolled asthma compared partly controlled and well controlled asthma (table 3). There were no significant differences of IgE between well controlled asthma Pregnant women and women without asthma ( $p>0.05$ ). Kittipong et al reported serum IgE was significantly higher in subjects with uncontrolled allergic asthma than in those with well-controlled ( $1075.4 \pm 420$  vs.

703.5 ± 355 IU/mL,  $p < 0.001$ ). Asthmatic subjects had a higher rate of caesarean section, but no differences in perinatal outcome, including birth weight, were found.<sup>14</sup> It is of great importance for physicians to optimally treat asthmatic females during pregnancy and encourage mothers be adherent to asthma medications. A significant increase in asthma risk was demonstrated among children whose mothers had poor control and increased severity of asthma during pregnancy. Asthma influences the outcome of pregnancy and also pregnancy can affect asthma severity, but the underlying immunological mechanisms of this interaction are not fully understood. This study found that IgE had a role in pathogenesis of asthma pregnancy and also can be a marker of uncontrolled asthma in pregnancy. Another finding of this study that the levels of IgE in well controlled asthma pregnancy subjects decreased to same levels in pregnant women without asthma. The conclusion of this study: serum IgE levels were higher in pregnant women with asthma compared to pregnant women without asthma. Serum IgE levels were higher in pregnant women with uncontrolled asthma compared to partly controlled and well controlled.

There was no conflict of interest in this study.

Limitations: This study contains several limitations. The sample of IgE serum was collected only one time and the subject were not followed until labor to assess outcome of the baby and mother with asthma in pregnancy.

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