

9.0.
Arabic summary

Plasma level of D-dimer in patients with Chronic Idiopathic Urticaria

Thesis

*Submitted for partial fulfillment of a MasterDegree
in Dermatology, Venereology and Andrology*

By :

Nelly Mohammed Hussein Ismail

M.B, B.CH,

Ain Shams University

Under The Supervision of :

Prof.Dr. Nader Fouad Mohamed Ragab

*Professor of Dermatology, Venereology and Andrology
Faculty of Medicine, Ain Shams University*

Assis.Prof.Dr. Samar Abdallah M. Salem

*Assis. Professor of Dermatology, Venereology and
Andrology
Faculty of Medicine, Ain Shams University*

***Faculty of Medicine
Ain Shams University
2008***

بِسْمِ اللَّهِ الرَّحْمَنِ
الرَّحِيمِ
وَقُلْ رَبِّي زِدْنِي عِلْمًا
{114}

صدق الله العظيم

سورة طه.....آية 114

Acknowledgements

*I would like to express my deepest thanks and
respect to **Dr. Nader Fouad M. Ragab** Professor of*

Dermatology, Venereology and Andrology, Ain Shams University, for his valuable supervision, guidance and kind advice throughout this work.

*Special thanks and deepest gratitude to **Dr. Samar Abdallah M. Salem**, assistant professor of Dermatology, Venereology and Andrology, Ain Shams University, for her good support, continuous supervision and unlimited help during this work.*

I would like to thank my family for their kindness, support, and much needed encouragement.

Plasma level of D-dimer in patients with Chronic Idiopathic Urticaria

*Protocol for thesis
Submitted for partial fulfillment of a Master Degree
in Dermatology, Venereology and Andrology*

By :

Nelly Mohammed Hussein Ismail

M.B, B.CH,
Ain Shams University

Under The Supervision of :

Prof.Dr. Nader Fouad Mohamed Ragab

Professor of Dermatology, Venereology and Andrology
Faculty of Medicine, Ain Shams University

Assis.Prof.Dr. Samar Abdallah M. Salem

Assis. Professor of Dermatology, Venereology and
Andrology
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2008

INTRODUCTION

Chronic urticaria (CU) is a common skin disorder characterized by the recurrent eruption of short-lived wheals accompanied by redness and itching for at least six

weeks (**Greaves, 2000**). However, it is not a single disease but a cutaneous reaction pattern for which there are multiple potential causes. The clinical expression of the disease varies from one patient to another in duration of activity, morphological features of the lesion and its histopathological basis (**Tharp et al., 1990**). Chronic idiopathic urticaria (CIU) is a common form of chronic urticaria in which no precise causal factors can be identified (**Champion, 1990**).

Results of a number of in vitro studies performed suggest an auto-immune pathogenesis for chronic idiopathic urticaria, but several aspects remain ill-defined or even contradictory. It was generally accepted that auto-antibodies to IgE or to high affinity IgE receptors which were commonly regarded as the most relevant pathogenic factor in the disease, can be detected in sera of a proportion ranging from 25% to 50% of patients with chronic

idiopathic urticaria (**Hide et al., 1993, Niimi et al., 1996, Tong et al., 1997**).

Recently, an activation of coagulation cascade via the tissue factor pathway has been observed in most of patients with chronic idiopathic urticaria. Also, indirect evidence of the possible involvement of coagulation cascade came from the observation that the proportion of skin test-positive patients rises substantially if autologous plasma is injected instead of autologous serum (about 80% Vs 50%) suggesting that clotting destroys a plasma factor that is some how involved in the skin reaction (**Asero et al., 2006**).

The recent information indicates that chronic urticaria is characterized by an activation of the extrinsic pathway of coagulation leading to the formation of thrombin which might be responsible for generating C5a and increasing vascular permeability. On the other hand, the excess of fibrin formation is counter-balanced by enhanced fibrinolysis as demonstrated by the increase in D-dimer levels (**Asero et al., 2007**).

D-dimer is a breakdown product by the degradation of cross linked fibrin by the plasmin due to any etiology (**Freyburger et al., 1998**).Also, it is produced in all

situations in which coagulation and fibrinolysis are activated (**Goldstien et al., 2001**).

Thrombus formation is normally followed by an immediate fibrinolytic response by plasmin causing the release of fibrin degradation products -predominately containing D-dimer- into the circulation. So, the absence of D-dimer implies that thrombosis is not occurring and negative D-dimer assays have an important role in excluding any diagnosis of coagulation (**Kelling et al., 2004**).

In recent studies D-dimer levels were found to be higher in patients with slight to moderate chronic idiopathic urticaria than in a group of age and sex matched normal controls and were significantly elevated in a selected group of patients with severe exacerbation of chronic idiopathic urticaria proving that the coagulation cascade is activated up to the production of fibrin as a result of the generation of thrombin. That was further supported by the dramatic drop of D-dimer levels which were extremely high during an

acute phase of severe chronic urticaria and perfectly normal after remission (**Asero et al., 2007, Asero et al., 2008**).

New therapies targeting anticoagulants are currently considered in treatment of chronic urticaria according to clinical studies which were performed to investigate the effect of warfarin in treating patients with chronic idiopathic urticaria unresponsive to anti-histamines, these patients responded to warfarin showing complete resolution of symptoms and some of them had a dramatic response (**Berth et al., 1988, Barlow and Greaves, 1992, Parslew et al., 2000**).

Also, a case report study showed a marked clinical improvement in a patient with chronic urticaria after been treated with subcutaneous heparin and remained completely recovered after fifteen months of treatment. If heparin was discontinued or the dose was reduced deterioration occurred. This supports the involvement of coagulation cascade in the pathogenesis of chronic urticaria. (**Chua and Gibbs, 2005**).

Aim of the Work:

The aim of this work is to estimate the plasma levels

of D-dimer in patients with chronic idiopathic urticaria, to assess its possible role in CIU and to correlate such levels with the disease severity.

Patients And Methods:

This study will include:

- Twenty patients with CIU after taking their consent.
- Ten patients with CU with a known cause are also selected after taking their consent.
- Ten healthy persons will be also included as a control group.
- All persons (patients & controls) will be subjected to:
 - 1) Full history taking.
 - 2) General examination.
 - 3) Dermatological examination.
 - 4) Other investigations as required to exclude possible causes of chronic urticaria.
 - 5) Blood samples will be obtained from patient and controls, and plasma D-dimer levels will be measured by the ELISA Method.
- Statistical analysis of the results will be performed.

The Thesis will include:

- 1 - Introduction and Aim of the Work.
- 2 - Review of Literature.
- 3 - Patients and Methods.
- 4 – Results.
- 5 – Discussion.
- 6 - Summary and Conclusion.
- 7 – References.
- 8 - Arabic Summary.

References:

- Asero R, Riboldi P, Tedeschi A and Cugno M (2006): Plasma of patients with chronic urticaria shows signs of thrombin generation and its intradermal injection causes wheal-and-flare reactions much more frequently than autologous serum. J Allergy Clin Immunol, 117: 1113-1117.
- Asero R, Riboldi P, Tedeschi A, Cugno M and Meroni P (2007): Chronic urticaria: A disease at a cross road between autoimmunity and coagulation. Autoimmunity Rev, 7(1): 71-76.
- Asero R, Tedeschi A, Coppola R, Griffini S, Paparella P and Riboldi P (2007): Activation of the tissue pathway of blood coagulation in patients with chronic urticaria. J Allergy Clin Immunol, 119: 705-710.

- Asero R, Riboldi P, Tedeschi A, cugno M, Griffini S and Bonanni E (2008): Severe chronic urticaria is associated with elevated plasma levels of D-dimer. *Allergy*, 63(2): 176-180.
- Barlow RJ and Greaves MW (1992): Warfarin in the treatment of chronic urticaria and angioedema. *Br J Dermatol*, 126: 415-6.
- Berth Jones J, Hutchinson PE, Wicks ACB and Mitchell VE (1988): Chronic urticaria with angioedema controlled by warfarin. *Br Med J*, 297:1382-3.
- Champion RH (1990): A practical approach to urticarial syndromes, a dermatologist's view. *Clin Exp Allergy*, 20: 21-4.
- Chua SL and Gibbs S (2005): Chronic urticaria responding to subcutaneous heparin sodium. *Br J Dermatol*, 153: 216-7.
- Freyburger G, Trilland H, Labrouch S, Gauthier P, Javorschi S and Bernard P (1998): D-dimer strategy in thrombosis exclusion. *Thromb Haemost*, 79: 32-7.
- Goldstien MN, Kollef MH, Ward S and Gage BF (2001): The impact of the introduction of rapid D-dimer assay on the diagnosis evaluation of suspected pulmonary embolism. *Arch Intern med*, 161:567-71.

- Greaves MW (2000): Chronic urticaria. J Allergy Clin Immunol, 105: 664-27.
- Hide M, Francis DM, Grallan EH, Hakimi J, Kochan JP and Greaves MW (1993): Auto-antibodies against the high affinity IgE receptors as a cause of histamine release in chronic urticaria. N Eng J Med, 328: 1599-604.
- Keeling DM, Mackiel J, Moody A and Watson HG (2004): The diagnosis of deep venous thrombosis in symptomatic out-patients and the potential assessment of D-dimer assay to reduce need for diagnostic imaging. Br J Haematol, 124: 15-25.
- Niimi N, Francis DM, Kermani F, Odonell BF, Hide M and Kobazablack A (1996): Dermal mast cell activation by auto-antibodies against the high affinity IgE receptors in chronic urticaria. J Invest Dermatol, 106: 1001-6.
- Parslew K, Ashworth J and Fredmann PS (2000): Warfarin treatment of chronic idiopathic urticaria and angioedema. Clin Exp Allergy, 30: 1161-5.
- Tharp MD, Levin MI and Fireman P (1990): Atlas of allergy. Newyork: Gover Medical Publishing, 16: 2-15.
- Tong LJ, Balakrishnan G, Koch JP, Kinet JP and Kaplan AP (1997): Assessment of autoimmunity in patients with chronicurticaria. J Allergy Clin Immunol, 99: 461-5.

مستوي مركب د-ديمر في بلازما مرضى الأرتيكاريا
مجهولة السبب

رسالة بحثية

توطئة للحصول على درجة الماجستير في الأمراض الجلدية والتناسلية

مقدمة من

الطبيبة/ نيللي محمد حسين إسماعيل
بكالوريوس الطب والجراحة
جامعة عين شمس

تحت إشراف

أ.د/نادر فؤاد محمد رجب

أستاذ الأمراض الجلدية والتناسلية والذكورة
كلية الطب - جامعة عين شمس

أ.م.د/سمر عبدالله محمد سالم

أستاذ مساعد الأمراض الجلدية والتناسلية
والذكورة

كلية الطب - جامعة عين شمس

كلية الطب

جامعة عين شمس

2008

المقدمة

يعتبر مرض الأرتيكاريا المزمنة من اضطرابات الجلد الشائعة والتي
تتميز بالطفح الجلدي المتكرر قصير الأجل مصحوباً باحمرار وحكة لمدة