Relation of cardiovascular disease to acute phase reactants in chronic haemodialysis patients

Submitted for partial fulfillment of master degree in Internal Medicine

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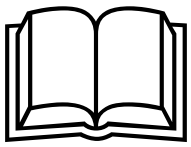
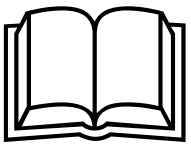

Introduction and

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A growing awareness of heart disease in individuals with kidney disease as a major public health concern has increased sharply because of the revelation that there are millions of Americans with reduced kidney function **(Berl et al., 2006).**

This fact coupled with the understanding that many individuals with CKD don't reach dialysis because they die of heart disease, has expand the concern about heart disease in both patients with CKD and patients with ESRD **(Keith et al., 2004).**

Heart disease is leading cause of death in approximately half of patients with ESRD **(USRDS, 2004).**

The two clinical presentations of heart disease in patients with kidney disease are atherosclerotic vascular disease (particularly CAD) and left ventricular hypertrophy **(Berl et al., 2006).**

Inflammation has recently been associated with atherosclerosis and malnutrition in ESRD, and this link has led to the development of malnutrition, inflammation, atherosclerosis (MIA) hypothesis. This describes a syndrome whereby raised levels of pro-inflammatory cytokines (such as IL-1, IL-6 and TNF-α) are a common link between malnutrition, inflammation, and atherosclerosis**(Stenvinkel , 2001).**

Also anaemia appears to be an important element linking elevated cytokines levels with poor patient outcomes. Several mechanisms for cytokine-induced anaemia have been proposed, including intestinal bleeding, impaired iron metabolism and suppression of bone marrow erythropoiesis and erythropoietin production **(Stenvinkel , 2001).**

A newly identified iron regulator, hepcidin, appears to communicate body iron status and demand for erythropoiesis to intestine, and in turn, modulates intestinal iron absorption. Hepcidin was first purified from human blood and urine as anti microbial peptide and was found to be predominantly expressed in the liver. A lack of hepcidin expression has been associated with iron overload and over-expression of hepcidin results in iron-deficiency anaemia in mice. These observations support the role of hepcidin as a signal that limits intestinal iron absorption. Hepcidin expression is also affected by hypoxia and inflammation and is decreased in hemochromatosis patients **(Nutr, 2004).**

In the recent report, Wrighting and Andrews showed that the inflammatory cytokine IL-6 directly regulated hepcidin through induction and subsequent promoter binding of signal transducer and activator of transcription 3(STAT3) **(Wrighting et al., 2006).**

Hepcidin is consistent with type II acute phase protein **(Nemeth et al., 2003).**

Aim of work

The aim of this work is to assess the possible relation between acute phase reactants including hepcidin as acute phase reactant type II and cardiovascular morbidity in chronic haemodialysis patients.

بسم الله الرحمن الرحيم

و من يتق الله يجعل له مخرجا

و يرزقه من حيث لا يحتسب

صدق الله العظيم

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LIST OF ABBREVIATIONS

AHA	American heart association
CKD	Chronic kidney disease.
CVD	Cardiovascular disease
CV	Cardiovascular
CHD	Chronic haemodialysis.
CRP	C reactive protein
CAD	Coronary artery disease
CRF	Chronic renal failure.
CSF	Cerebro spinal fluid.
CDC	Centers of disease control
C/EBP	Ccaa/enhancer binding protein
DPG	Di phosphoglycerate
ESRD	End stage renal disease
ECG	Electro cardio gram.
ECHO	Echo cardiography.
ESR	Erythrocyte sedimentation rate.
FBS	Fasting blood sugar
GFR	Glomerular filtration rate
Hgb	Haemoglobin.
HsCRP	Highly sensitive C reactive protein.
HD	Haemodialysis.
HDL	High density lipoprotein.
HAMP	Hepcidin anti microbial peptide gene
HFE	HFE gene is located on short arm of chromosome 6.
HIF	Hypoxia inducible factor.
IHD	Ischemic heart disease.
LVH	Left ventricular hypertrophy
LV	Left ventricle.
LDL	Low density lipoprotein.
LVMI	Left ventricular mass index.
MIA	Malnutrition, inflammation, atherosclerosis.
PTH	Para thyroid hormone
RT-PCR	Reverse transcription PCR.
STAT3	Signal transducer and activator of transcription 3
TSAT	Transferrine saturation.
TNF	Tissue necrosis factor
TIBC	Total iron binding capacity
TG	Triglyceride