

## Maternal stress in pregnancy based on Holmes-Rahe questionnaire and umbilical cord IgE

Reza Bidaki<sup>1</sup>, Mehran Karimi<sup>2</sup>, Mahdiyeh Mojibyan<sup>2</sup>, Hosein Hadi Nodoshan<sup>2</sup>, Asghar Zare<sup>2</sup>, Parivash Rafiee<sup>2</sup>, Zahra Saberi<sup>2</sup>

<sup>1</sup>Rafsanjan university of medical sciences, <sup>2</sup>Shahid Sadoughi University Of Medical Sciences & Health Services , Yazd, Iran.

### Abstract:

**BACKGROUND:** pregnancy is a stressful period in woman life and environmental changes can affect on its qualification. Maternal stress is a risk factor on pregnancy that may affect the fetal immune system and predispose newborn to allergy.

**METHODS:** In this descriptive-analytic study, 290 pregnant women in third trimester were questioned about stress events in pregnancy by Holmes-Rahe Stress Score Questionnaire and also umbilical cord and maternal serum IgE levels were determined.

**RESULTS:** We found that 50.3% of pregnant women had mild , 30.7% had moderate and 19% had high stress during the first and second trimester. Umbilical cord IgE(Uc IgE ) was high in 24%, 54% and 70.9% of neonates from women with mild, moderate and severe stress respectively(P=0.001). Uc IgE was significantly more in neonates of mothers with higher serum IgE.(50.5% vs 36.2%) (P =0.018) .

**Conclusion.** Findings of this study indicated that high stress during pregnancy which determined by Holmes-Rahe questionnaire had a significant correlation with Uc IgE.

**Keywords:** Holmes-Rahe questionnaire, Pregnancy stress, Umbilical cord IgE(Uc IgE)

### Introduction:

Alteration in our routines even grateful ones can be stressful. Psychological stress is a particular relation between the person and environment that is appraised by the person exceeding his or her resources and threatening well-being.( 1,2)

Psychic factors and allergic diseases have a reciprocal relationship so that psychic factors predispose to allergic diseases and in other hands allergic diseases affect on psychic conditions negatively.( 3)

In 1968-1969, 28% of women expressed nervousness, and 36% stated that they experienced stress. By 2004-2005, The percentage of women who experienced the born stress was more than doubled, to 75%.(4)

It seems that stress full life is increasing for women, and it is a worrying case , especially for pregnant women and their infants. The pregnancy is a stress full period and environmental changes can affect on its qualification. Stress Not only during the pregnancy period may cause pregnancy complications such as preeclampsia, preterm labour and low birth weight, but also it may affect immunocompetence in offspring which h underlying mechanisms are not well understood.(5) Stress during pregnancy may effects on the immune system of the fetus and may result in predisposing newborn to allergy.(6) Many studies evaluate results of longitudinal of stress during pregnancy in children. Stress-elicited disruption

of immunity begins in utero, for example it is a significant association between stress in pregnancy and eczema in first 2 years of life.(7)

HPA axis(Hypothalamus-Pituitary-Adrenal axis) can be stimulated to amplify fetal glucocorticoid excess, as well as to activate additional elements of the fetal stress response (ie, catecholamines) affecting the developing immune system .(5,8)Stress during pregnancy change immune system response in cytokines production by mononuclear cells so that IL-8 ,TNF- $\alpha$ ,IL-3 increase and INF- $\gamma$  decrease.(6,9,10)Some of the mediators released by the HPA axis seem to be capable of suppressing the immune function.(11)

Recently, concerns have been focused on the possibility of preventing atopic diseases during pregnancy. Evidence proposed a positive relationship between cord blood IgE and allergic sensitization(12). Many studies have found that cord blood IgE levels between 0.9 and 1.3 IU/mL are associated with significantly increased risk for allergies. High Uc IgE of around 1.0 IU/ml has been suggested as a predictor in western children.(13)

In a study,the effect of parental history of allergic disease and the level of Uc IgE was enquired and showed that neonates with atopic mothers have a high level of Uc IgE but for atopic fathers this was not true, and this association was only obvious in infant girls.(14) Lin and colleagues showed that the high mother's serum IgE and maternal psychosocial factors, including family income and nervousness are risk factors for increased Uc IgE levels. They concluded that psychosocial factors are potentially important risk factors for elevated cord blood IgE.( 1)

#### Material and Methods:

This is a descriptive analytic study, and cases included 320 pregnant women referred to Sadoghi (public) and Mojibian (Private) hospitals questioned in the third trimester from January until July, 2009. Exclusion criteria were maternal underlying conditions, including psychiatric disorders, thyroid disease, using Psychiatric drugs and alcohol, family history of depression, mental illness and high cord blood IgA level. In addition to assessment of maternal anxiety and Uc IgE, other variables, including, birth weight, gestational age and sex were also evaluated. First part of designed questionnaires consisted of general information, and part two was Holmes-Rahe questionnaire .Every questionnaire was filled by the mother or nurse. Then at the time of delivery 2 ml venous blood was withdrawn from mother and 5 ml of cord blood, collected in laboratory tubes.Sample was centrifuged and serum was separated and frozen at - 20 c°.

In this study cut of point for maternal serum IgE was 100 IU/ml and for Uc IgE was 0.35 IU/ml. After data collection, data analysis was done by SPSS 16 software and using independent t-test , Mann-whitney and Chi-square test and  $P < 0.05$  was considered significant.

#### Results:

##### Demographic Data

The average age of women ranged from 16 to 40 years (  $25.7 \pm 5.11$ ).Mean birth weight was  $3124 \pm 415$  grams (Minimum. 1600 g. & Max. 4350 g.).141 women (48.6%) had their first delivery, 82 (28.3%) the second, and 67 (23.1%) had their third delivery. Cesarean section was performed in 97 cases (23.4%). A total of 139 (47.9%) male and 151 (52.1%) female neonates were recruited into the present study (Table 1).

20 infants (6.9%) had birth weight less than 2500 grams (LBW) and percentage of infants with normal weight and above 4000 grams were 91.4% and 1.7% respectively. Gestational age at birth in 34 infants

(11.7%) were below 37 weeks, 251 infants ( 86.6%) between 37 to 40 weeks and in five infants (1.7%) more than 42 weeks. (Table 1)

Based on Holmes-Rahe questionnaire mild, moderate and severe stress during pregnancy was 50.3%,30.7% and19% respectively. (Table 2)

**Maternal serum &Cord blood IgE**

Uc IgE level was high in 24%, 54% and 70.9% of pregnant women with mild, moderate and severe stress respectively( $p<0.001$ )(Table 3).

105 mothers (36.2%) had high and 185 mothers (63.8%) had low serum IgE levels. Furthermore,170 infants (58.8%) had low and 120 (41.2%) infant had high Uc IgE. Median level of maternal and Uc IgE were 61.15 IU/ml and 0.2 IU/ml respectively.

In male newborns, 62 cases (44.6%) and in female newborn, 57 cases (37.7%) had high Uc IgE ( $P =0.236$ ). Also results showed that 50.5% of mothers with high serum IgE, delivered babies with high Uc IgE, while this was recorded 36.2% in mothers with low serum IgE ( $P =0.018$ ). There was a not linear relationship between maternal and Uc IgE( $P =0.111$ ,  $r =0.018$ ).Also 11 infants (55%) with birth weight below 2500 g and 108 (40%) infants with birth weight over 2500 grams had high Uc IgE . ( $P =0.258$ ).

Pearson's correlation test showed the linear association between pregnancy maternal stress based on Holmes-Rahe questionnaire and cord blood IgE levels .( $R$  sq linear 0.192 )(Diagram: 1 )

Table 1: Frequency distribution of parity, delivery type, gestational age, newborn sex and birth weight

| Variables        |                | No. | Percent |
|------------------|----------------|-----|---------|
| Number of parity | One            | 141 | 48.6    |
|                  | Two            | 82  | 28.3    |
|                  | Three and more | 67  | 23.1    |
| Delivery type    | C/S            | 97  | 23.4    |
|                  | NVD            | 193 | 66.6    |
| Newborn sex      | Male           | 139 | 47.9    |
|                  | Female         | 151 | 52.1    |

|                 |                 |     |      |
|-----------------|-----------------|-----|------|
| Birth weight    | <2500(gram)     | 20  | 6.9  |
|                 | 2500-4000(gram) | 265 | 91.3 |
|                 | >4000(gram)     | 5   | 1.7  |
| Gestational age | <37 weeks       | 34  | 11.7 |
|                 | 37-42 weeks     | 251 | 86.6 |
|                 | >42 weeks       | 5   | 1.7  |

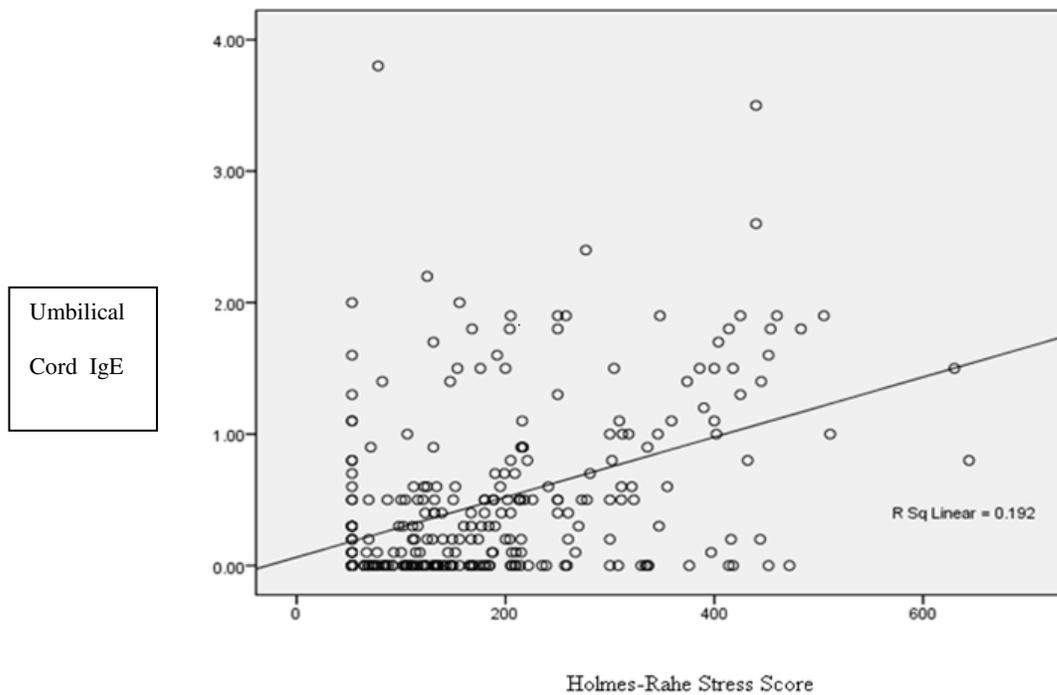
Table 2.Frequency of maternal stress score based on Holmes-Rahe questionnaire

| Holmes-Rahe stress score | Number<br>(%)  |
|--------------------------|----------------|
| Mild stress<150          | 146<br>(50.3%) |
| Moderate Stress=150-299  | 89<br>(30.7%)  |
| Severe stress>300        | 55(19%)        |
| Total                    | 290(100%)      |

Table 3. Correlation between Uc IgE and pregnancy stress scores

| Holmes- Rahe stress score    | Uc IgE (IU/ML)<br>(percent) |              |
|------------------------------|-----------------------------|--------------|
|                              | IgE<0/35                    | IgE≥0/35     |
| <150<br>(Mild stress)        | 111<br>(76)                 | 35<br>(24)   |
| 299-150<br>(Moderate Stress) | 41<br>(46)                  | 48<br>(54)   |
| ≥300<br>(Sevier stress)      | 16<br>(29.1)                | 39<br>(70.9) |

Diagram: Distribution of Uc IgE as Holmes-Rahe stress score in pregnancy.



**Discussion:**

Our study showed that antenatal stress is common in pregnant women in our area and a significant relationship exist between stress severity during pregnancy and Uc IgE (P=0.001). There was also a significant relationship between maternal serum IgE and Uc IgE (P=0.018). We didn't find any association between Uc IgE and gender, birth weight, and gestational age.

Pregnancy is known to be a major public health concern and pregnant women confront many life challenges and they have an increased risk for becoming involved stress. The consequences of stress during pregnancy on mother and fetus, and the long-term effects on child health status, have been shown in several studies. Pregnancy stress causes changes in perinatal immunomodulation and may finally bring on allergic diseases in children. (15,8,16)

High maternal stress in the first six months after delivery is associated with a greater allergen specific proliferatives response, higher total IgE levels and increased production of TNF- $\alpha$  and reduced INF- $\gamma$  in their children. (8)

Correlational studies suggest that pregnant mothers who have chronic psychological stress are more likely to abuse or neglect their children after they are born (11,17). According to this thread and the results of our findings which showed that during pregnancy moderate to high stress level is considerable therefore, the intervention of our health system is necessary to reduce stress in pregnancy.

Countries with the lowest stress levels report fewer problems over economics, health, employment, and violence than countries with higher stress levels. (18) In most developing countries, medical services, employment, economic state is low and lack of medical care can significantly increase national stress rates which those most affected by this stressor are women and children.

Stressful events undergo during pregnancy may be conveyed to babies as an increased risk for allergic disease. (19) In a study 9.5% of the women engaged with general anxiety disorder (GAD) at some point in pregnancy. (20)

However, our study showed nearly half pregnant women had moderate to severe stress during pregnancy. These findings show that pregnancy in our area is more stressful, and it may be due to differences between various economic, familial, social, environmental and race/ethnicity factors. Thus we emphasize to an establishment interventional program to decrease the stress during pregnancy and this maybe make allergic disease percentages decreased too.

Furthermore, culture and lower levels of education play a role in the production of stress. For example, women in Pakistan have particularly stressful life because of their lack of control over their lives. (21,22) It is estimated that 66% of women tolerated anxiety and depressive disorders in Pakistan. (22). Iran is in proximity of Pakistan and Turkey, and similarities are between both countries and stress patterns would be expected similar.

In a Turkish study, obese women had a higher score compared to normal weight women on family issues within the stress factors scale. (23)

Obese pregnant women attending an intervention program seem to have the same risk of experiencing anxiety and/or depressive symptoms as do obese and postnatal women in general. (24)

40% of Iranian adults (that nearly 48% of them belong to the women group) are low physical activity. Physical inactivity, particularly in females, is common in Iran. (25)

In our study, this item not be assessed but Exercise is an ideal method to help cope with environmental stressors. It will also give feeling more energetic and ready for an opponent with day's conflict. Exercise can help ease labor and decrease some of the anxiety associated with the unwilling labor or delivery.

In a study in Turkey, working women had higher levels of stress than non-working women. working women in sub scales of immune system and susceptibility to stress scale had a higher average score than non-working women. (26)

Some studies showed that the relationship between gender and IgE is significant, as U<sub>c</sub> IgE levels in infant boys are a higher than girls (14). It may justify higher prevalence of allergic diseases in boy infants. Lin et al found that male sex as a risk factor for high cord blood IgE level. (1) In our study, the percentage of male infants with high IgE was more than female newborns but this difference was not significant (P=0.236) and perhaps it is due to the low sample size.

Maternal IgE does not pass away from the placenta, but some studies showed that maternal and U<sub>c</sub> IgE levels are related with each other. One study on 100 mothers and newborns found a significant relationship between cord IgE and serum IgE of mothers with a history of allergy, but there is no

relationship in mothers having no history of allergy( Shilpa and colleagues). (27) High mother's serum IgE and maternal psychosocial factors are risk factors for elevated cord blood IgE levels (Lin and et., al).(1)We suggest that high maternal IgE level as a probable risk factor for child allergy because our study showed mothers who had higher serum IgE level had high Uc IgE levels, and the relationship is significant. As these findings, it can logically be hypothesized that reducing maternal stress before and during pregnancy may improve the fetal outcomes.

These findings emphasize the importance of the psychological health of pregnant women in developing countries. Furthermore, better coping abilities may help to improve feelings of pregnancy among females. Women in developing countries may experience the greater stresses than women in modern societies, and they are more likely to admit due to mental health problems.

It's very important for pregnant women who have close and continuous interactions with their close friends and family members, because their conflicts , challenges , anxiety and stress will be decrease. We advise pregnant women in our province should be trained for stress and anger management. The people must be educated about effects of stress on the pregnancy outcome in order to reduce the incidence of asthma and allergic diseases.

### **Conclusion:**

Stress is a substantial public health problem among pregnant women in Iran. Findings of this study indicate that pregnancy maternal stress score which determined by Holmes-Rahe questionnaire had a significant correlation with umbilical cord IgE. Pregnancy stress increases umbilical cord blood and maternal serum IgE. So that mothers who had higher IgE, had been newborn with higher IgE levels, that may be effective in predisposing to allergy and asthma in future life.

### **An acknowledgment:**

This research is from the student thesis and sponsored by Research deputy of Yazd sadoghi University of Medical Sciences. Furthermore, acknowledgments from laboratory science master degree students and nurses of gynecology ward in both Sadoghi and Mojibian hospital.

### **References**

1. Lin YC, Wen HJ, Lee YL, Guo YL. School of Dentistry, Kaohsiung Medical University, Kaohsiung, Taiwan Are maternal psychosocial factors associated with cord immunoglobulin E in addition to family atopic history and mother immunoglobulin E? *Clin Exp Allergy*. 2004 ;34(4):548-54.
2. Elizabeth R. McAnarney, MD; Catherine Stevens-Simon, MD Maternal Psychological Stress/Depression and Low Birth Weight Is There a Relationship? *Am J Dis Child*. 1990;144(7):789-792.
3. Chida Y, Hamer M, Steptoe A. A Bidirectional Relationship Between Psychosocial Factors and Atopic Disorders: A Systematic Review and Meta-Analysis *Psychosomatic Medicine* 70:102-116 (2008).

4. Middle-aged women experience more stress but have lower blood pressure. Africa's leading daily medical news. 2009. Bizcommunity.com.
5. Michelle Judith Sternthal, PhD, Michelle Bosquet Enlow, PhD, Sheldon Cohen, PhD, Marina Jacobson Canner, MA, John Staudenmayer, PhD, Kathy Tsang, MHA, and Rosalind J. Wright, MD, MPH, Boston and Amherst, Mass. Maternal interpersonal trauma and cord blood IgE levels in an inner-city cohort: A life-course perspective. *Journal of Allergy and Clinical Immunology*, 2009;124 (5) :954-960.
6. Wright. Rosalind J, Cynthia M. Visness, Agustin Calatroni, Mitchell H. Grayson, Diane R. Gold, Megan T. Sandel, Aviva Lee-Parritz, Robert A. Wood, Meyer Kattan, Gordon R. Bloomberg, Melissa Burger, Alkis Togias, Frank R. Witter, Rhoda S. Sperling, Yoel Sadovsky, and James E. Gern. Prenatal Maternal Stress and Cord Blood Innate and Adaptive Cytokine Responses in an Inner-city Cohort. *American Journal of Respiratory and Critical Care Medicine*. 2010; 182:25-33.
7. Sausenthaler. S. Stress-related maternal factors and childhood eczema. *J Investig Allergol Clin Immunol* 2009;19:481-487.
8. Wright. Rosalind J, Robyn T. Cohen and Sheldon Cohen. The impact of stress on the development and expression of atopy. *Current Opinion in Allergy and Clinical Immunology*. 2005;5:23-29.
9. Ana Elisa Fusaro, Cyro Alves de Brito, Eliana Futata Taniguchi, Bruno Pacola Muniz, Jefferson Russo Victor, Noemia Mie Orii, Alberto José da Silva Duarte, and Maria Notomi Sato. Balance between early life tolerance and sensitization in allergy: dependence on the timing and intensity of prenatal and postnatal allergen exposure of the mother. *Immunology*. 2009 ; 128(1pt2): 541-550.
10. Suzanne C. Segerstrom and Gregory E. Miller .  
Psychological Stress and the Human Immune System: A Meta-Analytic Study of 30 Years of Inquiry. *Psychol Bull*. 2004 ;130(4):601-30.
11. Stratakis CA, Chrousos GP. Neuroendocrinology and pathophysiology of the stress system. *Ann N Y Acad Sci* 1995;771:1-18.
12. A Sadeghnejad, W Karmaus, S Davis, R J Kurukulaaratchy, S Matthews, S H Arshad  
Raised cord serum immunoglobulin E increases the risk of allergic sensitisation at ages 4 and 10 and asthma at age 10. *Thorax*. 2004 ; 59(11): 936-942.
13. Shirakawa T, Morimoto K, Sasaki S, Taniguchi K, Motonaga M, Akahori W, Akahori S, Akahori T, Ohmori H, Kuroda E, Okabe K, Yugari K, Yamana M. Effect of maternal lifestyle on cord blood IgE factor. *Eur J Epidemiol*. 1997 ;13(4):395-402.
14. Johnson. C. C, Owanby. D. R and Peterson. E. L. Parental history of atopic disease and concentration of cord blood IgE. *Clinical and Experimental Allergy*. 1996;26:624-629.

15. Abigail L. Fowden, Dino A. Giussani and Alison J. Forhead . Intrauterine Programming of Physiological Systems: Causes and Consequences. *Physiology*, 2006; 21( 1): 29-37.
16. J Montoro, J Mullol, I Jáuregui, I Dávila, M Ferrer, J Bartra, A del Cuvillo, J Sastre, A Valero. Stress and allergy. *J Investig Allergol Clin Immunol* 2009;19(1): 40-47.
17. Naja Rod Nielsen; Tage S. Kristensen; Peter Schnohr; Morten Grønbæk. Perceived Stress and Cause-specific Mortality Among men and Women: Results From a Prospective Cohort Study. *American Journal of Epidemiology*. 2008;168(5):481-491.
18. Sandra Ketcham. Countries with Lowest Stress Levels.2011.
19. Salynn Boyles. Pregnancy Stress Ups Kids' Asthma Risk. *Health and pregnancy*. 2010;Webmed.
20. Buist A, Gotman N, Yonkers KA. Generalized anxiety disorder: Course and risk factors in pregnancy. *J Affect Disord*. 2011 Jan 24. [Epub ahead of print]
21. N. HUSAIN, I. B. CHAUDHRY. Life stress and depression in a tribal area of Pakistan .*The British Journal of Psychiatry* (2007) 190: 36-41.
22. DB Mumford, K Saeed, I Ahmad, S Latif and MH Mubbashar Stress and psychiatric disorder in rural Punjab. A community survey. *The British Journal of Psychiatry* (1997) 170: 473-478
23. N. Sanlier, N. Unusan. The Relationship Between Body Weight and Stress and Nutritional Status in Turkish Women .*Pakistan Journal of Nutrition* 2007 ;6 (4): 339-344.
24. Claesson IM, Josefsson A, Sydsj G. Prevalence of anxiety and depressive symptoms among obese pregnant and postpartum women: an intervention study. *BMC Public Health*. 2010 Dec 16;10:766.
25. Esteghamati A, Khalilzadeh O, Rashidi A, Kamgar M, Meysamie A, Abbasi M. Physical activity in Iran: results of the third national surveillance of risk factors of non-communicable diseases (SuRFNCD-2007). *J Phys Act Health*. 2011;8(1):27-35.
26. Nevin Sanlier, Fatma Arpacı. A study into the effects of stress on woman's health. *Humanity & Social sciences journal* 2(2):104-109, 2007.
27. Shah Shilpa, Bapat MM .Parental history of allergy, maternal serum IgE & cord serum IgE. 2006 ;60 (1) : 13-18 .