# Role OF Measurement of ADAM TS 13 in Patients with Suspected Microangiopathy

Thesis

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in Clinical Hematology

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بسم الله الرحمن الرحيم
وَاتَّقُوْا اللّٰهَ وَيُعَلِّمُكُمُ اللّٰهُ
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Marwa EL-Hosiny EL-Metwaly Nada

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# List of Abbreviations

| Abbr. | Full-term |
|---|---|
| **ADAMTS13** | A disintegrin and metalloproteinase with thrombospondin type 1 motif, member 13 |
| **ADP** | Adenosine di-phosphate |
| **ATP** | Adenosine triphosphate |
| **CAMP** | Cyclic adenosine monophosphate |
| **CBC** | Complete Blood Count |
| **COX1** | Cyclooxygenase-1 |
| **EHEC** | Enterohemorrhagic E. coli. |
| **ELISA** | Enzyme-linked immunosorbent assay |
| **GP** | Glycoproteins |
| **HIT** | Heparin-induced thrombocytopenia |
| **HLA** | Human leukocyte antigen |
| **HIV** | Human Immunodeficiency virus |
| **HUS** | Hemolytic-uremic syndrome |
| **IV.IG** | Intra venous immunoglobulin |
| **MAHA** | Microangiopathic hemolytic anemia |
| **NSAIDS** | Non-steroidal anti-inflammatory drugs |
| **OCS** | Open canalicular system |
| **RBCs** | Red blood cells |
| **SD** | Standard deviation |
| **SPSS** | Statistical Program for Social Science |
| **TGF-β** | Transforming growth factor beta |
| **TIA** | Transient ischemic attack |
| **TMAs** | Thrombotic microangiopathies |
| **TTP** | Thrombotic thrombocytopenic purpura |
| **TXA**2 | Thromboxane A2 |

| | |
|---|---|
| **ULVWF** | **:** Ultra large multimers of von Willebrand factor. |
| **VWF** | **:** Von Willebrand factor |
| **CNS** | **:** Central nervous system |
| **RBC** | **:** Red Blood Cell |
| **D+HUS** | **:** diarrhea with hemolytic uremic syndrome |
| **DIC** | **:** Disseminated intravascular coagulation |
| **ANA** | **:** Antinuclear antibody |
| **HSCT** | **:** Hematopoietic stem cell transplant |
| **TF** | **:** Thrombin generation and tissue factor |
| **FFP** | **:** Fresh frozen plasma |
| **FRM** | **:** Fibrin-related markers |
| **SF** | **:** Soluble fibrin |
| **AT** | **:** Antithrombin |
| **TM** | **:** Thrombomodulin |
| **APTT** | **:** Activated partial thromboplastin time |
| **MCP** | **:** Membrane co-factor protein |
| **C** | **:** Complement |
| **ST2** | **:** Suppression of tumorigenicity 2 |
| **PI** | **:** Plasma Infusion |
| **P P** | **:** Plasmapheresis |
| **sST2** | **:** Soluble form of suppression of tumorigenicity 2 trans-membrane ligand |
| **ST2L** | **:** Suppression of tumorigenicity 2 trans-membrane ligand |
| **ARF** | **:** Acute renal failure |
| **SP** | **:** Signal peptide |
| **PCR** | **:** Polymerase chain reaction |
| **mRNA** | **:** Messenger Ribonucleic acid |
| **TSP1** | **:** Thrombospondin type 1 |
| **CUB** | **:** Complement Urchin epidermal growth factor, and Bone morphogenetic protein) domains |

**FFP** : Fresh frozen plasma
**TM** : Trans membrane domain
**HSCs** : Hepatic stellate cells
**UL** : Ultra large
**CMV** : Cytomegalovirus
**HELLP** : Hemolysis, elevated liver enzymes, and low platelet count) and preeclampsia.
**DNA** : Deoxyribonucleic acid
**SLE** : Systemic Lupus Erythematosus
**VEGF** : vascular endothelial growth factor
**HSCT** : Hematopoietic stem cell transplant
**TA-TMA** : Stem cell transplant associated thrombotic microangiopathy
**RDW** : Red cell distribution width
**PT** : Prothrombin time
**BUN** : Blood urea nitrogen
**LDH** : Lactate dehydrogenase
**MRI** : Magnetic resonance imaging
**NSAID** : Non-steroidal anti-inflammatory
**E-coli** : *Escherichia coli*
**aHUS** : Atypical Hemolytic-uremic syndrome
**t HUS** : Typical Hemolytic-uremic syndrome
**ESRD** : End stage renal disease
**MCP** : Membrane co-factor protein
**IL** : Interleukin
**FDPs** : Fibrin Degradation Products
**FSPs** : Fibrin split products
**TF** : Tissue Factor
**PAI-1** : Plasminogen Activator Inhibitor-1
**IgG** : Immunoglobulin G
**GVHD** : Graft versus host disease

**IFN** : Interferon
**TNF** : Tumer necrosis factor
**CKD** : Chronic kidney disease
**SF** : Soluble fibrin
**FRMs** : Fibrin related markers
**AT** : Antithrombin
**T.Bill** : Total Bilirubin
**D.Bill** : Direct Bilirubin
**MCV** : Mean corpuscular volume
**AST** : Aspartate transaminase

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**Abstract**

**Microangiopathy:** a disorder involving the small blood vessels. thrombotic microangiopathy formation of thrombi in the arterioles and capillaries; proposed name for a syndrome that would include both thrombotic thrombocytopenic purpura and hemolytic uremic syndrome ***(Mosby's Medical Dictionary, 9th edition. © 2009, Elsevier)*** In our study we measured adamts13 in microangiopathy in thrombotic thrombocytopenic purpura, microangiopathic hemolytic anemia , hemolytic uremic syndrome , DIC .we made comparison between sever deficiency of adamts13 level <10% and moderate deficiency of adamts13 level >10%. ADAMTS13 (a disintegrin and metallo-proteinase with a thrombospondin type 1 motif, member 13)-also known as von Willebrand factor-cleaving protease (VWFCP)-is a zinc-containing metalloprotease enzyme that cleaves von Willebrand factor (vWf), a large protein involved in blood clotting. It is secreted in blood and degrades large vWf multimers, decreasing their activity ***(Levy et al. 2005).*** The ADAMTS13 gene maps to the ninth chromosome (9q34). ***Levy GG, Motto DG, Ginsburg D (2005).***

**Aim of the study:** The aim of such study is to assess the role of measurement of ADAMTS13 in adult patients with suspected microangiopathy.

**Subjects and methods:** The study will be conducted on 90 subjects including: 60 patients suspected microangiopathy compared to 30 healthy control subjects in Ain Shams University Hospitals, inpatient departments & out-patient clinics.

***The subjects will be divided into two groups:***

- Group 1 (60 subjects): patients with suspected microangiopathy.
- Group 2 (30 subjects): healthy control subjects.

***Including criteria:***

- Adult at or larger than 18 years old.
- Suspected microangiopathy (such as progressive microangiopathy hemolytic anaemia with or without thrombocytopenia, edema, effusion, organ failure.

***All patients will be subjected to the following:***

Detailed history taking and physical examination.

Laboratory investigations including:

- Complete blood picture (CBC) and peripheral blood film (with schistocytes), reticulocytic count, serum ferritin and erythrocyte sedimentation rate (ESR).
- Coagulation profile: prothrombin time (PT), and activated

partial thromboplastin time (aPTT).

- Metabolic profile including renal function tests (s.creat , urea ,Na & K) ,Liver function tests (SGOT , SGPT, total & direct Bilirubin, Total protein & albumin).
- Serum LDH.

Other investigation as needed for diagnosis.

Measurement of ADAMTS13 level in prepheral blood (ELIZA)

**Ethical aspects:**

The study will be initiated after obtaining approval of Ethical Committee of faculty of Medicine Ain Shams University.

***Statistical analysis of results***

***CONCLUSION:***

TTP and other TMAs remain diagnostically difficult and emergency condition and need to rapid investigation. Measurement of ADAMTS13 is more important in diagnosis but till now is not used as routine laboratory investigation in these cases because it is very expensive and we hope using widely in the futures.

**Key words:** thrombotic microangiopathy, ADAMTS13, thrombotic thrombocytopenic purpura