ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #099

1. Title:
Fibrinolytic Mechanism and Atherosclerosis

2 . Writing Group:
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3. Timeline:
Measurements of fibrinolytic factors will begin as soon as the case and controls are identified.

4. Rationale:
Fibrinolytic mechanism is responsible for clearing of fibrin clot. Fibrinolysis is initiated by release of tissue-type plasminogen activator (tPA) from endothelial cells. tPA converts plasminogen into plasmin which degrades fibrin into fragments one of which is D-dimer. To keep tPA in check, type-1 inhibitor of tPA (PAI-1) is also released from endothelial cells. PAI-1 neutralizes tPA. Clinical studies have shown that the PAI-1 levels are increased in myocardial infarction and venous thrombosis. Comparison of the levels of PAI-1, tPA and D-dimer in cases and controls in the ARIC will lead to a better understanding of the role of fibrinolytic variables in atherosclerosis.

5. Main Hypothesis:
The proposed study is test the hypothesis that increased PAI-1 levels and/or reduced tPA are risk factors of early atherosclerosis. Furthermore, reduced fibrinolysis will be manifested by a reduced level of D-dimers.

6. Data Request:
PAI-1, tPA and D-dimer will be measured in plasma samples stored at -70 degrees C in the freezer of Central Hemostasis Laboratory by standardized ELISA assay. Case and control code numbers will be provided by CC. The laboratory technicians are unaware of the identity of the samples. Data will be transmitted to CC where they will be analyzed. Data needed include characteristics of cases and controls and their tPA, PAI-1 and D-dimer values.

Keywords: Fibrinogen, hemostasis, case-control