DECLARATION

I, Alick Mwambungu, do hereby declare that this dissertation presents my own work and that all the sources I have quoted have been indicated and acknowledged by means of complete references. I further declare that this dissertation has not previously been submitted for a degree, diploma or other qualifications at this or another University. It has been prepared in accordance with the guidelines of Master of Science Dissertations of the University of Zambia.

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CERTIFI CATE OF APPROVAL

This dissertation of Alick Mwambungu is approved as partial fulfillment of the requirement for the award of the degree of Master of Science in Pathology (Haematology) by the University of Zambia.

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DEDICATION

I wish to dedicate this work to my family for the encouragement I got from the beginning of my studies. To my wife Chiti and my children Naomi, Chikutwe and Sean, your understanding and patience helped me achieve what looked like an impossible journey especially when priorities changed, with school taking up most of the financial share at the expense of what the majority might consider necessities in life.

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ABSTRACT

Background: Patients with diabetes mellitus have a high risk of atherothrombotic events. Eighty percent of patients with diabetes mellitus die due to thrombosis, and 75% of these deaths are due to cardiovascular complications. A cross-sectional analytical study was conducted at Ndola Central Hospital between November 2012 and April 2013 with the main objective of determining the hypercoagulability state of type 2 diabetes mellitus (T2DM) patients.

Method: Prothrombin time (PT), Activated partial thromboplastin time (APTT),von Willebrands factor (vWF) and Fibrinogen concentrations were measured in 213 T2DM patients and 172 non-diabetic healthy participants. vWF and fibrinogen were used as proxy biomarkers for hypercoagulability in T2DM patients. A structured questionnaire was used to capture Age, sex, duration of diabetes mellitus and knowledge on T2DM of study participants. Body weight and body height were also measured and Body mass index (BMI) calculated.

Results: The mean fibrinogen concentration for T2DM patients (4.3±2.5g/l) was significantly higher than control participants (2.3±1.6g/l). Mean vWF concentration was also significantly higher in T2DM patients (7.4±4.1 IU/ml) than in control participants (2.6±2.2 IU/ml) P=0.004. The mean APTT in T2DM patients was significantly shorter than in control study participants P=0.000. Prevalence of hypercoagulability among T2DM patients was significantly higher [126(59.2%)] than in the control participants [22(12.7%)]. Female type 2 diabetic participants had higher proportion of hypercoagulability than male participants 88(73.3%) and 38(40.9%) respectively P=0.000. Age ,Sex, glycaemic control, Obesity and duration of T2DM were found to be independent risk factors for hypercoagulability in T2DM participants with the AOR of 4.42(95% CI 2.77-10.63), 1.45(95% CI 1.19-3.16), 6.12(95% CI 2.27-8.36),5.28 (95% CI 3.01-8.21),4.54(95% CI 2.88-10.59) and 5.28(95% CI 3.01-8.21) respectively. APTT was found to be a probable marker of hypercoagulability in T2DM patients due to its high sensitivity (93.7%), Specificity (95.4%) PPV (96.7%), NPV (91.2%) and had a strong statistically significant correlation with vWF; R= -0.783 P=0.001.

Conclusion: T2DM patients are more hypercoagulable than non-diabetic healthy individuals and female T2DM patients were more hypercoagulable than male patients. APTT may be introduced as a marker for hypercoagulability in T2DM after conducting a prospective study to follow-up T2DM patients and determine how many will develop thrombosis in future.

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LIST OF ABBREVIATIONS

AGEs- Advanced Glycation End Products

ANOVA- Analysis of Variance

APTT– Activated Partial Thromboplastin Time

BMI- Body Mass Index

CEBM -Center for evidence Based Medicine

Da- Dalton

DBP – Diastolic Blood Pressure

DM- Diabetes Mellitus

EDTA-Ethylenediaminetetraacetic acid

ENOS- Endothelial Nitric Oxide synthase

FBC- Full Blood Count

FBG – Fasting Blood Glucose

HbA1C-Glycated Haemoglobin

IFG-Impaired Fasting Glucose

MOH – Ministry of Health

NCH – Ndola Central Hospital

NO- Nitric Oxide

OPD- Out patient Department

PAI- Plasminogen activator inhibitor

PEDF- Pigment Epithelium Derived Factor

PT – Prothrombin Time

PPV- Positive Predictive Value

ROS- Reactive Oxygen Species

SBP – Systolic Blood Pressure

TAT- Thrombin-Antithrombin complex

TF-Tissue factor

tPA- Tissue plasminogen activator

T2DM- Type 2 Diabetes Mellitus

UNFPA- United Nations Population Fund

UNZA-BREC- University of Zambia Biomedical Research Ethics Committee

VTE-Venous thromboembolism

VWF – von Willebrands factor

WHO – World Health Organisation

ZDHS-Zambia Demographic health Survey

DEFINITIONS AND ACRONYMS

Advanced Glycation End Products – Proteins or lipids that become covalently bonded to a sugar molecule such as glucose without the controlling action of an enzyme.

Atherosclerosis – A condition in which an artery wall thickens as a result of the accumulation of fatty materials such as cholesterol.

Atherothrombosis- atherosclerotic lesion disruption with superimposed thrombus formation.

Body Mass Index- A proxy for human body fat based on an individual's weight and height. Calculated by dividing individual's body mass by the square of his or her height.

Fibrinolysis- Breakdown of fibrin, usually by the enzymatic action of plasmin.

Haemostasis- Arrest of bleeding by the physiological properties of vasoconstriction and coagulation or by surgical means.

Hypercoagulability- Abnormality of blood coagulation that increases the risk of thrombosis.

Plasminogen- An inactive precursor of a serine protease plasmin.

Prostacyclin- A member of the family of lipid molecules known as eicosanoids. Inhibits platelet activation and is also an effective vasodilator.

Reactive Oxygen Species-Molecules or ions formed by the incomplete electron reduction of oxygen.

Thrombosis- Formation of a blood clot inside a blood vessel, obstructing the flow of blood through the circulatory system.

Thromboxane- Any of several substances that are produced especially by platelets, formed from endoperoxides, cause constriction of vascular and bronchial smooth muscle and promote blood clotting.

Tissue factor- Cell surface receptor for factor VIIa, necessary for initiation of the extrinsic coagulation pathway.