# CARDIOVASCULAR RISK FACTORS IN HEMODIALSIS PATIENTS

# THESIS

SUBMITTED FOR PARTIAL FULFILLMENT

OF THE MASTER DEGREE OF

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By

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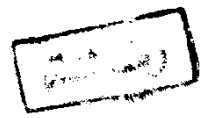

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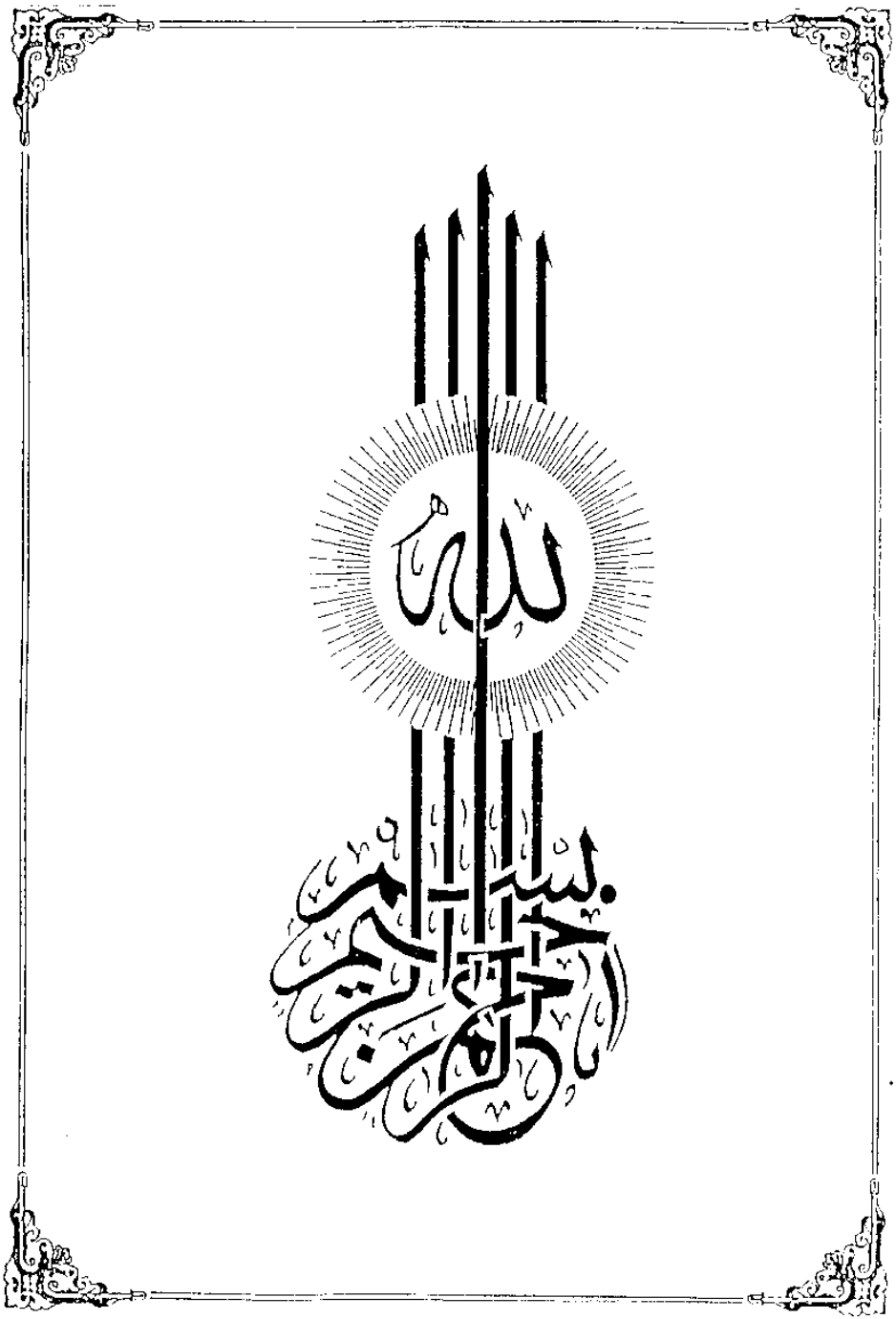

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# C O N T E N T S

# INTRODUCTION AND AIM OF WORK

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The introduction of long term hemodialysis provided a therapy which allowed patients with chronic renal failure to stay alive without requiring early and successful renal transplantation. However, analysis of survival of patients undergoing hemodialysis in the early 1970's revealed a high incidence of atherosclerotic complications in hemodialysis patients and that cardiovascular disease and, in particular, coronary artery disease, increased with the duration of dialysis (Lindner et al., 1974).

Considerable attention has been paid to the factors involved in this accelerated atherosclerosis, with a view both to reducing the morbidity and mortality of uremic patients and to throwing light on the cause of the atherosclerotic process itself.

Potential risk factors such as hyperlipidemia and hypertension have high prevalence in hemodialysis patients (Lowrie et al., 1974). These risk factors have been implicated in the development of atherosclerosis in chronic hemodialysis patients as they have been strongly associated with cardiovascular disease in the general population.

However, epidemiological evidence for the association between the prevalence of risk factors and this accelerated atherosclerosis is still lacking and even the concept of accelerated atherosclerosis in chronic hemodialysis patients has recently been criticized (Burke et al., 1978 and Rostand et al., 1979).

While atherosclerosis may not be accelerated by end-stage renal disease or hemodialysis per se, the fact remains that the death rate from cardiac causes in the overall hemodialysis population is high. The situation may be better understood by reviewing risk factors for cardiovascular disease that may occur in general population and analyzing the specific effects of hemodialysis on these risk factors. (Scharf et al., 1980).

In this study, major cardiovascular risk factors are evaluated in these patients with an attempt to determine their prevalence and possible contribution to cardiovascular disease.

# REVIEW OF THE LITERATURE

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## Introduction:

Coronary heart disease is a multifactorial process. In the nonuremic population the major established risk factors are serum total cholesterol ( and its low density lipoprotein and high density lipoprotein cholesterol content), blood pressure, carbohydrate tolerance, cigarette smoking and left ventricular hypertrophy detected on electrocardiography (Kannel et al., 1983).

Each of these risk factors and other additional factors are reviewed with the following guidlines:

1. Epidemiological association with coronary heart disease and the strength of this association in the general population.
2. The possible pathogenetic mechanisms by which it contributes to cardiovascular disease.
3. Its prevalence in chronic renal failure and the possible pathogenetic mechanisms.
4. Effect of chronic hemodialysis.

# 1- HYPERLIPIDEMIA

## Introduction:

Lipids are not soluble in water and they circulate in association with specific proteins in the form of plasma lipoproteins. Four classes of specific lipoproteins circulate in the plasma : (Goodman, 1976).

1. Chylomicrons are composed mainly of triglycerides and represent the transport form of dietary triglycerides.
2. Very low density lipoproteins are composed mainly of endogeneous triglycerides.
3. Low density lipoproteins carry cholesterol and normally represent the circulating form of most of the plasma cholesterol.
4. High density lipoproteins are composed of approximately half proteins and half lipids and they contribute to about one quarter of the plasma cholesterol.

## Hyperlipidemia and Hyperlipoproteinemia:

Since an elevated lipid level means that there is an elevated level of one or more lipoproteins, hyperlipidemia can be translated into hyperlipoproteinemia by classifying the paients according to the type of lipoprotein elevated (Fredrickson, et al.,1965).

The Fredrickson classification : (Fredrickson et al.,1965)

Type 1: Hyperchylomicronemia

Criteria : Chylomicrons present, pre-beta normal or slightly elevated.

The alpha and beta decreased:

This condition is rare and always familial possibly due to a genetic disorder of lipoprotein lipase. There has been no correlation to cardiovascular disease.

Type II: Hyperbetalipoproteinemia

Criteria: Increased total cholesterol due to an increased beta-lipoprotein cholesterol (LDL). Alpha cholesterol (HDL) is usually normal or low.

Type II a: Normal pre-beta (VLDL), normal triglycerides, plasma clear.

Type IIb: Increaased pre-beta and triglycerides,plasma clear to slightly turbid with no creamy layer.

This is one of the most common familial forms of hyperlipoproteinemias.

Secondary causes: Myxedema, myelomas, liver disease and nephrotic syndrome.

Type III : "Broad Beta" or "Beta-migrating VLDL"

Criteria: Cholesterol and triglyceride elevated and the plasma is turbid. This abnormal lipoprotein has broad beta electrophoretic motility but spearates with VLDL in the ultracentrifuge. The condition is rare and is commonly genetic.

Type IV: Carbohydrate induced endogenous hypertriglyceridemia.

Criteria: Increased pre-Beta, increased triglycerides, normal or slightly elevated total cholesterol, Alpha and Beta lipoprotein usually normal.

Secondary causes: Diabetes mellitus, pancreatitis, Obesity and contraceptive pills.

Type V: Mixed lipemia.

Criteria: Increased exogenous and endogenous triglycerides, chylomicron present, pre-Beta increased, Beta normal or slightly increased.

Secondary causes : Diabetes mellitus, myxedema, alcoholism, pancreatitis and nephrotic syndrome.

Hyperlipidemia and Atherosclerosis :

1. Very low density lipoprotein-triglyceride:

A direct correlation of these particles with risk was found in univariate analysis. However, no independant

impact was seen for VLDL or triglycerides when adjusted for the influence of other risk factors (Rhoads et al., 1976 and Castelli, 1984).

It has been suggested that the VLDL correlation with risk is derived from secondary association and that the triglyceride itself may not be atherogenic (Gordon et al., 1977). Moreover, Heyden et al. 1980 found no significant differences in triglyceride concentrations in examinees with coronary heart disease compared to the population without it.

2. Cholesterol :

Epidemiological studies of the evoluation of coronary heart disease in human population have for many years emphasized the importance of serum total cholesterol as a precursor of coronary heart disease. The association is strong, dose related and found in both sexes (Rhoads et al., 1976 and Pooling Project Research group, 1978).

It has been noted that at any level of cholesterol, the risk varies widely according to the dose of other risk factors and by its partition in the lipoprotein fractions (Gordon et al., 1977).

Low density lipoprotein (LDL):

Low density lipoprotein-cholesterol correlates best with total cholesterol. It could be used to predict the risk of coronary heart disease in person older than 50 and up into his eighties (Gordon et al., 1977). LDL-cholesterol is superior to the total cholesterol as a measure of atherogenic cholesterol (Kannel et al.,1979).

High density lipoprotein (HDL):

It has been shown that the plasma HDL appears to be reduced in several conditions with an increased risk of developing ischemic heart disease, and on the other hand high levels of HDL may protect against the development of atherosclerotic coronary artery disease ( Miller and Miller, 1975).

A highly significant inverse relationship was found between the prevalence of coronary heart disease and the level of HDL-cholesterol. In contrast, a highly significant correlation was found between the prevalence of coronary heart disease and the level of serum total cholesterol or LDL-cholesterol (Rhoads et al., 1976).