# Steady-State Serum Levels of Vascular Cell Adhesion Molecule-1 in Children with Sickle Cell Disease: Relevance to Stroke Risk and Disease Severity

**Thesis**
**Submitted for partial fulfillment of the MD degree in Pediatrics**


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**2014**

بسم الله الرَّحْمَنِ الرَّحِيمِ

(قَالُواْ سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ

الْعَلِيمُ الْحَكِيمُ)

صَدَقَ اللّه الْعَظِيْم

سورة البقره اية(32)

**ACKNOWLEDGMENTS**

First of all, thanks to Allah for giving me the strength to complete this work.

This thesis would not have been possible without the help, support and patience of my supervisors. I would like to thank ***Prof. Dr. Mona Hassan El-Tagui,*** Professor of Pediatrics, Faculty of medicine, Cairo University, for her outstanding supervision and guidance. Every step I moved forward is indispensable without her encouragement and keen insights.

I would like to thank***Dr. Mona Kamal El-Ghamrawy,*** Assistant Professor of Pediatrics, Faculty of medicine, Cairo University, for her continuous support, generous advice and valuable guidance in this work.

I would like to express my sincere gratitude to ***Dr. Foad Abdelmonem Abdullah,*** Assistant Professor of Neurology, Faculty of medicine, Cairo University for his remarkable efforts, considerable help and guidance for whole of this work.

And I would like to express my gratitude and appreciation to ***Dr. Fadwa Saied Abdel Azzim,*** Lecturer of Clinical and Chemical Pathology, Faculty of medicine, Cairo Universityfor her remarkable efforts, considerable help and guidance for this work.

Last but not least, I would like to express my appreciation to my whole family specially my wife for her great patience, help & support.

Finally, I dedicate this work to my daughter and son, whom I feel great hope for better future for me, my family & my country every time I look at their eyes.

# Abstract:

Our study conducted on **85** patients with SCD aged 2-18years, **8.4%** of patients showed high risk study and **12.0%** were conditional. One high risk patient had the qualifying velocity in ACA only. Regression analysis showed transfusion & HU dose are protective against stroke. Mean VCAM level was **1438.12** ± **848.2 ng/ml** for cases enrolled & significantly higher than of normal population. Levels also was higher in patient with normal TCD (**P.038).** However, correlation of VCAM level with TAMMvel using showed +ve correlation with **(P.041).** Levels were higher in HbSβ subgroup**,** with positive correlation with bilirubin level and frequency of blood transfusion**.** In SS subgroup, VCAM level was significantly correlated with severity frequency (**P≤.001)** and duration (P ≤ **.001**) of VOCs. Level was lower with HU treatment (**P.041**).



**Keywords:**

Sickle cell anaemia – Stroke –VCAM-1 – Transcranial Doppler – TCD – SCD

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# ABBREVIATIONS

| | |
|---|---|
| **ACA** | ANTERIOR CEREBRAL ARTERY |
| **ACS** | ACUTE CHEST SYNDROME |
| **AIS** | ACUTE ISCHEMIC STROKE |
| **ALT** | ALANINE TRANSIFRASE |
| **APCs** | ANTIGEN PRESENTING CELLS |
| **AVN** | AVASCULAR NECROSIS |
| **BIF** | BIFURCATIONAL ARTERY |
| **BUN** | BLOOD UREA NITROGEN |
| **CBC** | COMPLETE BLOOD COUNT |
| **CT** | COMPUTED TOMOGRAPHY |
| **ELISA** | ENZYME LINKED IMMUNOSORBENT ASSAY |
| **ESRD** | END-STAGE RENAL DISEASES |
| **FV** | FLOW VELOCITY |
| **GFR** | GLUMERULAR FILTRATION RATE |
| **HB** | HEMOGLOBIN |
| **HU** | HYDROXYUREA |
| **ICA** | INTERNAL CAROTID ARTERY |
| **ICH** | INTRACRANIAL HEMORRHAGE |
| **IL** | INTERLEUKIN |
| **KFTs** | KIDNEY FUNCTION TESTS |
| **LDH** | LACTATE DEHYDROGENASE |
| **LFTs** | LIVER FUNCTION TESTS |
| **MCA** | MIDDLE CEREBRAL ARTERY |
| **MRI** | MAGNETIC RESONANCE IMAGING |
| **NO** | NITRIC OXIDE |
| **NSAIDs** | NON-STEROIDAL ANTI-INFLAMMATORY DRUGS |
| **PCA** | POSTERIOR CEREBRAL ARTERY |
| **PT** | PROTHROMBIN TIME |
| **PTT** | PARTIAL THROMBOPLASITN TIME |
| **RBCs** | RED BLOOD CORPUSCLES |
| **SCD** | SICKLE CELL DISEASE |
| **STOP** | STROKE PREVENTION TRIAL IN SICKLE CELL ANEMIA |
| **TAMMVEL** | TIME-AVERAGED MEAN OF THE MAXIMUM VELOCITY |
| **TCD** | Transcranial Doppler |
| **TIA** | TRANSIENT ISCHEMIC ATTACK |
| **TNF** | TUMOR NECROTIC FACTOR |
| **VCAM-1** | VASCULAR CELL ADHESION MOLECULE-1 |
| **VLA-4** | VERY LATE ANTIGEN-4 |
| **VOC** | VASO-OCLUSIVE CRISIS |

# Introduction

Sickle cell disease (SCD) is one of the commonest genetic disorders world-wide and is the most common inherited hematological disease affecting humans **(Steinberg, 2001).**

SCD has its cardinal features of chronic hemolytic anemia and recurrent painful episodes. These and all other elements of the disease are the result of mutant sickle cell hemoglobin (Hb S) within the red blood cells (**Yogen et al, 2005)**.

This mutant Hb S is produced as a result of a mutation in the β-globin gene that changes the sixth amino acid from glutamic acid to valine **(Benz, 2010).**

Substitution of valine for glutamic acid on the outer surface of the Hb S molecule reduces solubility and polymerization of Hb S when deoxygenated, which leads to sickling and poor deformability of polymer-containing erythrocytes that results in occlusion by this sickle red cells of the microvasculature. (**Yogen et al, 2005)**.

Approximately half the individuals with homozygous HbS disease experience vaso-occlusive crises (VOC). The frequency of crises is extremely variable. Some individuals have as many as 6 or more episodes annually, whereas others may have episodes only at great intervals or none at all **(Maakaron, 2011).**

These VOCs, which are considered the key feature of SCD, are the end result of a series of red cell, endothelial, monocyte and platelet interactions **(Corrina, 2006).**

The red cell adheres to the endothelium through a series of mechanisms, either directly via exposed red cell membrane phosphatidylserine or sulfated glycans, or by using soluble adhesion molecules (e.g., integrins, thrombospondin, high-

molecular-weight von Willebrand factor and/or vascular cell adhesive molecule–1 (VCAM-1)) as a bridge **(Corrina2006).**

VCAM-1 which plays a very important role in the pathophysiology of VOC and stroke is an immunoglobulin-like adhesion molecule expressed on activated endothelial cells and participates in neointima formation after vascular wall injury, because it facilitates monocyte infiltration into injured arteries or/and directly enhances smooth muscle cell proliferation **(Klaus &Yuqing2001).**

Moreover, a study conducted at 2011 concluded that levels of VCAM-1 were significantly higher in subjects with severe SCD **(Dworkis et al., 2011).**

As stroke -which has devastating consequences on children- affects approximately 11% of SCD patients younger than 20 years of age **(Dworkis et al., 2011)**, detection of high risk patients and those liable for strokes is very critical in management of those patients **(Adams, 2001).**

Careful screening with trans-cranial Doppler (TCD) ultrasonography and treatment with chronic blood transfusion will likely reduce the number of strokes in children with sickle cell anemia **(Bruce, 2007).**

TCD is a well-established predictor of future cerebrovascular symptoms, it can measure flow velocities in the large intracranial arteries. The narrowing of these arteries, which leads to cerebral infarction, is characterized by an increased velocity of flow therefore, estimating the flow velocity across intracranial arteries helps identifying children at risk of stroke due to increased cerebral velocities (**Colombatti et al., 2009).**

# AIM OF WORK

Our aim is to estimate serum levels of VCAM-1 and correlate it with findings of trans-cranial Doppler and clinical condition in children with sickle cell anemiaTo determine its value as a predictive marker for stroke in sickle cell disease and to identify any association, if present, between serum VCAM-1 levels and disease severity, transfusion therapy and treatment given is also our objective.