

## Serum IL-13 Level in Pregnancy Related Pruritus

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### Abstract

Background: Interleukin is an activated T helper 2 cell-secreted pleiotropic cytokine. It is a kind I immune response counterregulatory mechanism and has become a major regulator for Type II cytokine driven immune reactions. The pathophysiologic alterations generated by allergic inflammation in numerous tissues are suspected of being a more central mediator. The new transient ankyrin potentials 1-dependent and histamine-independent method produce chronic pruritus and the expression of TRPA1 in AD skin is essential to the beginning and support of chronic AD itch. Goals: The objective of this research was to assess the amount of IL in pregnant women with pruritus complaints. Method: 60 pruritus-related pregnant patients were included in this research. They were (27.9 ± 4.5) years of age. In addition to 30 healthy pregnant women without pruritus, the control group was taken. Any patient was excluded from the trials; any pruritus identified as a special dermatological illness (eczema, parasites, hives, fungal infections), bile bladder illness, liver problems (cirrhosis, acute fatty liver, hepatitis), hypertension and diabetes. For liver, immunoglobulin E and eosinophil, all patients were investigated. Serum IL- level was assessed using enzyme-linked immunosorbent test kits commercially available. Results: Pruritus pregnant women had substantially greater eosinophilic counts, ig E as opposed to control group (p to 0.001 each). The total, direct, bilirubin, bile acid, aspartate aminotransferase (AST), aminotransferase (ALT), total of cholesterol (CT), triglyceride (TG), low-density lipoprotein (LDL), fasting blood glucose (FBG), post-brandal glucose (PB G) in relation to the control group were not significantly higher for the pregnant female with pruritus (P>0.05). Pruritus associated with pregnancy was substantially greater in IL- compared to control group (P<0.001). IL- substantially increased in the first, second and third quarters. IL in the third quarter was substantially greater than in the second quarter (P<0.001 each). No significant relationships were identified in all the individuals (P>0,05 for each) between the concentrations of oesophilic count, immunoglobulin E (IgE) and IL- vs. gravity and foetal gender. Conclusion: The findings of this research show that IL is greater for patients with more severe pruritus and may explain the higher IL level for these patients, so that early detection of IL levels may contribute towards improved pregnant pruritus treatment.

**Key words:** Il-, pregnancy, pruritus.

### 1. Introduction

Pruritus is an undesirable sensation that leads to a desire to scratch. It is the most prevalent sign of the skin. The systemic differential diagnosis is usually caused by xerosis (dry skin) or eczema, which reaches as many as cirrhosis, haematological disturbances, infections, medicines responses and malignancies. Frequently disregarded, pruritus may seriously affect the quality of life [1].

Jizziness is a frequent symptom among pregnant women, with up to 14 to 23%. The frequency in various populations is 0.7 to 5%. Genetic and environmental factors contribute to their prevalence among the world's populations [2].

Atopic dermatitis driver (AD). He is a powerful mediator of the induction and effector stages of inflammation of type 2 [3]. It supports the synthesis of immunoglobulin E (IgE) and shares the alpha receiver subunit with IL-4 [4]. It promotes chronic pruritus through a new and histamin-dependent transient receptor potential ankyrin 1 (TRPA1) and the expression of TRPA1 in the AD skin is essential in initiating and maintaining chronic itching [5].

The purpose of this research is to analyse the amount of IL in the pregnant women of pruritus patients to determine the involvement of IL in pruritus pathogenesis in pregnant women.

### 2. Subjects and methods

#### 2.1. The study population

This was a cross sectional case control study. Patients were included in this study were from outpatient clinic of Dermatology, Venereology and Andrology Department of Benha University Hospitals in the period between July 2019 and March 2020 after the approval by Research Committee at Faculty of Medicine, Benha University. The present study included 60 pregnancy related pruritus patients. Their mean age was (27.9 ± 4.5) years. In addition to 30 healthy pregnant females without pruritus, were taken as a control group. Every subject was informed about the aim of the study and an informed consent was obtained from each individual before sample collection. Any subject was presented with any of the following conditions was excluded from the study; any pruritus diagnosed as specific dermatologic condition (eczema, parasites, hives, fungal infections), gall bladder disease, liver diseases (cirrhosis, acute fatty liver, hepatitis), hypertension and diabetes. Patients were subjected to full history-taking including; onset, course, and duration of pruritus, stress factors, and history of itching in previous pregnancy and outcome of previous pregnancy with itching. All patients were evaluated

for liver function test, immunoglobulin E and eosinophil. ELISA assays:

Five ml of venous blood were used for the production of serum and ethylene diamine tetra acetic acid (EDTA) plasma for the measurements of IL- was obtained. Serum was obtained after coagulation of the blood at room temperature (+22°C) for 60 min. Blood for both serum and plasma was centrifuged at 2500 rpm for 10 min. Serum and plasma were stored at -20°C until analysis.

## 2.2. Statistical Analysis

The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). Data were presented and suitable analysis was done according to the type of data obtained for each parameter. Student T Test was used to assess the statistical significance of the difference between two study group means. For the comparison

of the three groups' means, one way analysis of variance (ANOVA) was used. Chi-Square test was used to examine the relationship between two qualitative variables. Fisher's exact test: was used to examine the relationship between two qualitative variables when the expected count is less than 5 in more than 20% of cells. Correlation analysis: To assess the strength of association between two quantitative variables. The correlation coefficient defines the strength and direction of the linear relationship between two variables. P is significant if <0.05 at confidence interval 95%.

## 3. Results

Pregnant females with pruritus had significantly higher eosinophilic count, Ig E when compared to control group (P<0.05). In addition, pregnant females with pruritus had non significantly higher total, direct bilirubin, bile acid, AST, ALT, TC, TG, LDL, FBG, PBG when compared to control group (P>0.05) Table (1).

**Table (1)** Difference of laboratory data between cases and control groups.

	Control (N=30)			Pregnancy Related Pruritus (N=60)			P
	Mean	±	SD	Mean	±	SD	
Eosinophils (X10 <sup>9</sup> /L)	0.3	±	0.1	0.9	±	0.2	<0.001
Ig E (IU/mL)	63.3	±	.9	94.3	±	5	<0.001
Total bilirubin (mg/dL)	1.1	±	0.05	1.5	±	0.2	0.143
Direct bilirubin (mg/dL)	0.3	±	0.02	0.5	±	0.2	0.115
Bile acid (mmol/L)	6.1	±	0.4	7	±	0.6	0.287
AST (U/L)	39.9	±	4.1	42.5	±	3.3	0.173
ALT (U/L)	44.1	±	3.8	46.5	±	6.5	0.292
Cholesterol (mg/dL)	197	±	4.4	214.3	±	36.8	0.172
TG (mg/dL)	167.6	±	15.5	174.8	±	.9	0.6
LDL (mg/dL)	109.5	±	15.2	115.7	±	14.3	0.326
HDL (mg/dL)	61.2	±	9.2	54.3	±	15.4	0.218
FBS (mg/dL)	116.7	±	8.8	122.5	±	9.1	0.182
PPBS (mg/dL)	7.3	±	14.9	144.5	±	.2	0.267

Pregnancy related pruritus had significantly higher IL- level when compare to control group (P<0.001) Table (1).

## 4. Discussion

Pruritus is a symptom of numerous nervous system illnesses that affect a wide human population and is treated using variable-access pharmacology drugs. Chronic itch is a big unmet health concern affecting 20% of the world's population [6]. Pruritus occurs about 15% of pregnancy and makes women distressed and also carries an extra danger to the foetus [7]. Pruritus during pregnancy is the main dermatological symptom. A variety of PSDs, such as PEP, pemphigoid gestationis and pruritus gravidarum, are accompanied by intense scratching and scratching in addition to the underlying or acquired dermatoses. The treatment of pruritus during pregnancy needs judicious attention due to possible implications on the baby [8].

Interleukin- is a powerful mediator of inflammation induction and effector stages of type 2.

It also affects the change of the class to IgE and eosinophil chemotaxis [9]. It generates chronic pruritus by a new TRPA1, reliant on histamine, and is crucial for the onset and continued support of chronic pruritus in AD skin (dermal sensory nerves, mast cells, and epidermis) [5].

In this research, the eosinophilic count and Ig E of pregnant women were considerably greater in comparison with the control group (P<0.001 for each).

These results agree on the preceding findings of Puri et Al [10]. The results reported significant eosinophilic differences in the number of atopic pregnant women with nipple eczema compared to non atopic pregnant women with nipple eczema (P<0.01), whereas the serum IgE levels between the two groups were not statistically significant. Martina et al. [11] observed, on the other hand, no significant

variations in Ig E between pregnant women with allergy symptoms in relation to control patients ( $P < 0.01$ ). The variance between outcomes may be explained by the variety in sample size, ethnic variances and genetic and racial background.

Singh and Sidhu [12] observed there was no significant increase in blood bilirubin ( $P=0.055$ ), however the levels of AST and ALT in pregnant women with IC cholestasis were considerably higher ( $P=0.029$ ;  $P=0.011$ ).

Pregnancy intrahepatic cholestasis is a syndrome which is characterised in the second part of pregnancy by pruritus. Besides pruritus, clinical jaundice has been used to define ICP; greater rates of foetal complications than when diagnosis has been based on high bile acid and transaminase. Serum bile acid elevation is thought to be the best laboratory marker for diagnosing the problem. Bile acids have been investigated as suspected pruritogens most comprehensively. In individuals with cholestasis, skin tissue concentrations of bile acids are raised and are linearly proportional to serum levels. In addition, the binding resin cholestyramine improves the removal of bile salts and alleviates pruritus [14].

This is in line with Yousri et al.[15] studies, which indicated that blood levels of total IgE and IL- increased substantially to heterozygous AG and homozygous GG than homozygous AA in atypical, asthma nonatopic and allergic patient groups ( $P < 0.001$  for each). In addition, serum IL- levels may be employed for the detection of allergic disorders as a biochemical marker. IL- was involved in allergic illness development, including atopic dermatitis. IL- was only manufactured in the skin and resulted in the occurrence of a chronic inflammatory phenotype characterised by xerosis and pruritus eczematotic lesions, dermal infiltration of CD4+T cells, mastcells, eosinophils, macrophages and the cells of Langerhans, chemical and cytokine upregulation, including thymic lymphopoietin stromal and fibrosis skin remodelling and increased vasculature. The cutaneous phenotype was supplemented by higher IgE and IgG1 serum total and enhanced IL-4 and IL- output by CD4+ lymphoid cells and mononuclear peripheral blood cells. IL- is a powerful dermal inflammation stimulant [16]. IL4 and IL levels in skin biopsies in individuals with atopic dermatitis have been demonstrated to correlate with IL-31, recognised pruritogen [17]. The skin's dermal expression of IL- resulted in a persistent pruritus inflammatory skin disease similar to eczema [16].

The findings showed that the esinophilic count, IgE and IL- concentrations vs. gravity and sex of the foetus were not significantly associated in all tested patients ( $P>0.005$  for each).

In allergic type I responses, immunoglobulin E antibodies play a vital role. In B cells, IL- is capable of inducing an immunoglobulin isotype switch to IgE. T cells have been polyclonally activated to generate IL- and subsequently IgE secretions in

cultures with isolated T and B cells of allergic asthma patients and non atopic controls. The total quantity of IgE generated between patients and controls was not substantially different. In addition, the generation of IgE in both patients and controls was markedly decreased when IL-4 anticorps were neutralised during culture. Neutralizing IL- however resulted in a substantially higher reduction of IgE production in the patient group. There was a greater patient IL- production, however the IL-4 production was not substantially different. A more extensive investigation of IL- production shows that patients' T cells are less responsive to a negative IL-controlled signal [18].

## 5. Conclusion

In the present study, we concluded that expression of is higher in more severe pruritus related pregnancy patients and that could be explained by higher level in those patients, so the early recognition of IL- level might help in better management of pruritus in pregnancy.

## 6. Recommendations

The findings of this investigation should be evaluated in view of their limitations as a very small sample size was included in the current investigation. It is advised from the findings of this research that: Assessment of serum in various forms of pregnant pruritus. Additional investigations are required to determine the specific pathways through which IL- contributes to pruritus-related pregnancy pathophysiology. Measurement of pruritus-related pregnancy levels is important before and after therapy.

## References

- [1] D.Nowak, J.Yeung. Diagnosis and treatment of pruritus. Canadian Family Physician.vol. 63(12),pp. 918-924, 2017.
- [2] K.Prusova, L.Churcher, A.Tyler, A.Lokugamage. Royal College of Obstetricians and Gynaecologists guidelines: How evidence-based are they? J Obstet Gynaecol.vol. 34(8),pp. 706-711,2014.
- [3] N.Gandhi, G.Pirozzi, N.Graham. Commonality of the IL-4/IL- pathway in atopic diseases. Expert Rev Clin Immunol.vol. (5),pp.425-437,2017.
- [4] K.Eyerich, N.Novak. Immunology of atopic eczema: overcoming the Th1/Th2 paradigm. Allergy.vol. 68(8),pp.974-982,2015.
- [5] M.Oh, S.Oh, J.Lu, H.Lou, A.Myers, Z.Zhu. TRPA1-dependent pruritus in IL-induced chronic atopic dermatitis. J Immunol.vol. 191(11),pp. 5371-5382, 2014.
- [6] J.Meng, M.Steinhoff. Molecular mechanisms of pruritus. Curr Res Transl Med.vol. 64(4),pp.203-206,2016.

- [7] Sharma C, Talukdar R. Pregnancy with Pruritus: Our Experience. *IOSR J Dental Med Sci.* 2019; 18(4): 46-51.
- [8] E.Weisshaar, R.Witteler, T.Diepgen, TA.Luger, S.Ständer. Pruritus in pregnancy. A frequent diagnostic and therapeutic challenge. *Der Hautarzt; Zeitschrift für Dermatologie, Venerologie, und verwandte Gebiete.*vol.56(1),pp. 48-57,2005.
- [9] N.Gandhi, G.Pirozzi, N.Graham. Commonality of the IL-4/IL- pathway in atopic diseases. *Expert Rev Clin Immunol.*vol. (5),pp. 425-437, 2017.
- [10] N.Puri, A.Puri. A study on dermatoses of pregnancy. *Our Dermatol Online.*vol. 4(1),pp. 50-56,2013.
- [11] A.Martina, F.Anne, Y.Jonsson, M.Persson, J.Ernerudh, G.Berg. Total and allergen-specific IgE levels during and after pregnancy in relation to maternal allergy. *J Repro Immunol.*vol. 81(1),pp.82-88, 2009.
- [12] G.Singh, K.Sidhu. Cholestasis of pregnancy: a prospective study. *Med J Armed Forces India.*vol.64(4),pp. 343-345,2008.
- [13] A.Morton, J.Laurie. The biochemical diagnosis of intrahepatic cholestasis of pregnancy. *Obstet Med.*vol. 12(2),p.76-78, 2019.
- [14] M.Bechtel. Pruritus in pregnancy and its management. *Dermatologic Clin.*vol. 36(3),pp. 259-265,2018.
- [15] H.Yousri, S.El-Tarhouny, S.Shalaby, R.Mohamed, T.Hassan. Interleukin- receptor A1 gene polymorphism and IL- serum level in atopic and non-atopic Egyptian children. *Immunol Invest.*vol.40(5),pp.523-534,2011.
- [16] T.Zheng, M.Oh, S.Oh, J.Schroeder, A.Glick, Z.Zhu. Transgenic expression of interleukin- in the skin induces a pruritic dermatitis and skin remodeling. *J Invest Dermatol.*vol. 129(3),pp.742-751, 2009.
- [17] M.Neis, B.Peters, A.Dreuw, J.Wenzel, T.Bieber, C.Mauch, T.Krieg. Enhanced expression levels of IL-31 correlate with IL-4 and IL- in atopic and allergic contact dermatitis. *J Allergy Clin Dermatol.*vol. 118(4),pp.930-937,2006.
- [18] J.Ingram, M.Kraft. IL- in asthma and allergic disease: asthma phenotypes and targeted therapies. *J Allergy Clin Immunol.*vol. 0(4),pp.829-42, 2012.