THE PREVALENCE AND NUTRITIONAL CAUSES OF HYPOGLYCAEMIA IN PATIENTS WITH END- STAGE RENAL FAILURE (ESRF) ON MAINTENANCE HAEMODIALYSIS (MHD) AT KENYATTA NATIONAL HOSPITAL NAIROBI, KENYA

Anastacia Wanjiku Kariuki

Thesis presented in partial fulfillment of the requirements for the degree of
Master of Nutrition at the University of Stellenbosch

Study Leader(s): Prof. M.G. Herselman

Co Study Leader(s): Prof. D. Labadarios
Prof. S.O. Mc'Ligeyo
Dr. J.K. Kayima

Statistician: Prof. D.G. Nel

March 2008

DECLARATION

I, Anastacia Kariuki, declare that this thesis is my own original work and that all sources have been accurately reported and acknowledged, and that this document has not previously in its entirety or in part been submitted at any university in order to obtain an academic qualification.

Signature  Date: 26 February 2008

ABSTRACT

BACKGROUND: Although hypoglycaemia is a known complication of haemodialysis, there is little information about its prevalence among patients on maintenance haemodialysis.

OBJECTIVE: To determine the prevalence of hypoglycaemia in patients on maintenance haemodialysis in Kenyatta National Hospital (Nairobi, Kenya) and to identify potential nutrition-related causes of hypoglycaemia.

METHODS: A cross-sectional, descriptive and observational study design was followed. Patients who had been on chronic maintenance haemodialysis for 3 months or longer were included in the study which was carried out from May 8 through to June 30, 2006. Random blood glucose levels were determined at baseline, 15 minutes, 30 minutes and 45 minutes, and at hourly intervals thereafter until the end of the dialysis session. The prevalence of hypoglycaemia (a blood glucose level less than 3.9 mmol/L) was then determined for the duration of haemodialysis. The relationship between minimum blood glucose levels and dietary intake, anthropometric status, primary diagnosis, co-morbid and socio-demographic factors, prescribed medication and dialysis related factors was determined.

RESULTS: Among the 51 haemodialysis patients who participated in the study, the prevalence of hypoglycaemia was 16% (n=8). Eight percent (n=4) of these patients were however already hypoglycaemic on initiation of dialysis. Dietary intake of niacin ((r=0.31; p=0.02), riboflavin (r=0.30; p=0.03) and vitamin B_6 (r=0.30; p=0.03) showed a significant relationship with blood glucose levels. The relationships between hypoglycaemic episodes and insulin administration (p=0.06), and between blood glucose levels and BMI (r=0.25; p=0.08 and protein intake (r=0.26; p=0.07) approached significance. There was no significant relationship between blood glucose levels and the duration of haemodialysis (p=0.942), hours of haemodialysis (p=0.27) and the dialysate solution used (p=0.12).

CONCLUSIONS: Hypoglycaemia was present in 16% of patients on maintenance haemodialysis. Potential nutritional parameters which may have contributed to lower blood glucose levels in this study include a lower dietary intake of niacin, riboflavin, and vitamin B_6. Lower protein intake and lower BMI was marginally associated with low blood glucose levels.

OPSOMMING

MOTIVERING: Alhoewel hipoglisemie ‘n bekende komplikasie van hemodialise is, is min inligting beskikbaar oor die prevalensie van hipoglisemie in pasiënte op langtermyn hemodialise.

DOELWIT: Om die prevalensie van hipoglisemie onder pasiënte op langtermyn hemodialise by die Kenyatta Nasionale Hospitaal (Nairobi, Kenya) te bepaal, asook om potensiële voedingverwante oorsake van hipoglisemie te identifiseer.

METODE: ’n Dwarssnit, beskrywende en observasie studie ontwerp is gevolg. Pasiënte wat vir 3 maande of langer op chroniese instandhoudings hemodialise behandeling was is by die studie ingesluit wat vanaf 8 Mei to 30 Junie 2006 uitgevoer is. Lukraak bloedglukose vlakke is bepaal by basislyn, 15 minute en 45 minute, en met uurlikse intervalle daarna tot aan die einde van die dialise sessie. Die prevalensie van hipoglisemie (’n bloedglukose vlak kleiner as 3.9 mmol/L) is bepaal vir die duurte van die dialise sessie. Die verband tussen minimum bloedglukose vlakke en dieetinname, antropometriese status, primêre diagnose, ander onderliggende siektes, sosiodemografiese faktore, voorgeskrewe medikasie en dialise verwante faktore is bepaal.

RESULTATE: Die prevalensie van hipoglisemie onder die 51 hemodialise pasiënte wat aan die studie deelgeneem het, was 16% (n=8). Agt persent (n=4) van hierdie pasiënte was egter alreeds hipoglisemies met die aanvang van dialise. Dieetinname van niasien (r=0.31; p=0.02), riboflavien (r=0.30; p=0.03) en vitamine B_6 (r=0.30; p=0.03) het ’n betekenisvolle verband met bloedglukose vlakke getoon. Die verband tussen hipoglisemiese episodes en insulien toediening (p=0.06) en tussen bloedglukose vlakke en LMI (r=0.25; p=0.08) en proteïen inname (r=0.26; p=0.07) was byna betekenisvol. Daar was geen betekenisvolle verband tussen bloedglukose vlakke en die duurte van hemodialise (p=0.942), ure op hemodialise (p=0.27) en tipe dialisaat (p=0.12) nie.

GEVOLGTREKKING: Hipoglisemie was teenwoordig in 16% van pasiënte op langtermyn hemodialise. Potensiële voeding faktore wat moontlik tot die laer bloedglukosevlakke in hierdie studie bygedra het was lae inname van niasien, riboflavien en vitamine B_6. Laer proteïen inname en LMI het ’n byna betekenisvolle verband met laer bloedglukose vlakke getoon.

DEDICATION

To my loving husband Phil for the moral support that kept me going from the start of this academic programme. To my lovely daughter, baby Lauryn who has been my long-life treasure to be adored by nature, and to all those who prayed for me and wished me the best in life. Thanks a lot for all your support.

ACKNOWLEDGEMENT

First and foremost I wish to pass my sincere gratitude to Professor M.G Herselman who took her precious moments to discuss any issue that rose-up in relevance to this study and who kept encouraging me throughout this study programme.

I wish to thank and acknowledge the great assistance and guidance offered to me by my supervisors Professors Demetre Labadarios and Mc' Ligeyo. As for Dr. Kayima, "You offered me a shoulder and I lent on it". God bless you all for all your kind support.

I also acknowledge the efforts of Professor D.G Nel who assisted me in the data analysis section and Mr. Bosco who was always there in making sure that all the laboratory quality measures were applied during the drawing and analysis of blood samples. Without their effort, this work would not have been a success. And most of all to you, "mum" Florence Mwathi, you lifted me up when the going got too tough; no words can gratify your efforts.

I wish to acknowledge all the renal-unit patients for giving me their consent to carry out the research and the renal management team for the key role you played during the data collection period.

To the Kenyatta National Hospital and University of Stellenbosch Research and Ethics committees, it was an honour to have this research approved by you. Thank you for the great time you took in reviewing this research.

To Roche Products Limited, thank you for the electronic weighing-scale and the height-chart without which nutritional assessment would have not been possible.

And to all who played any part in making this process a success, receive my sincere gratitude and acknowledgement.

LIST OF TABLES

LIST OF FIGURES

LIST OF ADDENDA

LIST OF ABBREVIATIONS

ACE	Angiotensin converting enzyme inhibitor
AFA	Arm fat area
AMA	Arm muscle area
ARF	Acute renal failure
BG	Blood glucose
CCB	Cardiac channel blockers
CED	Chronic energy deficiency
CHO	Carbohydrates
CI	Confidence Interval
CKD	Chronic kidney disease
CRF	Chronic renal failure
CrCl	Creatinine Clearance
D	Day
DPI	Daily protein intake
ESRF	End stage renal failure
GFR	Glomerular filtration rate
H2 Antagonist	Histamine 2 receptor antagonist
HD	Haemodialysis
KNH	Kenyatta National Hospital
KDOQI	Kidney Diseases Outcomes Quality Initiative
MHD	Maintenance haemodialysis

MDRD	Modification of diet in renal disease
MUFA	Mono-unsaturated fatty acids
NKF	National kidney foundation
PEM	Protein energy malnutrition
PPI	Proton pump inhibitor
PUFA	Poly-unsaturated fatty acids
QFFQ	Quantitative food frequency questionnaire
SD	Standard deviation
SFA	Saturated fatty acids
StatSoft	Statistica Statistical Software
USA	United States of America

DEFINITION OF TERMS

Access Route [1]

A surgically formed connection of an artery and vein or an implanted artificial conduit in the arm or leg to allow easy access to the bloodstream for processing blood through an artificial kidney and returning to the body (also called cannulae, fistula, shunt).

Arteriogram[2]

An x-ray test involving injection of dye into an artery. A renal arteriogram injects dye into the artery to the kidneys to see if the blood vessels are normal.

Artificial Kidney [3]

Also referred to as "dialyzer." A filtering device that removes excessive fluid and waste products from the bloodstream and corrects chemical imbalance of the blood.

Batch System [4]

A method of supplying dialysate that involves the preparation of a large amount of dialysate by mixing concentrated chemicals with large amounts of purified water.

Bath[5]

Dialysate fluid or bath is composed of fluids and chemicals similar to body fluids without the waste products. Waste products will flow from the blood into the dialysate and then be flushed away.

Blood Flow Rate [6]

The amount of blood passing through the artificial kidney each minute. This is determined by the speed at which the blood pump is set.

Blood pump[7]

A pump that is used to push the blood from the patient through the artificial kidney and back to the body.

Bubble-Trap[8]

The larger part of the arterial and venous bloodlines which eliminates air from the lines and prevents clots from entering the vein by "trapping" them in a filter.

Erythropoietin[9]

It is a hormone made in the kidney which stimulates special bone marrow cells to produce red blood cells.

Fistula[10]

A connection surgically made between an artery and a vein beneath the skin that ultimately allows a person to be connected to an artificial kidney machine.

High Flux Dialysis [11]

High blood pump speed and high efficiency haemodialysis treatment.

Hypoglycaemia [12]

Hypoglycaemia or low blood glucose is a condition in which the level of glucose in the blood drops below a certain point (< 2.5mmol/l). The condition manifests itself by a number of symptoms that usually disappear 10 to 15 minutes after eating sugar. For the purposes of this study hypoglycaemia was defined according to the criteria used in the renal- unit of the hospital (<1.79 clinical hypoglycaemia; 1.8–3.8 below normal; 3.9–11.1 normal random blood glucose; and >11.1 possibly diabetic).

Membrane[13]

In haemodialysis, the membrane refers to the cellophane-like substance in the artificial kidney through which wastes from the blood filter into the dialysate fluid

Negative-pressure[14]

Pulling pressure exerted in the dialysate compartment that causes excess water to be pulled from the blood compartment of the dialyzer across to the dialysate compartment.

Peritoneal Dialysis [15]

A process in which dialysate is introduced into the peritoneal cavity. The peritoneal membrane in the abdomen functions in the same way as the membrane in the artificial kidney.

PositivePressure[16]

In haemodialysis, referred to as "back pressure" or "venous drip chamber." Pressure exerted on the artificial kidney to cause removal of water from the blood. Increasing the positive pressure increases fluid removal.

Posterior Urethral Valves[17]

Found in male children; it is an obstruction in the urethra which slows the free flow of urine.

Prime [18]

The normal saline used to fill the lines and dialyzer and lines prior to dialysis.

Semi permeable membrane [19]

A material through which only certain particles may pass, and through which other particles will not pass. Dialyzers are semi-permeable membranes.

Shunt (external) [20]

Two small plastic tubes (cannulae) surgically implanted, one in an artery and one in a vein. When not on dialysis, the two are joined by a connector (bridge) forming a "shunt."

Ultrafiltration [21]

The process of removing water from the blood during dialysis by exerting positive or negative pressure on the blood in the artificial kidney.

TABLE OF CONTENTS

CHAPTER ONE: LITERATURE REVIEW

1.1 Introduction

The kidney performs many functions including salt and water balance, excretion of nitrogenous wastes, acid-base regulation, electrolyte homeostasis, bone metabolism, erythropoietin synthesis, and blood pressure control. The glomerular filtration rate (GFR) is generally considered the best measure of kidney function.[22-23]

Approximately 2 million tiny structures called nephrons found in the kidneys are used to eliminate waste products and regulate electrolytes in the body. Renal failure results when these nephrons begin to die off and consequently waste products and electrolytes can no longer be processed effectively.[24] As a result, there is an accumulation of waste products and the patient becomes intoxicated by the waste that the kidneys cannot filter. Electrolyte and fluid imbalances, anaemia, high blood pressure and acid-base abnormalities occur as the kidneys continue to deteriorate.[22-24]

Renal disease is prevalent worldwide in children, adolescents and adults. In America more than 50,000 people die each year because of kidney disease; more than 260,000 suffer from end stage renal disease and require dialysis or kidney transplantation; and more than 48,000 are waiting for kidney transplants.[25,26] In tropical Africa, the incidence of end stage renal failure (ESRF) stands at about 90 000-150 000 thousand people per annum. In Kenya, one of the leading nephrologists estimates the range to fall between 250-300 patients per year and only one tenth (25-30) of these patients are able to get dialysis. [27]

1.2 Chronic Kidney Disease (CKD)

1.2.1 Classification of CKD

Chronic kidney disease is defined by the National Kidney Foundation as kidney damage for three or more months, with or without a decrease in GFR accompanied by abnormalities of markers of kidney damage, or a GFR below 60 mL per minute per 1.73 m^2 for three months or more, with or without kidney damage.[28] It is usually accompanied by signs and symptoms of ureamia, or as the need for initiation of kidney replacement therapy for management of the complications of a decreased GFR.

CKD is quantified as a serum creatinine greater than 136µmol/l in women or 182 µmol/l in men or a decrease in GFR (Table 1.1).[29,30,31] In the early stages the patient usually has no symptoms but azotaemia is present . Levels of hormones such as erythropoietin, calcitriol, and parathyroid hormone (PTH) may also be abnormal. Symptoms, if present are mild and patients may have anaemia, hypocalcaemia, and hyperphosphataemia. This stage, if not intervened early, progresses to clinical uraemia and the onset of end-stage renal failure (ESRF) which requires the need for renal replacement therapy. The latter is initiated in the form of dialysis or a kidney transplant. Early identification of patients who will require renal replacement therapy is important since adequate preparation may decrease morbidity and also permit the evaluation of patient and family members for a living related renal allograft.[32]

Table 1.1: Classification of chronic kidney disease (CKD) by the National Kidney Foundation, USA[32]

Stage	Description	GFR* (ml/min)	Action Recommended
I	Kidney damage with normal or increased GFR	>90	Diagnosis and treatment to slow progression, cardiac risk reduction
II	Mild decrease in GFR	60-89	Monitor to estimate progression
III	Moderate decrease in GFR	30-59	Evaluate and treat complications
IV	Severe decrease in GFR	15-29	Prepare for renal replacement therapy
V	Kidney failure	< 15 or dialysis	Renal replacement therapy

*CKD-Chronic kidney disease

*GFR- Glomerular filtration rate

1.2.2 Causes of CKD

There are many causes of CKD (Table 1.2), including some very rare disorders. However, diabetes mellitus and/or hypertension are responsible for more than half of the cases of CKD and this can be attributed to high consumption of refined processed foods, sedentary lifestyles as well as high stress levels.[32] There are no such data available in Kenya but there is also no reason to believe that the pathophysiology is different in Kenyans and in Africa in general.

Table 1.2: Diseases associated with chronic kidney disease in America (CKD) [32]

Cause	% of Total CKD Cases
Diabetes mellitus	50-70
Hypertension	
Glomerulonephritis, cystic diseases, and other urologic diseases	20-25
Unknown cause	15

NKF-DOQI Guidelines 2006[32]

Diabetes Mellitus

Types 1 and 2 diabetes mellitus cause diffuse glomerulosclerosis, a silent disease that starts with early basement membrane thickening. With hyperglycaemia, glucose end products accumulate in the basement membrane of the glomerulus. Eventually, the glomerulus loses its semi-permeable selectivity and becomes leaky, which results in microalbuminuria. This progresses to proteinuria and, in about 10% of cases to nephrotic syndrome and diabetic nephropathy. [33] Type 2 diabetes has reached epidemic proportions in the United States and especially in developing countries. Those groups at greatest risk are African Americans, Mexican Americans, and Native Americans. [34-35]

In Kenya and Africa in general, current trends show that type 1 and 2 diabetes are on the rise and this is especially attributable to lifestyle changes. That is, consumption of high glucose and high fat diets with low physical activity. At Kenyatta National Hospital (KNH) for instance in 2003, 132 in-patient admissions and 32 fatalities were as a result of type 2 diabetes. There are however, no statistics available to substantiate this information.[36]

Hypertension

Increased pressure in the glomerulus leads to glomerulosclerosis. The signs and symptoms vary with the severity of hypertension. Proteinuria, nocturia, and casts are the usual signs, and there can be progression to azotaemia. Blacks, especially men, have a greater risk for CKD caused by

hypertension than do whites probably due to genetic composition and exposure to more refined processed and refined foods as compared to their white counterparts.[37]

Glomerulonephritis

Glomerular disease affects the glomeruli, causing alterations in glomerular membrane permeability, function, and structure. Primarily, it has an immune pathogenesis. But there are other non-immune causes of glomerular damage, such as diabetes and amyloidosis. Glomerular disease can be restricted to the kidney, such as membranous glomerulonephritis, or it can occur secondary to a multi-system disorder, such as systemic lupus erythematosus. Inflammation may resolve without scarring or progression to sclerosis, or it can progress at various rates from rapid to slowly progressive. Proteinuria, haematuria, dysmorphic red blood cells, and red cell casts are seen in urinalysis.[37]

Interstitial nephritis

Drugs and heavy metals such as lead are the primary causes of interstitial nephritis. Damage to the tubule leads to urine concentrating problems and pH and electrolyte imbalances. There is little or no proteinuria or red blood cells in the urine. [31-33]

Chronic pyelonephritis

Infection of the urinary tract with E. coli can cause a low grade inflammatory response which can lead to interstitial inflammation and tubular cell necrosis. The inflammation increases the pressure in the kidney capsule. When capsular pressure becomes greater than hydrostatic pressure, the GFR is reduced. The increased pressure also damages viable tissue.[33], [34, 37]

Cystic/hereditary/congenital kidney disease

Some of these causes of CKD include Alport syndrome (in men, accompanied by deafness), autosomal dominant polycystic kidney disease, medullary cystic kidney disease, and malformations of the urinary tract.[29, 34]

Obstructive disorders

These disorders include stones, cancer, and prostate enlargement, which cause mechanical blockage of urine flow. The increased capsular pressure opposes the hydrostatic pressure, which decreases the GFR. Eventually, the increased pressure causes damage to viable tissue. Hydronephrosis is the end result of obstruction[29, 38,39]

1.2.3 Risk factors of CKD

The risk factors for CKD are compounded by many of the risk factors for heart disease (Table 1.3).

Table 1.3: Risk and compounding factors in chronic kidney disease (CKD) [40]

CKD Risk Factors	Compounding risk factors for CKD	
	Cardiac Risk Factors	General Risk Factors
Diabetes Mellitus	Obesity	Age – CKD increases as age increases
Hypertension	Hyperlipidaemia	Race – non-white more prone to CKD
NSAID use	Cigarette smoking	High protein diet promotes CKD

Another classification of the risk factors for CKD by Levey et al. 2005[41] distinguishes between:

- Susceptibility factors (older age, family history, low birth weight, decrease in renal mass, ethnicity, and low income / education)
- Initiating factors (diabetes, hypertension, autoimmune disease, systemic and urinary tract infections, kidney stones, obstruction, drug toxicity and hereditary disease)
- Progression factors (higher levels of proteinuria and blood pressure, poor glycaemic control in diabetes, dyslipidaemia and smoking)
- End-stage factors (low Kt/V in dialysis patients, temporary vascular access, anaemia, hypoalbuminaemia, hyperphosphataemia and late referral)

1.2.4 Management of CKD[39]

1.2.4.1 Slowing the progression of CKD

Because of the complexity of the consequences of CKD, management should be multifaceted and tailored to the individual patient according to the National Kidney Foundation of the United States of America (Table 1.1).[22] The patient should be referred to a nephrologist when the serum creatinine is greater than 136µmol/l for women or > 182 µmol/l for men, or if the creatinine clearance is less than 70 ml/min.[40]

Renal function should be protected to avoid prerenal azotaemia by preventing dehydration, treating urinary tract infections promptly and by relieving urinary obstruction.[39,40] A focus on the role of diet shows that very low and low-protein diets of 0.3-0.6 g/kg supplemented with specific renal enteral supplements are indicated in the incipient phases of diabetic nephropathy and in most patients with chronic renal failure, to slow progression of disease and improve the patient's overall condition, contributing to improved survival in these patients which is in line with the NKF/KDOQI 2001 guidelines.[41-45] Low protein diets may retard the progression of renal failure and delay the need for dialysis therapy and at least 50% of the protein should be of high biological value. Primary results from the Modification of Diet in Renal Disease (MDRD) Study were, however, not conclusive regarding a beneficial effect of protein restriction on the deterioration of renal function.[41] Secondary analyses of the MDRD Study, although not definite, was more consistent with the hypothesis that protein restriction is beneficial. Clearly, further research is needed to clarify this issue. Studies by Walser *et al.* [42, 43] also document the safety of dietary protein restriction of several years' duration. The MDRD Study also revealed that adherence to a low protein diet, although challenging, can be enhanced with regular follow-up with a skilled dietitian. Physicians must, however, be mindful of the detrimental effect of malnutrition at the onset of ESRD on subsequent survival. [44] Frequent monitoring of protein and energy intake and nutritional status is necessary to assure the safety of patients following a low protein diet.

In patients with renal failure on dialysis, the studies reviewed do not support the prescription of a very low-protein diet with the aim of reducing the frequency of dialysis sessions since most patients already suffer from PEM at the initiation of haemodialysis.[45]

1.2.4.2 Treatment of complications of CKD

Control of blood pressure [46]

The optimal blood pressure for dialysis patients has not been firmly established. Although the Joint National Committee recommendation for blood pressure control in patients with CKD is to control and maintain blood pressure at levels <130/80 mm Hg with antihypertensives, lifestyle changes including a reduction in the intake of salt and fat, as well as increasing physical activity. Blood pressure control in patients on HD is complicated by the volume and electrolyte shifts surrounding the dialysis procedure that acutely changes blood pressure. Diabetic patients on dialysis may be more prone to postural hypotension and labile blood pressure than non-diabetic dialysis patients. A higher supine blood pressure may be necessary in order to prevent symptomatic postural hypotension in these patients. Individual judgment and patient evaluation is required to match goals with symptoms.[47]

Control of hyperglycaemia

Tight glucose control in diabetic patients by medicinal and dietary changes (i.e. avoiding refined sugars, increasing the intake of dietary fibre and maintaining a haemoglobin A1c < 7.0 mmol/l) as well as increasing the activity level is associated with a delay in the development of microalbuminuria, which may eventually lead to chronic renal failure. Controlling hyperglycaemia gives the primary care provider the opportunity to be aggressive in the treatment of the early stages of diabetes.[48]

Hyperglycaemia is also common in ureamic patients due to insulin insensitivity leading to hyperinsulinaemia. Endocrine and metabolic disorders are frequently observed during chronic renal failure. There is a state of resistance to many anabolic hormones and insulin-like growth factor-1(IGF-1). [49]

Avoid Nephrotoxins

It is important to avoid nephrotoxins and all non-steroid anti-inflammatory drugs (NSAIDs) to retard the progression of renal failure, including COX-2 inhibitors.[47] A short course of NSAIDs therapy may be permitted with renal monitoring. Monitoring the patient's over-the-counter drug use is of utmost importance. When the CrCl is less than 50 ml/min, dosages of medications that

are metabolized or excreted by the kidney should be adjusted. Some medications that should be adjusted are beta-blockers, allopurinol, H^2-receptor antagonists, penicillin, cephalosporins, digoxin, morphine, and codeine. Examples of medications that should be avoided, especially when the CrCl is less than 30 ml/min are contrast dyes, aminoglycosides, cimetidine, colchicine, probenecid, metformin, acarbose, and glyburide.[45,46,47]

Manage cardiac disease risk factors

Standard cardiac risk factor management includes stopping smoking, reducing alcohol intake, and initiating an exercise program. It is important to treat dyslipidaemia, and the goal low-density lipoprotein (LDL) should be below 2.5mmol/l.[48] Many factors related to the uraemic state may be associated with cardiac disease. Several of these factors like uraemia, hyperparathyroidism, and dose of dialysis are potentially amenable to correction.[49, 50]

Hyperhomocysteinaemia appears to be a risk factor for cardiovascular mortality/morbidity in uremia though the mechanism is yet to be investigated. Homocysteine levels are related to renal dysfunction, smoking, elevated blood pressure, and other cardiovascular risk factors and are higher in people with atherosclerosis than in those without. Daily administration of the combination of 2.5 mg folic acid, 50 mg vitamin B_6 and 1 mg vitamin B_{12} lowered homocysteine levels significantly but did not reduce the incidence of death from cardiovascular causes or myocardial infarction during a mean follow-up of 5 years in patients with vascular disease. It had no beneficial effects on major vascular events in a high-risk population with vascular disease and the results of this study did not support the use of folic acid and B vitamin supplements in the prevention of cardiovascular mortality.[51]

Treat anaemia with epoetin alfa

Kidney failure causes a normochromic normocytic anaemia due to decreased synthesis of erythropoietin. Epoetin alfa improves anaemia, which is the second leading cause of left ventricular hypertrophy. It will reduce left ventricular hypertrophy and also lead to increased energy and sense of well being [52]. Resistance to epoetin alfa treatment is seen if there is inflammation, infection or iron deficiency. This will resolve once the underlying condition is treated. Epoetin alfa treatment may also cause iron deficiency because iron is needed to produce

red blood cells (RBCs). Iron replacement, either by mouth or intravenously, will be an adjunct therapy while on epoetin alfa.[53]

Treat renal osteodystrophy[54]

Renal osteodystrophy is characterized by high levels of serum phosphorus with low or normal calcium levels, and hyperparathyroidism. [55-58] The K/DOQI guidelines[59] have focused on the control of both dietary phosphorus and calcium compared to the previous emphasis on phosphorus only. The recommended calcium-phosphorus product of 5.5 $mmol^2/l^2$ or less is based on research that showed an elevated product greater than 7.2 $mmol^2/l^2$ was associated with increased mortality by 34% in CKD. Dietary phosphorus restriction (foods such as dairy and legumes) is necessary in CKD as high circulating levels of serum phosphorus promotes calcium release from the bone.[59] Non dietary therapy includes the aggressive use of oral phosphate binders (preferably non-aluminum, non-magnesium containing) dosed with the phosphorus content of each meal to promote stool excretion and lower gut absorption. Some phosphate binders contain high levels of calcium, which may contribute to soft tissue calcification and an increased risk of cardiovascular calcification. Intravenous vitamin D can be administered during haemodialysis treatment or by oral therapy in peritoneal dialysis for the management of hypocalcaemia and prevention of renal osteodystophy.[56, 57, 58]

Guidelines for the use of phosphate binders in CKD [54-60]

Stages 3 and 4 CKD:

Advanced kidney disease leads to hypocalcaemia, hyperphosphotaemia and increased calcium phosphorous product and the consequences include increased likelihood of extra skeletal calcification and demineralization of bone .During this stage if phosphorus or intact PTH levels cannot be controlled within the target range, despite dietary phosphorus restriction, phosphate binders should be prescribed. Calcium-based phosphate binders are effective in lowering serum phosphorus levels and may be used as the initial binder therapy.

Stage 5 CKD:

The optimal use of vitamin D therapies cannot be considered in isolation but rather as part of a broader management of the divalent ion derangements of ureamia. Of crucial importance is the

control of hyperphosphataemia which remains difficult and unsatisfactory for large numbers of patients. Currently available dietary phosphate binders suffer from relative lack of efficacy and weak action and most have potential for real toxicity which has led to the advent of new and better drugs comprising alfacalcidol or calcitriol, both of which effectively attenuate secondary hyperparathyroidism and the target organ consequences thereof.[59] Three of these agents, namely 22-oxacalcitriol (Maxacalcitol), paricalcitol (Zemplar) and doxercalciferol (Hectorol), are now in clinical use for the treatment of secondary hyperparathyroidism. The main experience with 22-oxacalcitriol is in Japan and that with paricalcitol and doxercalciferol in the United States. 22-Oxacalcitriol differs from calcitriol only in the substitution of the carbon 22 with an oxygen atom, while both paricalcitol and doxercalciferol are vitamin D_2 (ergocalciferol) analogues. Doxercalciferol (1a-hydroxyvitamin D_2) is the vitamin D_2 equivalent of alfacalcidol and like alfacalcidol is a prodrug requiring hepatic 25-hydroxylation for full activation. Unlike alfacalcidol, however, doxercalciferol administration leads to generation of 1,24S-dihydroxyvitamin D_2 in addition to 1, 25-dihydroxyvitamin D_2. Both of these are potent vitamin D metabolites.[56-59]

In dialysis patients who remain hyperphosphataemic (serum phosphorus >1.78 mmol/l) despite the use of either of calcium-based phosphate binders or other non calcium, non aluminum, non magnesium-containing phosphate-binding agents, a combination of both non-calcium and calcium-based phosphate binders should be used. The total dose of elemental calcium provided by the calcium-based phosphate binders should not exceed 1,500 mg/day, and the total intake of elemental calcium (including dietary calcium) should not exceed 2,000 mg/day. Calcium-based phosphate binders should not be used in dialysis patients who are hypercalcaemic (corrected serum calcium of >2.54 mmol/l]), or whose plasma PTH levels are <16.5 pmol/l on 2 consecutive measurements.[54-60]

Non calcium-containing phosphate binders are preferred in dialysis patients with severe vascular and/or other soft-tissue calcifications. In patients with serum phosphorus levels >2.26 mmol/l, aluminum-based phosphate binders may be used as a short-term therapy (4 weeks), and for one course only, to be replaced thereafter by other phosphate binders to prevent aluminum retention and toxicity. In such patients, more frequent dialysis should also be considered.[54-60]

1.2.4.3 Dietary management

A complete discussion of the dietary management of CKD is beyond the scope of this thesis. However, the following are general guidelines for the nutritional management of patients on maintenance haemodialysis.[60-64]

Dietary Protein Intake (DPI)

Several prospective nutritional-metabolic studies have compared the effects of different levels of DPI on the nutritional status of patients on MHD. Most of these latter studies have been carried out in in-hospital clinical research centers, and hence, the numbers of patients studied have been small. Taken together, these studies suggest that a DPI of about 1.2 g/kg/d is necessary to ensure neutral or positive nitrogen balance in most clinically stable MHD patients. At least 50% of the protein ingested should be of high biological value.[45, 56] Protein of high biological value has an amino acid composition that is similar to human protein, is likely to be an animal protein, and tends to be utilized more efficiently by humans to conserve body proteins. The increased efficiency of utilization of high biological value protein is particularly likely to be observed in individuals with low protein intakes.[62-64]

In clinical practice, protein needs should be matched to the workload of the remaining kidney function (Stages1-4) or to the level of treatment (Stage 5). Stage 5 (dialysis) and transplantation exceed minimal recommended levels of protein intake for normal kidney function due to increased requirements. An emphasis is placed on high biological value protein containing a larger percentage of essential amino acids. This allows a lower total dietary protein intake to achieve a similar ratio of essential amino acids compared to a higher protein diet with a lower biological value. Although guidelines for 0.6-0.8 gm/kg/d are recommended in CKD, maintaining appropriate body protein stores and translating the diet from theory into food reality often necessitates liberalization of protein intake. Protein-calorie malnutrition occurs in patients when inadequate protein and/or inadequate calories are available to spare protein use as energy.[41-44, 61]

Energy intake

Dietary energy requirements have been studied in MHD patients under metabolic balance conditions. Dietary energy requirements were examined in six MHD patients while they ingested diets providing 25, 35, and 45 kcal/kg/d and a DPI of 1.13 g/kg/d for 21 days each. These studies indicated that the mean energy intake necessary to maintain both neutral nitrogen balance and unchanging body composition was about 35 kcal/kg/d. The finding that energy expenditure in MHD patients appears to be normal corroborates the observations from the aforementioned nitrogen balance and body composition studies.[61]

Sodium/Fluid

Sodium, as an extracellular electrolyte, helps regulate fluid balance. Filtration of sodium decreases in CKD as does fluid volume as urine. Sodium intake control is initiated when fluid retention occurs. Fluid intake must match urine output (Stages 1-4) or volume removed during treatment (Stage 5) in addition to any urine output remaining.

Haemodialysis patients without urine output should gain no more than approximately 0.9kg per day (representing fluid accumulation between treatments) to avoid fluid overload. This fluid restriction is more appropriately calculated using percentage of body weight or using a patient's "dry weight" (the weight when all extra fluid is removed, ideally post-dialysis weight) as a goal.[45, 61, 64]

Potassium intake[45, *61-64*]

Potassium may need to be restricted in the late stages of CKD so as to prevent hyperkalaemia and cardiac arrhythmia. Potassium restriction of 2000-2500mg/d (50-65mmol/d) or 1mmol/kg body weight is indicated in cases of hyperkalaemia. Non dietary causes of hyperkalaemia should be identified but the overall potassium restriction should not compromise the nutritional adequacy of the diet. Foods with high potassium content that need to be restricted in oliguric and anuric ESRF patients on dialysis include fruit, fruit juices and vegetables especially bananas, avocadoes, dried fruits, mushrooms, beetroot, spinach, potatoes and potato products, as well as

tomato based food products. Others include nuts and seeds, chocolate and strong coffee. However, some of these foods (such as vegetables) can be cut in small pieces, boiled in a lot of water to reduce the potassium content.

Calcium intake

The total elemental calcium intake (including both dietary calcium intake and calcium based phosphate binders) should not exceed 2000mg/day. The best food sources of calcium are also high in phosphorus which may contribute to the calcium and phosphorus imbalance in the blood. Medication to help raise the levels of calcium in the blood may be needed.[45, 56, 61-63]

Phosphorus intake

Phosphorus restriction to 0.8-1.0 g/day may become necessary in the early stages of the disease to prevent hyperphosphataemia, hypocalcaemia, and resulting hyperparathyroidism. Phosphorus is, however, abundant in meat products, especially liver, meat or yeast extracts, fish products (fish roe and fish with edible bones), eggs, milk and milk products which make dietary restriction difficult. Medications to bind phosphorus may therefore be required, especially in the late stage of CKD.[52-54] Both calcium-based phosphate binders and other noncalcium, nonaluminum-, and nonmagnesium-containing phosphate-binding agents (such as sevelamer HCl) are effective in lowering serum phosphorus levels. Either may be used as the primary therapy. In CKD patients (Stages 3 and 4), the serum level of phosphorus should be maintained at or above 0.87 mmol/l and no higher than 1.49 mmol/l. In CKD patients (Stage 5) and those treated with haemodialysis or peritoneal dialysis, the serum levels of phosphorus should be maintained between 1.13 to 1.78 mmol/l.[45, 56, 61-63]

Vitamins [60, 62]

a) *Water soluble vitamins.*

In the long-term, a low protein diet (LPD) or a very low protein diet (VLPD) present a risk of water-soluble vitamin deficiency. Low levels of riboflavin, of thiamin and even greater deficiency of pyridoxine were found in patients with CKD. Supplementation of 5 mg/day of pyridoxine in predialysis patients and 10 mg/day in MHD and CAPD patients are recommended.

Cyanocobalamine (B_{12}) and folic acid levels are normal in CKD, and supplements are not required. Ascorbic acid is often low in CKD patients on conservative or dialytic treatment and **intakes ranging from 60 to 200mg/d have been recommended by different authors. In general, patients treated with LPD and supplemented VLPD as well as those patients who are on dialysis must be supplemented with water-soluble vitamins on a routine basis. Consensus has not been reached on the optimal amounts that must be supplemented, but supplementation must be handled in a cautious manner as high amounts may lead to oxalosis.** Patients also treated with long-term vegetarian diets are also at risk of developing water-soluble vitamin deficiency.

(b) *Fat soluble vitamins.*

The plasma levels of vitamin A are frequently high in CKD due to an increase in retinol-binding protein which is normally catabolized by the kidneys. Supplements of fat-soluble vitamins A, E and K are not recommended because of the risk of intoxication in the presence of renal failure. The exception is vitamin D which may be indicated in patients with secondary hyperparathyroidism and renal osteodystrophy.[61-63]

Herbal products[64]

Herbal products of any kind should be avoided as they may be nephrotoxic / contaminated with heavy metals, it may contain harmful minerals and they may interact with prescribed drugs. Herbal remedies could be an important source of potassium in patients with renal disease especially in the presence of concomitant treatment with angiotensin converting enzyme (ACE) inhibitors.[57]

General guidelines[45, 56, 61-64]

- A dietician should be consulted early for the assessment and planning of dietary management.
- Adjust the diet according to laboratory findings for potassium, calcium and phosphorous.
- Maintain adequate fluid intake to prevent dehydration but at the same time avoiding fluid overload.
- Avoid mineral supplements as CKD patients may not tolerate them.

- If a patient has iron deficiency, gastrointestinal blood loss should be ruled out, and iron replacement therapy should be provided if needed.
- Vitamin supplementation especially water soluble vitamins.

1.2.4.4 Renal replacement therapy[65]

Dialysis: Dialysis is a treatment for people in the later stage of CKD. This treatment cleans the blood through the removal of wastes and excess water from the body. Normally, healthy kidneys do this work.[65, 66]

Sometimes dialysis is a temporary treatment. However, when the loss of kidney function is permanent, as in end-stage kidney failure, dialysis is required on a regular basis. The only other treatment for kidney failure is kidney transplant. There are two types of dialysis: *haemodialysis* and *peritoneal dialysis*. Peritoneal dialysis uses a filtration process similar to haemodialysis, but the blood is cleaned inside the body rather than in a machine. In this case, fluid and solute exchange occurs in the peritoneal cavity where the body takes in the solutes from the dialysate in exchange for the waste products. The membrane lining this cavity consists of a vascular wall, interstitium, mesothelium, and adjacent fluid films. The membrane helps in solute exchange through the process of osmosis [39, 53, 65]

Haemodialysis means, “cleaning the blood” - and that is exactly what this treatment does. Blood is circulated through a machine, which contains a *dialyzer* (also called an artificial kidney). The dialyzer has two spaces separated by a thin membrane. Blood passes on one side of the membrane and dialysis fluid passes on the other. The wastes and excess water pass from the blood through the membrane into the dialysis fluid, which is then discarded. The cleaned blood is returned to the bloodstream. [39, 53, 65]

Acute complications during haemodialysis [66]

Acute complication may occur during routine haemodialysis treatments (Table1.4)

Table 1.4: Common acute complications of haemodialysis [66, 67]

Complication	Prevalence (%)
Hypotension	25 - 55
Cramps	5 - 20
Nausea and vomiting	5 - 15
Headache	5
Chest pain	2 - 5
Back pain	2 - 5
Itching	5
Fever and chills	< 1
Hypoglycaemia	3 - 7

These complications of haemodialysis are generally caused by multiple underlying mechanisms and are poorly understood. Knowledge of their pathogenesis is further complicated by their often simultaneous occurrence. As an example, nausea, vomiting, headache, and/or chest pain may accompany hypotension with haemodialysis, which has many possible causes. Similarly, cramps may be associated with hypotension and are often very difficult to treat. [65-68]

Longer treatment times and a high rate of urea removal and/or ultrafiltration significantly enhance the incidence of headache, nausea, and vomiting during haemodialysis. [65-70] It is important to emphasize that longer treatment times alone may not necessarily be associated with adverse effects. The lack of such effects with extended haemodialysis treatment times and with nocturnal haemodialysis was reported in the dialysis center in Taussin, France, and indicates that length of treatment alone may be unimportant if the solute clearance rate is slow. [69, 70]
In addition, dialyzer membrane composition (cellulosic versus noncellulosic), surface area, and biocompatibility are not significant factors underlying these intradialytic symptoms.[71]

Since longer treatment times combined with high urea removal rates appear to be important, a variant of the dialysis disequilibrium syndrome may underlie these symptoms in many patients. Dialysis disequilibrium is thought to be due to water movement into the brain as a result of a reverse osmotic shift induced by urea removal.[65] This syndrome is common when dialysis is initiated and it should be considered in the non-compliant and/or inadequately dialyzed patient with chronic renal failure who develops nausea, vomiting, or headache while being aggressively

dialyzed. In this setting, initially altering the dialysis prescription in favour of less intensive and more frequent treatments may avoid these complications.[67]

Hypoglycaemia as a complication of haemodialysis [66-74]

A recent study done on the blood glucose profiles of Nigerian chronic renal patients on haemodialysis yielded a high prevalence of hypoglycaemia during haemodialysis. Blood glucose levels in this study were ranging between 1.7-8.2 mmol/l. Blood glucose concentration <3.9mmol/l was reported in 85 percent of the patients and with levels <2.5mmol/l in 50 percent of the patients during the haemodialysis process.[73]

Hypoglycaemia is not uncommon in the haemodialysis population, but there seems to be a lack of studies on its prevalence and causes. This is possibly due to the multiplicity of factors that may contribute to the development of hypoglycaemia. It is usually sudden in onset and presents with cold sweats, mental confusion and blurred vision. Once diagnosed it is easy to manage and that could be the main reason why it is not given the attention it deserves. However, prolonged, severe hypoglycaemia has been reported to cause brain damage and death because glucose is the main energy source of the brain. The blood glucose level at which symptoms of hypoglycaemia occurs which are shaking, sweating, mental confusion, blurred vision incoherent speech and in severe cases hypoglycemic coma is variable but has been generally accepted as a blood glucose <2.5 mmol/l. Treatment includes the administration of oral or IV glucose and the ingestion of sugar or sugary foods like sodas followed by a starchy snack/meal. The outcome is usually favourable.[70]

Potential causes of hypoglycaemia in patients on haemodialysis

Many factors (Figure 1.1) have been shown to contribute to the occurrence of hypoglycaemia during haemodialysis.

Renal disease - The renal disease itself is a major cause of hypoglycaemia as a result of the ureamic syndrome but the pathogenesis of hypoglycaemia in CKD is complex involving several factors and mechanisms. Glucose unavailability due to reduced substrate is thought to be the most important factor with poor appetite, nausea and vomiting contributing to the reduction of substrate. Pkes.et.al [66] reported that the contributing factors of hypoglycaemia in CKD patients in

their study were hepatic dysfunction, and drug side–effects (isoniazid, rifampin and propranolol) and the treatment of choice was intravenous glucose administration. Proper nutrition, the judicious use of any medication that has the potential for hypoglycaemia, the early detection and treatment of diseases and the use of glucose containing dialysate in haemodialysis patients can diminish the risks of this potentially lethal complication.[65-74]

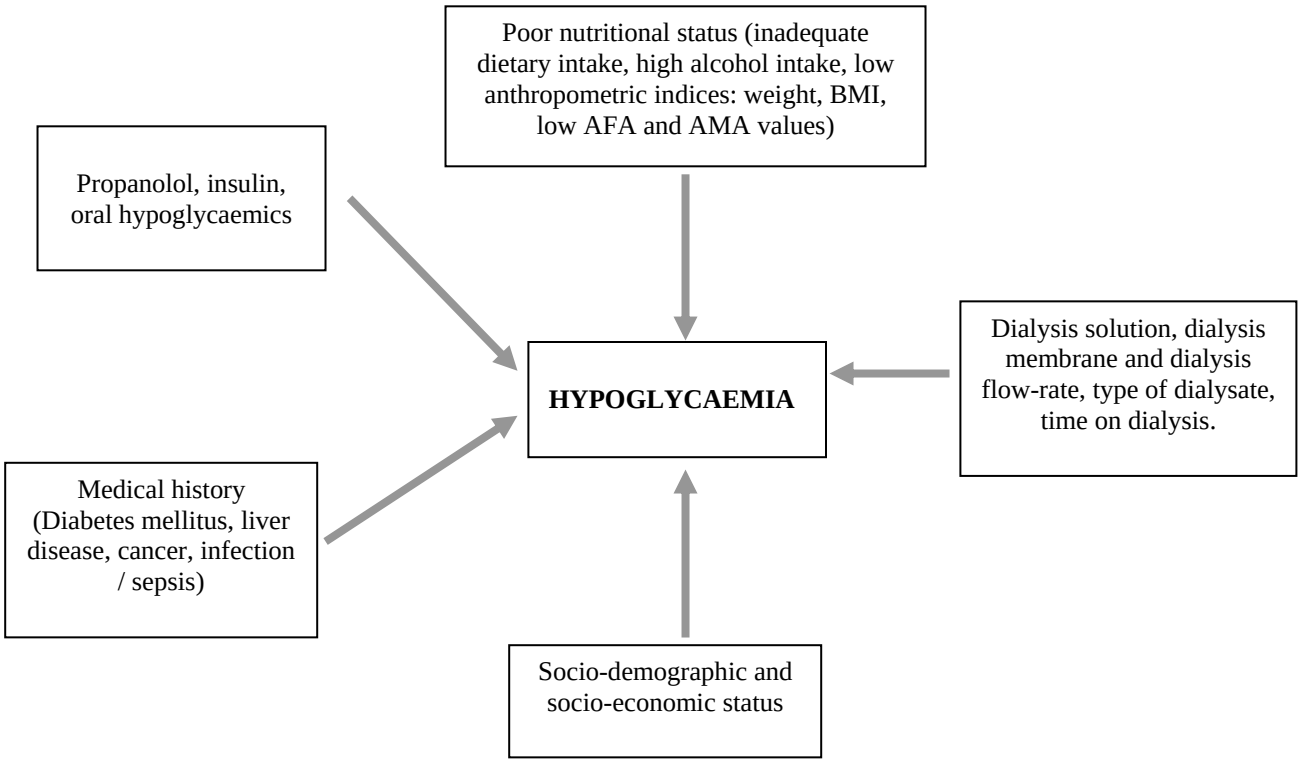


Figure 1.1: Conceptual framework showing the factors that may contribute to hypoglycaemia in haemodialysis patients.

Haemodialysis - The haemodialysis process is also a major contributor to hypoglycaemia. Though patients may have asymptomatic (without symptoms) hypoglycaemia while on haemodialysis and not be aware of it, those patients with an initial plasma glucose of 4.5 mmol/l or less and who do not eat during dialysis are particularly at risk and they should be dialyzed with a dialysis fluid containing at least 5.5 mmol/l glucose. In a study investigating the mechanism of hypoglycaemia caused by haemodialysis it was concluded that during

haemodialysis using a high bicarbonate dialysate, the haemodialysis induced decrease in plasma glucose was possibly a result of diffusion of glucose from plasma into erythrocytes.[68-70]

Medication- The medication the haemodialysis patient is taking could also play a major role in determining the plasma glucose levels of the patient. Such medication has been widely reported to cause hypoglycaemia especially in patients with inadequate food intake and also those on haemodialysis using glucose-free dialysate. Propranolol, which is widely employed in haemodialysis patients for the control of renin-dependent hypertension, has been investigated and infrequent reports have linked hypoglycaemia and propranolol, especially in complex situations such as malnutrition, anaesthesia and excessive insulin use. The many complications of renal disease dictate the use of multiple medications with varying side effects. Drugs such as phosphate binders, laxatives, diuretics and antibiotics may lead to altered taste, nausea, vomiting, constipation, diarrhea, anorexia, increased nutrient loss, increased nutrient need, dry mouth, gastro-intestinal (GI) distress, and malabsorption which are some of the common drug side effects that may affect nutritional intake leading to hypoglycaemia during haemodialysis.[65, 68]

Dialysis membrane- Studies have shown that the use of a low flux cuprophane membrane in haemodialysis leads to a loss of 4-9g of free amino acids and 8-10g of amino acids if patients eat during the treatment. Those using high flux dialyzers tend to lose even more amino acids and due to the high permeability of protein, albumin losses of about 25g are lost per session when higher filtration rates are used. Different reported studies have indicated that glucose molecules are also lost during each haemodialysis session but the actual amount has not been calculated.[69-70]

Dialyzer Re-use - Re-use of dialyzers is a routine procedure in most dialysis centers for cost saving purposes. Although usually small amounts of proteins are lost during a single haemodialysis, Kaplan et al [72] reported markedly increased protein losses when polysulphone membranes were reprocessed many times with bleach or formaldehyde. After 20-25 re-uses, up to 17g of protein were lost during one haemodialysis session. [71-72] since protein losses during haemodialysis therapy are inevitable; the nutritional status of the haemodialysis patient is becoming vulnerable especially if the patient is already malnourished on entering haemodialysis.

With the re-use of dialyzers glucose is lost and the amount is dependant on the type and the times of re-use.[68-72]

Alcohol- Hypoglycaemia is often seen in malnourished chronic alcoholics. Patients with alcohol induced hypoglycaemia usually present in coma or semi-coma 2 to 10 hours after alcohol ingestion. The presenting physical findings may include hypothermia, tachypnea, and the smell of alcohol on the breath.[72-74]

Sepsis- Sepsis can cause hypoglycaemia, more often in elderly patients with underlying liver and renal disease. It has also been described in a 6-month-old patient with Neisseria meningitis and in other patients in whom no cause for hypoglycaemia other than sepsis was present.[74]

Hepatic Disease- Co-morbid disease, including hepatic disease, is common in patients on haemodialysis. Diffuse, severe liver disease, in which 80 to 85 percent of the liver is functionally impaired or destroyed, may result in hypoglycaemia due to impaired glycogenolysis and gluconeogenesis. Diseases such as acute hepatic necrosis, acute viral hepatitis, Reye's syndrome, and severe passive congestion have been implicated. Metastatic or primary liver neoplasia may cause hypoglycaemia if a large portion of the liver is involved, but liver metastases usually do not produce hypoglycaemia.[75]

Extrapancreatic Neoplasm- Hypoglycaemia may be associated with, or caused by, neoplasms of virtually every histopathologic type. Hypoglycaemia-causing tumors may be unsuspected and discovered during systemic evaluation of a patient with fasting hypoglycaemia; or hypoglycaemia may occur as a late or preterminal event in a patient with known neoplasia.[76]

Malnutrition- Malnutrition in patients on haemodialysis has been documented by many studies and a high prevalence of protein-energy-malnutrition (PEM) is quite evident.[76] The prevalence of PEM in chronic renal failure is reported to be between 30-76% and is particularly common in elderly patients, especially those with chronic renal failure secondary to diabetes mellitus. A high prevalence of PEM is observed in patients commencing haemodialysis and those patients who are malnourished at the onset of dialysis therapy are likely to stay malnourished one to two years

later.[75, 78-83] Patients presenting with protein-energy malnutrition are more likely to present with hypoglycaemia during haemodialysis due to diminished glycogen stores. Also, a strong risk factor for both morbidity and mortality in connection with chronic dialysis has been observed in patients with PEM. Reduction in anthropometric measurements, low concentrations of visceral proteins such as serum albumin, abnormalities in plasma and muscle amino acid profiles are some of the indices of malnutrition that have been identified in these patients. (Table1.5)

Table 1.5: Indices of malnutrition in haemodialysis patients [79-83]

Indices of malnutrition in haemodialysis patients
1. Reduction in anthropometric measurement (weight, BMI, mid-upper arm circumference, and skinfold thickness)
2. Serum albumin <40g/L
3. Abnormal plasma and muscle amino-acid profiles.
4. Low percentage of ideal body-weight (<85%)
5. Low IGF-1,transferrin,and pre-albumin levels

*BMI-Body mass index *IGF-Immunoglobulin factor

PEM is multi-factorial and is dependent on nutritional, metabolic, hormonal and inflammatory factors. Other factors considered causing PEM in chronic renal failure include: insulin resistance, increased glucagon concentrations, secondary hyperathyroidism and reduced thyroid hormone concentrations. [79-83]

In the haemodialysis population malnutrition has a number of causes, many of which are common to all forms of renal replacement therapy. These include: anorexia, inadequate intake, increased nutrient losses, abnormal nutrient metabolism, altered nutrient absorption, inadequate dialysis, catabolism of dialysis, blood loss, co-morbid conditions or superimposed illnesses, endogenous and exogenous uraemic toxins, drug-nutrient interactions, endocrine disorders, and stresses of renal replacement therapy. Psychological and socioeconomic factors may also play a role in the development of malnutrition.[80-83]

Malnutrition and hypoglycaemia are encountered in CKD patients on haemodialysis due to diminished glycogen stores often associated with ESRF patients on MHD. Hypoglycaemia in the majority of these patients is however asymptomatic. To reduce the potentially serious risks

associated with hypoglycaemia, efforts should be made to diagnose and treat hypoglycaemia in the MHD population. Proper nutrition and adequate energy intake should be ensured in all the patients on haemodialysis. Blood glucose evaluation should be done more often in both diabetic and non-diabetic CKD patients. Glucose containing dialysate fluid should be used in HD patients and if this is not feasible, glucose drinks should be given in cases where presentations of hypoglycaemia have been identified. During the HD procedure, patients should be encouraged to eat at regular intervals to replace the glucose losses.[83]

1.2.4.5 Patient Education [23, 39, 80]

Patient education should begin at the time of diagnosis and continue throughout the CKD course. The patient needs to know his or her prognosis and treatment options to make informed decisions. Advance directives should be discussed early and reviewed when the patient's condition changes. Renal replacement treatment should be included in the advance directives. The options for renal replacement therapy include haemodialysis, peritoneal dialysis, or kidney transplantation.The nurse practitioner can assume the role of the primary care provider for patients with CKD, working closely with the nephrologists. [24, 26, 39, 75] The primary care provider should screen, identify, and do the initial evaluation of patients with CKD for referral to the nephrologist, provide day-to-day management of patients, and provide patient education. The patient should receive immunizations for hepatitis A and B, especially before renal transplantation.[24] The nephrologist should provide more extensive patient assessment, strategic guidance, and specific recommendations for patient care, and patient education. The renal dietitian should assist the patient in the planning and implementation of dietary guidelines in relation to nutritional assessment (anthropometry, subjective global assessment, dietary interviews and diaries) and integration of the results. The patient with his/her family should be counselled on the appropriate nutrient intake. With early detection and management, and in coordination with the nephrologist, the renal dietitian and the primary care provider have the opportunity to reduce or delay the progression to end-stage kidney failure.[25, 26, 39, 75, 79-83]

1.2.5 Statement of the problem

It has been observed that hypoglycaemia occurs frequently at Kenyatta National Hospital's renal unit with most patients presenting with cold sweats and mental confusion. The effects of

hypoglycaemia have been observed in both diabetics and non-diabetics on MHD. No clinical tests are done to analyze the blood glucose level once these symptoms appear but the patient is given intravenous glucose and in severe cases haemodialysis is discontinued. The potential causes of this hypoglycaemia have not been investigated but may include poor nutritional status, composition of dialysate, dialysis flow rate, dialyser re-use, dialysis membrane, co-morbid disease and medication.

Socio-economical factors may also play a role since haemodialysis is a very expensive procedure and rarely fully covered by insurance bodies. Patients on haemodialysis also have medical conditions which place high financial demands on them which include purchasing of drugs/medicine,surgery and special consultations due to the multi-systemic nature of the disease. Basic living needs also bring more challenges since all haemodialysis units in Kenya are situated in the cities where the cost of living is much higher. Due to these economic factors many patients may therefore not be able to afford dialysis two or three times per week on a regular basis and this may lead to inadequate dialysis, which in turn may compromise the nutritional status of patients as a result of poor or inadequate feeding.

Patients on haemodialysis should be given ongoing medical attention throughout the haemodialysis process to prevent such potentially serious complications such as hypoglycaemia. The team comprising of the nephrologist, technical staff, the renal nurse, renal dietician and renal counselor should attempt to encourage the haemodialysis patients so as to ensure that patients accept their medical conditions and continue with treatment modalities. During the haemodialysis process, vital signs should be monitored closely so that any abnormality arising is dealt with immediately. Unfortunately this is not the case at Kenyatta National Hospital. Blood pressure and temperature are monitored on an hourly basis from the start to the end of the four hours haemodialysis process but blood glucose levels are not. Patients going into hypoglycaemia are identified when they start exhibiting symptoms like cold sweats and mental confusion, which also takes a keen nurse to notice as uraemic signs can also present with mental confusion and incoherence in speech.

Once a patient on haemodialysis presents with any hypoglycaemic signs or symptoms, a random blood glucose test should be done before the intravenous infusion of highly concentrated

dextrose solution. Furthermore, there needs to be standard guidelines governing the volume and amount of dextrose to be infused in accordance to the extent of hypoglycaemia, which is also not the case at Kenyatta National Hospital. At Kenyatta National Hospital Renal Unit, the symptoms of hypoglycaemia are managed with 50% dextrose given intravenously with the amount varying from one nurse to the other because the unit does not have existing standards. Moreover, patients presenting with asymptomatic hypoglycaemia may suffer in silence during haemodialysis, only to complicate the process further. These reasons then, served as the motivation for this study.

1.2.6 Purpose of the study

The purpose of the study was to assess the prevalence of hypoglycaemia among patients with end stage renal failure on maintenance haemodialysis at Kenyatta National Hospital Renal Unit and to identify potential nutrition-related causes of the hypoglycaemia.

CHAPTER TWO: METHODOLOGY

2.1 Aim of the Study

The aim of the study was to assess the prevalence of hypoglycaemia among the patients with end-stage renal failure on MHD and to identify potential nutrition-related causes of the hypoglycaemia.

2.2 Objectives

- To determine the prevalence of hypoglycaemia in patients on MHD
- To determine the nutritional status of patients on MHD
- To determine the relationship, if any, between hypoglycaemia and nutritional status, the presence of co-morbid disease, prescribed medication, dialysis-related variables and socio-demographic status of the patient.

2.3 Hypotheses

The following null hypotheses were tested in the study:

2.3.1 There is no significant relationship between blood glucose concentrations and the following independent variables:

- parameters of nutritional status
- socio-demographic status
- co-morbid disease
- prescribed medication
- dialysis-related variables

2.4 Research Design

A prospective descriptive, cross-sectional, observational study design was followed.

2.5 Study Area and Population

The research study was carried out at the Kenyatta National Hospital's Renal-Unit. Kenyatta National Hospital is a teaching and referral hospital located about 2 km from Nairobi, the capital city of Kenya. Being a referral hospital, its renal unit is the oldest in the country, having started

its first haemodialysis programme in 1984 and it is also the largest dialysis unit in Kenya. Currently 200 patients are on maintenance haemodialysis twice per week in this unit and on average, 20 patients are dialyzed daily. Patients being managed in this unit come from different parts of the country as well as from the East Africa and the Great Lakes regions. The renal unit manages all types of renal diseases and other modes of treatment include peritoneal dialysis as well as kidney transplantation.

2.6 Sample Size and Sampling Techniques

The following selection criteria were used in selecting patients for the study.

- Patients with end-stage renal failure with or without diabetes mellitus.
- Patients who had never had kidney transplantation.
- On MHD for not less than 3 months.
- Older than 18 years.
- Able to participate in the study and giving written informed consent.

2.7 Data Collection Instruments

2.7.1 Logistical considerations

The renal unit total population of patients on MHD was 200 of whom 100 patients met the inclusion criteria. All patients who met the inclusion criteria were considered for inclusion in the study. If a patient was willing to take part in the study, an appointment was scheduled. Fifty five patients out of 100 patients were enrolled to the study but 45 of these patients were excluded for reasons shown in Figure 2.1.

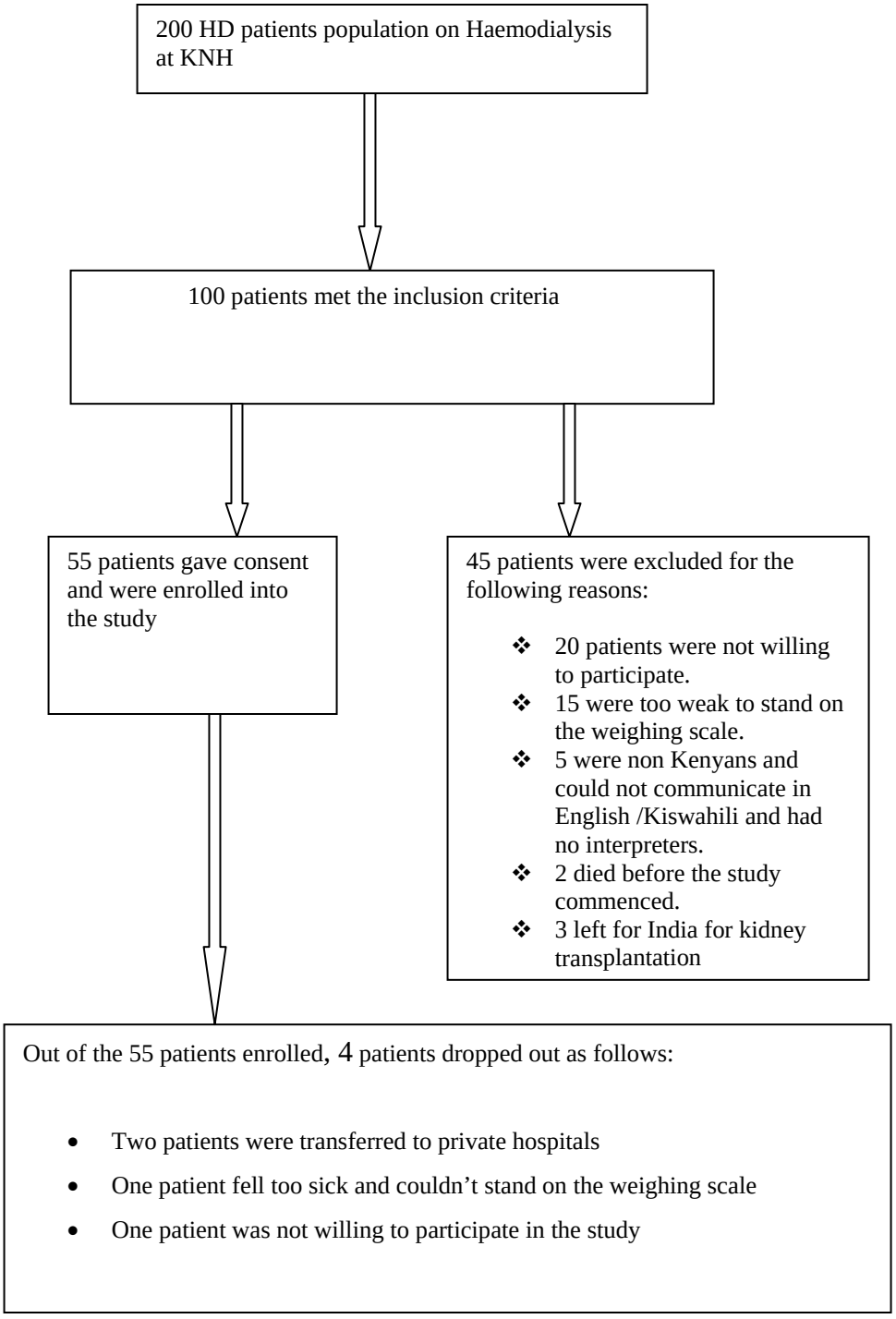


Figure 2.1: A flowchart showing the enrollment of patients to the study.

2.7.2 Obtaining socio-demographic, economic and medical history, drugs / medication and dialysis information.

The following socio-demographic data was obtained by means of a structured questionnaire (ADDENDUM 1):

- Age
- Gender
- Marital status
- Occupation
- Ethnicity
- Residence
- Housing
- Employment
- Grants and income.

For the medical history, drugs/medications and dialysis procedures, patients' medical files were retrieved for the recording of their primary diagnosis and any co-morbid condition that may have been present as well as the patient's dialysis history. The relevant dialysis detail for the day on which patients were tested for hypoglycaemia was also recorded. These included frequency and length of the dialysis sessions, type of dialysate fluid, and dialysis membrane used during haemodialysis. Clinical experiences during dialysis sessions (especially hypoglycaemic signs and symptoms e.g. disequilibrium, hunger, cold sweats, mental confusion) were recorded. This information was obtained from the nurses' records, observations / questioning of the patients.

2.7.3 Anthropometric data.

The researcher obtained height, weight, mid upper arm circumference (MUAC) and multiple skinfold measurement (triceps, biceps, suprailiac and sub scapular) using standard equipment and standardized techniques. The principal investigator collected the anthropometric and dietary intake data. All the measurements were taken thrice and the average was used for further analyses (ADDENDUM 2). [84-85]

2.7.3.1 Weight

Weight was taken after dialysis (dry weight) and it was determined using a standardized Xenical personal electronic scale measuring weight to the nearest 0.1 kg. Patients were asked to wear light hospital gowns and weight was taken with the patient barefoot. To ensure privacy, all anthropometric measurements were taken when the curtains were drawn around the participant's bed. [84-85]

2.7.3.2 Height

Height was determined using the "Xenical Lose weight gain health" height chart mounted on the wall. The patient was asked to stand with heels together, arms to the side, legs straight, shoulders relaxed and the head in the Frankfort horizontal plane ("look straight ahead"). Heels, buttocks, scapulae (shoulder blades) and back of the head were positioned against the vertical surface of the stadiometer. Height was measured in centimeters to the nearest 0.001 m after maximum inhalation. [84-85]

2.7.3.3 Mid-Upper Arm Circumference (MUAC)

The MUAC was measured with a non-stretchable flexible tape. The patient was asked to stand with his/her elbow relaxed, with the right arm hanging freely to the side. The mid-point was located by measuring from the acromion to the olecranon and marking the mid-point with a pencil. The tape was placed round the upper arm, directly over the pencil mark at the mid-point on the posterior aspect (back) of the upper arm. The tape was pulled just snugly enough around the arm to ensure contact with the medial side of the arm and elsewhere. Measurement was recorded to the nearest 0.1 cm. [84-85]

2.7.3.4 Triceps skinfold measurement

The triceps skinfold measurement was taken with the patient standing with his or her feet together, shoulders relaxed and arms hanging freely at the sides. The posterior surface of the right upper arm was located which was in the same area as the marked midpoint for the upper arm circumference. The fold of skin was grasped together with the subcutaneous adipose tissue gently with the forefingers approximately 1.0 cm above the point at which the skin was marked.

With the jaws of the calipers perpendicular to the length of the fold, the thickness of the skin was measured with a John Bull's calipers to the nearest 0.2 mm, 3 seconds after the caliper jaws have been released. Three measurements were taken and an average calculated. [84-85, 88, 89]

2.7.3.5 Biceps skinfold measurement

The same procedure used for the triceps skinfold was followed, but with the measurement of the biceps at the front of the upper arm (instead of the back, as with the triceps) the level was the same as for the triceps and arm circumference and the location was in the midline of the anterior part of the arm. [84-85, 88, 89]

The patient was asked to stand with his/her feet together, shoulders relaxed and arms hanging freely at the sides. Standing behind the patient's right side, the investigator rotated the right arm so that the palm is facing forward. Locating the point on the anterior surface of the right arm in the same area as the marked midpoint of the upper arm circumference, the fold of skin and subcutaneous adipose tissue of the anterior surface of the upper arm was grasped. This was in the midline of the upper arm and about 1.0 cm above the marked line on the middle of the arm. [84-85, 88, 89]

2.7.3.6 Subscapular skinfold measurement

The patient was asked to stand erect with relaxed shoulders and arms and the back of the examination gown or garment opened. Palpating for the inferior angle of the scapula a fold of skin and subcutaneous adipose tissue was grasped directly 1.0 cm below and medial to the inferior angle. The skin-fold formed a line about 45 degrees below the horizontal, extending diagonally toward the right elbow. Placing the jaws of the caliper, perpendicular to the length of the fold about 1.0 cm lateral to the fingers, and with the top jaw of the caliper on the mark over the inferior angle of the scapula. The same procedure as for the triceps skin fold was used. [84-85, 88, 89]

2.7.3.7 Supra-iliac skinfold measurement

The patient was asked to stand erect with feet together and arms hanging loosely by the sides. When necessary, the arm was abducted slightly to improve access to the site. Palpation of the

iliac crest followed. The skin was grasped at an oblique angle, just posterior to the midaxillary line below the natural cleavage lines of the skin. The skinfold was aligned inferomedially at 45 degrees to the horizontal, following the general procedure above. [84-85, 88, 89]

2.7.3.8 Body-mass index (BMI) [86, 87]

The BMI was calculated by relating the averages of the weight and height taken using the following formula:

$$BMI = \frac{\text{Weight (kg)}}{\text{Height (m)}^2}$$

BMI was classified according to the recommended cut-off points (Table 2.1)

Table 2.1: BMI classification [86, 87]

BMI	**CLASSIFICATION**	**BMI ASSOCIATED HEALTH RISKS**
<16	Grade 3 CED*	Increased risk
16-16.9	Grade 2 CED	Increased risk
17-18.5	Grade 1 CED	Low risk
18.5-24.9	Normal	Average risk
>25	Overweight	
25-29.9	Pre-obese	Increased risk
30-34.9	OB class 1	Moderate risk
35-39.9	OB class 2	Severe risk
>40	OB class 3	Very severe risk

WHO 2002 [87]* CED = Chronic Energy Deficiency

2.7.3.9 Arm fat area (AFA) and arm muscle area (AMA) [88]

AFA and AMA was calculated from the triceps skinfold thickness and the arm circumference using prediction equation methods by Frisancho [88] as shown below.

$$AMA\ (cm^2) = \frac{[MUAC\ (cm) - (3.14*TSF\ (cm)]^2}{4*3.14}$$

$$AFA\ (cm^2) = \frac{MAC\ (cm) * TSF\ (cm)}{2} - \frac{3.14 * TSF\ (cm)^2}{4}$$

AMA and AFA were classified and interpreted as follows:-

Below <5th centile…. Low
5 – 10th centile ……. Borderline
10 – 90th centile….. Normal
90 - 95 centile…….. High
above 95th centile….Very High

2.7.3.10 Percentage body fat [81]

Raw data and the computing formulas were entered in Excel and the following equations were calculated to obtain the percentage body fat values: [85, 90]

- Compute sum of the biceps, triceps, subscapular and suprailiac skinfolds (Σ)
- Compute the logarithm (Σ)
- Compute body density (D) from the equations for men or women
- Calculate the fat mass (kg) = weight (kg) * [4.95/D-4.5]
- Calculate % body fat = fat mass (kg) /weight (kg)* 100

The patients were then classified according to their percentage body fat (Table 2.2).

Table 2.2: Classification of percentage body fat [90]

Classification	**Women (% body- fat)**	**Men(% body- fat)**
Low	< 8%	< 5%
Acceptable (Lower end)	9-23%	6-15%
Acceptable (Upper end)	24-31%	16-24%
Too high	> 32%	> 25%

2.8 Dietary Intake.

Nutritional assessment on all patients on haemodialysis had been done at the initiation of haemodialysis. Dietary counseling was aimed at replacement of nutrients lost during the haemodialysis and educating the patient on the importance of eating adequate amounts of food prior to commencing haemodialysis based on the following:

- Current weight(dry weight)
- Dietary history
- Body Mass Index (BMI)
- Patients food likes and dislikes
- Nutrient losses during haemodialysis.

For this study, information on dietary intake was obtained using two dietary assessment methods, the 24 hour-recall and a structured quantified food frequency questionnaire (QFFQ) (ADDENDUM 3 and 4 respectively). With the 24-hour recall method, patients were requested to recall all the foods eaten in the 24 hours preceding the day of the study. Snacks, beverages, alcohol and any herbal or commercial nutritional supplements taken were included.[91] In addition, the 24-hr recall was also completed for a dialysis day and a weekend day, and the average of the three 24-hr recalls was calculated. The QFFQ contained a list of all the foods commonly consumed by the different ethnic communities of Kenya. The list was sub-divided into various food groups. Portion sizes were estimated using fresh food models that were packed in various food containers of 100 g each. Various fresh fruit models were presented to the patients to estimate the portion size consumed. For the fluids (water, beverages, alcohol, fruit juice and soups) different cups of different capacities (100 ml, 200ml, 500ml and 1litre) were used. Household tablespoons and teaspoons were used to estimate the quantities of glucose, cooking oil/fat, salt, spreads and spices. The National Food Consumption Survey (NFCS-QFFQ 1 1999), which has been used in South Africa to assess dietary intake for children of ages between 1-9 years was used as a basis in the formatting of the questionnaire. Dietary intake questionnaires were face validated using previous dietary data recorded at the initiation of haemodialysis. For those questions where values were missing, or the answers incomplete, the patient was given the questionnaire on the subsequent visit to complete it. All the questionnaires used in this research

were approved by the University of Stellenbosch, Department of Human Nutrition and ratified by all the study leaders before being used as research instruments.

2.9 Obtaining Biochemical Data (Addendum 5 and 6)

Serum glucose

Laboratory data was collected by a laboratory technician trained and experienced in medical laboratory techniques. The laboratory technician drew 2 ml blood from the patients during the haemodialysis sessions. All the patients on haemodialysis were on glucose free dialysate solutions. Blood was drawn from the afferent dialysis lines and analyzed immediately using a Precision QID glucometer model Q8751-4076 Abbott laboratories, United Kingdom, UK), which is used at Kenyatta National Hospital Laboratories for the analysis of blood glucose. Serum blood glucose concentration was analysed sequentially at the start of the dialysis session and then every 15 minutes for the first hour on dialysis and thereafter every hour until the end of dialysis. Those patients whose dialysis was discontinued due to hypoglycaemia or dialysis disequilibrium were recorded.

The same laboratory technician also assisted the investigator in blood sampling and procedures to ensure the following laboratory quality control measures:

- That the glucometer had read a controlled solution and was in good working condition.
- That the blood being analyzed was not contaminated with spirit or bleaching agents like jik.
- That the glucometer's sensor was placed in a water-free area at all times.
- The coefficient of variation was 0.86 percent. Normality of the patient's glucose concentration was interpreted according to the Kenyatta National Hospital laboratories defined normal range (Table 2.3).

Table 2.3: Kenyatta National Hospital renal unit reference normality* ranges of serum glucose [92]

Parameter	Reference range
Random blood glucose	3.9- 11.1mmo/l

* Kenyatta National Hospital renal unit reference ranges (2005)[92]

Hypoglycaemia or low blood glucose is a condition in which the level of glucose in the blood drops below a minimum concentration (< 2.5mmol/l). The condition manifests itself by a number of symptoms that usually disappear 10 to 15 minutes after eating sugar. For the purposes of this study hypoglycaemia was defined according to the criteria used in the renal- unit of the hospital which is blood glucose <3.9mmol/l .[12, 66-74] Hypoglycaemia in this study was further classified using the following cut-off points (<1.79 = clinical hypoglycaemia; 1.8–3.8 = below normal; 3.9–11.1 = normal random blood glucose; and >11.1 possibly diabetic).

2.10 Pilot Study.

A pilot study was conducted on 7 haemodialysis patients not taking part in the study, but otherwise representative of the study group, to test the socio-economic and demographic, medical and dietary intake questionnaires for content, comprehension and structure. Adaptations were made as necessary before it was used in the main study. The 24-hour recall questionnaire was adapted to include snacks in between meals. Different examples of snacks were listed to enable the patient to give the correct snack taken. In the QFFQ questionnaire, food items were renamed using the local language for better comprehension. A vegetable like capsicum was referred by the name “hoho” while amaranth was referred to as “terere”.

2.11 Data Analysis

A statistician appointed by the Faculty of Health sciences, University of Stellenbosch, was consulted for the data analysis.

Data from the laboratory tests and questionnaires was entered into an Excel spreadsheet in the format required which allowed the computation of frequencies, percentiles, means and standard

deviation in order to estimate patterns, trends as well as relationships between blood glucose levels and other relevant variables.

The Food meter UK (7) statistical package was used in the analysis of nutrient content while the Stat Soft Inc. (2004) STATISTICA data analysis software system (version 7)[93] was used to analyse the other variables.The following blood glucose categories were used for the classification of the blood glucose values.[92]

1 = <1.79 (clinical hypoglycaemia)
2 = 1.8 – 3.8 (Below normal)
3 = 3.9 – 11.1 (normal random blood glucose)
4 = >11.1 (possibly diabetic)

Both descriptive and inferential statistics were used where applicable. Due to the relatively low prevalence of hypoglycaemia, the relationship between blood glucose and independent variables was based on the minimum blood glucose level experienced by participants as per the above categories. All patients with hypoglycaemia were included in the analysis including those who presented with hypoglycaemia at baseline. The analysis of variance (ANOVA) was used to determine whether there were significant differences between two or more groups or sample at a selected probability level. The probability level used in this study was $p < 0.05$. Regression statistics were used in finding out whether the independent variables predicted given dependent variables. Chi-square test was used to establish relationships between two variables that were categorical in nature.

In testing the magnitude of the relationship between two variables and their direction, Spearman's rank correlation coefficient was used.[94]

2.12 Ethics Considerations.

2.12.1 Ethics review committee.

The protocol was approved by the Committee for Human Research, Faculty of Health Sciences, University of Stellenbosch N05/12/196 as well as the Ethics Committee of Kenyatta National Hospital N1/2857 [Appendices 5 (A and B)].

2.12.2 Informed consent

Written informed consent was obtained from each participant. The standard informed consent form of the Faculty of Health Sciences of the University of Stellenbosch was adapted for use in this study and translated in Kiswahili language (Addendum 7).

2.12.3 Patient confidentiality

Patient's identification information was omitted from the study related material to ensure participants confidentiality. Patients who presented with symptomatic hypoglycaemia were noted on a separate sheet and the nurse in the unit was informed for appropriate intervention.

CHAPTER THREE: RESULTS

3.1 Description of Subjects

Fifty five out of the 100 patients on MHD who met the selection criteria were enrolled in the study. Four patients were excluded due to the following reasons:

- Two patients were transferred to private hospitals
- One patient fell too sick and couldn't stand on the weighing scale
- One patient was not willing to participate in the study.

The mean age for the study population was 47 years [Standard Deviation (SD) 13.4)] (Table 3.1) .The majority of the participants were males (71%), married (86%), unemployed (46%) and falling within the low income group (46%) and therefore were depending on the hospital's credit facility to maintain haemodialysis. Sixty three percent were living in the urban area of the hospital for proximity and economic reasons, and the majorities were living in informal housing (65%) and were from Kikuyu ethnicity (47%).The other Kenyan ethnic groups were poorly represented in the sample. The Kikuyu community is the largest in the country with one third (about 10 million) of the country's population (about 30 million) being from this ethnic group. There were two non-Kenyans in the study population, one from southern Sudan and the other from Uganda.

In terms of co-morbidity and haemodialysis-related factors (Table 3.2), study participants had been on MHD for a mean period of 39.2 (13.4) years. Bicarbonate dialysate solution was used in the majority of participants (68.6%) and all were dialysed using diacetate membranes since this was the only type in stock at the time of the study. The majority of participants was dialyzed for 4 hours twice a week (80%) and had a blood flow rate of 285-500ml/min.

Table 3.1: Socio-demographic characteristics of the study population (n = 51)

Parameter	**Number (%)**	**Interclass Difference** **P-value (Chi square-test)**
Age in years: Mean (SD)	47(13.4)	-
Gender Males Females	 36(71) 15(29)	**0.46**
Marital status Married Single Divorced	 44(86) 6(11) 1(2)	**0.44**
Occupation Not employed Own business Civil servant Farmer Retired	 24(46) 4(8) 10(20) 7(14) 6(12)	**0.20**
Residence Urban Peri-urban Rural	 32(63) 7(14) 12(24)	**0.44**
Monthly income Low (<Ksh 5,000) Middle (Ksh 5,000-10,000) High (> Ksh 15,000)	 37(73) 10(8) 4(20)	**0.88**
Housing Temporary Semi-permanent Permanent	 33(65) 6(12) 12(24)	**0.40**
Ethnicity Kikuyu Taita Kisii Baganda Embu Kalenjin Kamba Mijikenda Luo Ogiek Borana Meru Luhyia	 24(47) 2(4) 3(6) 1(2) 1(2) 5(10) 3(6) 2(4) 2(4) 1(2) 2(4) 2(4) 3(6)	**0.26**

Table 3.2: Co-morbidity and dialysis features of the study participants (n=51)

Parameter	**Number (%)**	**Interclass Difference p-value (Chi square-test)**
Co- morbidity		**0.06**
Diabetic nephropathy	15 (30)	
Hypertension	51 (100)	
Sepsis/Infection	3 (6)	
Hepatitis B	4 (8)	
Dialysis sessions per week		**0.94**
One	9 (18)	
Two	41(80)	
Three	1(2)	
Time on HD, months		**Not applicable**
Means (SD) [range]	39.2 (13.4) [3-204]	
Dialysate		**0.12**
Bicarbonate	35 (69)	
Acetate	16 (31)	
HD Membrane		**Not applicable**
Diacetate	51 (100)	

3.2 Prevalence of Hypoglycaemia during Haemodialysis:

3.2.1 Blood glucose (BS) concentrations during haemodialysis

The prevalence of hypoglycaemic episodes (<3.9 mmol/L) varied from 8% at baseline to 0% at 4 and 5 hours (Figure 3.1), with a prevalence of 16% for the full duration of haemodialysis, including baseline. Two percent of the participants presented with hypoglycaemia between the first and third hours of haemodialysis. None of the 7 patients who were dialysed for 5 hours experienced a hypoglycaemic episode. During the haemodialysis process patients were allowed to eat as per the renal-unit meal schedule and all the patients used glucose free dialysate solution.

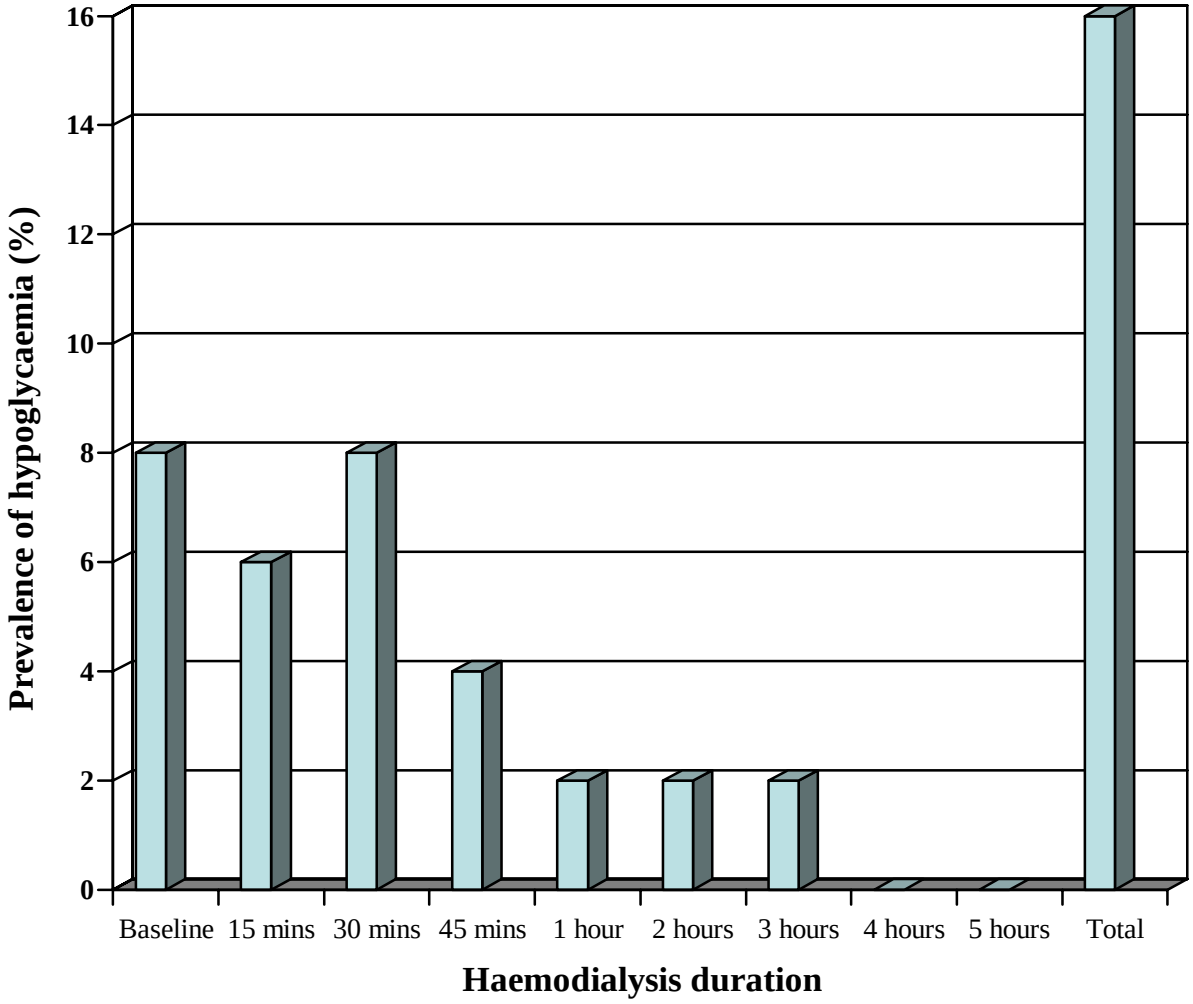


Fig.3.1: Prevalence of hypoglycaemia during haemodialysis (n=51)

3.2.2: Mean blood glucose concentration during haemodialysis

There was a significant statistical (though not clinically so) decline in mean blood glucose (BG) levels from 8 mmol/L at baseline to 6 mmol/L at 4 hours (Figure 3.2, p=0.0097). Mean blood glucose levels during MHD fluctuated within normal ranges for most of the patients. From the 1st hour of MHD onwards no new cases presented with clinical hypoglycaemia (<1.79 mmol/L). In 3 of the 4 participants with clinical hypoglycaemia, haemodialysis was discontinued as they could not tolerate the haemodialysis (Table 3.3).

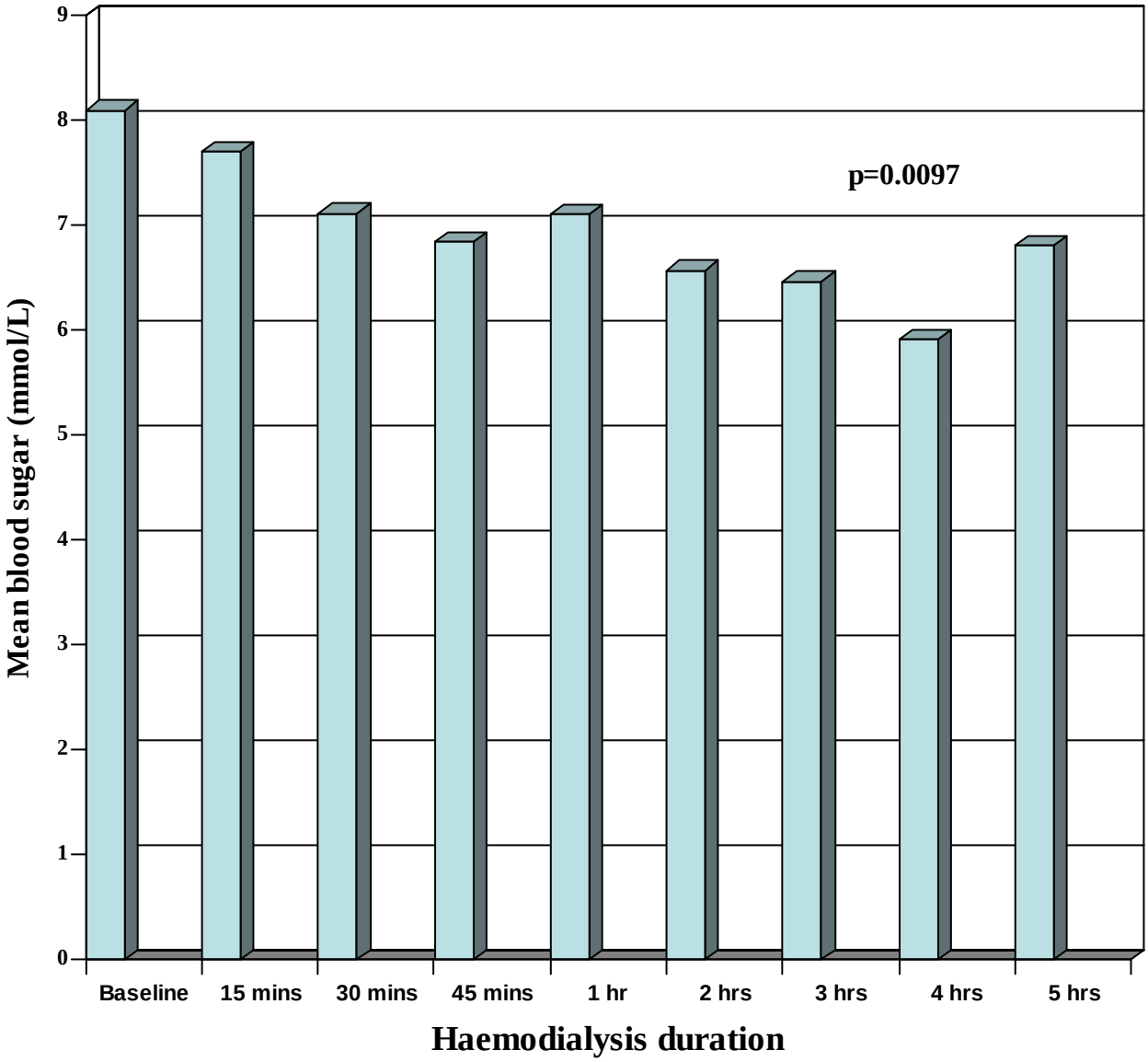


Fig.3.2: Mean blood glucose concentration during haemodialysis (n=51)

Table 3.3: Mean blood glucose concentration, range, SD, 95% CI and classification of participants according to blood glucose categories (n=51)

	Blood glucose levels (mmol/L)			BG range categories (mmol/L) Number (%) of subjects in each category				Participants in whom HD was discontinued
	Mean (SD)	**Range**	**95% CI**	**<1.79**	**1.8 – 3.8**	**3.9 – 11.1**	**>11.1**	**Number (%)**
Baseline, before HD	8 (0.8)	1.6-22.4	6.0-10.1	1(2)	3(6)	11(22)	36(71)	-
15 Min	7.7(0.8)	1.6-20.8	5.5-9.8	1(2)	2(4)	21(41)	27(53)	-
30 Min	7.1(0.8)	1.7-19.7	4.9-9.2	1(2)	3(6)	21(41)	26(51)	-
45 Min	6.8(0.9)	2.1-17.8	4.5-9.1	-	2(4)	21(41)	28(54)	1(2)
1 Hr	7.1(0.8)	3.0-12.9	4.9-9.2	-	1(2)	17(33)	33(65)	2(4)
2 Hr	6.5(0.6)	3.6-12.9	5.1-8.1	-	1(2)	22(44)	28(54)	-
3 Hr	6.4(0.5)	3.5-13.7	5.2-7.8	-	1(2)	27(53)	23(46)	-
4 Hr	6.0(0.3)	2.3-19.5	5.0-6.8	-	2(4)	23(46)	26(51)	-
5 Hr	6.8(0.8)	4.7-11.2	4.7-8.9	-	-	36(71)	15(29)	-

BG=blood glucose
HD=haemodialysis

Three patients were discontinued from haemodialysis due to severe hypoglycaemia - one after 45 minutes and two after 1 hour of haemodialysis respectively. From their diet histories they had not eaten for the last 2-3 days and one had intractable vomiting and was not retaining any solid or liquid food. These patients were also underweight with BMI of 15.6, 16.8 and 17.7kg/m^2 respectively.

3.2.3: Symptoms of hypoglycaemia during haemodialysis

Seven of the 51 participants presented with symptoms compatible with hypoglycaemia. These symptoms were retrieved from the patients' haemodialysis files where they had been recorded by the clinician in charge of the renal unit of KNH. Hunger and generalized weakness were the symptoms most frequently experienced (Table 3.4).

Table 3.4: Symptoms of hypoglycaemia experienced during haemodialysis (n=7)

Signs/symptoms of hypoglycaemia	**Number of patients* (%)**
Mental confusion	3 (15)
Cold sweats	2 (10)
Generalized body weakness	5 (25)
Hunger	6 (30)
Shaking	4 (20)

*More than one symptom was experienced per patient (See also Table 3.5)

With regard to the cluster of symptoms and the corresponding blood glucose levels of the 7 participants who presented with symptoms of hypoglycaemia (Table 3.5), all of the participants with the exception of participant No.18 experienced at least one hypoglycaemic episode. In 3 participants blood glucose levels remained below normal throughout the dialysis procedure whereas 2 subjects also experienced hyperglycaemic episodes.

Table 3.5: Cluster of hypoglycaemic symptoms in participants (n=7)

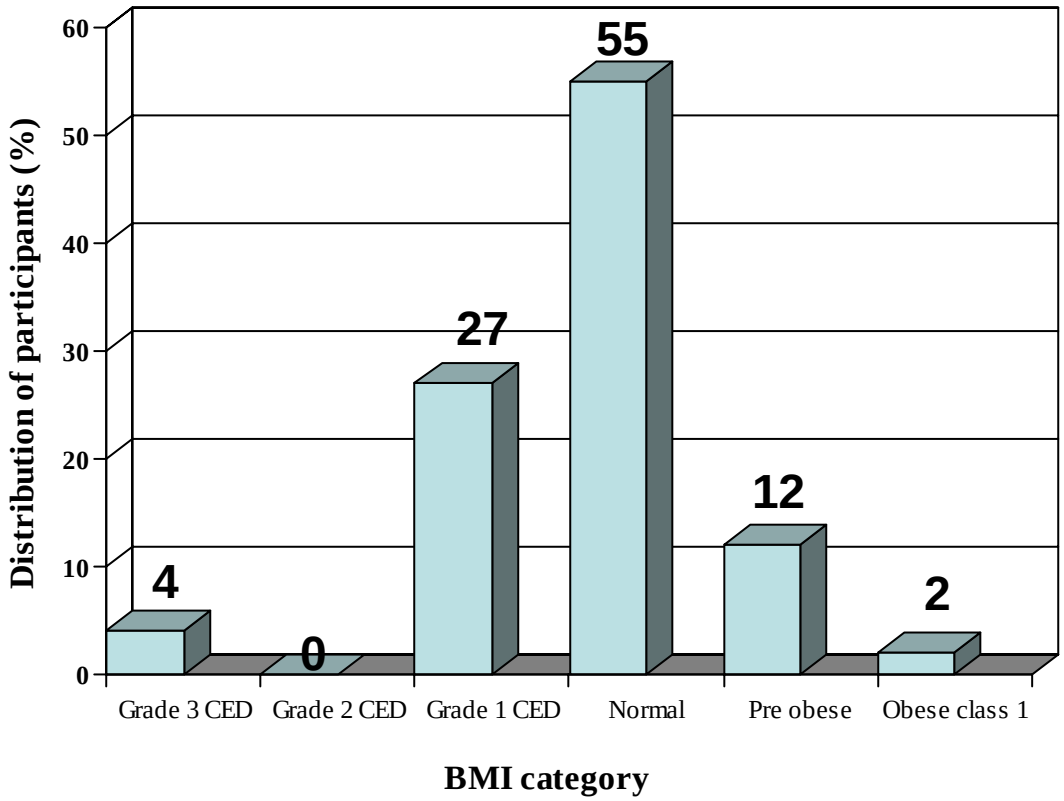
	Cluster of hypoglycaemic symptoms	**Blood glucose level, mmol/L Mean (range)**	**Potential risk factors for hypoglycaemia**
Patient no. 21	Confusion, hunger, weakness, shaking	2.9(2.1-3.5)**	Nausea, vomiting and anorexia
Patient no. 18	Confusion	6.6(5.7-7.7)	Insulin, fasting
Patient no. 13	Weakness,hunger,shaking	2.5(1.9-3.1)**	Anorexia, nausea
Patient no.23	Cold sweats, weakness, hunger	5.1(1.6-10.5)	Poor and inadequate oral intake, hepatic disease, nausea and vomiting
Patient no.2	Confusion, cold sweats, weakness, hunger, shaking	4.6(2.3-6.1)	Poor and inadequate oral intake, nausea vomiting and hepatic disease,
Patient no.38	Weakness, hunger, shaking	1.8(1.6-2.4)**	Insulin
Patient no.8	Hunger, shaking	5.1(3.6-8.3)	Poor appetite

** Dialysis was discontinued

3.3: Description of the Anthropometric Status

3.3.1 Body mass index (BMI) classification

More than 50% of subjects had a BMI between 18.5-24.9kg/m^2 (Figure 3.3). According to the WHO this BMI is normal with average risks.[57] Twenty-seven percent of subjects were classified as grade 1 chronic energy deficient (CED) and 12% as pre-obese. Only a small minority were classified at the extreme ends (CED grade 3 and obesity class 1).



CED - chronic energy deficiency

Figure 3.3: Distribution of Body Mass Index (BMI) of the participants included in the study (n=51)

3.3.2 AFA and AMA Classification

The majority of the participants had AFA (60%) and AMA (88%) below the 5th percentile indicating low fat and muscle compartments (Figure 3.4). A small percentage of subjects had borderline low AFA (22%) and AMA (6 %). A normal fat and muscle compartment was seen in 28% and 6% of the participants. There was no participant above the 90th percentile classification.

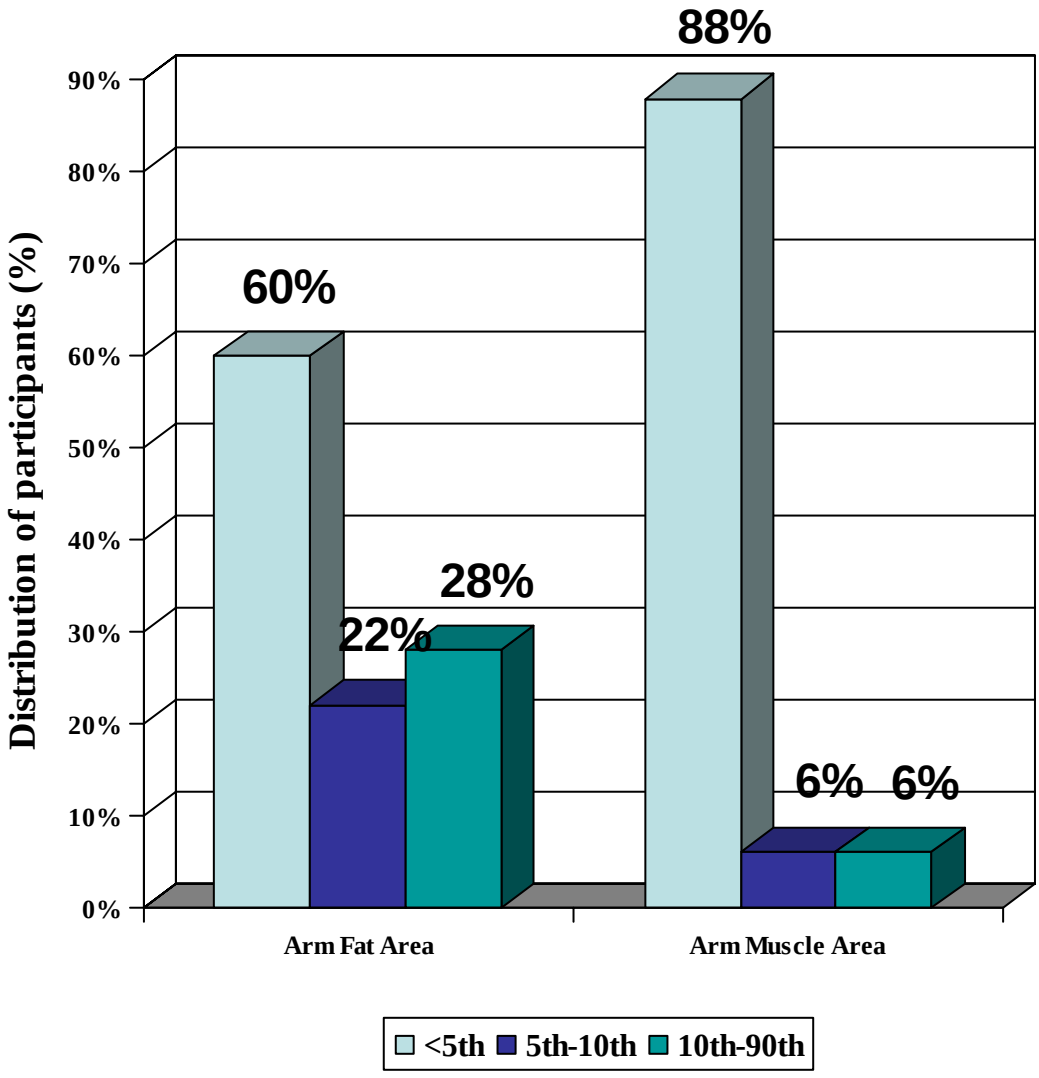


Figure 3.4: Classification of arm fat area and arm muscle area (n=51)

3.3.3 Body Fat Classification

Percentage body fat was classified as “acceptable upper” or “too high” in 53% and 12% of participants (Figure3.5) respectively. In 35% of participants, body fat was classified as “acceptable low” while no participant was classified in the “too low” body fat category.

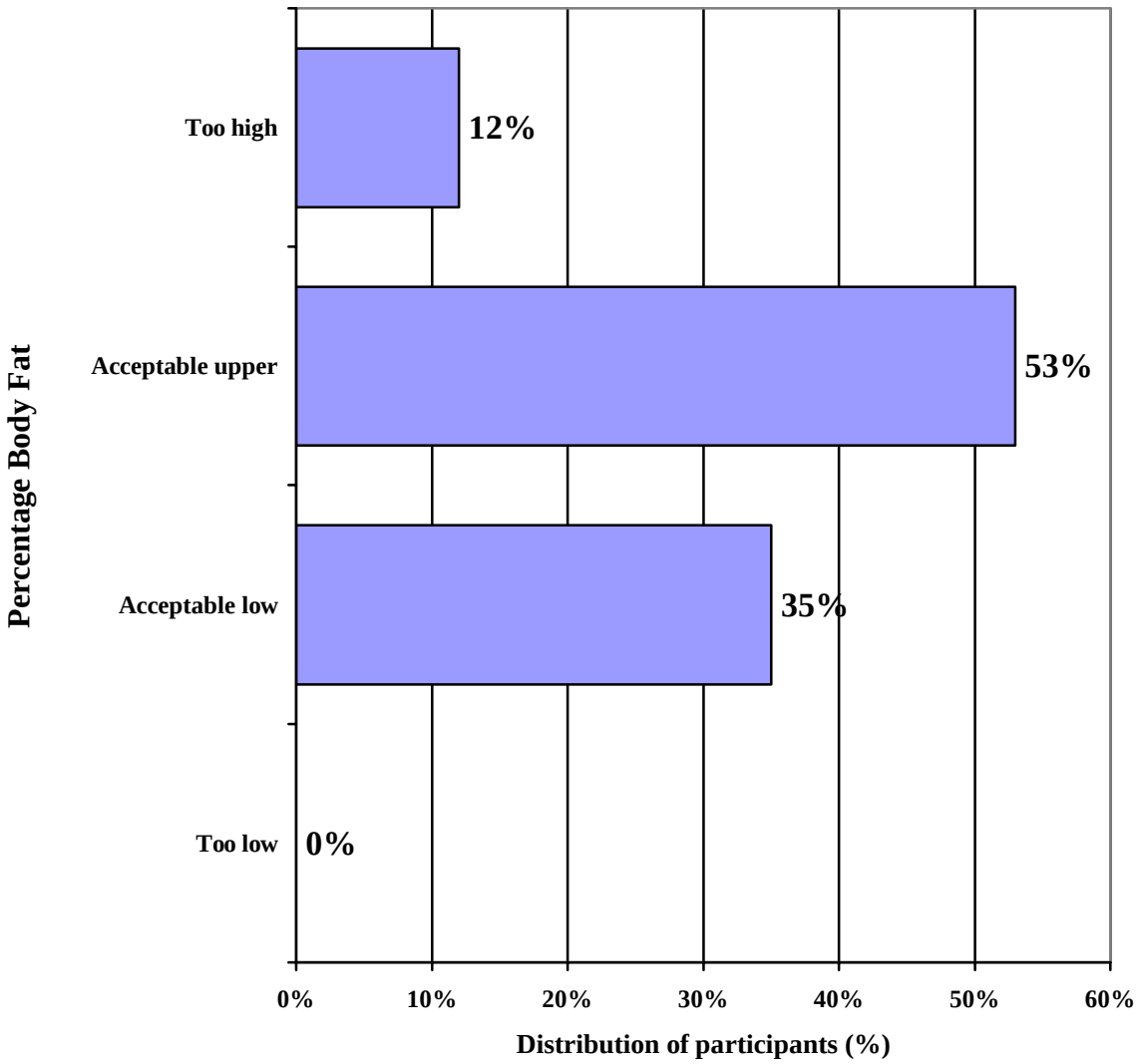


Figure 3.5: Classification of participants’ percentage body fat (n=51)

3.4 Description of Dietary Intake

3.4.1 24-hour recall and QFFQ nutrient intake summary

In general more than 50% of subjects had a low intake of protein, energy, MUFA, and niacin (both 24-hr recall and QFFQ) (Table 3.6). With the exception of PUFA (p=0.18009) and MUFA (p=0.3296), all nutrients showed significant differences when comparing the results of the 24hr recall and the QFFQ.

Table 3.6: Description of the intake of macronutrients

Nutrients	**Recommendation for patients on HD**	**Intake[mean (SD)]**			**% of subjects with intake below recommendation**		**% of subjects with intake above recommendation**	
		24-Hr recall	**QFFQ**	**P value**	**24-Hr recall**	**QFFQ**	**24-Hr recall**	**QFFQ**
Prot (g/kg IBW)	1.2	0.98(0.06)	1.10(0.05)	0.00014	71	69	24	31
Energy (cal/kg IBW)	<60 yrs: 35 >60 yrs: 30-35	19.92(0.96)	20.76(0.9)	0.0073	96	96	4	2
Total Fat (%TE)	20-35	29.39(1.24)	31.17(1.05)	0.00831	16	6	29	20
PUFA * (%TE)	5-10%	9.07(0.4)	9.59(0.4)	0.18009	4	6	37	39
MUFA** (%TE)	10-15%	10.32(0.7)	9.38(0.3)	0.3296	55	63	18	4
SFA*** (%TE)	5-10%	9.78(0.4)	12.25(0.53)	0.00000	2	2	45	69
CHO (%TE)	50-60	51.0(1.54)	47.6(1.3)	0.00000	47	61	20	6

Table 3.7: Description of the intake of micronutrients without supplements

Vitamin	Recommendation for patients on HD	Intake without supplements [mean (SD)]			% of subjects with intake below recommendation		% of subjects with intake above recommendation	
		24-Hr recall	QFFQ	P value	24-Hr recall	QFFQ	24-Hr recall	QFFQ
Pyridoxine (mg/d)	**Males** 1.3 (19-50 yrs) 1.7 (51-70 yrs) **Females** 1.3 (19-50 yrs) 1.5 (51-70 yrs)	 1.82(0.8) 1.21(0.5) 1.42(0.56) 1.0(0.6)	 1.4(1.4) 0.8(0.9) 1.1(1.05) 0.54(1.2)	 0.0008 	 20 73 30 60	 70 87 70 100	 80 27 70 40	 30 13 30 -
Thiamin (mg/d)	**Males**:1.2 **Females** : 1.1	11.54(1.0) 1.4 (0.8)	0.83(0.7) 0.93(0.9)	0.00001	39 40	81 73	61 60	19 27
Riboflavin (mg/d)	**Males**:1.3 **Females**: 1.1	1.4 (0.8) 1.46 (0.7)	0.93(0.9) 0.73(0.7)	0.00000	44 33	86 87	56 67	14 13
Niacin (equivalents/d)	**Males**:16 **Females**: 14	1.5 (0.95) 1.1 (0.6)	1.64(0.9) 1.3 (0.6)	0.0044	100 100	100 100	- -	- -

There were significant relationships between hypoglycaemia and all the selected micronutrients (Table 3.7). The intake of micronutrients was quantitatively derived with the exclusion of the contribution of the supplements to the diet. Micronutrients derived from supplements alone could not be estimated because the supply of supplements was from various external sources as

participants opted to buy supplements externally because they may have been cheaper and negotiable compared to the hospitals' fixed prices.

3.5: Relationship between minimum blood glucose levels and Socio-demographic Variables.

There was no significant relationship between hypoglycaemia and socio-demographic variables (Table 3.8).

Table 3.8: Relationship between minimum blood glucose levels and socio-Demographic/economic variables (n=51)

Independent variables	**Correlation coefficient[a]**	**P-value (chi square test / spearman's correlation[b])**
Gender, male versus female	-	0.46
Age, years	0.12 [b]	0.41 [b]
Marital status classification [c]	-	0.44
Occupation classification [c]	-	0.20
Residence classification [c]	-	0.44
Income classification [c]	-	0.88
Ethnicity classification [c]	-	0.26
Housing-type classification [c]	-	0.40

[a]Correlation coefficient not applicable to chi square tests

[b] Spearman correlation coefficient

[c] Classification as defined in Table 3.1

3.6: Relationship between minimum blood glucose levels and Co-morbid Disease and Haemodialysis factors.

There was no relationship between hypoglycaemia and co- morbid disease or haemodialysis factors (Table 3.9).

Table 3.9: Relationship between minimum blood glucose levels and co-morbid disease and dialysis factors (n=51)

Independent variable	**p-value (Chi square-test)**
Diabetes (yes *versus* no)	0.18
Sepsis/Infection (yes *versus* no)	0.41
Hepatitis B (yes *versus* no)	0.19
Dialysis sessions/week (1 *versus* 2 *versus* 3)	0.94
Dialysate solution (acetate *versus* bicarbonate)	0.12
Hours of HD per session (3 *versus* 4 *versus* 5)	0.27
Duration of HD (months)	0.58 (r = -0.08)*
Blood-flow rate (ml/min)	1.00 (r = 0.00)*

* Spearman correlation coefficient HD – haemodialysis

3.7: Relationship between Hypoglycaemia, Medication and Supplements

Of all the medication/ supplements the patients were receiving, insulin therapy was the only variable that showed a trend for higher risk of hypoglycaemia (Table 3.10; p=0.06)

Table 3.10: Relationship between hypoglycaemia and medication and supplements (n=51)

Independent variable (yes *versus* no)	**p-value(chi square test)**
Oral hypoglycaemics	0.70
Insulin	**0.06**
Beta-Blockers	0.40
Angiotensin converting enzyme inhibitors	0.38
Cardiac channel blockers	0.52
Phosphate- binders	0.26
H2 Antagonists	0.35
Proton Pump Inhibitors	0.40
Vitamin D	0.48
Multivitamin	0.87
Protein supplement	0.81
Erythropoietin	0.76
Folate	0.15
Calcium supplement	0.64
Other supplement	0.55

3.8 Relationship between Minimum Blood Glucose and Nutritional Parameters

Lower vitamin B6 (r=0.30; p=0.03), niacin (r=0.31; p=0.02) and riboflavin (r=0.30; p=0.03) intakes as determined from the QFFQ showed significant relationships with lower blood glucose levels. Lower BMI (r=0.25; p=0.08) and lower protein intake (r=0.26; p=0.07) showed a trend for a higher risk for hypoglycaemia (Table 3.11).

Table 3.11: Relationship between minimum blood glucose levels and nutritional parameters (n=51)

Nutritional parameter	**Spearman's Correlation (r)**	**p-value**
BMI (continuous data)	0. 25	**0.08**
AMA percentile classification	-	0.5836 [a]
AFA percentile classification	-	0.4768 [a]
Protein, g/kg IBW		
24 Hr- recall	0.26	**0.07**
QFFQ proteins g/kg IBW	0.26	**0.07**
Energy, cal/kg IBW		
24 Hr- recall	0.08	0.58
QFFQ energy, calorie/kg IBW	0.1	0.50
Fat intake (low, normal or high)		
24 Hr- recall	-	0.1955 [a]
QFFQ Fats (low, normal or high)	-	0.2888 [a]
Carbohydrates, g/day		
24 Hr- recall	-0.01	0.94
QFFQ carbohydrates g/day	-0.05	0.71
Pyridoxine (B6), mg/d		
24 Hr- recall	0.05	0.72
QFFQ vitamins B6,mg/day	0.30	**0.03**
Riboflavin (B2),mg/d		
24 Hr- recall	0.20	0.17
QFFQ Vitamin B2,mg/day	0.30	**0.03**
Niacin, mg/d		
24 Hr- recall	0.25	0.08
QFFQ Niacin,mg/day	0.31	**0.02**
Thiamin(B1), mg/d		
24 Hr- recall	0.22	0.13
QFFQ Vitamin B1,mg/day	0.14	0.31

[a] Chi square test for categorical data

CHAPTER FOUR: DISCUSSION

4.1 Prevalence of Hypoglycaemia

This study showed that 16% percent of ESRF patients on HD in the Kenyatta hospital, Kenya, experienced hypoglycaemia during the course of HD which is consistent with those of several other studies.[67-74] It should be noted, however, that 8% were already hypoglycaemic at baseline before initiation of HD, for reasons that were not investigated. An example is a recent study done on the blood glucose profile in Nigerian chronic renal patients on HD which reported an even higher incidence of hypoglycaemia during haemodialysis with blood glucose levels <3.9mmol/l in 85% and <2.5mmol/l in 50% of the HD patients. According to the authors of this Nigerian study, the patients were non-diabetics and were not allowed to eat during the 4 hours of haemodialysis presumably to assess the effects of haemodialysis on blood glucose during a fasting state. This may partially explain the large variability in the prevalence of hypoglycaemia between the Nigerian study and the current study where patients continued with their meal sessions as is always the case at KNH.[73]

In the interpretation of the findings of different studies one should keep in mind that different studies have used different hypoglycaemia cut –off points and categorization depending on the model type of the glucometer and other variables like medical factors which may partially explain the variation in results.

In this study participants presenting with hypoglycaemia reported or exhibited confusion, cold sweats, shaking with hunger and generalized weakness as the most common symptoms. Some study participants had to be discontinued from the HD process due to severe hypoglycaemia within the first hour of HD. In these participants factors like hepatic disease, PEM and inadequate oral intake may have contributed to the severity of hypoglycaemia. Though other studies have assessed hypoglycaemia during HD in ESRF patients few have assessed the hypoglycaemic symptoms in cluster hence the lack of reference studies for comparison with these findings.

4.2 Potential Causes of Hypoglycaemia

Potential causes of hypoglycaemia in this study were multifactorial ranging from poor dietary intake, presence of a co-morbid disease, PEM, vomiting, anorexia, fasting, and medication to the use of glucose free dialysis solution.

4.2.1 Dietary intake

None of the macronutrients showed a significant relationship with the prevalence of hypoglycaemic episodes. Dietary intake of most of the major nutrients was below the recommended daily intake among the haemodialysis patients both in the 24 hr recall and QFFQ dietary intake assessment methods. Significant differences between the 24 hr recall and QFFQ may be due to under/overestimation of food intake during the respective periods. It may also have been due to real differences due to different time periods that have been assessed (usual intake *versus* intake in the preceding 24 hours). Among the study population, protein intake as determined by the 24 hour recall and QFFQ was lower than the recommended 1.2g/kg for MHD patients at a mean of 0.97g/kg/d and 1.09g/kg/d respectively. Daily protein intake (DPI) is often reported to be low in MHD patients with the amino-acids and protein losses during haemodialysis averaging between 6-12 grams of amino-acids per haemodialysis increasing the protein demands further. A number of publications have described the mean DPI of individuals treated with MHD to vary from about 0.94 to 1.0 g protein/kg/d.[45,56,61-63] Few studies have directly assessed the dietary protein requirements for MHD patients and no prospective long-term clinical trials have been conducted in which patients are randomly allocated to different dietary protein levels to study the effects of protein intake on morbidity, mortality, or quality of life.[81]

Energy intake was also below the recommended intake of 30-35kcal/kg, with average intakes of 20 kcal/kg in the 24 hour recall and 21kcal/kg in the QFFQ. Energy intake did not have any significant relationship with blood glucose levels as patients were encouraged to eat during haemodialysis as is the usual practice at KNH.

During haemodialysis the intake of high carbohydrate energy giving foods like bread, potatoes, yams, chapattis and arrowroots is very important in the prevention of hypoglycaemia. Patients who presented with hypoglycaemia may have not had a meal prior to the commencement of haemodialysis, as hunger was the symptom reported by most of the patients who suffered hypoglycaemia. One patient however, presented with asymptomatic hypoglycaemia but did not complain of hunger as he had taken his meals prior to the HD process. The short term consequences of hypoglycaemia include generalized weakness, blurred vision and poor concentration but in severe cases it may be fatal.

Renal failure patients require vitamin replacement therapy that addresses the specialized needs of renal failure. Chronic renal failure has an impact on the absorption, metabolic actions and elimination of vitamins in comparison to vitamin handling in persons with normal kidney functions. There are several causes of vitamin derangements in chronic renal failure patients (either a deficiency or an excess) resulting from a restrictive renal diet, the removal of water soluble vitamins by the dialysis procedure, the accumulation of unidentified uraemic toxins and the interaction of medications upon the absorption and activity of specified nutrients.[94] Vitamin B_6 ($p=0.03$), niacin ($p=0.02$) and riboflavin ($p=0.03$) as determined from the QFFQ (but not the 24-hr recall) showed significant positive relationships with minimum blood glucose levels in this study, indicating higher levels of blood glucose with higher intakes of the respective vitamins. Micronutrient losses during haemodialysis, restriction of fruits and leaching of vegetables may have contributed to the significant relationship and between minimum blood glucose levels and vitamin B_6, niacin and riboflavin.

A positive correlation between minimum blood glucose levels and dietary intake of vitamin B_1, known as thiamin, has been expected (but not confirmed) as thiamin serves as a catalyst in carbohydrate metabolism.[94] Rich food sources high in thiamin include liver, heart, and kidney meats, eggs, leafy green vegetables, nuts, legumes, berries, wheat germs, and enriched cereals. Vitamin B_2, or riboflavine, also helps to metabolize carbohydrates[94] and it is abundant in mushrooms, milk, meat, liver, dark green vegetables, and enriched cereals, pasta, and bread. Niacin helps to release energy from nutrients and food sources rich in niacin are chicken,

salmon, tuna, liver, nuts, dried peas, enriched cereals, and dried beans. [94] Vitamin B_6 chief dietary sources include whole grains, bread, liver, green beans, spinach, avocados, and bananas.[94]

Some patients had to be discontinued from haemodialysis due to severe hypoglycaemia. Although the causes and mechanisms of hypoglycaemia in ERSF are multifactorial, it is possible that food intake during haemodialysis was an important and significant predictor of the sustainability of normal blood glucose levels during the haemodialysis process, since diminished glucose availability due to reduction in substrate is thought to be the most important mechanism leading to hypoglycaemia.

Poor appetite, nausea, vomiting, and inadequate dietary intake as complications of the renal disease and the haemodialysis procedure have previously been reported to be the main cause of malnutrition in the HD population.[79-83] Patients presenting with hypoglycaemia as earlier reported may have not had a meal prior to dialysis which may have been the cause of energy deprivation as was noted by the low mean dietary intake of the major nutrients which were below the recommendations of the haemodialysis populations. Indeed malnutrition was present in 50% of participants in the current study which is comparable to reports of 38% and 43.2% malnutrition rates reported by other studies.[79-83]

4.2.2 Anthropometric status

Anthropometrically, BMI was the only index that showed a trend towards a positive relationship with minimum blood glucose levels (the higher the BMI the higher the blood glucose levels) but this was not significant. Over 50% of the participants had a normal BMI and 27% had Grade 1 CED. According to the AMA and AFA values over fifty percent of the participants had low muscle and fat stores. Thirty five percent of the participants had a low percentage body fat but still within the acceptable range as a result of poor/inadequate dietary intake which may have been secondary to anorexia, nausea, poor appetite, depression and economic deprivation.
High BMI in this group may have been partly due to a positive fluid balance since only one patient (2%) was able to have the stipulated 3 sessions of haemodialysis weekly. BMI does not

give a differentiation of the fat and the fat-free mass and with inadequate dialysis patients may have left with positive fluid balance confounding the actual “dry” weight post dialysis. These findings therefore conclude that many patients in this study suffered from PEM.

4.2.3 Other

Insulin injections showed a higher trend for risk of hypoglycaemia. Patients who were diabetic and on insulin injections may have avoided carbohydrate foods and were therefore not able to replace the glucose losses during haemodialysis though this was not assessed in the diabetic participants in this study. There were no significant relationships between minimum blood glucose levels and the presence of co-morbid disease or infections.

4.2.3.1 Use of glucose free dialysate solution

The use of glucose- free dialysate for HD patients may have contributed to the common occurrence of hypoglycaemia during dialysis. All subjects in this study were dialysed using a glucose-free dialysate; hence, the contribution of glucose-free dialysate towards hypoglycaemia could not be assessed. Other studies, however, have indicated that hypoglycaemia is common during HD and is mostly seen in patients on glucose free dialysis solution.[73-77] Jayme and co-workers[96] studied both diabetics and non-diabetics on HD and concluded that asymptomatic hypoglycaemia was frequent when glucose free dialysis solution was used. The mean plasma glucose level was significantly higher (138.2 + 96.3 vs. 120.7+ 75.9: p=0.0392) when 90mg/dl of glucose solution was added to the dialysis solution compared to glucose free dialysate. Diabetic patients were most affected.

Glucose balance during HD is dependent on the glucose concentration of the substitution fluid. The use of glucose-free solutions does not contribute to an improvement in the metabolic control of patients with impaired glucose utilization, as has been falsely assumed. Glucose free dialysate results in a glucose loss accounting for 40 to 80 g/day depending on the filtration volume, which must be compensated for by an activation of endogenous gluconeogenesis mainly from amino acids, thus promoting protein breakdown. Glucose loss during the use of glucose-free solutions

must be considered when evaluating the energy balance of the patient, and it must be replaced by nutritional therapy.[71], [73, 77]

Alberto and co-workers[78] also studied HD associated protein catabolism with and without glucose in the dialysis fluid among eight patients on HD and concluded that addition of glucose to the dialysis fluid may help the energy balance. It however did not appear to reduce the negative effects of HD on protein metabolism.

4.2.3.2 Socio-economic factors

From an economic perspective, participants in the present study may have been having inadequate food intake due to the following reasons. Firstly, almost half of them were not employed and may have adapted to other forms of meeting their basic needs like food by either selling the assets they had acquired during the employment period, or receiving rations from their families, friends and other humanitarian sectors. Due to this economic deprivation, KNH management and the Government of Kenya was offering credit facilities to these patients to be able to meet the haemodialysis treatment. Secondly, over half of the study population lived in the urban centre for proximity and cost effective purposes since dialysis centres are located in the urban cities of Kenya. Patients therefore had to rent houses to be able to access the dialysis facilities which may have resulted in the reduction of the food budget to be able to live within the urban set-up.

4.3 Significance of the Study

The study findings showed that hypoglycaemia is not uncommon among patients on haemodialysis in the renal- unit of KNH and that hypoglycaemia should receive a higher attention from the renal team than is normally the case. Both symptomatic and asymptomatic symptoms of hypoglycaemia were reported with the majority of the patients exhibiting hypoglycaemic symptoms reporting that they had not eaten before dialysis. Some potential causes of hypoglycaemia that were identified in this study that need to be considered in future management include poor/inadequate dietary intake of vitamins (niacin, thiamin and vitamin B6)

and protein, a lower BMI, the use of insulin during haemodialysis (for diabetics) as well as the use of glucose free dialysis solution. Proper management and prevention of hypoglycaemia will benefit patients on HD since hypoglycaemia may be fatal if untreated. In general, such measures may improve dialysis outcome which may reduce morbidity and mortality resulting from prolonged hypoglycaemia, especially in the asymptomatic cases.

These study findings will also alert the clinicians managing renal patients on haemodialysis regarding the need to advise patients on how to prevent the occurrence of hypoglycaemia during the haemodialysis process. Secondly, the findings will enlighten health care providers especially nutritionists/dieticians managing the haemodialysis population to appropriately advise the patients on the appropriate foods to take and the correct number of portions during the haemodialysis process. However, these findings should be seen as preliminary and need to be confirmed by additional large studies.

4.4 Limitations of the Study

The study had several limitations:

1. The study was carried out only on patients with end-stage renal failure who had been on dialysis for at least 3 months and who could stand on the weighing scale and against a mounted height chart. Patients who did not meet this inclusion criterion were excluded from the study even though they were still on haemodialysis. The study therefore cannot give a proper presentation of all the patients on haemodialysis.

2. The study was carried out at Kenyatta National Hospital (KNH), and the sequence of haemodialysis and dialysis procedures used in Kenyatta National Hospital could be totally different from that used in other haemodialysis centers. Therefore the findings of this study should not be generalized to other haemodialysis units.

3. Participants were studied once only, hence it is uncertain how reproducible the results are.

4. The sample size was small, resulting in a relatively small number of patients presenting with hypoglycemia which were not enough for more powerful statistical analysis.With larger numbers it might have been possible to identify more risk factors for hypoglycemia.

5. The study did not assess the influence of the patient's access routes or dialysis prescription on blood glucose levels. It will be important for future studies of this nature to consider them for more detailed analyses.

6. The study did not include the waist and hip circumference measurements for the assessment of central obesity. These measurements may be important in predicting the patient's adiposity status, and should be considered in future studies. Waist and hip circumference may be useful especially in poor economic settings since they require cheap tools (tapes) which are easy to use in a very short time.

7. Available data in this study did not allow the assessment of a dose-response relationship between medication and minimum blood glucose. This should be considered in future studies where patients are followed up for a longer time.

8. Future studies should assess the presence of hypoglycaemic symptoms by asking the participants at each venesection, rather than relying on the physician's or nursing notes.

CHAPTER FIVE

SUMMARY, CONCLUSION AND RECOMMENDATIONS

5.1 Summary and Conclusion

The main conclusion is that a 16% prevalence of hypoglycaemia was found in this study, with 8% already being hypoglycaemic at baseline, before initiation of HD. Most patients presenting with hypoglycaemia were symptomatic and 3 out of the 51 patients had to be discontinued from HD due to severe hypoglycaemia. Malnutrition was also present among the study population with 60 % and 80% of the participants presenting with AFA and AMA values below the 5th percentile respectively.

The potential risk factors that were identified include poor/inadequate food intake prior to the start of dialysis, low intake of niacin, thiamin, vitamin B6 and protein, low BMI, use of insulin, and glucose free dialysate.

During the haemodialysis process, those patients who had not eaten before HD developed hypoglycaemia and were peripherally injected with a high concentration of intravenous glucose solution. Patients presenting with severe hypoglycaemia were discontinued due to the severity of the condition.

5.2 Recommendations

Based on the results from this study it is recommended that:

- During haemodialysis patients should be encouraged to eat small frequent meals to prevent the occurrence of hypoglycaemia. It's also important that all patients who are on parenteral and enteral feeds continue to be fed as per their feeding regimes so that they may not become hypoglycaemic during the haemodialysis process, or be dialysed using glucose containing solutions
- All nurses should be trained on signs and symptoms of hypoglycaemia so that they can be able to educate the patients adequately on how to identify these signs and symptoms as well as how to prevent hypoglycaemia.

- ❖ All patients should undergo routine nutritional assessment to identify those who are at risk of malnutrition and interventions sought adequately.
- ❖ All patients on regular HD should be encouraged to eat meals and snacks provided by the renal-unit during sessions of HD to prevent hypoglycaemia.
- ❖ A protocol specific for each renal unit should be formulated.
- ❖ All patients should be adequately monitored for hypoglycaemia during HD. Patients presenting with cold sweats, blurred vision, and shaking should have a random blood glucose test and given intravenous 50 % dextrose to restore normal vital signs followed with a snack.
- ❖ All patients with diabetes especially those on insulin should be discouraged from taking/injecting their medication before dialysis or consideration must be given for a reduction of the dosage, due to the glucose losses associated with HD. They should also be encouraged to carry sweets in case they experience any of the hypoglycaemic signs during HD.
- ❖ The renal-unit management team should consider the use of glucose containing haemodialysis solutions in all patients to prevent hypoglycaemia.

5.3 Recommendations for Further Research

1. A similar prospective study should be replicated in other government hospitals, private hospitals and private dialysis centres in Kenya and on larger sample sizes.
2. Further studies could be done to explore the prevalence of hypoglycaemia in acute renal failure on HD since it’s more catabolic and severe as compared to chronic renal failure.
3. A similar study would be necessary for those patients less than three months on haemodialysis with morbidity complications.
4. Comparison of the effects of glucose and non-glucose containing solutions in the haemodialysis population should be investigated, especially in limited resource settings.

LIST OF REFERENCES

1. Hirth RA, Turenne MN, Woods JD, et al.Vascular access in newly treated U.S. haemodialysis patients: Predictors and trends. J Am Med J Ass1996; 276:1303-1308.

2. Rettig R and Levinsky NG. Kidney Failure and the Federal Government. Washington, DC: National Academy Press, 1991.

3. Port FK, Wolfe BA, Mauger EA, et al. Comparison of survival probabilities for dialysis patients vs. cadaveric renal transplant recipients. Am Med J Ass 1993; 270 (11):1339-1343.

4. Shinzato T, Nakai S, Akiba T, Yamazaki C, et al. Survival in long term haemodialysis patients: Results of the annual survey of the Japanese society for dialysis therapy. Nephro Dial Transplant 1997; 12:884-888.

5. Collins AJ, MA JZ, Umen A, et al. Urea index (Kt/V) and other predictors of haemodialysis patient survival. Am J Kidney Dis 1994; 23:272-282.

6. Carlson DM, Duncan DA, Naessens JM, et al. Hospitalization in dialysis patients. Mayo Clin Proc 1984; 9:769-775.

7. Churchill DN, Taylor DW, Cook RJ, et al. Canadian haemodialysis morbidity study. Am J Kidney Dis. 1992; 3:214-234.

8. Valderrabano F, Berthoux F, Jones E, et al. Report on management of renal failure in Europe, XXV, 1994: End stage renal disease and dialysis report. Nephro Dial Transplant 1996; 11 (Suppl 1):20-21.

9. Cristol JP, Bosc JY, Badiou S, et al. Erythropoietin and oxidative stress in haemodialysis: Beneficial effects of vitamin E supplementation. Nephro Dial Transplant 1997; 12:2312-2317.

10. Ifudu O, Dawood M, Homel P, et al. Excess morbidity in patients starting uremia therapy without prior care by a nephrologist. Am J Kid Dis 1996; 28:841-845.

11. Levin NW. Dialyzer reuse. A currently acceptable practice. Semin Dial 1993; 7:1232-1242.

12. Wolfson AB, Singer I. Hemodialysis-related emergencies - Part 1. J Emerg Med 1987 Nov-Dec; 5(6): 533-43.

13. Parker TF 111, Wingard RL, Husni L, et al. Effect of the membrane biocompatibility on nutritional parameters in chronic haemodialysis patients. Kidney Int 1996; 49:551-556.

14. USRDS. ADR. Bethesda, MD: NIH, NIDDK, April 1997. Available: http://www.usrds.org. Accessed: 26 February 2007: chapter 21, p.49-60

15. Hylander B, Barkeling B, Rossner S. Eating behaviour in continous ambulatory peritoneal dialysis and haemodialysis patients. Am J Kidney Dis 1992; 20:592-597

16. USRDS. ADR. Bethesda, MD: NIH, NIDDK, April 1998; Table G-19. Available: http://www.usrds.org. Accessed: 17 July 2005: chapter 24, p. 774-778

17. USRDS. ADR. Bethesda, MD: NIH, NIDDK, April 1998; Appendix, Table G-43. Available: http://www.usrds.org. Accessed: 12 March 2006: chapter 17, p. 153-157

18. Pastan S, Bailey J. Dialysis therapy. N Engl J Med 1998; 338(20): 1428-1437.

19. Keshaviah PR, Nolph KD. Protein catabolic rate calculations in CAPD patients. ASAIO Trans 1991; 37:400-402

20. Brenner BM, Rector FC Jr, eds. The Kidney. 6th ed. WB Saunders, Oxford. 1999; chapter 4: 453-460.

21. Ifudu O. Care of patients undergoing haemodialysis. N Engl J Med 1998; 339(15): 1054-1062.

22. K/DOQI Clinical Work Group. Clinical practice guidelines for chronic kidney disease. Am J Kidney Dis. 2006; 39(Suppl 1):S1-S266.

23. Campoy, S. Early renal insufficiency for primary care. Program and abstracts of the national conference for Nurse Practitioners Session 309, Baltimore, Maryland. 2001. November 7-10.

24. Consensus Development Conference panel morbidity and mortality of renal dialysis: a NIH consensus conference statement. Ann Intern Med; 1994. 121:62-70.

25. Lancaster L ed. Core Curriculum for Nephrology Nurses. 4th ed. Pitman, American Nephrology Nurses Association, New York 2001; vol 5, p. 128-140.

26. Eknoyan G, Lameire N, and Barsoum R, et al. The burden of kidney disease: Improving global outcomes. Kidney Int 2004; 66:1310-1314.

27. Kayima, J. Consultant Physician and Nephrologist, Senior Lecturer, Nairobi University, Kenya: Personal interview, 4 May. 2007.

28. Johnson CA, Levey AS, Coresh J, Levin A, Lau J, et al . Clinical practice guidelines for chronic kidney disease. Part 1. Definition, disease stages, evaluation, treatment and risk factors. Am Fam Physician 2004; 70:869 - 876

29. Levey AS. Measurement of renal function in chronic renal disease. Kidney Int 1990; 38:167-184.

30. Brown SCW, O'Relly PH. Iohexol clearance for the determination of glomerular filtration rate in clinical practice. Evidence for a new gold standard. J Urol 1991; 146: 675-679.

31. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron 1976; 16:31-41.

32. National Kidney Foundation Kidney Disease Outcomes Quality Initiative. Available: http://www.kidney.org/profession/doqi/index.cfm.2001. Accessed: 2005, 20 August.

33. Eknoyan G, Hostetter T, Barkris GL, et al. Protenuria and other markers of chronic kidney disease: A position statement of the National Kidney Foundation (NKF) and the National Institute of Diabetes Digestive and Kidney Diseases (NIDDK). Am J Kidney Dis 2003; 42:617-622.

34. Ter Wee PM. Initial management of chronic renal failure. In: Cameron S, Davidson AM, and Grunfeld JP et al. (Eds). Oxford Textbook of Clin Nephrol 1992; 1173-1195.

35. US Renal Data Systems. Available: http://www.usrds.org. Accessed: 5 July 2005: chapter 13, p. 1225-1230

36. KNH Department of planning and Data unit. Consulted: 24 July 2007.

37. Tierney LM, MCPhee SJ, Papadakis MA. Current medical Diagnosis and Treatment. New York: Mc Graw Hill. 2001.

38. Levey AS, Eckardt K, Tsukamoto Y, et al. Definition and classification of chronic kidney disease: A position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int 2005; 17: 2089-2100.

39. Kausz AT, Levey AS. The care of patients with chronic kidney disease: What we must do and who should do it? J Gen Intern Med 2001; 17:658-662.

40. K/DOQI Clinical Work Group. Quality initiative clinical practices guidelines. Am J Kidney Dis 1997; 30 (Supp 2 and 3): 967-1198

41. Levey AS, Greene T, Beck G, Caggiula AW, Kusek JW, et al. Dietary protein restriction and the progression of chronic renal disease: What have all the results of the MDRD study shown? J Am Soc Nephrol 1999; 10: 2426 - 2439

42. Walser M. Does prolonged protein restriction preceding dialysis lead to protein malnutrition at the onset of dialysis? Kidney Int 1993; 7: 1139–1144

43. Coresh J, Walser M, Hill S. Survival on dialysis among chronic renal failure patients treated with a supplemented low-protein diet before dialysis. J Am Soc Nephrol 1995; 6: 1379–1385

44. Owen WFJ, Lew NL, Liu Y, Lowrie EG, et al. The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing hemodialysis. N Engl J Med 1993; 329: 1001–1006.

45. K/DOQI Nutrition Work Group. Clinical practice guidelines for nutrition in chronic renal failure. New York, National Kidney Foundation; 2001.

46. The seventh report of the Joint National Committee on the prevention, detection, evaluation and treatment of high blood pressure: JNC-7 report. JAMA 2003; 289:2560-2570.

47. Ruggenenti P, Perna A, Remuzzi G, and et al. On the behalf of the GISEN Group: renal function requirement for dialysis in chronic nephropathy patients on long-term ramipril; REIN follow-up trial. Lancet 1998; 352:1252-1256.

48. K/DOQI Clinical Work Group. Clinical practice guidelines for managing dislipidaemias in chronic kidney disease. Am J Kidney Dis.2003; 41(suppl 3):S1-S92.

49. Fadde GZ, Haffar SM, Perna AF, et al. On the mechanism of impaired insulin secretion in chronic renal failure. J Clin Invest 1991; 87:255-261

50. Murphy SW, Palfrey PS. Screening for cardiovascular disease in dialysis patients. Curr. Opin Nephrol Hypertens 1996; 5:532-540.

51. Tonelli M, Bohm C,Pandeya S, et al. Homocysteine lowering with folic acid and B vitamins in vascular disease. N Engl J Med 2006; 39: 1567-1577.

52. Nissenson AR, Fine RN, Gentile DE (eds). Clinical Dialysis, 3rd ed. Appleton & Large, Norwalk Connecticut, 1995, chapter 5:67-76.

53. National Kidney Foundation. Clinical practice guidelines: 2000 updates; Executive summaries; haemodialysis adequacy, peritoneal dialysis adequacy, vascular access, anaemia. New York, National Kidney Foundation; 2000.

54. Cunningham J. Parathyroid pathophysiology in Uraemia. Nephrol Dial Transplant 1996; 11:S106- S110.

55. Pareitt AM. The hyperparathyroidism of chronic renal failure: a disorder of growth. Kidney Int. 1997; 52: 3-9.

56. Zarazaga A, Garina de Lorenzo L, Garcia Luna P et al. Nutritional support in chronic renal failure: systematic review. Clin Nutr 2001; 20:291-299.

57. Block GA, Hulbert-Shearon TE, Levin NW, et al. Association of serum phosphorus and calcium phosphate product with mortality risk in chronic haemodialysis patients: A national study. Am J Kidney Dis 1998; 31:607-617.

58. Cunningham J. New Vitamin D analogues for osteodystrophy in chronic kidney disease. Paediatr Nephrol 2004; 19:705-708.

59. K/DOQI Clinical Work Group. Clinical practice guidelines for bone metabolism and disease in chronic kidney disease. Am J Kidney Dis 2003; 38:1358-1360

60. Beto JA, Vinod K. Medical nutrition therapy in chronic kidney failure: intergrating clinical practice guidelines. J Am Diet Assoc 2004; 66: 652-670.

61. Beto JA. Which diet for which renal failure: Making sense of the options. J Am Diet Assoc 1995; 95:898-903.

62. Toigo G, Aparicio M, Attrian P, et al. Expert working group report on nutrition in adult patients with renal insufficiency (part 1 of 2). Clin Nutr 2000; 19:197-207.

63. Mitch WE, Klahr S. Handbook of Nutrition and the Kidney. 4th ed. Philadelphia, PA: Lippincott Williams and Wilkins. 2002; chapter 3: 24-28.

64. Saxena AK, Panbotra BR. Herbal remedies: renal tragedies. Swiss Med Wkly 2003; 133:188-189.

65. Held PJ, Port FK, Wolfe RA, et al. The dose of haemodialysis and patient mortality. Kidney Int 1996; 50:550-556.

66. Pkes, Cunovic D. Spontaneous hypoglycaemia associated with renal failure-a preventable life threatening complication. Acta Med Croatica 1994; 48:207-10.

67. Zarate A, Gelfand M, Novello An, et al. Propranolol associated hypoglycaemia in patients on maintenance haemodialysis. Int J Artif Organs 1981; 6:130-4.

68. Jackson MA, Holland MR, Nicholas J, et al. Occult hypoglycaemia caused by haemodialysis. Clin Nephrol 1999; 51: 242-7.

69. Hakim RM, Held PJ, Stannard DC, et al. Effect of dialysis membrane on mortality of chronic haemodialysis patients. Kidney Int 1996; 50: 566-570.

70. Campbell PJ, Gerich JE. Mechanisms for prevention, development and reversal of hypoglycaemia. Adv Intern Med 1988; 33:205.

71. Ibrahim MA, Labib B, Sallam B, et al. Effect of dialyzer reprocessing on glucose homeostasis. Haemodialysis International. 2005; 9 (1): 79

72. Kaplan AA, Halley SE, Lapkin RA, et al. Dialysate protein losses with bleach processed polysulphone dialyzers. Kidney Int 1995; 47:573-578.

73. Agbo J A, Semhar BA. Prevalence of hypoglycaemia in diabetics on haemodialysis. African Med J 2004; 3:132-134

74. Takahashi A, Kubota T, Shibahara N, et al. The mechanism of hypoglycaemia caused by haemodialysis. Clin Nephrol 2004; 62: 362-8.

75. Ikizler TA, Wingard RL, Hakim RM. Nutrition in end-stage renal disease. Kidney Int 1996; 50:343-357.

76. Leypoldt JK, Cheung AK, Carrol CE, et al. Effect of dialysis membranes and middle molecule removal on chronic haemodialysis patient survival. Am J Kidney Dis 1999; 33:349-355.

77. Wathen RL, Keshaviah P, Hommeyer P, et al. The metabolic effects of haemodialysis with and without glucose in the dialysate. Am J Clin Nutr 1978; 31:1870-1875.

78. Gutierrez A, Bergstrom J and Alvestrand A. Haemodialysis-associated protein catabolism with and without glucose in the dialysis fluid. Kidney Int 1994; 46:814-822.

79. Linda M. Malnutrition: Detection and prevention. Proceedings for the ISPD; the V111th congress of the ISPD, Seoul Korea, 23-26 August. 1998. Abstract no. 2.

80. K/DOQI Nutrition Work Group. Clinical practice guidelines for nutrition in chronic renal failure. Am J Kidney Dis 2000; 35 Suppl (2): 887-890.

81. Sehgai AR, Leon J, Soinski JA. Barriers to adequate protein nutrition among haemodialysis patients. J Ren Nutr 1998; 8:179-187

82. Pernnigton CR. Disease-associated malnutrition. Postgrad Med J 1998; 74:65-71.

83. Sullivan DH. The role of nutrition in increased morbidity and mortality. Clin Geriatr Med 1995; 11:661-74.

84. Aparicio M, Cano N, Chaveau, et al. nutritional status of haemodialysis patients' French national cooperative study. Nephrol Dial Transplant 1999; 14:1679-1686.

85. Blummenkrantz MJ, Kopple JD, Gutman YK. Methods for assessing nutritional status of patients with chronic renal failure. Am J Clin Nutr 1980; 33:1567-1585.

86. WHO Expert Committee. Physical Status: The use and interpretation of anthropometry. WHO Technical Report series. Geneva, World Health Organization. 1995.

87. WHO Technical Report series. The Problem of Overweight and Obesity. In Obesity: Preventing and Managing the Global Epidemic. Report of a WHO Consultation. Geneva, WHO, 2002.

88. Frisancho AR. New norms of upper limb fat and muscle areas for assessment of nutritional status. J Clin Nutr.1981; 34:2540-2556

89. Lee RD and Niemann DC. Nutrition Assessment. 3rd ed. London, McGraw Hill:Grune & Stratton 2003, Chapter 6, p. 230-252

90. Durnin JVGA, Womersley J. Body fat assessment from total body density and its estimation from skinfold thickness. Brit J Nutr 1974; 32:77-97.

91. Sehmi JK. National food composition tables and the planning of satisfactory diets in Kenya. E A Med J 1993; 1: 51-150.

92. KNH-Renal unit laboratory. Blood glucose reference normality values: 2005.

93. Statistica Stat soft. Inc. 2004. Data analysis software system (version 7). Available at www.statsoft.com.

94. Durn OJ and Clarke V.A. Applied Statistics: Analysis of Variance and Regression.1974.John Wily and Sons, New York, chapter 10, p. 300-315

95. Makoff R. Appropriate vitamin therapy for dialysis patients. Semin Dial 1997; 10:272-277.

96. Jayme EB, Aline S, Diego M, et al. Glucose-added dialysis fluid prevents asymptomatic hypoglycaemia in regular haemodialysis. Am J Kidney Dis 2007; 24:254-266

APPENDIX 1: BUDGET

DESCRIPTION OF EXPENSES	APPROPRIATE COST (KENYA SHILLING)
Precision QID glucometer	150000
Blood glucose electrodes	50000
Digital weighing scale	6000
Height meters / charts	4000
MUAC Tapes	2000
Stationery	3000
Statistician	1500(per hour)
Research Assistant's fee	5000
Laboratory tests	100000
Photocopies and printing	10000
Total	330000

APPENDIX 2: WORK SCHEDULE

Aspect of research	Appropriate amount of time needed	Date
Data collection	2months	June-July
Data analysis	1month	August
Report of results	2months	September-October
Final adjustments / additional time needed.	1month	November

APPENDIX 3: RESEARCH INSTRUMENTS

ADDENDUM 1

PART. A

SOCIO-DEMOGRAPHIC, ECONOMIC, AND MEDICAL HISTORY QUESTIONNAIRE

Patient: No……

ID. No ……..

1. Age in years____

2. Sex

1= [] Female 2= [] Male

3. Marital Status

1= [] Single 2= [] Married 3= [] Divorced 4= [] Widowed

4. Occupation

1= [] Teacher 2= [] Farmer 3= [] Doctor 4= [] Nurse 5= [] Student

6= [] Businessman/woman 7= [] Not employed

5. Residence

1= [] Urban 2= [] Peri-urban 3= [] Rural

Ethnicity

7. Income (Ksh per month)

8. Housing type

1=permanent 2=semi-permanent 3=temporary

PART. B

MEDICAL HISTORY

1. Primary Diagnosis.

1= [] Diabetes 2= [] Hypertension 3= [] Nephritis 4= [] Cardiovascular disease

5= [] Gout 6= [] any other (specify)……..

2. Co-morbid disease

1= [] Liver disease 2= [] Infections 3= [] Cancer 4[] Diabetes Mellitus

5= [] other (specify)……

3. Haemodialysis data

a. Period of haemodialysis (months) _____

b. Dialysate solution

1= [] Bicarbonate solution (glucose free)

2= [] Acetate solution (glucose free)

c. Duration of Dialysis in hours

d. Blood flow rate (ml/min)

e. Dialysate flow rate (ml/min) _____

f. Membrane type

1= [] Diacetate

2= [] Polysulfone

3= [] other (specify)

g. Dialysis sessions per week

1= [] Once

2= [] Twice

3= [] Thrice

4. Medication

Hypoglycemic

[] Oral hypoglycemic

[] Insulin (specify)

Anti-Hypertensives

[] ACE Inhibitors

[] Angiotensin11 Receptor Blockers (ARBs)

[] Cardiac Glycosides

Anti-Ulcer

[] H2 Antagonist

[] Proton Pump Inhibitors (PPIs)

[] Phosphate binders

[] Lipid lowering agent

[] HBV vaccine

[] Folate

[] Erythropoietin Hormone (EPO)

[] Any other (specify)……..

5. Supplementation

[] Calcium [] Vitamin D

Name (s) Name (s)

Composition Composition

Dose Dose

Frequency Frequency

[] Protein [] Multivitamin

Name (s) Name (s)

Composition Composition

Dose Dose

Frequency Frequency

[] Any other (specify)…….

Name (s)

Composition

Dose

Frequency

6. Alternative supplements (please state the dose and the frequency and any special method used during preparation)

[] Kamirithu herbs

Name (s)

Dose

Frequency

Method of preparation

[] Herbal tea (s)

Name (s)

Dose

Frequency

Method of preparation

[] GNLD products

Name (s)

Dose

Frequency

Method of preparation

[] Tianshi products

Name (s)

Dose

Frequency

Method of preparation

[] Swissgarde products

Name (s)

Dose

Frequency

Method of preparation

[] Any other (please specify as below)

Name (s)

Dose

Frequency

Method of preparation

ADDENDUM 2

ANTHROPOMETRIC ASSESSMENT

ID.NO:							**Date:**					
Weight (kg)				**Height (m)**				**BMI(kg /m2)**	**MUAC (cm)**			
Wt 1	Wt 2	Wt 3	Av. wt	Ht 1	Ht 2	Ht 3	Av. Ht		Muac 1	Muac 2	Muac 3	Av. Muac

Skinfold- thickness

Triceps(mm)				**Biceps(mm)**				**Sub-scapular(mm)**				**Supra-iliac(mm)**			
Mmt 1	Mmt 2	Mmt 3	Av. mmt	Mmt 1	Mmt 2	Mmt 3	Av. mmt	Mmt 1	Mmt 2	Mmt 3	Av. mmt	Mmt 1	Mmt 2	Mmt 3	Av. mmt

*Mmt-Measurement

ADDENDUM 3

24-Hour Recall Method

ID.NO		**Date:**		
PREVIOUS EATEN FOODS	**Description of food item**	**Cooking method used**	**Amount Eaten (Household measure)**	**Amount Eaten (GRAMS/DAY**
Early breakfast Brown bread White bread Arrowroots Sweet-potatoes Porridge Cake Chapatti Other (specify)				

Breakfast Brown bread White bread Arrowroots Sweet-potatoes Porridge Cake Chapatti Other (specify)				

Lunch Beef stew Fried beef Roast beef Chicken stew Fried chicken Roast chicken Stewed beans Stewed green-grams Ugali Chapatti boiled rice Fried rice Mashed potatoes Matoke Steamed cabbages Fried cabbages Fried kales Steamed kales vegetables				

Fried traditional vegetables Steamed traditional Other (specify) Supper/Dinner Beef stew Fried beef Roast beef Chicken stew Fried chicken Roast chicken Stewed beans Stewed green-grams Ugali Chapatti boiled rice Fried rice Mashed potatoes Matoke				

Steamed cabbages Fried cabbages Fried kales Steamed kales Fried traditional vegetables Steamed traditional vegetables Other (specify Snacks Biscuits Cakes Bread Pancakes Sweets Other (specify)				

Beverages Tea Coffee Soya Milo Drinking chocolate Other (specify)				
Fruits Mangoes Oranges Tangerines Pawpaw Apples Grapes Watermelon Ripe bananas Other (specify)				

Alcohol Beer Spirit Wine Traditional brew Other (specify)				
Dairy Fresh milk Yoghurt Mala Butter Cheese Ghee Other (specify)				

ADDENDUM 4

QUANTITATIVE FOOD FREQUENCY QUESTIONNAIRE (QFFQ).

ID.NO				**Date:**				
FOOD ITEM	**HOW OFTEN?**							
CEREALS AND GRAINS PRODUCTS.	Cooking method	Per day	Per week	Per month	Per year	Rarely /never	Portion size	Amount in g/day
Brown bread								
White bread								
Sweet bread								
Bread(fried with an egg)								
Cornflakes								
Macaroni								
Maize meal								
Maize(white on cob &toasted)								
Rice								
Sorghum(Red)								
Weetabix								
Wheat flour(Whole meal)								
Wheat flour (Home baking)								
Other (specify)								
STARCHY ROOTS & TUBERS								
Arrow root (boiled)								
Cassava(boiled)								
Potato sweet(boiled)								
Other (specify)								
GRAIN LEGUMES & LEGUME PRODUCTS								
Green gram(boiled)								

Beans(dry)								
Other(specify)								
NUTS								
Coconut (fresh)								
Groundnut a).roasted (unsalted) b)Roasted & salted								
Other (specify)								
VEGETABLES & THEIR PRODUCTS								
Cabbage (boiled)								
Kale (sukuma wiki)								
Lettuce								
Managu (Nightshade)								
Ndania (Coriander leaves)								
Spinach (boiled)								
Brinjals(Egg plant)								
Hoho (capsicum)								
Onion (Red)								
Pumpkin (raw with peel)								
Pumpkin (Raw without peel)								
Other (specify)								
FRUITS								
Apple								
Avocado								
Bananas raw (boiled)								
Bananas ripe								
Dates (dried)								

Grapes (pale green variety)								
Lemon juice								
Lime juice								
Mango Ripe								
Orange fruit								
Orange juice								
Pawpaw								
Passion fruit juice								
Pears Common (Raw)								
Pineapple pulp								
Plums								
Guavas Ripe								
Tangerine Pulp								
Tangerine Juice								
Tree Tomato								
Water Melon								
Other (specify)								
SUGARS AND SYRUPS								
Honey								
Sugar white Native brown								
Sugar cane (mature)								
Other (specify)								
MEAT, POULTRY AND EGGS								
Beef liver								
Beef steak(stewed)								
Beef minced (stewed)								
Beef Rump-steak(fried)								
Chicken Roast (meat & skin)								

Chicken meat-Boiled, boned								
Egg boiled Hen								
Egg Yolk								
Egg Scrambled								
Goat meat (cooked and moderately Fat								
Goat liver								
Pork chops (loin grilled)								
Fish Fillet (whole, dried & salted)								
Fish dried (unspecified)								
Nile perch (dried)								
Other (specify)								
MILK & MILK PRODUCTS								
Butter (cow milk)								
Camel's Whole milk								
Cheese Cottage (cow milk whole fresh)								
Cow milk (whole)								
Cow milk (skimmed)								
Cow milk powder (whole)								
Cow milk dried skimmed								
Yogurt (cow's whole milk)								
Other (specify)								
OILS & FATS								
Cooking oils (not fortified)								
Fish liver oil								

Hydrogenated oils e.g. Kimbo, Kasuku etc								
Lard/ Animal fats								
Margarine (fortified)								
Salad oil								
Sunflower oil								
Other (specify)								
BEVERAGES								
Beer lager								
Traditional Beer (specify) …….								
Cider (dry)								
Cider (sweet)								
Coconut water								
Coconut milk								
Orange juice								
Mango juice (canned)								
Passion fruit juice								
Commercial soft drinks								
Spirit (vodka, Gin, whisky etc)								
Sugar cane juice								
Tomato juice								
Wine (red)								
Wine (white & dry)								
Wine (white & sweet)								
Other (specify)								
SPICES & CONDIMENTS								
Black pepper (dry)								
Chili (fresh)								

Chili (dry)								
Coriander leaves(dhania)								
Curry powder								
Ginger (dry)								
Garlic (dry)								
Other (specify)								
MISCELLANEOUS								
Biscuits (salt)								
Biscuits (sweet)								
Cakes (various fancy iced)								
Chapattis (made without fat)								
Chapattis (made with fat)								
Ice cream (dairy)								
Mayonnaise								
Omelet								
Pancakes								
Pea nut butter								
Potato chips								
Potato crisps								
Scones								
Tomato sauce								
Other (specify)								

ADDENDUM 5

BIOCHEMICAL ASSESSMENT

Date **ID.No**	**Serum glucose (mmol/l)**
At baseline(start)	
After 15minutes	
After 30 minutes	
After 45 minutes	
After 1 hour	
After 2 hours	
After 3 hours	
After 4 hours	
After 5 hours (end)	

ADDENDUM 6

SIGNS OF HYPOGLYCAEMIA

Date:

ID.NO.

[] Mental confusion [] Cold sweats [] Generalized body weakness

[] Hunger [] Shaking [] Dizziness

[] Difficulty speaking [] Inability to concentrate

[] Tiredness

APPENDIX 4: CONSENT FORM

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

TITLE OF THE RESEARCH PROJECT:

THE PREVALENCE AND CAUSES OF HYPOGLYCEMIA IN PATIENTS WITH END-STAGE RENAL FAILURE ON MAINTENANCE HAEMODIALYSIS AT KENYATTA NATIONAL HOSPITAL RENAL UNIT, NAIROBI, KENYA

REFERENCE NUMBER:

PRINICIPAL INVESTIGATOR: Anastacia Wanjiku Kariuki

ADDRESS: P.O Box 30924 –00100, Nairobi, Kenya

CONTACT NUMBER: (CELLPHONE) 0721-283491

You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Also, your participation is entirely voluntary and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part.

This study has been approved by the Committee for Human Research at Stellenbosch University and will be conducted according to the ethical guidelines and principles of the South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What is this research study all about?

The study will be conducted at the Kenyatta National Hospital Renal unit only. The total number of patients will be 50.The patients to be included in the study will be selected using a simple computerized method where the researcher does not have any control over which patients are selected.

The study aims to investigate the prevalence and causes of low blood glucose during haemodialysis. Potential causes may include dialysis, the nutritional status of the patient, the presence of disease, certain medication and the type and the time of the last meal eaten before dialysis.

The study will involve analyzing blood glucose levels nine times (9) before dialysis and at regular intervals after the onset of haemodialysis. For this purpose, a very small amount of blood will be obtained from the bloodlines (total volume of 2 mls or about ½ teaspoon).

Anthropometric measurements will be carried out after dialysis and will include weight, height and four skinfold measurements, as well as the mid-upper arm circumference. During dialysis, the dietitian to determine dietary intake will interview the patient.

Why have you been invited to participate?

You have been invited to take part in this study because of the following reasons:

You are on long-term haemodialysis treatment.

You have been on haemodialysis for more than three (3) months

You are older than 18 years.

What will your responsibilities be?

During the haemodialysis session you will be required to give about 2 ml (½ teaspoon) of blood for the analysis of the blood glucose. After dialysis you must be available for measurement of your weight, height, mid upper arm circumference and four skinfold sites. You must also be available for an interview with the dietitian to report on your food intake.

Will you benefit from taking part in this research?

You may or may not benefit directly from the study. The study aims to benefit those patients

experiencing low blood glucose levels during dialysis by identifying and correcting the causes.
The renal-unit management will also be informed of the results of the study so that the necessary steps can be taken to prevent the occurrence of low blood glucose during dialysis.

Are there any risks involved in your taking part in this research?
No risks or discomfort will be exposed to the participant in the study. The blood to be used for biochemical analysis will be drawn from the catheter/fistula.

If you do not agree to take part, what alternatives do you have?
You will continue with your dialysis as scheduled. Normal dialysis procedures will be continued and all vital signs observed without any discrimination or inferior treatment.

Who will have access to your medical records?
The information collected will be treated as confidential, and if it is included in a thesis, a publication in a professional journal, the identity of the participant will remain anonymous.
Once the study is completed, the findings of the outcome will be explained to the individual patients during haemodialysis and a presentation of the same will be done during the renal-consultative meeting held on every Wednesday of the week.

What will happen in the unlikely event of some form injury occurring as a direct result of you is taking part in this research study?
No direct injuries are foreseen as a direct consequence of the research. However, should hypoglycemia occur the nurse and/or doctor in the renal-unit will be promptly informed and intravenous glucose solution given.

Will you be paid to take part in this study and are there any costs involved?
No, the study will be carried out during your usual scheduled dialysis session in the renal unit.

Is there any thing else that you should know or do?
You should inform your family practitioner or usual doctor that you are taking part in a research

study and show him/her this letter so that he/she is informed.

You should also inform your medical insurance company that you are participating in a research study.

You can contact Prof. MC Ligeyo or Dr. Kayima at Tel 2726300 *43803 if you have any further queries or encounter any problems.

You can contact the Ethics Committee- Kenyatta National Hospital on 2726300 *44102 if you have any concerns or complaints that have not been adequately addressed by your study doctor.

You will receive a copy of this information and consent form for your own records.

By Signing below, I…….. agree to take part in a research study entitled:-

THE PREVALENCE AND CAUSES OF HYPOGLYCEMIA IN PATIENTS WITH END-STAGE RENAL FAILURE ON MAINTENANCE HAEMODIALYSIS AT KENYATTA NATIONAL HOSPITAL RENAL UNIT, NAIROBI, KENYA

I declare that:

I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.

I have had a chance to ask questions and all my questions have been adequately answered.

I understand that taking part in this study is voluntary and I have not been pressurized to take part.

I may choose to leave the study at any time and will not be penalized or prejudiced in any way.

I may be asked to leave the study before it has finished, if the study doctor or researcher feels it is in my best interests, or if I do not follow the study plan, as agreed to.

Signed at (*place*)……..On (*date*) ……..

…… ……..……..

Signature of Participant Signature of Witness.

Declaration by Investigator

I, Anastacia Wanjiku Kariuki declare that: -

I explained the information in this document to ……..…

I encouraged him/her to ask questions and took adequate time to answer them.

I am satisfied that he/she adequately understands all aspects of the research, as discussed above

I did/did not use a translator. (*If a translator is used then the translator must sign the declaration below.*

Signed at (*place*)…….. On (*date*) ……..

…….. ……..……

Signature of Investigator Signature of Witness.

Declaration by Translator

I (*name)* ……. Declare that: -

I assisted the investigator Anastacia Wanjiku Kariuki to explain the information in this document to (*name of participant*)…….. using the language medium of Kalenjin/ kikuyu/ Dholuo/ Luhyia/ kiswahili/.

We encouraged him/her to ask questions and took adequate time to answer them.

I conveyed a factually correct version of what was related to me.

I am satisfied that the participant fully understands the content of this informed consent document and has had all his/her question satisfactorily answered.

.

Signed at (*place*)…….. On (*date*) ……..

…….. ……..……

Signature of Translator. Signature of Witness.

APPENDIX 5: RESEARCH APPROVAL LETTERS

A) Kenyatta N.Hospital Ethics Approval Letter

REF: KNH-ERC /01/2857 Date:5th May 2006

Anastacia W. Kariuki
Dept. Nutrition
KNH

Dear Ms Kariuki,

RESEARCH PROPOSAL "THE PREVALENCY AND NUTRITIONAL CAUSES OF HYPOGLYCEMIA IN PATIENTS WITH END-STAGE RENAL FAILURE ON MAINTENANCE HEMODIALYSIS (MHD) AT THE RENAL- UNIT OF KENYATTA NATIONAL HOSPITAL, NAIROBI, KENYA."

This is to inform you that the Kenyatta National Hospital Ethics and Research Committee has reviewed and **approved** your above cited proposal.

On behalf of the committee, I wish you a fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of database that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely,

PROF. A N GUANTAI
SECRETARY, KNH-ERC

c.c. Prof K.M Bhatt, Chairperson, KNH-ERC
The Deputy Director CS, KNH
The Head, Nutrition Department, KNH
Supervisors: Prof. M G Herselman
Prof. D Labadarious
Prof. MC Ljsevo
Dr. Kayima

B) University of Stellenbosch Ethics approval letter

22 June 2006

Ms AW Kariuki
Discipline of Human Nutrition
Department of Interdisciplinary Health Sciences

Dear Ms Kariuki

RESEARCH PROJECT: **"THE PREVALENCE AND NUTRITIONAL CAUSES OF HYPOGLYCEMIA IN PATIENTS ON MAINTENANCE HEMODIALYSIS AT THE RENAL-UNIT OF KENYATTA NATIONAL HOSPITAL, NAIROBI, KENYA"**
PROJECT NUMBER : N05/12/196

My letter dated 25 April 2006 refers.

At a meeting that was held on 12 June 2006 the Committee for Human Research ratified the approval of the above-mentioned project.

Yours faithfully

CJ VAN TONDER
RESEARCH DEVELOPMENT AND SUPPORT (TYGERBERG)
Tel: +27 21 938 9207 / E-mail: cjvt@sun.ac.za

CJVT/cjvt

Copy to: Prof D Labadarios

C:\DOCUMENTS AND SETTINGS\EVISAGIE.000\MY DOCUMENTS\KMNI\PROJEKTE\2005\N05-12-196-002.DOC