

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

Thesis

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A decorative floral frame with a central yellow oval containing the text. The frame is adorned with green leaves and pink flowers.

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ
وَاتَّقُوا اللَّهَ وَيُعَلِّمُكُمُ اللَّهُ
وَاللَّهُ بِكُلِّ شَيْءٍ عَلِيمٌ

صَدَقَ اللَّهُ الْعَظِيمُ
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List of Abbreviations

<i>Abbr.</i>	<i>Full-term</i>
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
TMA_s	: Thrombotic microangiopathies
TTP	: Thrombotic thrombocytopenic purpura
TXA₂	: Thromboxane A ₂

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	: <i>Escherichia coli</i>
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	: Tumor necrosis factor
CKD	: Chronic kidney disease
SF	: Soluble fibrin
FRMs	: Fibrin related markers
AT	: Antithrombin
T.Bil	: Total Bilirubin
D.Bil	: 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 metalloproteinase 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 peripheral 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