ESTIMATION OF HIGH DENSITY LIPOPROTEINS IN YOUNG PATIENTS WITH PREMATURE CORONARY ARTERY DISEASE.

Thesis

Submitted for Partial Fulfilment of

The Master Degree in

Cardiology

BY

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1992

ACKNOWLEDGEMENT

I would like to express my deepest gratitude to Professor Aly Ramzy for his kind supervision and valuable suggestion.

Appreciative thanks to Assistant Professor Amal Aycub for her meticulous guidence. Indeed she offered me the greatest help.

My deep thanks to Dr. Lyla Abou El Magd, and the staff of Cardiology and Clinical Pathology Departments, Ain Shams University, for their helpful remarks and providing me with every possible reference about this subject.

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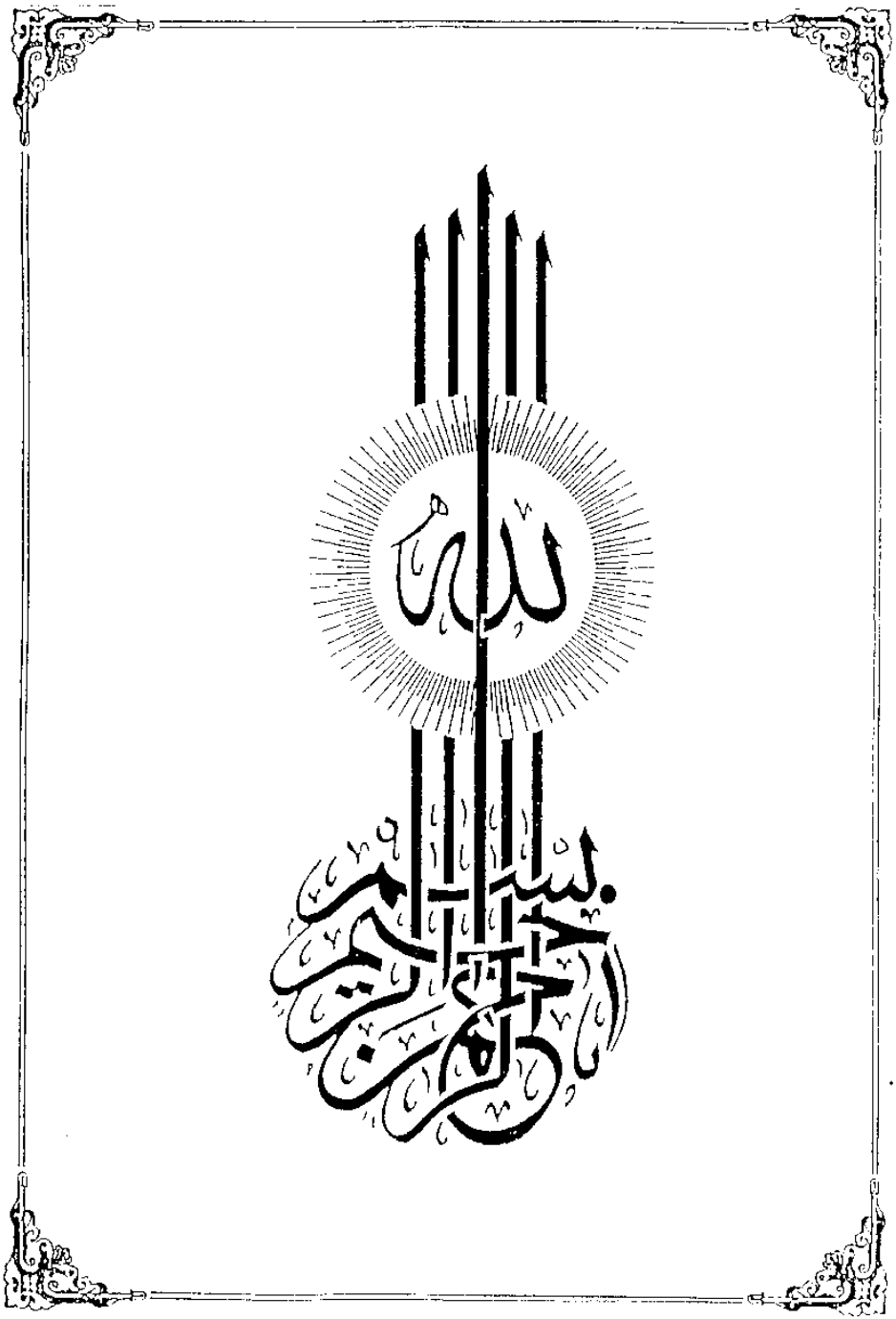

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I. INTRODUCTION AND AIM OF WORK

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Coronary Artery Disease

Coronary artery disease is perhaps the most important fatal disease in the western industrialized countries. In Egypt definite criteria of coronary artery disease were detected in 3.7 % of clerical employees, 1.6% of manual labourers and 1.3% of farmers. Angina was found in 10% of employees, 4.5 % of labourers and 1.3% of farmers. In addition mortality from ischemic heart disease in Egypt was three times more common in urban than in rural population (Dayme et al.,1978).

It has apparently increased in frequency since the early 1930s, especially in younger people. The data are hard to evaluated because death in a younger person is more important to be followed up by autopsy diagnosis , whereas the cause of death in an older person, epecially some one with known coronary disease, is not specifically confirmed at autopsy (Morgan , 1970).

Coronary artery disease in about 99 % of cases is due to atherosclerosis. In about 1% it is due to other vascular diseases such as syphilis and connective tissue disorders (e.g. systemic lupus erythromatosis) which are rare causes.

Coronary artery disease below the age of 40 years "Premature coronary artery disease" presented itself as a major problem, as it affects men in their peak.

The aetiology & pathogenesis of coronary atherosclerosis is still open for new theories, particularly the disease occuring in the young.

In recent years, great attention has been paid to the role played by high density lipoprotein cholesterol in protection against coronary atherosclerosis. Many reports discussed the beneficial effect of lipoprotein cholesterol fractions.

The aim of this work is to provide an understanding to the underlying risk factors which lead to coronary artery disease (C.A.D.) in young men below the age of forty with special reference to the lipid pattern, and evaluating the estimation of the high density lipoproteins fraction.

II. REVIEW OF LITERATURE

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Coronary Atherosclerosis

Etiology :

Many factors are considered contributary to development of coronary atherosclerotic heart disease. These include genetic and environmental factors as well as factors related to the blood and the blood vessel wall. These are considered as risk factors for development of the lesion (Di Girolamo, 1978).

Spcific Risk Factors

There is association of certain factors with coronary atherosclerosis. This has led to the formulation of a number of risk factors some major, some minor, some reversible and some irreversible. The presence of a risk factor in an individual patient gives no certainty of the presence or severity of coronary artery disease (C.A.D.), and those individuals without an identified high risk factor will be free of significant risk of developing C.A.D. (Epstein, 1971).

The mechanisms by which these risk factors operate to enhance the likelihood of atherosclerosis are not precisely known , nor is the pathogenesis of the disease

itself. Risk factors, however, correlate significantly with coronary angiographic findings (Vlietstra, et al., 1980).

Non Modifiable Risk Factors :-

1. Age.
2. Sex.
3. Familial history of premature coronary atherosclerotic heart disease.

Modifiable Risk Factors :-

Major :-

1. Increased serum lipid levels (Cholesterol, triglyceride).
2. Habitual diet high in total calories, fat , carbohydrate and salt.
3. Hypertension.
4. Cigarette smoking.
5. Carbohydrate intolerance.
6. Obesity.

Minor :-

1. Health benefits of physical activity.
2. Oral contraceptive use.
3. Personality type.

4. Psychosocial tensions.

5. Gout.

6. Prostaglandins. 7. Other factors.

(1) Age :

The development of atherosclerotic lesions are dependant on time, so age has a strong and consistent association with the lesion . In recent years the clinical manifestations of atherosclerosis have become more common and occur at an earlier age, but the pathologic process of atherosclerosis itself has not changed (Sokolow, 1981).

Reducing the possibility that non linear interactions of other variables with age and sex might obscure important result. An important finding was not only that increasing age and male sex were powerful risk factors for C.A.D., but also that their presence over whelmed or "washed out" the effect of other risk factors, that is, in the oldest group of males, other risk factors had only a weak effect. Conversely, in the absence of these two most important factors, that is, in females 45 years old or less, other risk factors such as cigarette smoking and serum cholesterol level had considerable importance (Vlietstra, et al., 1980).

(2) Sex :-

Men are prone to clinical manifestation of coronary atherosclerosis than women in childbearing age. After menopause however, there is rapid narrowing of sex difference in the incidance of C.A.D. The mechanisms by which the menopause influences coronary disease have not been established, but it may be due sex difference of blood lipids which is about 10 mg/dl in HDL cholesterol from Framingham data (from 55 mg/dl found often in women, to 45 mg/dl found often in men). This is associated with as much as a two fold increase in C.A.D. risk (Havel, 1979). It may also be due to difference in hematocrite, physical activity and protective effect of estrogen. The modest effect of estrogen is observed on HDL and LDL cholesterol (Di Girolamo, 1978). Estrogen lead to lowering LDL and VLDL cholesterol and triglyceride level, but elevation of HDL cholesterol (Bain,et al.,1981 & Heiss, et al.,1980).

C.A.D. though very rare in young women it can occur in association with one of the other major risk factors, as severe hypertension (diastolic pressure greater than 120 mmHg), 22% of those women (hypertensives) under 45 years of age had angina pectoris (Mackay,et al., 1980).

(3) Familial History of Premature Coronary Atherosclerotic Heart Disease :-

Familial occurrence of C.A.D. has been well documented in both family and twin. Familial nature of C.A.D. may be explained partly by the common environmental factors shared by the family members and partly by known genetic component of individual risk factors associated with C.A.D. Thus hyperlipidemia a potent precursor of C.A.D., has recently been shown in a large proportion of relatives of young patients with myocardial infarction (Rissanen, 1977).

In the younger age group, the family history of early onset of atherosclerotic heart disease was the strongest variable. This supports evidence that has demonstrated an increased risk of C.A.D. in relatives of people who have the onset of C.A.D. at an early age. Patients with positive family history were younger and had higher cholesterol levels and lower ratios of HDL cholesterol to total cholesterol (Holmes, et al., 1981).

The degree of familial aggregation of C.A.D. appeared to be similar in the non fatal myocardial infarction, fatal myocardial infarction and angina pectoris groups. However,

distinct differences between the groups were found as to the predominant clinical manifestation of the disease. While fatal C.A.D. predominated among the sibs in the fatal myocardial infarction group, non fatal C.A.D. was most common among the sibs of the angina pectoris probands, Asymptomatic form of C.A.D. appear, in fact, to be more common in the families of probands with angina-pectoris (Rissanen, 1979).

Rissanen in 1979, stated that there was somewhat an increased mortality from C.A.D. in mothers of the very youngest case probands. The three to four fold excess in the rate of C.A.D. among case sibs is reported, and this agrees with the reported two-to-tenfold increase in the rate of C.A.D. among brothers and two-to-fourfold increase among the sisters of affected men (Rose, 1964).

The relatively modest excess occurrence of C.A.D. in case relatives over that in reference relatives could be taken to suggest that familial factors play only a minor role in the causation of C.A.D. However, even this modest excess may indicate a substantial familial element in the disease. (Rissanen , 1979).

Familial aggregation of C.A.D. may be based on genetic factors but it is difficult to separate these from the influence of environment and traditions shared by family members. All major risk factors such as serum lipid levels, arterial blood pressure and blood sugar are likely to be under polygenic control. Monogenic familial hypercholesterolaemia is a rare disorder and , inspite of its high atherogenecity , it can account for a very minor fraction of genetic component of C.A.D. (Rissanen, 1977). In young persons with C.A.D. and strong family history, there is shortened platelet survival and these persons represented by subclinical disease. Little is known about how genetic factors contribute to the development and progression of C.A.D. in the young. One hypothesis is that the genetic factor may contribute to a hyperactive response by the arterial wall to the endothelial injury, that is, it might induce an exaggerated proliferation of smooth muscle cells or fibroblasts or excessive production of collagen. Alternative hypothesis is that the genetic factor may in some way lessen the resistance to the arterial endothelial damage or perhaps enhance the platelet arterial wall interaction.(Fuster,et al., 1981).