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Nutrition And Health Status Of Hemodialysis Patients In Dhaka, Bangladesh

Tanjina Rahman
Wayne State University

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TANJINA RAHMAN

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DEDICATION

This work is dedicated to my father, *Ghazi Ghulam Rahman (LATE)* who always encouraged me towards the dream and success of my life with his enormous love and blessings till his last breath.

And,

my mother, *Mina Sultana*, my husband, *Nayeem Jamaly*, and my brother *Gazi Nayeem Rahman* who also supported and motivated me selflessly and never forget to pray for my success every day and night which made it possible for me to complete this work.

"You have been there for me, no matter what choices I might have made….you lovingly repaired my broken spirit, helped me plot a new course, and set me free to fly on my own once again, There is no greater love than that. You will always be special to me, and no matter where life takes me, I will remember you with love."

-Marilyn K Deacon.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

AD: Atherogenic Dyslipidemia

ADAT: Appetite and Diet Analysis Tool

ADPKD: Adult Polycystic Kidney Disease

APKD: Adult Polycystic Kidney Disease

ASN: American Society of Nephrology

BMI: Body Mass Index

BUN: Blood Urea Nitrogen

CRF: Case Report Form

CRP: C-Reactive protein

CKD: Chronic Kidney Disease

CKD-MBD: Chronic Kidney Disease-Mineral Bone Density

C-G Eq.: Crockfilt-Gault Equation

CGN: Chronic glomerulonephritis

CVD: Cardiovascular Disease

DL: Dyslipidemia

DM: Diabetes Mellitus

DN: Diabetic Nephropathy

DEI: Dietary Energy Intake

DPI: Dietary Protein Intake

EBPG: European Best Practice Guidelines

EDTA: Ethylene Diamine Tetra-acetic Acid

eGFR: Estimated GFR

ESRD: End Stage Renal Disease

ESHA: Nutrition Analysis and Food Processor Software

FA: Fatty Acid

FTNS: Food Technology and Nutrition Science

GFR: Glomerular Filtration Rate

HD: Hemodialysis

HDL-C: High Density Lipoprotein Cholesterol

HGS: Hand Grip Strength

HTN: Hypertension

Hr-QoL: Health related Quality of Life

IDL-C: Intermediate Low-density Lipoprotein Cholesterol

ISN: International Society of Nephrology

ISRNM: International Society of Renal Nutrition and Metabolism

ISAK: International Society of Anthropometrics and Kinanthropometry

INFS: Institute of Nutrition and Food Science

IQR: Interquartile range

KDIGO: Kidney Disease: Improving Global Outcomes

KDOQI: Kidney Disease Outcomes Quality Initiative

KD-QoL: Kidney Disease Quality of Life

KFB: Kidney Foundation Bangladesh

KFHRI: Kidney Foundation Hospital and Research Institute

Kt/V: Dialyzer clearance of urea multiplied by the dialysis time and divided by the volume of distribution of urea, approximately equal to the patient's total body water

LDL-C: Low Density Lipoprotein Cholesterol

LH: Lithium Heparin

MICS: Malnutrition Inflammation Complex Syndrome

MIS: Malnutrition Inflammation Score

MAC: Mid-upper Arm Circumference

MAMC: Mid Arm Muscle Circumference

MD: Mixed Dyslipidemia

MHD: Maintenance Hemodialysis

MUFA: Monounsaturated fatty acids

NHANES: National Health and Nutrition Education Survey

NIH: National Institute of Health

NKF: National Kidney Foundation

NSTU: Noakhali Science and Technology University

P: Phosphorous

PEW: Protein-Energy Wasting

pmp: Per million population

Pro:Protein

PTH: Parathyroid Hormone

pts.: Patients

PUFA: Polyunsaturated fatty acids

RLS: Restless Leg Syndrome

RRT: Renal Replacement Therapy

Sr.: Serum

SD: Standard Deviation

SPSS: Statistical Package for Social Sciences

TAG: Triglycerides

TC: Total Cholesterol

TIBC: Total Iron Binding Capacity

TSF: Triceps Skin Fold

URR: Urea Reduction Ratio

USRDS: United States Renal Data System

VLDL: Very Low-density Lipoprotein

CHAPTER 1 INTRODUCTION

Chronic kidney disease (CKD) in Bangladesh

Bangladesh is a small but heavily populous country in the world. It is as big as the state of Iowa in USA, with a population density of almost 3000 persons per square mile, while the population density of Iowa state is only 50 persons per square mile. Revised version of world population prospectus in 2019 stated that, in 2016, the total population in Bangladesh was 161,376,708. This makes it the 8th most populous country in the world [1]. Dhaka is the capital and largest city of Bangladesh and in 2018,World Bank reported that, the population in Dhaka could be as high as 20 million by 2015 [2]. Therefore, in 2016, it was 18 million and in 2020, the population reaches to 21 million. In past decades, communicable diseases were responsible for majority of morbidity and mortality in Bangladesh. For that reason, much of health care costs in Bangladesh is invested in poverty alleviation, birth control, clean drinking water supply, maternal and child health, and the removal of infectious and communicable disease [3]. However, due to epidemiological transition, the disease pattern changed from communicable and infectious diseases to non-communicable diseases like hypertension, diabetes, cardiovascular disease and CKD [4]. Due to the higher burden of treatment cost and existing government policy, the treatment for CKD is given a low priority in this region despite the fact that, the prevalence of CKD is 18 million among people living in both rural and urban settings in Bangladesh[3].

About 35,000-40,000 people reach end stage renal disease (ESRD) and 40,000 patients die due to CKD each year in Bangladesh. In 2004, kidney disease care was available in 6 out of 13 government hospitals and dialysis facilities were available in 4 of the 13 university hospitals. There were also 10 private hospitals that provide treatment facilities for renal patients. There was only one renal transplant center in government and another in the

private sector [5]. In 2014, there were around 84 dialysis centers in Bangladesh, of which, half were situated in Dhaka city. Remaining were in other six large cities of the country. However, at that time, available facilities could hardly cover only 9000 to 10,000 new patients (one-third) for twice weekly dialysis and the remaining 66% of patients had no access to hemodialysis [6]. As the treatment of ESRD is very expensive and off limits for the majority of Bangladeshi people, 70% of patients start on dialysis and stop treatment after 3 to 6 months because they can no longer afford it [3]. However, the current capacity of both public and private hospitals can provide facilities to only 10% of the affected people. The remaining patients die without any prior treatment and due to inaccessibility and unaffordability of services. In October 2017, 'Bangladesh Tribune'- an online Newspaper published that, around 20 million people in Bangladesh are suffering from kidney disease, of which, 8 lacs (800,000) require dialysis but only 30 thousand were able to receive it. Based on their report, there were 101 dialysis centers across Bangladesh in 2017 with around 1300 to 1500 non-functional dialysis machines, but the number is very low, and at least 1,000 more centers with fully functional machines are needed to treat the large number of patients.

In this chapter, there will be a brief introduction of the organ-Kidney, its structure and function, abnormalities in its function and different types of kidney diseases with an emphasis on CKD, ESRD and its complications and current scenario in Bangladesh.

Kidney-its structure and functions

The kidneys are a pair of bean-shaped organs-each weighing about 150 g in male and 135g in female. Both kidneys lie in the retroperitoneal space, left one on a slightly upper position than the right one. It is a complex organ with highly specialized cells. Its functional unit is called, "nephron", where each kidney has about 1 to 1.3 million of nephrons. Each nephron consists of a glomerulus with bowman's capsule and a long tubule, segmented into

distinct parts-proximal tubule, loop of Henle, distal tubule, and collecting duct (Figure **1-1**). Major functions of nephrons are-*a) Filtration*-Glomeruli generates ultrafiltrate of the plasma, *b) Reabsorption*-Tubules selectively reabsorb substances from the ultrafiltrate, and *c) Secretion*- Tubules secretes substances into the urine. Major function of the kidneys is the correction of the composition and volume of body fluid that deviate from the normal range due to food intake, metabolism, exercise and environmental factors, which in case of a normal individual could take place within an hour or so. Another important function is the excretion of urea, toxin and foreign metabolites and the formation of urine [7]. Typically, kidneys receive 1700 L of blood per day for filtration where large and negatively charged molecules are restricted. Then glomeruli form 180 L of urine per day, of which, 99% is reabsorbed by the tubules (sodium, potassium and glucose), thus each day, 1 to 2 L of urine with other waste products, toxins, organic acids and extra minerals are excreted from the body via kidneys. Kidneys are also responsible for the production of hormones and enzymes, such as-renin (catalyze angiotensin, a vasoconstrictor peptide and regulate blood pressure), erythropoietin (a glycosylated protein with 165 amino acids that stimulates the maturation of red blood cells in bone marrow), and activation of the most active form of vitamin D, 1-25-Dihydroxy Calciferol (D3) that aid in calcium and phosphate balance in the body and maintain bone health. Kidneys help to regulate ion concentration (sodium, potassium and calcium) to maintain homeostasis balance, regulate pH of blood plasma via excretion of excretion of hydrogen ion and reabsorption of bicarbonate ion to maintain acid-base balance in the body [7-9] (Table **1-1**).

Different Types of kidney diseases

There are various types of kidney disease such as-urinary tract infection (UTI) with symptoms of frequent urination with burning sensation, pain in lower abdomen and fever,

azotemia with an elevation of blood urea nitrogen (BUN) and creatinine level, nephrotic syndrome with damages the filtering unit that allow them to leak protein into the urine, focal segmental glomerulosclerosis (FSGS), and uremia with a raised level of urea and other nitrogenous wastes in the blood [7]. In 2012, KDIGO (Kidney Disease: Improving Global Outcomes) defines acute kidney injury (AKI) as an increase in serum creatinine level by more than 0.3 mg/dl within 48 hours or urine volume of less than 0.5 ml/kg body weight/hour for more than 6 hours with sudden, temporary, or sometimes fatal loss of kidney function. It occurs due to injury, surgery, NSAIDS overdose or myocardial infarction (MI). The condition is often reversible with short term treatment and kidney function improves [10].

Chronic Kidney Disease (CKD)

Definition and classification: CKD is considered as one of the major public health problems worldwide. In developed countries, the mortality rate due to CKD is alarmingly high. It is a gradual, progressive and irreversible loss of kidney function over a long period, classified based on glomerular filtration rate (GFR) or albuminuria, when a patient's GFR falls below 60 ml per minute per 1.73 m^2 for more than 3 months or when a patient's urine albumin-to-creatinine ratio is over 30 mg of albumin for each gram of creatinine (Figure **1-2**) [11]. According to the National Kidney Foundation (NKF) Kidney Disease Outcome Quality Initiative (K/DOQI) guidelines, CKD is defined as, " *a chronic disease state in that irreversible, structural, or functional abnormalities of the kidney, with or without a decreased glomerular filtration rate (GFR), are present for at least three consecutive months*" [12]. Based on CKD-EPI (chronic kidney disease epidemiology collaboration) equation, which is better than MDRD (modification of diet in renal disease study) equation for a clinical setting, estimated GFR (eGFR) is used to classify different stages of CKD[13]. There are five stages of CKD from stage 1 (normal or somewhat reduced kidney function) to

stage 5 or ESRD or a complete renal failure with a GFR of less than 15 ml/min/1.73m^2 (Figure **1-3**). When CKD reaches to stage 5 or ESRD, patients require renal replacement therapy (RRT) either by dialysis or transplantation as a life-saving approach. ESRD is a devastating medical, economic and social problem.

Incidence and prevalence: Globally, the incidence of CKD was 214.63 per million population in 1990, which was increased to 288.53 per million population in 2016 [14]. In developed countries (e.g. USA), the incidence of ESRD was 378 per million population and the prevalence was 2128 per million in 2015[15]. The incidence of ESRD in developing countries was 34 (Algeria) to 240 (South Africa) per million population in 1999 [16]. USRDS report revealed that, in 2016, the incidence rate of ESRD in the United States (US) was 373.4 per million population (pmp) per year, a total of 124,675 new cases reported to have ESRD. The prevalence rate of ESRD was 2160.7 pmp, a total of 726,331 prevalent cases of ESRD based on December 31, 2016 data in the US. Overall, CKD stages 1 to 5 increase from 13.6% in 2012 to 16.1% and CKD stages 3 to 5 rises from 6.2 to 7.5% in 2016 (Figure **1-4**)[15]. Studies done in rural and urban areas of Bangladesh to assess the prevalence of CKD are combined in table **1-2**, where, in one study, prevalence of CKD in Bangladesh was reported as 26%[17]. In 2015, Das et al. showed that, prevalence of stage 2 CKD was 24% and mostly in female.[18]. Although the prevalence of ESRD in Bangladesh is unknown, it could be 200 to 250 per million population per year and the incidence rate will be higher than the prevalence rate [6]. The prevalence of CKD among urban Bangladeshi population has been estimated at 16% to 18% [17], and of them 11% were in stage III to V [19]. In Bangladesh, incidence of ESRD could be 100 per million or 16100 new patients develop ESRD each year for a population of 161 million as the population in Bangladesh in 2016 is 161 million[1, 5].

Accurate assessment of the incidence and prevalence of ESRD becomes difficult in Bangladesh due to lack of proper renal registries of patients.

Etiology: Based on United States Renal Data System (USRDS) Annual report, prevalence of CKD among diabetics is 36% (2013-2016) and 31% among hypertensive individual (2013-2016)[15]. Highest correlation was observed between age and eGFR and between hypertension (HTN) and albuminuria. Among adult NHANES participants in 2013-2016, prevalence of CKD was highest (21%) among individuals aged more than 60 years, followed by self-reported cardiovascular disease (SR-CVD) (26.3%), DM (18.7%), HTN (16%) and higher BMI (7.3%). An albumin-creatinine ratio (ACR) of more than 30 mg/g was most common among individuals with DM (27%), followed by those with HTN (21%), aged+ 60years (17.3%), with SR CVD (14.8%), and of higher BMI (12%). The presence of both eGFR <60 and ACR ≥30 was most common with SR-CVD, at 11%, followed by DM at 8.5%, those aged 60+ years (6%), with HTN (5.6%), and with higher BMI (2.6%) (Figure **1-5**)[15]. One study conducted in Bangladesh among ESRD patients, not on dialysis showed that, 18.3% had ischemic heart disease, 38% had heart failure and 9% had left ventricular hypertrophy. Patients with DM experienced more CVD events compared to their non-diabetic counterparts [20]. Another screening study conducted in a public place in Dhaka city, Bangladesh among 634 normal individuals showed that, 12.8% of individuals participated in the study had CKD, of which, 6% were in CKD stage 3 and these patients had a higher body mass index and systolic blood pressure, and majority of them were aged above 60 years[21]. In 2012, Ahmed et. Al. conducted a study in six hemodialysis centers in Bangladesh and found that, glomerulonephritis and diabetic nephropathy were the most common causes of ESRD and hypertension was also associated with them[22]. A cross-sectional study

conducted in rural Bangladesh showed that, microalbuminuria and overt-proteinuria are common among rural Bangladeshi people with hypertension [23].

Treatment options: There are two ways to treat a patient if he has kidney failure – dialysis, or renal transplant. However, the number of kidneys available for transplant is very low. So, dialysis remains the only option for a patient to survive until he got a transplant. In 2016, 35% of new ESRD patients in the US were reported to receive little or no pre-ESRD nephrology care[15]. Options for renal replacement therapy include either dialysis hemodialysis (HD) or peritoneal dialysis (PD) or transplantation of kidney (best treatment option) (Figure **1-6**). A patient can also choose "no renal replacement therapy or comfort care" that leads to certain death within a few months and also known as "conservative kidney management" [24]. USRDS revealed that, in 2016, 63% of patients received HD (98% of which was on in-center and 2% on home HD), 7% received PD and 29.6% received kidney transplantation as treatment option[15]. In Bangladesh, treatment facilities are available only in major cities and many patients travel a long distance to seek care.[25]. Around 80% of kidney failure patients cannot afford the treatment cost of profitable centers and approximately 66% patients have no access to any kind of treatment facilities as the existing facilities can hardly accommodate only 9,000-10,000 new patients [6]. Even though there is improvement in dialysis technique and patient care [15], patients are reported to have poor quality of life [26]. In Bangladesh, outcome of that small number of patients who can access hemodialysis is not great. Survival of HD patients was estimated in a study which showed 1, 3 and 5 year survival rate of 90%, 75% and 55% respectively [27].

Complications due to CKD: Due to a reduction in the number of functional nephrons, kidneys become less flexible to different solutes in CKD and there is reduced renal clearance, waste excretion and accumulation of proinflammatory cytokines, metabolic acidosis, reactive

oxygen species, and formation of advanced glycation end products (AGE) [28, 29]. *Metabolic acidosis* is an early symptom in patients with CKD. It gets worsen as the disease progresses to ESRD and may affect other organic function- cardiovascular system, central nervous system, pulmonary function, inflammatory process, immunity and metabolism[30]. *Impaired oxidative balance* in dialysis patients are partly due to increased production of reactive oxygen species, reduced clearance, and weak antioxidant defense mechanism [31]. *Insulin resistance* may occur due to reduced catabolism of insulin and glucagon[32]. Altered hormone production also leads to anemia[33] and mineral and bone disorder (CKD-MBD) [34]. *Anemia* with a hemoglobin level of less than 11 g/dL results in poor quality of life and higher cardiovascular mortality and morbidity in ESRD patients[35]. In case of *CKD-MBD*, as GFR declines, 1-α-Hydroxylase enzyme, responsible for the conversion of vitamin D into its active form became inactive, results in increased production of parathyroid hormone (hyperparathyroidism), diminished absorption of calcium ion from the intestine, overproduction of phosphorous in blood (hyperphosphatemia), all of which lead to the release of calcium from bone and leads to mineral-bone disorder (MBD) [36]. *Malnutrition and chronic infection*, common in dialysis patients also triggers anemia, that eventually induce inflammation, oxidative stress, and cardiovascular complication in the long run[37, 38]. *Hypoalbuminemia* is another important risk factor for these patients and a serum albumin level of less than 3.8 g/dl is associated with malnutrition [39, 40]. It is also associated with high rate of CVD mortality [41]. Several non-nutritional factors are also associated with hypoalbuminemia (infection, inflammation, fluid overload, inadequate dialysis and metabolic acidosis). Additionally, around 20% of ESRD patients die due to *treatment complication*[42]. One study conducted in Bangladesh in 2012 showed that, prevalence of anemia was almost 97%, prevalence of hypocalcemia and hyperphosphatemia was around 50% in a group of

CKD stage 5 patients, not on dialysis. 23% of these patients also had an elevated calcium-phosphate product [20]. It has been also noted that, cardiovascular (CVD), cerebrovascular, and peripheral vascular diseases are more common causes of high rates of morbidity and mortality among CKD patients [43]. Patients with CKD have a higher risk of developing CVD, stroke and dyslipidemia, a compromised antioxidant system, metabolic abnormalities and early death [44]. Mortality among dialysis patients and the possible causes behind it have been studied in different countries and shows markedly different patterns based on to timely access to pre-ESRD medical care, management of biochemical abnormalities in advanced CKD, access to quality of ESRD medical care, and ESRD education and support service [45]. The situation is even worse in Bangladesh, where little focus is given to prevent the occurrence of chronic disease. More focus is given on eradication of infectious and communicable disease, birth control, and maternal and childhood mortality [3]. There is limited access to treatment facilities, and little government support is available for patients with CKD.

Inflammation: Inflammation is a physiological response, defined as, *" a localized adaptive response, elicited by injury or destruction of tissues that serves to destroy, dilute, or sequester both the injurious agent and the injured tissue"* [46]. It may arise due to prolonged poor appetite, skeletal muscle wasting, hypercatabolism, hormonal imbalance, and atherosclerosis, all of which are common in dialysis patients [47]. Assessment of inflammation in case of Bangladeshi ESRD patients was not properly documented to the best of our knowledge, only in one study, it was reported that, C-reactive protein (CRP) was present in 78% of CKD stage 5 (not on dialysis) pateints, which is one of the markers of inflammation [20]. Another study showed that, Bangladeshi ESRD patients with a high CRP had a low serum albumin level (a marker of malnutrition) and experienced high

cardiovascular events and concluded that, inflammation may play a role in both the progression of cardiovascular disease and malnutrition among ESRD patients[48].

Dyslipidemia: Advanced CKD patients including ESRD on dialysis also develop dyslipidemia [49]. Dyslipidemia in CKD is characterized by increased level of triglyceride (TG) and very low density lipoprotein (VLDL), varying level of LDL-C and a decreased level of plasma HDL-C [50]. Unlike dyslipidemia in normal individual, total cholesterol (TC) and low density lipoprotein (LDL-C) are within normal range or even lower among CKD patients with dyslipidemia. However, there was no large prospective study conducted in ESRD population to assess the relation between CVD risk and dyslipidemia[51]. Dialysis patients with lower level of TC or LDL-C are also at very high risk of all cause and cardiovascular mortality, likely due to inflammation and malnutrition[52]. Dyslipidemia is a contributing factors to the developoment of atherosclerosis [49]. In normal metabolism, HDL-C promotes reverse-cholesterol transport system by the uptake of cholesterol from extrahepatic tissue and maturation of HDL particle. However, in CKD, this system becomes dysfunctional and also promotes LDL-oxidation (Figure **1-7**) [53]. In a cross sectional study conducted in Bangladesh in 2012, it was found that, patients on maintenance hemodialysis (MHD) showed a different pattern of dyslipidemia-a low HDL-C, high TG and an altered TC to HDL-C ratio when compared to healthy control[54].

Cardiovascular disease (CVD): The risk of developing CVD is 10 to 30 times higher among CKD patients compared to general population (Figure **1-8**)[15]. Prevalence of some common types of CVD in dialysis patients include-coronary artery disease (66%), left ventricular hypertrophy (75%), and cardiac failure (40%) [15, 55]. CVD risk is also higher among patients undergoing HD (Figure **1-9**)[15]. There are both traditional and non traditional risk factors, responsible for the development of CVD in CKD. Traditional risk

factors include-diabetes melitus, hypertension, sedentary lifestyle, smoking, dyslipidemia and family history whereas non-traditional risk factors include-inflammation, malnutrition, oxidative stress, endothelial dysfunction, uremic toxin, and altered mineral metabolism (Figure **1-10**) [53]. Various exposures that increase the cardiovascular disease burden in ESRD patients involve-comorbidities, inflammmation and oxidative stress, nutrient loss due to dialysis process itself, limited intakes of antioxidents due to dietary restrictions as well as genetic attributes [56]. One study showed that, prevalence of ischemic heart disease, heart failure, arrhythmia and left ventricular hypertrophy was 18.3%, 38%, 4.7% and 9% among Bangladeshi CKD stage 5 patients not on dialysis[20].

Malnutrition: Malnutrition among renal patient is termed as either 'Uremic malnutrition', or "Renal Cachexia' or 'Protein-energy wasting (PEW)' or 'malnutrition-inflammation complex syndrome (MICS)', malnutrition inflammation atherosclerosis (MIA) syndrome, kidney disease wasting' and is associated with the prevalence of morbidity and mortality among these patients [57]. Malnutrition or PEW is considered as a common problem among adult HD patients [58]. The concept of PEW was proposed in 2007 by the International Society of Renal Nutrition and Metabolism (ISRNM) "*as a state of nutritional and metabolic derangements in patients with CKD characterized by simultaneous loss of systematic body protein and energy stores, leading ultimately to loss of muscle and fat mass and cachexia*" [57]. Studies suggested that, patients undergoing dialysis have reduced muscle mass and fuel reserves [59]. In a recent study, ISRNM proposed a "PEW" score, which if high, could indicates systemic inflammation, muscle wasting and malnutrition among MHD patients [60]. One-third of MHD patients having malnutrition have a high mortality risk [40]. Causes of PEW in CKD include decreased protein and energy intake, hypermetabolism, metabolic acidosis, decreased physical activity, decreased anabolism, comorbidities, and

dialysis related factors which is shown in Table **1-3** [59]. Figure **1-11** shows that, as the CKD progresses from stage 1 to stage 5 and GFR decreases, complications, such as malnutrition, hyper catabolism, uremic toxin, and inflammation increase, all of which will lead to PEW and further complications which may cause even death [57]**.** Figure **1-12** shows that, PEW is related with increased frailty and depression, cardiovascular disease and infection-all of which may create volume overload, oxidative stress, endocrine disorder, anemia, anorexia, acidosis, poor nutrient intake and more nutrient loss during dialysis[57]. One study, conducted in Saudi Arabia revealed that HD patients have a tendency toward developing malnutrition and are at high risk of both morbidity and mortality [61]. Another study conducted in 2018 showed that, prevalence of malnutrition among Bangladeshi ESRD patients on MHD was 16.9%[62]. Global prevalence of PEW, based on a meta-analysis of 90 studies from 34 countries including 16,434 patients, has been estimated at between 28-54% (25^{th}-75^{th} percentile) [63]. However, data on prevalence of PEW in different countries around the world are poorly defined due to lack of gold-standard methods/definition to diagnose PEW (Table **1-4**). Combination of MICS, along with inflammation and dyslipidemia are responsible for increased incidence of atherosclerosis among hemodialysis patients [64].

Importance of the Nutritional Management in CKD

A common trend seen among dialysis patient is that, dietary intake becomes inadequate during transition from non-dialysis to dialysis period. Often patients don't meet their recommended intake, based on NKF/KDOQI guidelines for HD patients. Transition from non-dialysis dependent CKD to dialysis dependent ESRD is a critical phase for each patient and requires a combination of clinical, nutritional, and psychological assessments [65]. Nutritional indicators can be directly linked to patient's physiological status and

outcomes. Therefore, careful and appropriate selection of food is crucial to address such problems.

Several epidemiological studies done in different countries showed that patients with kidney disease have limited understanding of their illness and know little about renal specific diet practice, where, patients with abnormal laboratory values for serum albumin, phosphorus, potassium, low body mass index (BMI) (<23 kg/m^2), poor muscle mass and muscle strength and poor dietary intake were considered as patients having poor existing renal-specific nutrition knowledge [66]. Studies have also shown promising results for educational intervention among dialysis patients in fluid management, exercise and adaptation to treatment [44], and also showed better results in controlling diet-related incidence of hypertension, hyperphosphatemia, hyper/hypokalemia and protein-energy wasting, thus reduce further deterioration in renal function[67]. One study showed that, dialysis patients who received one diet counseling session by a registered dietitian showed significant improvement in their health status as assessed by their body mass index and biochemical parameters compared to patients who did not receive any nutrition support [68]. Another study from Taiwan showed that, provision of nutrition education among predialysis patients helped to keep stable or improve their physiologcal status and reduced further deterioration of renal function by eliminating patients's delusion about the use of Chinese herbs [69]. A study recently conducted in Bangladesh also mentioned that, illiteracy might be a reason for increased prevalence of malnutrition among renal patients [62].

Inadequate nutrient intake is a major contributing factor to the development of PEW among ESRD patients on MHD[12]. Nutritional management involves maintaining a good nutritional status as well as establishing normal serum chemistry via adequate intakes of all macro and micronutrients[8]. Nutritional management in renal disease is challenging for

clinicians since the outcomes of dialysis depends on the adequacy of both the dialysis treatment and the dietary intake and nutritional status of the patient [70]. Various dietary restrictions are traditionally imposed on dialysis patients, whereas little evidence exists to their benefits [71]. The goals for nutrition therapy for dialysis patient is to provide them with an attractive and palatable diet, control edema and serum electrolytes, prevent nutritional deficiencies, renal osteodystrophy, and cardiovascular complications. Aims of dietetic intervention among dialysis patients should be to optimise their nutritional status, keep renal biochemistry within safe limits, control blood pressure, blood glucose, and fluid overload, and thus make dietary advice as practical as possible to aid compliance. For this reason, all renal patients should have adequate renal specific dietetic or nutritional support [72].

Protein: According to a simplified historical scheme on main focus in diets for CKD patients it has shown that, in the first Era, "Potassium" was considered to be the main killer with “Hyperkalemia” being the main concern. Therefore, fruits and vegetables were regarded as the forbidden foods. In the second Era, as soon as dialysis become efficient and survival rates increased, "Hyperphosphatemia" was identified as the main enemy and milk and its products were banned from the diet for these patients to avaoid vascular calcification. Then, in the third or present Era, "Protein-energy-wasting" or malnutrition was identified as the compromised health status. Thus a diet high in both calorie and protein is recommended (Table **1-5**) [73].

A high blood urea level may increase protein carbamylation and production of reactive oxygen species, thus leads to oxidative stress, inflammation, endothelial dysfunction, and cardiovascular disease [74]. A diet containing 0.6 to 0.8 g/Kg body weight/day of protein where, half of the protein comes from high biological value protein sources such as-dairy products or egg and the remaining from plant sources can fulfill dietary needs of an adult

with moderate to advanced CKD [75]. To reduce the prevalence of PEW among children and malnourished patients, a protein intake of at least 0.8 g/Kg body weight/day is recommended [76]. A randomized controlled clinical trial conducted in CKD stage 3 to stage 5 patients in Brazil showed that, patients' adherence to a low protein diet can be improved with provision of nutrition education[76]. A prospective cohort study (ARIC) assessed the association between the dietary protein sources and incident CKD and during a follow up of 23 years showed that, high intake of red and processd meat was associated with a high risk of CKD, compared to a diet rich in nuts, legumes and low-fat dairies using a 66-item food frequency questionnaire (FFQ) [77].

However, a low-protein diet should not be prescribed to CKD stage 4 and stage 5 patients with poor appetite and weight loss [78]. To manage increase loss of protein due to ongoing dialysis procedure, K/DOQI recommended around 1.2 to 1.3 g of protein/Kg body weight/day for a typical hemodialysis patient [79].

Phosphorus: A major role of kidney is to maintain phosphorus homeostasis. In individuals with CKD, high dietary phosphorus burden could worsen hyperparathyroidism and renal osteodystrophy, promote vascular calcification, and cardiovascular events, and thus increase mortality. Hyperphosphatemia is defined as an abnormal high serum phosphorus level of more than 1.46 mmol/L, a common metabolic anomalis in advanced CKD [80]. It is associated with coronary artery calcification, development of secondary hyperparathyroidism, left ventricular hypertrophy, mineral bone disorder and cardiovascular and all-cause mortality [81]. When phosphorus builds up in blood, it also pulled calcium from bones and cause weak and fragile bones. It also forms crystals which accumulates in joint, muscle, skin, blood vessels and heart and cause pain in bones, poor blood circulation, and damage heart [80]. In a Dialysis Outcomes and Practice Pattern Study (DOPPS) cohort study, it was revealed that

altered mineral metabolism (laboratory values for serum albumin, calcium, potassium, sodium, phosphorus, hemoglobin, vitamin D, urea, creatinine fall both above or below the K/DOQI recommended range) is related with high mortality rate among patient. The appropriate use of dialysate calcium concentration, use of food items with low Phosphorus to protein ration, phosphorus binders, vitamin D supplementation will improve patients' outcome [82].

The quantity and bioavailability of phosphorus differs with the type of dietary protein intake. Gastrointestinal absorption of phosphorus is lower for plant due to phytates than for meat [83], also processed foods have higher phosphorus burden due to the use of food additives [84]. Organic phosphate in fresh plant food has an absorption rate of 20% to 50% and in animal-based food, it is 40% to 50%, whereas, the absorption rate is more than 90% in inorganic phosphate from processed foods and carbonated drinks. Thus type of phosphate (organic or inorganic) is an important consideration for patients' education [85, 86]. Restriction of dietary phosphorus to less than 800 mg/day is recommended for CKD patients [79]. However, controlling hyperphosphatemia is associated with poor outcomes among dialysis patients who are at high risk of protein-energy wasting, and an individualized dietary approach incorporating the use of phophate binders should be recommended for dialysis patients [75]. Controling dietary phosphorus is quite challenging in real-life settings. Effective strategies include restriction of phosphorus rich food, selection of fresh food mostly from plant origin, adoption of boiling as a prefered cooking method, avoid foods with preservatives, fast food, and street food. Boiling causes demineralization of food by reducing phosphorus as well as sodium, potasium, and calcium content in both vegetables and animal-derived products. The degree of mineral los is proportional to the amount of boiling water that is used, the size of the pieces, the cooking time, and the absence of the peel for plants.

Studies showed that, boiling reduces 51% of P from vegetables, 48% from legumes, and 38% from meat [87].

Phosphorus (P) to Protein (Pro) ratio (mg of P/g of Pro): Ideally, a beneficial diet for a hemodialysis patient should be high in protein and low in bioavailable phosphorus. Because, PEW results from a reduction in protein intake due to the restriction of dietary phosphorus intake. Both low dietary protein (Pro) intake, high dietary phosphorus (P) intake and high ratio of dietary P/Pro intake are associated with increased mortality in hemodialysis patients [88]. A favorable P to Pro ratio of 10 to 12 mg/g is recommended by NKF KDOQI [89]. It has been showed that, a P/Pro ratio of a whole egg is more than 14 mg/g of protein, whereas, the ratio is less than 2 mg/g of protein in case of a egg white [90]. Nutrition education is necessary in this regard. To help in selecting foods with lower phosphorus content via different cooking methods, phosphorus bioavailability, a phosphorus pyramid is developed by National Kidney Foundation considering loss of phosphorus via different cooking methods, phosphorus bioavailability, and P to Pro ratio and is widley used as a popular, visual nutrition education tool for CKD patients (Figure**1-13**)[91].

Sodium and Fluid: Hypernatremia takes place when dietary sodium intake is high, that may lead to fluid retention, rise in blood pressure, and shortness of breath. In patients with CKD, dietary sodium restriction is recommended to control fluid retention and hypertension and to improve cardiovascular risks [92]. A dietary sodium intake of less than 4g/day is recommended for overall management of CKD and a sodium intake of less than 3g/day is recommended for specific management of fluid retention and hyponatremia. Additionally, patients with stage 3 and above should limit fluid intake to less than 1.5 L/day. Adjustment should be made based on hot climate and other associated condition of fluid loss [93]. There is little information about the dietary habits of Bangladeshi renal patients.

Common cooking practice showed the use of excess dietary salt due to poor health literacy and unawareness among Bangladeshi CKD patients in East London [94]. K/DOQI recommended a dietary sodium intake of 750 to 2000 mg a day and fluid intake of 750 to 1500 ml a day for a typical hemodialysis patients [89].

Potassium: Potassium imbalance is another common cause of morbidity among dialysis patients. For most people, fresh fruits and vegetables, rich in potassium are considered as healthy choice due to high fiber and vitamin content and low acidogenecity [95]. In epidemiological studies, both low (<4.0 mmol/L:hypokalemia) and high (>5.5 mmol/L:hyperkalemia) plasma potassium levels are related to rapid progression of kidney disease [96]. Though hypokalamia is more commong among hospitalized patients or patients undergoing peritonial dialysis, hyperkalamia is most common among hemodialysis patients due to excess intake and inadequate removal. Regulating dietary intake of potassium is difficult for patients who are also told to reduce intakes of phosphorus, sodium, water, and carbohydrates while having diabetes as a comorbidity. Excessive dietary potassium restriction can expose patients to less heart-healthy and more atherogenic diet and constipation [97]. Appropriate cooking method in order to leach potassium from fruits and vegetables should be adopted to avoid hyperkalemia. In hemodialysis patients with hyperkalemia, a dietary potassium intake of less than 3 g/day with a balanced intake of fiber-rich (20 to 25 g/day) fresh fruits and vegetables is recommended by K/DOQI [89].

Summary with Specific Aims

There is a rising trend in the incidence and prevalence of CKD in Bangladesh. Every year around 35,000-40,000 people reach ESRD and about 40,000 people die from kidney disease. Malnutrition and inflammation contributes to the high rates of mortality among dialysis patients. HD patients have a greater risk for cardiovascular disease, stroke and dyslipidemia, a compromized antioxident system, cognitive dysfunction, metabolic abnormalities, hospitalization, and all cause mortality. The main goals of treating patients with CKD are to slow down disease progression and prevent CVD and atherosclerotic complications. Nutrition and life-style modifications might play a key role to improve the outcomes. However, no single method can assess the overall nutritional and health status of a patient undergoing HD and a combination of multiple approaches should be employed to understand this issue. One such approach could be to assess the impact of improved nutrition knowledge on the nutritional and health status of HD-CKD patients. Therefore, by providing patients a renal-specific nutrition and health related counseling, it may be possible to improve dialysis outcomes as well as nutrition and health status of this population group in a resource-poor setting. To the best of our knowledge, no study has been done in Bangladesh to assess the current nutrition and health status of hemodialysis patients and see the impact of renal-specific nutrition knowledge on their overall quality of life.

The goal of this Ph.D. ***proposal*** is to document the extent of nutrition and health status of patients undergoing HD in a resource poor setting. The ***central hypothesis*** is that, high morbidity and mortality in HD patients in Bangladesh is in part attributed to poor nutrition and nutritional knowledge. The ***rationale*** for this research proposal is that, once the basis for poor nutrition and lack of nutrition knowledge has been established, appropriate interventions can be provided to renal patients in this resource-poor setting which may result

in an improvement in their quality of life. The information will also serve as a basis for training support staff to disseminate nutrition information in dialysis units across Bangladesh. To test my hypothesis I proposed the following specific aims:

Specific Aim I:

To assess the current nutrition and health status of hemodialysis patients in a specialized renal hospital in Dhaka, Bangladesh.

Specific Aim II:

To document the prevalence of protein energy wasting (PEW) based on criteria from the International Society for Renal Nutrition and Metabolism (ISRNM) among the existing hemodialysis patients.

Specific Aim III:

To develop culturally acceptable renal-specific nutrition information and evaluate its impact on patients' renal nutrition-related knowledge

Tables and Figures

Tables

Table 1-1. Kidney Functions [9].

	Functions
Waste elimination	Removal of metabolic waste products (urea, creatinine, uric acid) and elimination and detoxification of drugs and toxins
Fluid balance	Involve in removal and reabsorption of water to maintain fluid balance (via action of antidiuretic hormone, atrial natriuretic peptide, aldosterone)
Acid-base regulation	Involve in secretion, excretion and reabsorption of H^+, HCO_3^-, NH_4^+, PO_4^{++} to maintain blood pH
Electrolyte balance	Involve in excretion and reabsorption of electrolytes such as sodium, potassium, chloride, and bicarbonate to maintain homeostasis
Mineral metabolism	Control of mineral metabolism through endocrine synthesis (1,25-dihydroxycholecalciferol and 24, 25-dihydroxycholecalciferol) and excretion of phosphorous
Endocrine functions	Regulation of systemic blood pressure (renin, angiotensin, prostaglandin, nitric oxide, sodium homeostasis and production of erythropoietin
Metabolic process	Regulation of metabolic process (gluconeogenesis, lipid metabolism) Degradation and catabolism of peptide hormones (insulin, glucagon, parathyroid hormone) and low molecular weight protein (β_2-microglobulin and light chain)

Source: Handbook of Nutrition and the Kidney, 2010 [9]

Table 1-2. Prevalence of Chronic Kidney Disease (CKD) in Bangladesh

Reference	Year	Place	Age, Year	Diagnostic Criteria	No. of pts	Prevalence (%)	Type of study
Huda et al.[98]	2010	Urban	15-65	Spot quantitative urine protein, Creatinine clearance and eGFR (CG/BSA and MDRD)	1000	MDRD:13.1, C-G Eq: 16	Cross sectional
Das et al.[99]	2010	Urban		eGFR, albuminuria	1200	MDRD:7.2, C-G Eq: 9.9	Cross sectional
Hasan et al.[100]	2012	Rural	18-65	Urine for albumin, Sr. creatinine, RBS	1240	MDRD:19.5, C-G Eq:19	Cross sectional
Fatema et al.[21]	2013	Urban	18-70	Spot quantitative urine protein and eGFR (MDRD)	634	12.8	Screening
Anand et al.[17]	2014	Urban	>30	Spot quantitative urine protein and eGFR (CKD-EPI)	402	26	Cross sectional
Khanam et al.[101]	2016	Urban	18-80	K/DOQI Guideline	1317 (T2-DM)	13.9	

MDRD: modification of diet in renal disease, C-G: Cockcroft-Gault formula, eGFR: estimated glomerular filtration rate, ACR: albumin creatinine ratio, CKD-EPI: chronic kidney disease epidemiology

Table 1-3. Causes of PEW in CKD patients [59]

		Causes of PEW in CKD patients
1		**Decreased protein and energy intake**
	a	Anorexia
		i. Dysregulation in circulating appetite mediators
		ii. Hypothalamic amino acid sensing
		iii. Nitrogen-based uremic toxins
	b	Dietary restrictions
	c	Alterations in organs involved in nutrient intake
	d	Depression
	e	Inability to obtain or prepare food
2		**Hypermetabolism**
	a	Increased energy expenditure
		i. Inflammation
		ii. Increased circulating proinflammatory cytokines
		iii. Insulin resistance secondary to obesity
		iv. Altered adiponectin and resisting metabolism
	b	Hormonal disorders
		i. Insulin resistance of CKD
		ii. Increased glucocorticoid activity
3		**Metabolic acidosis**
4		**Decreased physical activity**
5		**Decreased anabolism**
	a	Decreased nutrient intake
	b	Resistance to GH/IGF-1
	c	Testosterone deficiency
	d	Low thyroid hormone levels
6		**Comorbidities and lifestyle**
	a	Comorbidities (diabetes mellitus, CHF, depression, coronary artery disease, peripheral vascular disease)
7		**Dialysis**
	a	Nutrient losses into dialysate
	b	Dialysis-related inflammation
	c	Dialysis-related hypermetabolism
	d	Loss of residual renal function

Source: Etiology of the protein-energy wasting syndrome in chronic kidney disease: a consensus statement from the International Society of Renal Nutrition and Metabolism (ISRNM) [59]

Table 1-4: Prevalence of malnutrition among HD patients in different countries

Author	Country	Sample Size	Prevalence (%)
Campbell et. Al. 2013[102]	Australia	213	23.5
Alharabi et.al. 2012[103]	Saudi Arabia	269	48.7
Harvinder et.al. 2016[104]	Malaysia	155	59
Srivastava et al. 2012[105]	India	135	43.0
Wardani et al. 2019[106]	Indonesia	71	66

Analysis was done in HD patients

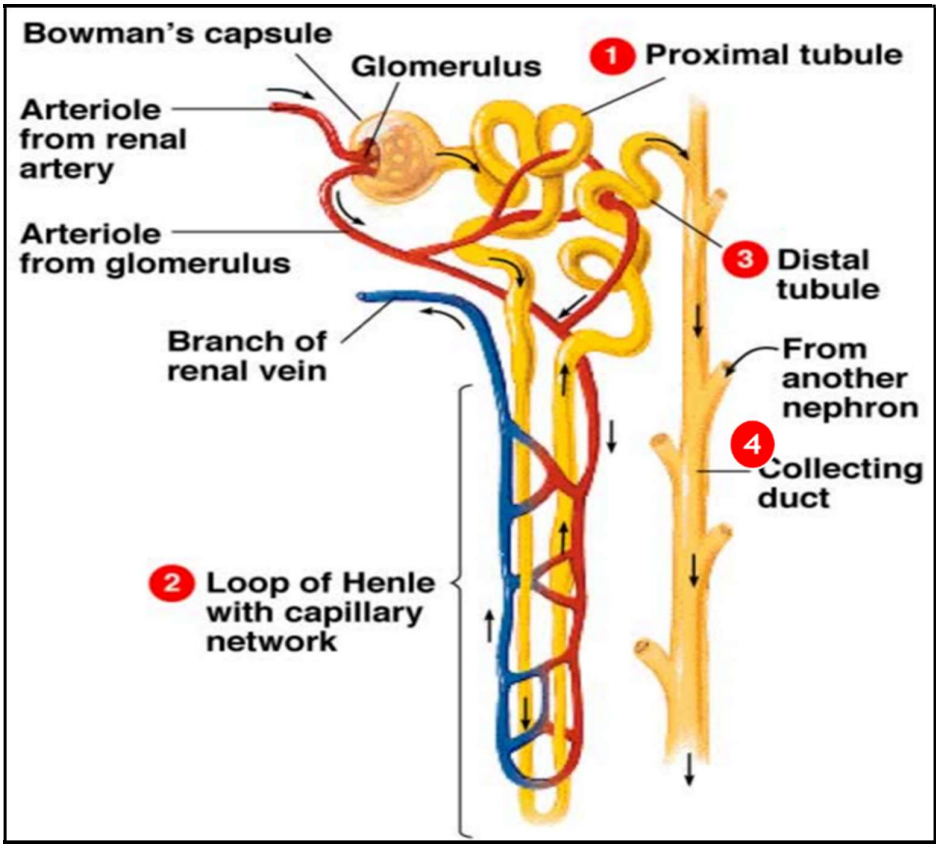
Table 1-5: A simplified historical scheme of the main focuses in diets for patients on chronic hemodialysis[73]

Period	**The 'Main Enemy'**	**The Risks**	**Dietary Indications**
First Era	Potassium	Hyperkalemia can be deadly	Restrictions on fruits and vegetables
Second Era	Phosphate	Vascular calcification, vascular ageing	Restrictions on cheese, milk and derivatives
Third Era	Malnutrition	Risk of death is higher in malnourished patients	Increased protein and calorie intake

The definition of each period is approximate, as each one merges with the next, and the first warnings on malnutrition are as old as dialysis itself, while we should always keep in mind the short-term risks of hyperkalemia and the long-term importance of hyperphosphatemia [73].

Figures

Figure 1-1. Overview of Kidney Structure



Source: Overview of Kidney Function and Structure [7]

Figure 1-2. Percentage of NHANES 2013-2016 participants, in the various CKD (eGFR and albuminuria) risk categories (KDIGO 2012)[15]

				Albuminuria categories			
				A1	A2	A3	
				Normal to mildly increased	Moderately increased	Severely increased	
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol	Total
GFR categories (ml/min/1.73 m^2)	G1	Normal to high	≥90	54.9	4.2	0.5	59.6
	G2	Mildly decreased	60-89	30.2	2.9	0.3	33.5
	G3a	Mildly to moderately decreased	45-59	3.6	0.8	0.3	4.7
	G3b	Moderately to severely decreased	30-44	1.0	0.4	0.2	1.7
	G4	Severely decreased	15-29	0.13	0.10	0.15	0.37
	G5	Kidney failure	<15	0.01	0.04	0.09	0.13
			Total	89.9	8.5	1.6	100

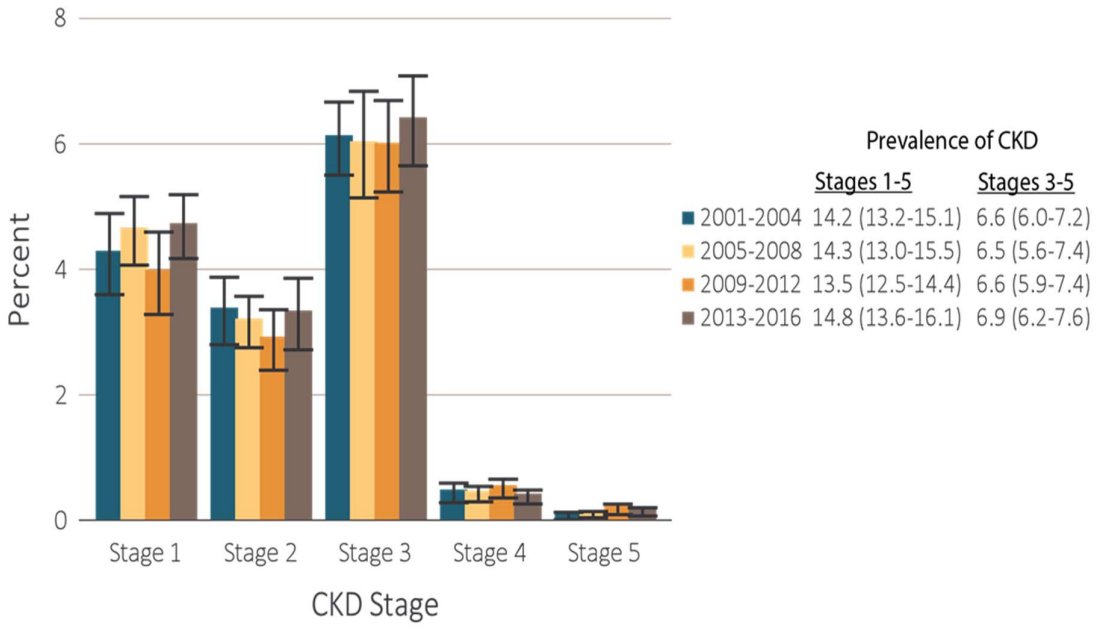
Data source: USRDS Annual Data Report, 2018 [15].National Health and Nutrition Examination Survey (NHANES), 2001-2004, 2005-2008, 2009-2012 & 2013-2016 participants aged 20 and older. Single-sample estimates of eGFR and ACR; eGFR calculated using the CKD-EPI equation. Low risk: eGFR ≥60 ml/min/1.73 m^2 and ACR <30 mg/g; moderately high risk: eGFR 45-59 ml/min/1.73 m^2 or eGFR ≥60 ml/min/1.73 m^2 and ACR 30-300 mg/g; high risk: eGFR 30-44 ml/min/1.73 m^2 or eGFR 45-59 ml/min/1.73 m^2 and ACR 30-300 mg/g or eGFR ≥60 ml/min/1.73 m^2 and ACR >300 mg/g; very high risk: eGFR <30 ml/min/1.73 m^2 or eGFR 30-44 ml/min/1.73 m^2 and ACR 30-300 mg/g or eGFR ≥60 ml/min/1.73 m^2 and ACR >300 mg/g.
Abbreviations: ACR, urine albumin/creatinine ratio; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate; KDIGO, Kidney Disease: Improving Global Outcomes CKD Work Group.

Figure 1-3. Stages of Chronic Kidney Disease[107]

Stages	Description	GFR (ml/min/1.73 m2)	
Stage 1	Kidney damage with normal kidney function	90 or higher	
Stage 2	Kidney damage with mild loss of kidney function	89 to 60	
Stage 3a	Mild to moderate loss of kidney function	59 to 45	
Stage 3b	Moderate to severe loss of kidney function	44 to 30	
Stage 4	Severe loss of kidney function	29 to 15	
Stage 5	Kidney Failure	Less than 15	

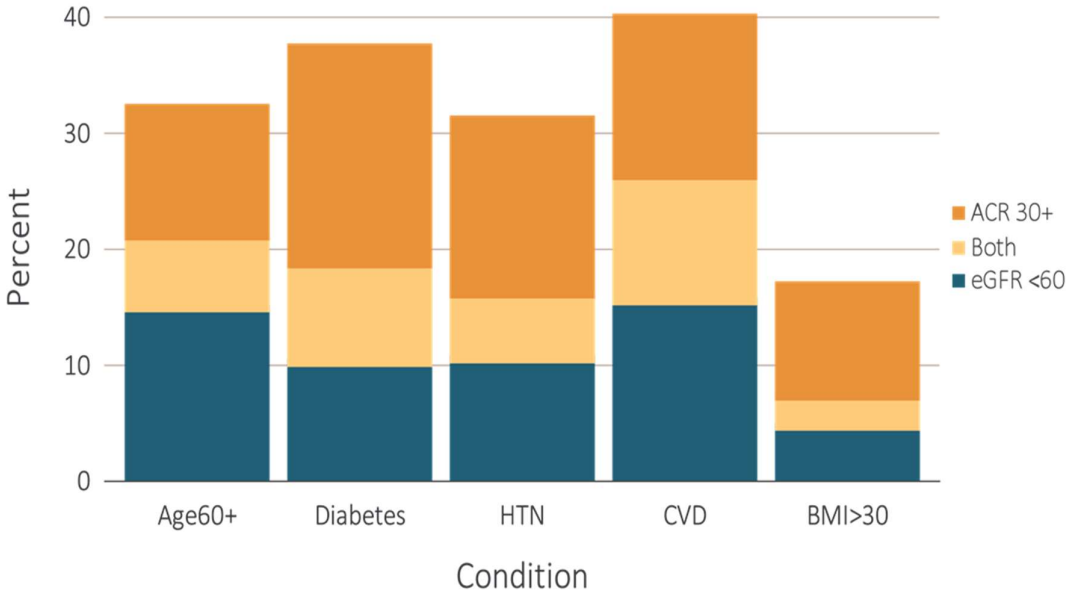
Source: National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification.[107]

Figure 1-4: Prevalence of CKD by stages among NHANES participants (2001-2016)[15]



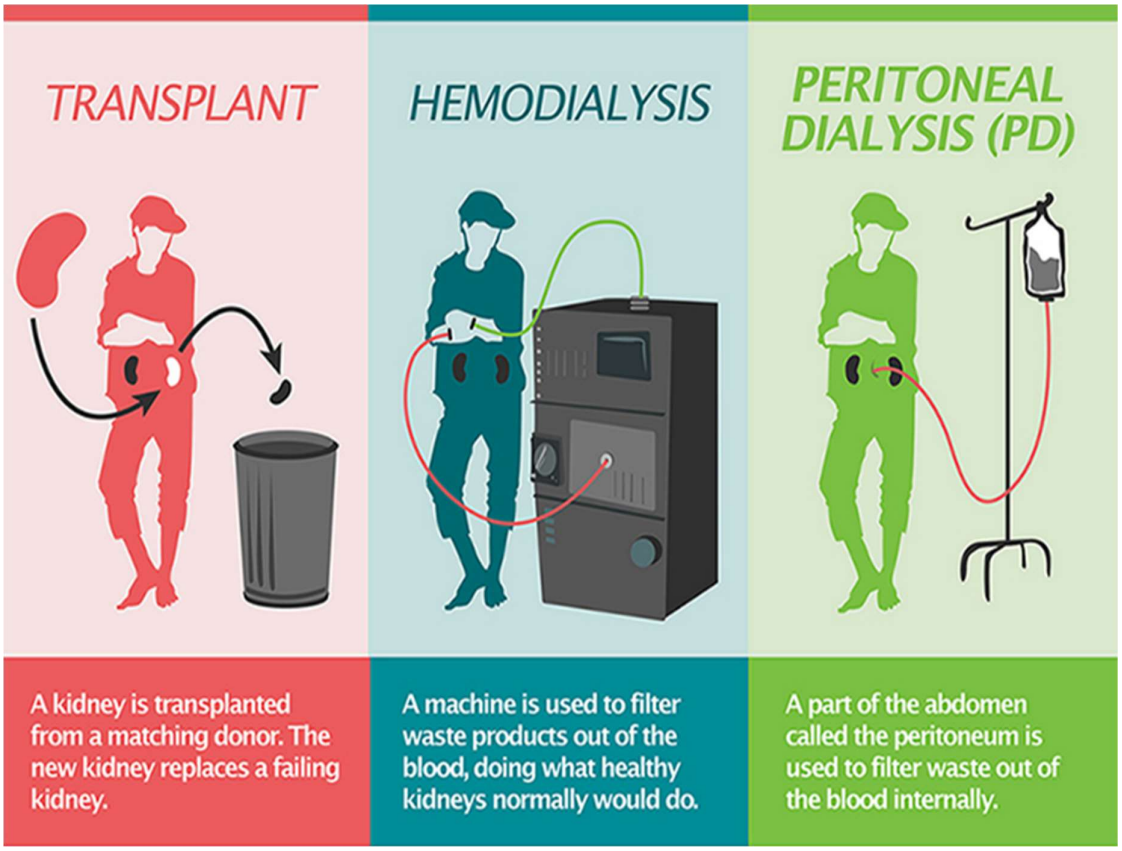
Data Source: National Health and Nutrition Examination Survey (NHANES), 2001-2004, 2005-2008, 2009-2012 & 2013–2016 [15], participants aged 20 & older. Whisker lines indicate 95% confidence intervals. Abbreviation: CKD, chronic kidney disease.

Figure 1-5: Distribution of markers of CKD in NHANES participants with diabetes, hypertension, self-reported cardiovascular disease and obesity, 2013-2016[15]



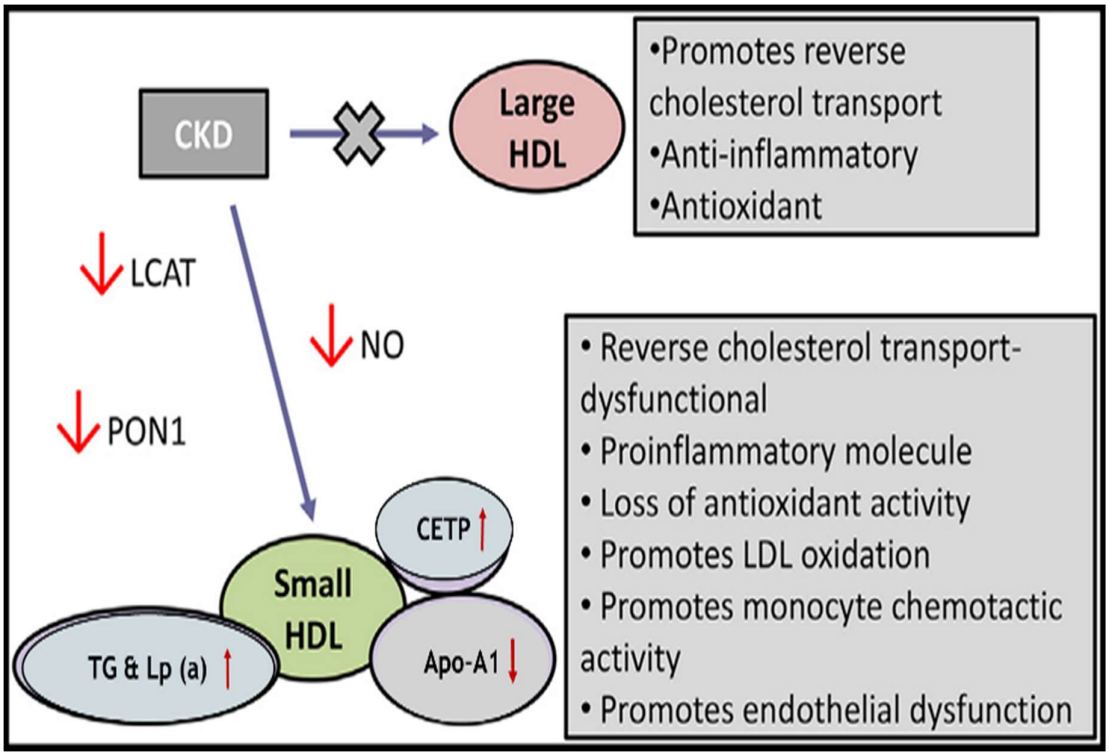
Data Source: National Health and Nutrition Examination Survey (NHANES), 2013-2016 [15], participants age 20 & older. Single-sample estimates of eGFR & ACR; eGFR calculated using the CKD-EPI equation. Abbreviations: ACR, urine albumin/creatinine ratio; BMI, body mass index; CKD, chronic kidney disease; SR CVD, self-reported cardiovascular disease; eGFR, estimated glomerular filtration rate; HTN, hypertension.

Figure 1-6: Treatment options for Renal Replacement Therapy (RRT)



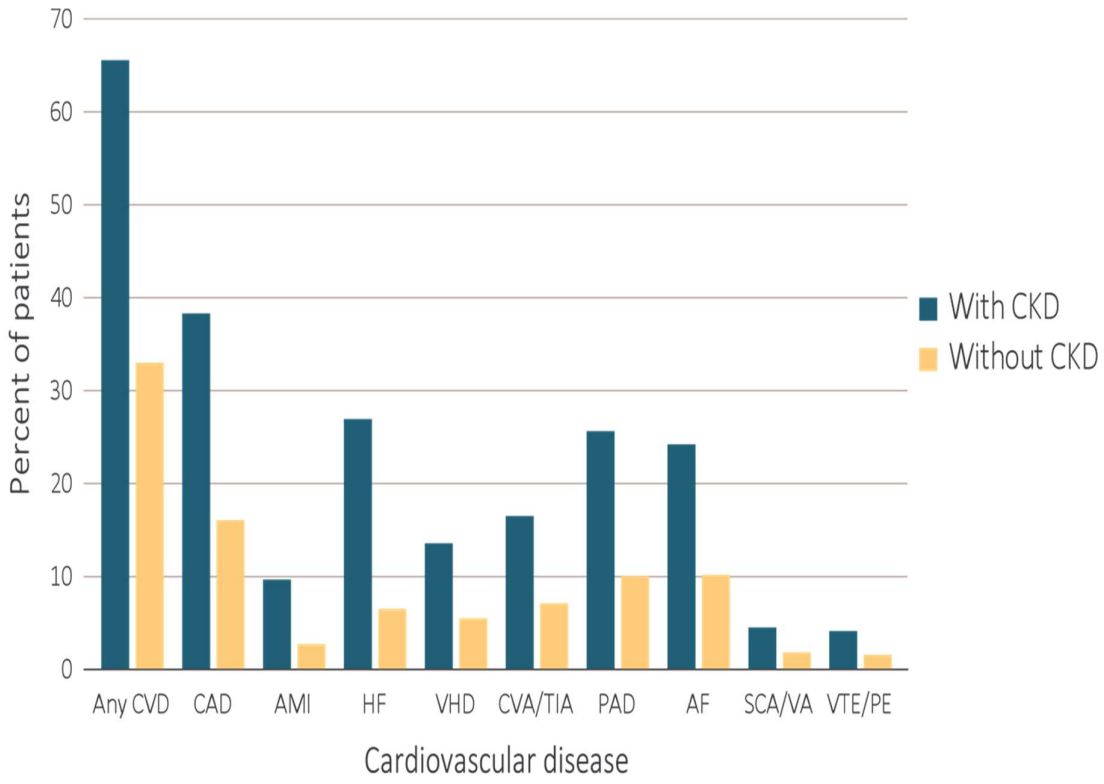
Source: Adopted from Internet

Figure 1-7. Changes in HDL Function mediated by CKD [53]



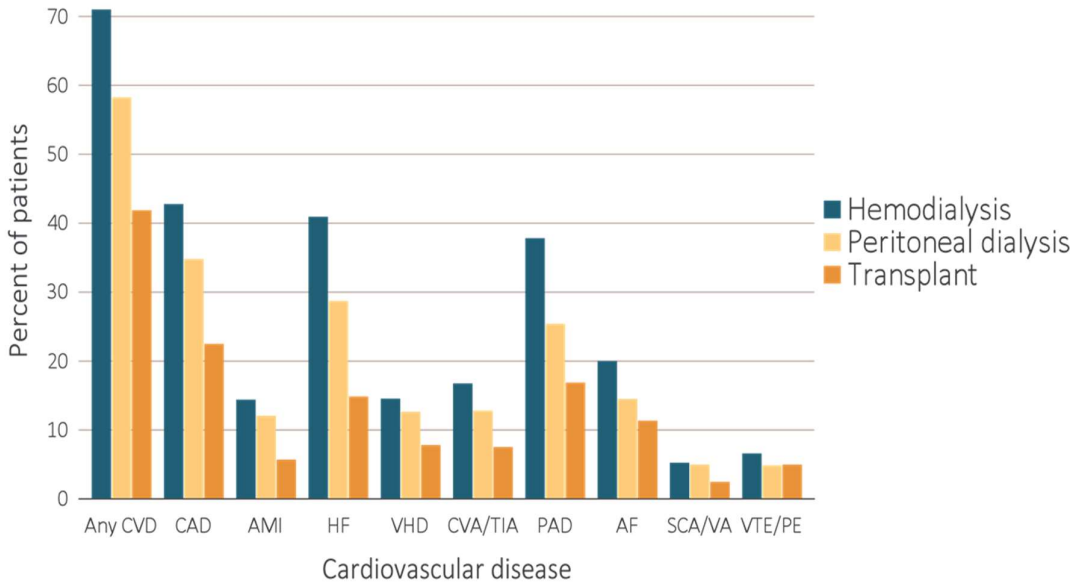
Source: Cholesterol Metabolism in CKD [53]

Figure 1-8: Prevalence of common cardiovascular diseases in patients with or without CKD, 2016 [15]



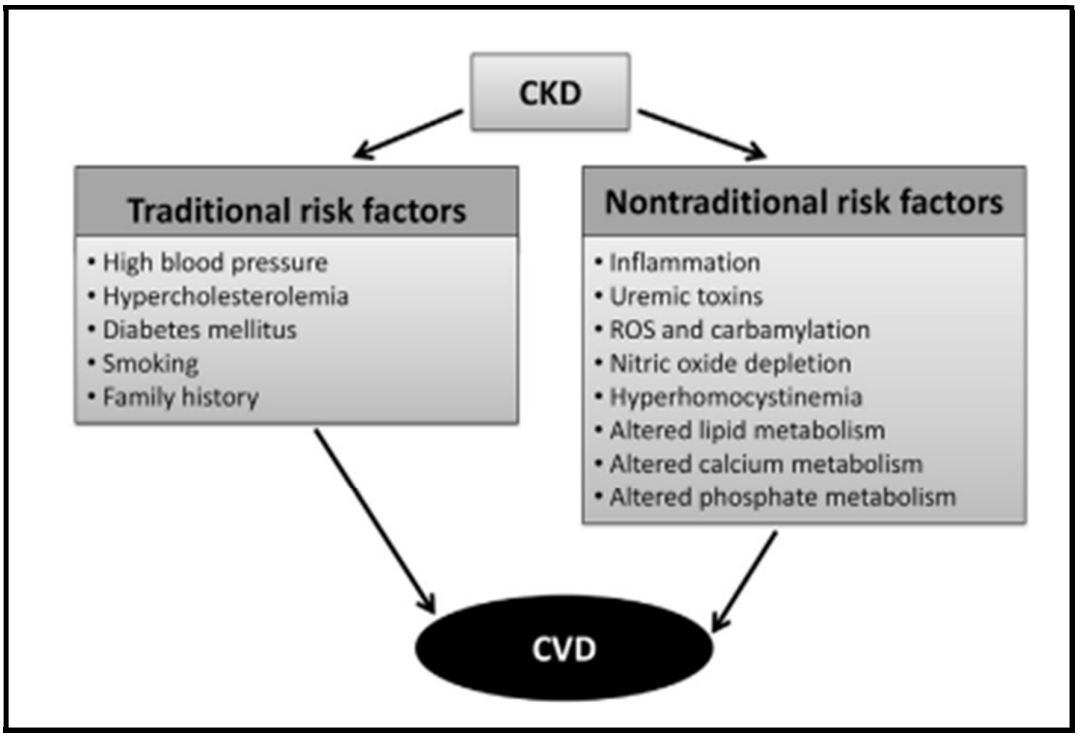
Source: USRDS Annual Data Report [15]. Abbreviations: AF, atrial fibrillation; AMI, acute myocardial infarction; CAD, coronary artery disease; CKD, chronic kidney disease; CVA/TIA, cerebrovascular accident/transient ischemic attack; CVD, cardiovascular disease; HF, heart failure; PAD, peripheral arterial disease; SCA/VA, sudden cardiac arrest and ventricular arrhythmias; VHD, valvular heart disease; VTE/PE, venous thromboembolism and pulmonary embolism

Figure 1-9: Prevalence of cardiovascular diseases in adult ESRD patients by treatment modality, 2016[15]



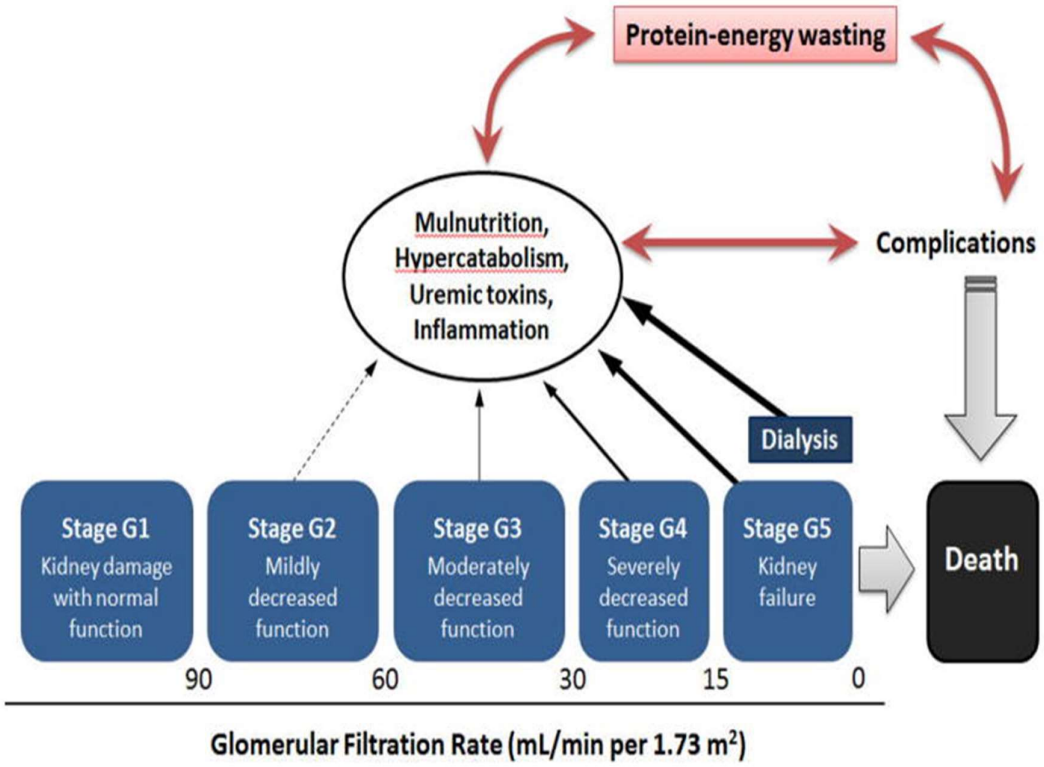
Data Source: Special analyses, USRDS ESRD Database [15]. Abbreviations: AF, atrial fibrillation; AMI, acute myocardial infarction; CAD, coronary artery disease; CVA/TIA, cerebrovascular accident/transient ischemic attack; CVD, cardiovascular disease; HF, heart failure; PAD, peripheral arterial disease; SCA/VA, sudden cardiac arrest and ventricular arrhythmias; VHD, valvular heart disease; VTE/PE, venous thromboembolism and pulmonary embolism.

Figure 1-10: CVD Risk Factors in CKD [53]



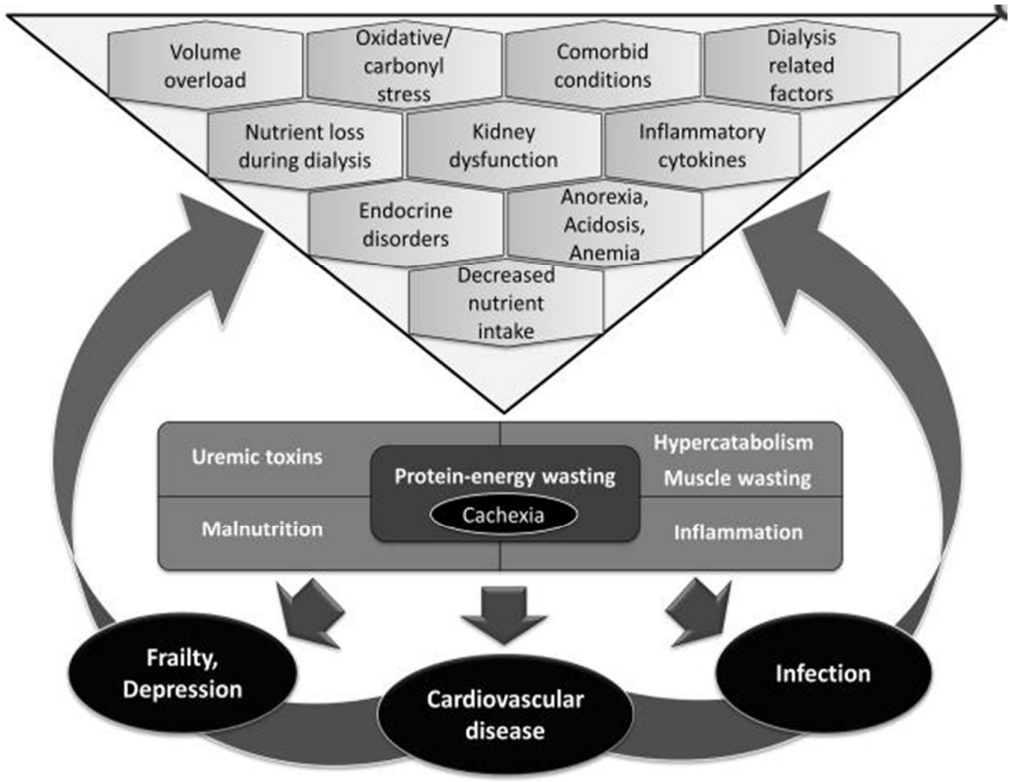
Source: Cholesterol Metabolism in CKD [53]. Chronic kidney disease (CKD) and cardiovascular disease (CVD) risk factors and their interplay. Traditional risk factors are found in both the CKD and non-CKD population. Nontraditional risk factors may result from or be worsened by CKD and negatively affect the cardiovascular system in the CKD population. Abbreviation: ROS, reactive oxygen species.

Figure 1-11: The Conceptual Model for CKD progression, and its consequences [57]



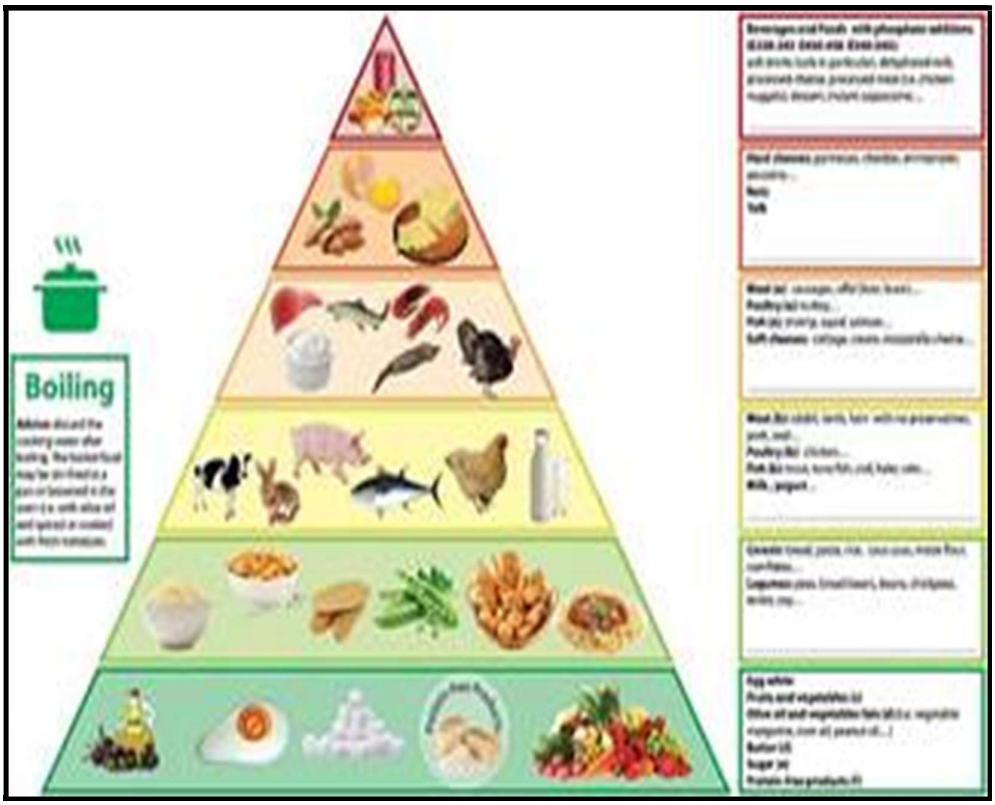
Source: Latest consensus and update on protein-energy wasting in chronic kidney disease [57]

Figure 1-12: The conceptual model for etiology of PEW in CKD and direct clinical implications [57]



Source: Latest consensus and update on protein-energy wasting in chronic kidney disease [57]

Figure **1-13.** The Phosphorous Pyramid [91]



Source: The “phosphorus pyramid”: a visual tool for dietary phosphate management in dialysis and CKD patients [91].

CHAPTER 2 METHODOLOGY

General Study Design

The purpose of **specific aim I** was to examine the current health and nutritional status of HD patients. A total of 133 patients on MHD from Kidney Foundation Hospital and Research Institute, Dhaka, Bangladesh (in 2017 and 2018) were assessed based on anthropometric, biochemical and clinical parameters in this cross-sectional study. Lipid and lipoprotein subfractions were analyzed and patients with dyslipidemia were characterized using triglycerides (TG) to high density lipoprotein cholesterol (HDL-C) ratios of > 3.8 and < 3.8 as well as the Adult Treatment Panel (ATP) III, 2013 guidelines. Patients' data were also analyzed based on gender and twice weekly vs thrice weekly dialysis in order to measure any differences between these two groups.

The goal of **specific aim II** was to identify patients with poor nutritional and health status. Patients were assessed for protein energy wasting (PEW) based on ISRNM proposed diagnostic criteria. We explored prevalence of PEW at KFHRI where more than 3.5 lacs (3,60616) dialysis sessions were offered for patients with kidney failure over the last 16 years in KFHRI and as the recent meta-analysis of global prevalence of PEW across 36 countries did not have any data for Bangladesh [63].

The goal for **specific aim III** was to develop an educational tool for improving renal-specific nutrition knowledge among hemodialysis patients in the form of a "Nutrition Booklet". A further objective was to improve adherence to renal-specific diet among dialysis patients.

Study site- Kidney Foundation Hospital and Research Institute (KFHRI)

Kidney Foundation Hospital and Research Institute (KFHRI) is a specialized hospital in Dhaka, Bangladesh. Twenty-two percent of the ESRD patients received renal replacement therapy (RRT) and are managed with HD initially. Also, 50% of kidney transplantation are performed in KFB each year. The survival rate for both HD and kidney transplant patients in KFHRI is better than any other facilities in Bangladesh and other Asian countries [3].

Ethics and Human Subjects Issues

A total of 133 MHD patients were assessed between 2017 and 2018. A pilot study in 2017 and the clinical trial, "Palm Tocotrienol in Chronic Hemodialysis Study (PATCH)" in 2018 were both approved by the ethics board of both KFHRI and Wayne State University (WSU), while the PATCH study was further approved by the Institutional Review Board of Wayne State University (IRB#123314MP4F), where, 102 were enrolled in a clinical trial assessing the impact of supplementation with 300 mg of tocotrienols or placebo (PATCH clinical trial NCT 02358967) by the local hospital staffs. The data reported in the current study from the "PATCH participants" were collected prior to the start of their supplementation. Inclusion criteria was ESRD patients undergoing MHD treatment for at least 3 months and more than 18 years old. Informed written consent was obtained from all patients. Where needed consent forms and case report forms were translated into the Bangla language, approved by bi-lingual nephrologists and registered lawyer (Figure **3-1**).

Anthropometric assessment

To facilitate anhtropometric data collection, two phases of training were implemented. Initially a training workshop was conucted at KFHRI for nurses, medical doctors and the local nutrionists. Next, another training session at KFHRI was conducted by members of the

research team, just prior to data collection, again involving nurses, medical doctors and resident nutrionists. In both sessions, training was provided by individuals who were Level 3 certified by the International Society for Anthropometry and Kinanthropometry (ISAK) for anthropometric assessments. For data collection, patients were assessed by 2-3 teams of 3-4 individals per team. Each team included a hopsital nephrologist, staff member and a research team member. Anthropometric assessments included measurement of height and post-dialysis weight, and calculating Body Mass Index (BMI) of a patient using the Quetelet's index [108]. Before or after dialysis session, mid-arm circumference (MAC) was measured for each subject in a standing position using a non-stretchable Lufkin® tape (Apex Tool Group, LLC, NC, USA). Also, triceps skinfold thickness (TSF) was measured using Lange skinfold calipers (Lange Skinfold Calipers, Power System, Tennessee, USA). Mid-arm muscle circumference was then calculated using the standard formula: [MAMC=MAC-(3.14 x TSF)] [109]. Protocol from the International Society for Advancement of Kinanthropometry (ISAK) was followed. Handgrip strength for each patient was measured by taking three readings with a rest period of at least 1 min between trials from the non-fistula hand using a Jamar Hand-grip dynamometer (BK-7498; Fred Sammons, Inc., Burr Ridge, IL). The measurements were taken to assess muscle strength of the patient. The measurement was taken before or after the dialysis session while the patient was in sitting position and standard protocol from the American Society of Hand Therapists was used [110].

Nutritional assessment

There is no formal dietetics program or specialized nutrition program with practicums in renal nutrition in Bangladesh and most nutrionists are indviduals who took some nutrition courses as undergraduates. 'No' dietitian with skills was available, routine nutrition assessment as per KDOQI/ ISRNM was not been performed in the hospital. In such

circumstances, dietary data collection was a big challenge and training was given to hospital dietitian before data collection. For nutrition data collection, initially a training workshop was conucted at KFHRI for nurses, medical doctors and the local nutrionists. Afterwards, one member affiliated with the hospital site attended a two week training workshop in Malaysia with other members of the research team. During this visit, shadowing of staff in local dialysis units was arranged. A final training session at KFHRI was conducted by members of the research team, just prior to data collection. The training was provided by individuals who were registered dietitians (accreditation from Austalia and USA).

In both 2017 and 2018, only one-day 24-hour diet recall data were collected and analyzed from all the patients. Then dietary data were analyzed using ESHA Food Processor Nutrition Analysis and Fitness Software, version 11.3.285. For mixed dishes, that were not in the existing data base, ingredients were entered in the recipe builder within the software and approximately 150 Bangladeshi recipes were thus prepared based on recipes available for some common foods in Bangladesh from “Food Composition Table for Bangladesh” (Figure **2-2**) [111] and established recipes available from online. Ingredients available in both "ESHA" and “Food Composition Table” were used and some were also collected from “online sources” and were verified by searching various food database website and comparing them.

Basal Metabolic Rate (BMR) was calculated using Harris-Benedict Equation: [*men: 66.5+(13.75 x body weight in Kg) +(5.0 x height in cm) - (6.76 x Age in years)] and [*women:655+(9.6 x body weight in Kg) +(1.8 x height in cm) -(4.7 x age in years)] [112, 113].

When their weight was <95% or >115% of the standard body weight, we used adjusted edema-free body weight and when the value was between 95%-115%, we used actual body weight as recommended by NKF KDOQI (2000) guidelines[79].

To minimize systemic error, underreporting of dietary data was evaluated by calculating the ratio between reported energy intake (EI) and basal metabolic rate (BMR). Goldberg cut-off equations for EI: BMR (Energy Intake: Basal metabolic rate) can be used to determine the mean population bias in reported energy intake[114, 115]. However, as we do not have any physical activity value, here we directly compare energy expenditure with energy intake to determine under-reporters, with a ratio of EI:BMR<0.75 being used as a cut-off for under-reporters, more than 2.4 was considered over-reporters and the ratio of 0.75 to 2.4 being used as acceptable reporters [116]. It is often difficult to get an accurate picture of the dietary intake of patients due to the prevalence of high rates of underreporting among CKD patients and there is dispute on how to omit under-reporters while doing dietary evaluation especially in terms of total calorie, protein, dietary fiber, calcium and zinc intake[117, 118]

Blood sampling and Lipid measurements

Non-fasting blood smaples were collected into two sets of tubes, one containing Ethylene Diamine Tetraacetic Acid (EDTA) and one containing Lithium Heparin (LH). The use of non-fasting blood samples is consistent with recent reports and guidelines where it is noted that, they are valid predictors of cardiovascular disease risk [119]. Plasma samples were isolated by centrifugation at 3500 rpm for 10 minutes at 4^0C and multiple aliquots were immediately stored at -80^0C. They were subsequently transported to Wayne State University on dry ice via courier (World Courier Service, Bangladesh). Plasma total cholesterol (TC) and triglycerides (TG) were measured using enzymatic assays (Point Scientific Inc., Canton,

MI, USA). HDL-C was assessed in the supernatant after precipitating apo B lipoproteins with dextran sulfate and magnesium ion (Point Scientific Inc.). LDL-C was calculated using the Friedwald formula: [LDL-C=TC-HDL-C-(TG/5)]. HDL and LDL-subfraction were analyzed in plasma using the Lipoprint^{TM} polyacrylamide electrophoresis-based system (Quantimetrix Corporation, Redondo Beach, CA, USA) and were quantitated using the manufacturer's software[120]. HDL can be separated into 10 subfractions which can be grouped into large, intermediate and small HDL (Figure **2-3**). Similarly, LDL is separated into 7 subfractions, which can then be classified into three groups constituting of large, intermediate and small LDL (Figure **2-4**). This system is certified by FDA for clinical LDL subfraction measurements, while values for HDL are for research purposes only.

Sociodemographic data and medical history were collected for all patients. Data were also collected for different types of health-related questionnaire such as malnutrition inflammation score (MIS), appetite and diet analysis tool (ADAT), and health-related Quality of life (HR-QoL) from 102 patients in 2018.

MIS Form (Malnutrition inflammation score)

This is a new comprehensive scoring system with 10 components is an indicator of malnutrition-inflammation complex syndrome (MICS) and is also significantly correlated with measures of inflammation (C-Reactive Protein), anemia (Hematocrit), and nutritional status (Creatinine) as well as hospitalization and mortality of patients on maintenance hemodialysis (MHD) [46]. It combines the traditional 7 components of subjective global assessment along with body mass index (BMI), serum albumin level and total iron binding capacity (TIBC) to represent serum transferrin level. This score has validity and reliability to diagnose malnutrition among hemodialysis population [121]. A score >5 indicates malnourished. The MIS has 10 components, each with four levels of severity, from 0

(normal) to 3 (very severe). The sum of all 10 MIS components ranges from 0 (normal) to 30 (severely malnourished); higher score reflects a more severe degree of malnutrition and inflammation [46].

ADAT Form

It was developed to assess the appetite and factors affecting food intake in hemodialysis patients in accordance with dose of dialysis provided [122]. One study suggested that, poor appetite is correlated with increased proportion of malnourished dialysis patients [123]. It is a five-point scale, where, "1=very good', "2=good', "3=fair', "4=poor', and "5=very poor'. The lower the score, the better the appetite of a patient [124]. Thus, ADAT of scale one means very good appetite whereas, ADAT of scale five means very poor appetite.

Restless Leg Syndrome (RLS) Score Form

RLS is a sensory-motor disorder, usually occurs in lower limbs of the body during rest or sleep time and is related to poor sleep quality and depression [125]. Higher score means severity of RLS, Here, "0" point means "no symptom", 1-10 points meaning "mild symptom", 11-20 points meaning "moderate symptom", 21-30 points meaning "severe symptoms", and 31-40 points meaning "very severe symptoms". Restless leg syndrome scale: 0, None; 1 – 10, Mild RLS; 11-20, Moderate RLS, 21-30 Severe RLS, 31-40 Very Severe RLS. Patients reporting score '0' were excluded from analysis [126].

HR-QoL (Health Related Quality of life) and SF 36

Quality of Life (QoL) was assessed using an interviewer administered 36-item Short Form Health Survey (SF-36) questionnaire [127]. The KDQOL-36 is comprised of five subscales calculated separately: 1) SF-12 physical component summary (PCS), 2) SF-12 mental component summary (MCS), 3) burden of kidney disease, 4) symptoms of kidney

disease, and 5) effects of kidney disease. The two domains in SF-36, PCS used for assessing physical health status and MCS used for assessing emotional and psychological function contribute to the total QoL score [128]. It is an easy to use tool that can be use in the outcome assessment programs for dialysis patients [129]. KD- QoL Subscale scores range from 0 to 100, with lower scores indicating poor self-reported QOL [130]. It is also a clinically adequate and inexpensive method that gives a balanced estimation of nutritional status in dialysis patients [131]. The lower the score, the more malnourished the patient will be and it is a good way of assessing morbidity and mortality of HD patients.

Assessment of PEW patients (Specific Aim II)

PEW was diagnosed in the study patients based on anthropometric and biochemical measures as described by the International Society for Renal Nutrition and Metabolism (ISRNM) (Figure **2-5**) [57]. Data were utilized from four criteria with pre-established values - serum chemistry (albumin, prealbumin or cholesterol), body mass (BMI, unintentional weight loss over time or fat percentage), muscle mass (muscle wasting over time, MAMC or creatinine appearance) and dietary intake (using measures of DPI or DEI). If measures for 3 out of 4 major criteria were encountered, a patient was diagnosed as having PEW.

Development of culturally acceptable renal-specific 'Nutrition Booklet' for Hemodialysis patients (Specific Aim III)

The booklet was developed with input from Registered dietitians from USA and Malaysia, nephrologists, nutritionists, published dietary guidelines, scientific literature as well as the "Bangladeshi Food Composition Table" from the Institute of Nutrition and Food Science (INFS), University of Dhaka [111]. It included utilization of data from "Food Composition Table of Bangladesh" in order to assess protein, phosphorus, potassium and sodium content of ethnic and typically consumed Bangladeshi Food Stuffs and based on that,

list food based on its phosphorous to protein ratio and potassium content, construct meal plan and formulate a "Bangladeshi Phosphorus Pyramid", all of which could be used as a visual and user-friendly tool for the nutrition education of dialysis patients as well as of health care professionals and to improve existing renal-specific nutrition knowledge/food practice among the patients identified as having poor nutritional and health status. The booklet contained a translation of necessary nutrition related information and suggestions in the "Local (Bangla)" language as well as an analyses of 381 ethnic food items from the INFS data-base for renal-specific nutrients: protein, sodium, potassium, and phosphorous. The booklet was generated in "Bangla" and then translated into English and cross-checked by bilinguists.

Statistical Analysis:

The software, Statistical package for social science (SPSS) version 26 (IBM, Chicago, IL, USA) was used for data analysis. Descriptive statistics of continuous variables were reported as mean±standard deviation (SD), median (Interquartile range, IQR), and frequency or number (n) and percentage (%), depending on the distribution of variables. Categorical variables were presented as number (n) and pecentage. The normal distribution of continuous variables was assessed using Kolmogorov-Smirnov test. Differences between groups were analyzed using Student *t* test and Mann-Whitney's U test for normally distributed and non-normally distributed data, respectively. $p < 0.05$ was considered statistically significant. When there were more than two groups, a one way ANOVA (analysis of variance) test was used and in order to assess the difference among groups, Tukey's Post Hoc test was used. Correlations were evaluated using Pearson's and Spearman's rank crrelation test.

Figure 2-1. Study Flow Chart for Specific Aim I and Specific Aim II.

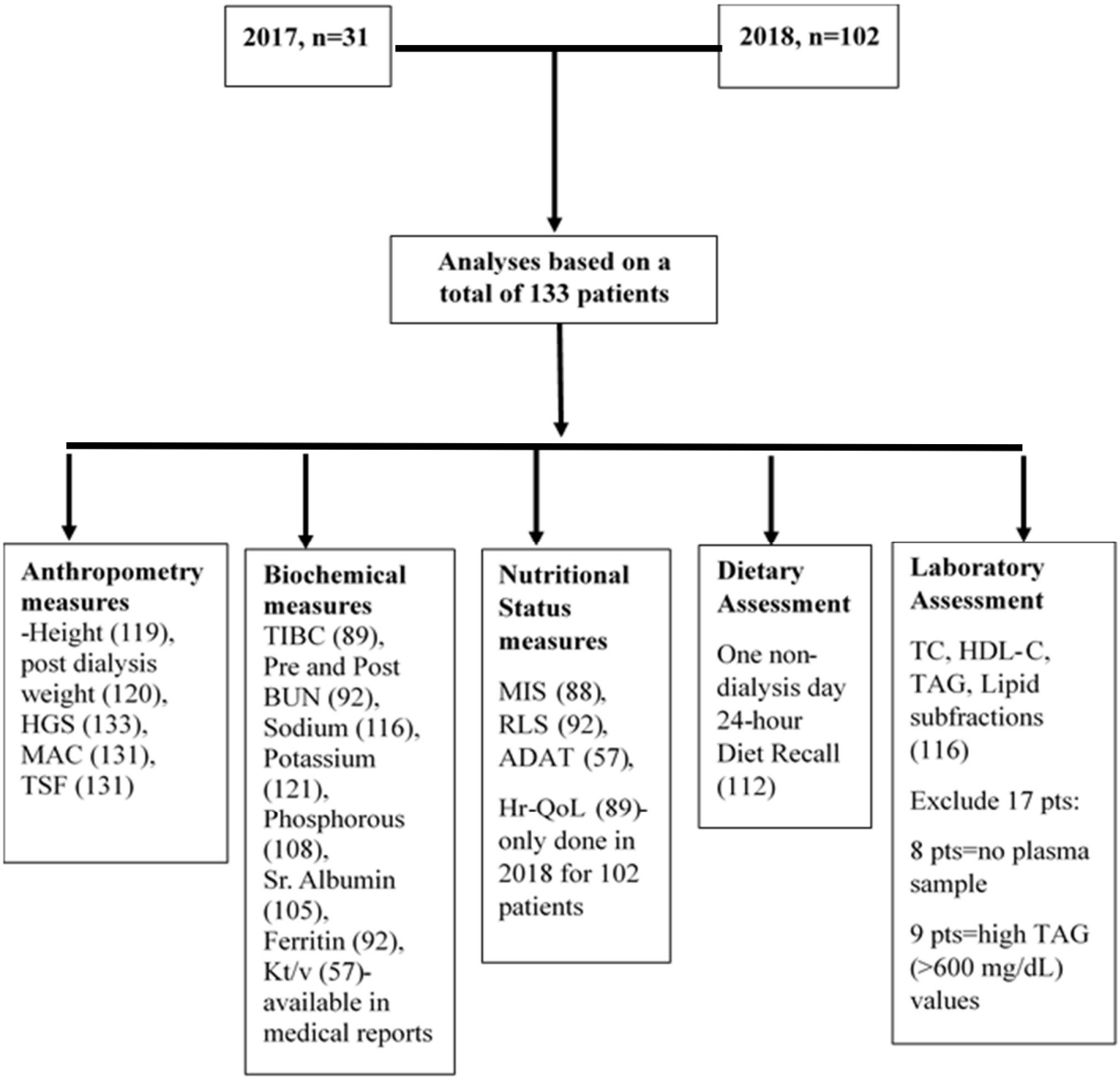


Figure 2-2. Recipe construction using Esha Food Processor Software

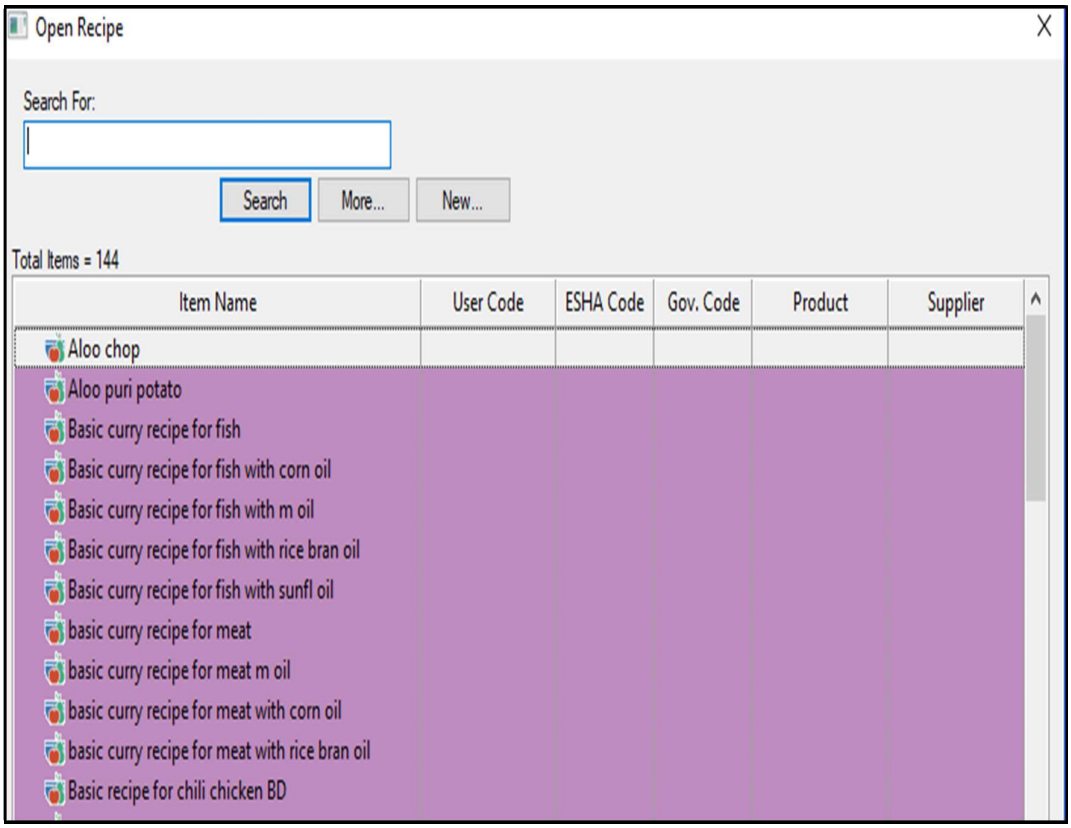
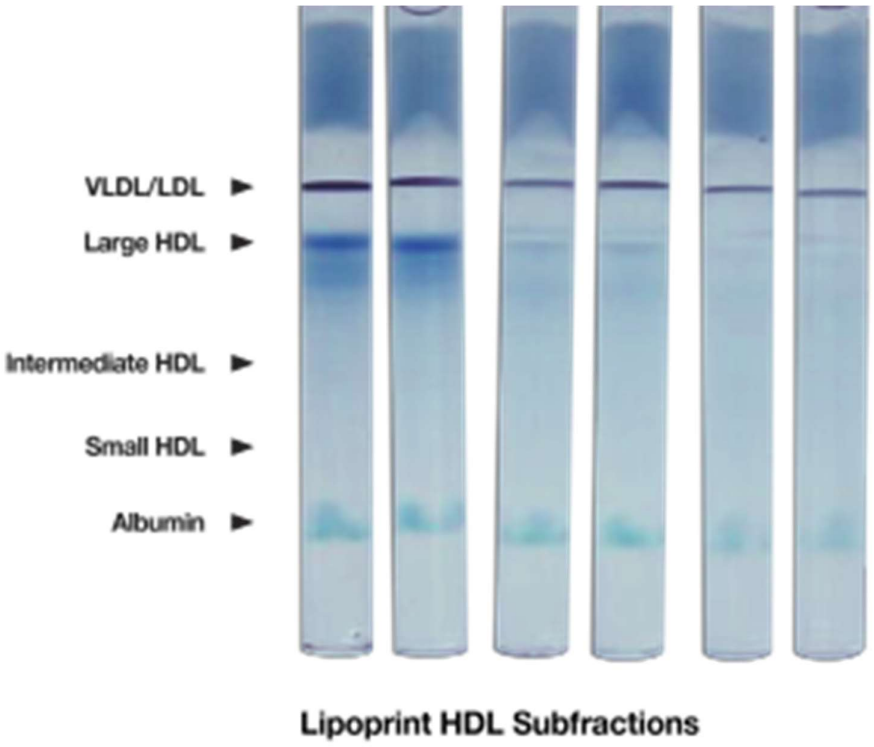
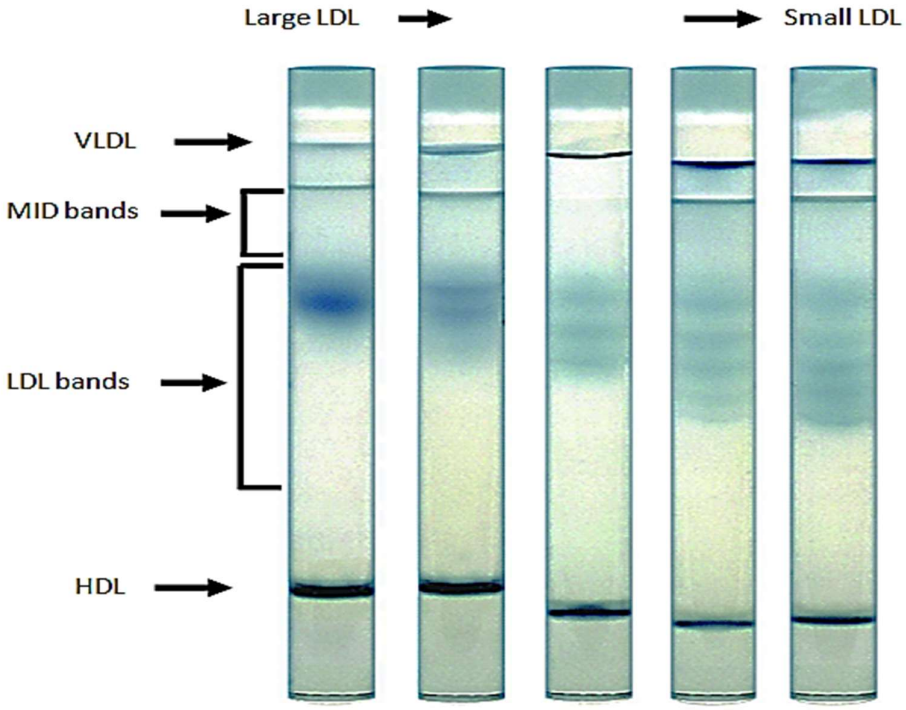


Figure **2-3.** HDL Lipoprint subfraction band separation on polyacrylamide gel tube



Source: Quantimetrix, Laboratory Lipoprint, 2019

Figure **2-4.** LDL Lipoprint subfraction band separation on polyacrylamide gel tube



Source: Quantimetrix, Laboratory Lipoprint, 2019

Figure 2-5. ISRNM Criteria for Clinical Diagnosis of PEW in CKD [132].

Criteria
Serum chemistry
Serum albumin < 3.8 g per 100 ml (Bromcresol Green)[a]
Serum prealbumin (transthyretin) < 30 mg per 100 ml (for maintenance dialysis patients only; levels may vary according to GFR level for patients with CKD stages 2–5)[a]
Serum cholesterol < 100 mg per 100 ml[a]
Body mass
BMI < 23[b]
Unintentional weight loss over time: 5% over 3 months or 10% over 6 months
Total body fat percentage < 10%
Muscle mass
Muscle wasting: reduced muscle mass 5% over 3 months or 10% over 6 months
Reduced mid-arm muscle circumference area[c] (reduction > 10% in relation to 50th percentile of reference population)
Creatinine appearance[d]
Dietary intake
Unintentional low DPI < 0.80 g kg^{-1} day^{-1} for at least 2 months[e] for dialysis patients or < 0.6 g kg^{-1} day^{-1} for patients with CKD stages 2–5
Unintentional low DEI < 25 kcal kg^{-1} day^{-1} for at least 2 months[e]

Source: A proposed nomenclature and diagnostic criteria for protein–energy wasting in acute and chronic kidney disease [132]. PEW:protein energy wasting, CKD: chronic kidney disease, BMI: body mass index, DEI: dietary energy intake, DPI: dietary protein intake. At least three out of the four listed categories (and at least one test in each selected category) must be satisfied for the diagnosis of kidney-disease related PEW. Optimally, each criterion should be documented on at least three occasions, preferably 2-4 weeks apart. [a]Not valid if concentrations are due to abnormally great urinary or gastrointestinal protein losses, liver disease, or cholesterol-lowering medicines. [b]A lower BMI might be desirable for certain Asian populations, weight must be edema-free mass, for example, post-dialysi dry weight. [c]Measurement must be performed by a trained anthropometrist, [d]Creatinine appearance is influenced by both muscle mass and meat intake, [e]Can be assessed by dietary diaries and interviews, or for protein intake by calculation of normalized protein equivalent of total nitrogen appearance (nPNA or nPCR) as determined by urea kinetic measurements.

CHAPTER 3 SPECIFIC AIM I: RESULTS-CURRENT NUTRITION AND HEALTH STATUS OF HEMODIALYISIS PATIENTS IN A SPECIALYZED RENAL HOSPITAL IN BANGLADESH

Results.

Overall Nutrition and Health Status of Bangladeshi Hemodialysis patients

Table **3-1**. demonstrated the mean values for demographic and clinical parameters. Data were collected from a total of 133 MHD patients in the present study, of which, 65 were males (49%) and 68, females (51%). The mean age for all patients was 50±13 years. Among all patients, 17% were in the "young adult" range of 18 to 35 years old, 45% were in the "middle-aged adult" range of 36 to 55 years old, and 38% were in the "older adult" range of more than 55 years old [133].

In this study, sixty-two percent (n=81) of patients underwent twice weekly dialysis. Average duration of dialysis was 3.8±0.4 hours. Mean dialysis vintage was 30±24.3 months. Hypertension (HTN) was reported to be the predominant causes of developing ESRD (39%), followed by HTN along with either diabetic nephropathy (DN) (28%) or chronic glomerulonephritis (CGN) (18%). Other (8%) reasons reported by the patients were-ADPKD (Adult polycystic kidney disease), postpartum complication, or unknown reason.

Table **3-2** demonstrated anthropometric assessments including measurement of Body mass index (BMI) from height and post-dialysis weight of a patient using the Quetelet's index [108]. BMI was calculated for 119 patients out of 133 patients as we had missing data for post-dialysis weight (n=13) and height (n=14). that, the mean BMI for all patients was 24.1±5.2 kg/m^2. Among all patients, 12% were in the "under-weight" range of less than 18.5 kg/m^2 , 52% were in the "healthy-weight" category of 18.6 to 24.9kg/m^2 , 24% were in the

"over-weight" category of 25-29.9 kg/m^2, and 13% were in the "obese" range of more than 30 kg/m^2 [134].

Another anthropometric assessment was the measurement of muscle mass on 131 out of 133 patients. Hand-grip strength was measured for all 133 patients. The mean values for mid-arm circumference (MAC), triceps skinfold (TSF), mid-arm muscle circumference (MAMC) and hand-grip strength (HGS) among all patients were 26.5±5.2 cm, 15.6±8.4 mm, 21.6±3.6 cm and 19.3±7.5 kg respectively.

Table **3-2** also demonstrated biochemical parameters which were analyzed in the hospital laboratory and available data were collected for the following parameters- TIBC or total iron binding capacity (n=89), urea reduction ratio (URR%) (n=92), sodium (n=116), potassium (n=121), serum albumin (n=105), phosphorous (n=108), ferritin (n=92), Kt/V (n=57). The mean values for these biochemical parameters were-TIBC, 242.2±63.9 mg/dL; URR%, 64.6±10.3; sodium (Na), 135.8±4 mEq/L; potassium (K), 5±0.7 mEq/L; phosphorous (P), 4.4±2.2 mg/dL; serum albumin, 3.7±0.6 g/dL; ferritin, 496.7±442.8 ng/ml; 18 patients with ferritin >2000 ng/ml; Kt/V, 1.3±0.4 respectively.

Table **3-3**. showed the plasma lipid profile and subfraction values of the study cohort. Nine patients were excluded from the analysis due to high TAG values (839.3±273.8 mg/dL) of more than 600 mg/dL because Friedwald equation for LDL-C estimation is not reliable if TAG level is high [135]. Another eight patients were excluded due to missing plasma sample. Therefore, data for 116 plasma samples are presented in the results of both lipid profile and subfraction.

The mean values for total cholesterol (TC), triglycerides (TAG), low-density lipoprotein (LDL-C) and high- density lipoprotein (HDL-C) were 154±40 mg/dL, 179±95 mg/dL, 84±31 mg/dL, and 35±11 mg/dL. For general population, reference values for TC,

TAG, and HDL-C are <200 mg/dL, <150 mg/dL, and ≥40 mg/dL. The average ratio of TC/HDL-C, LDL-C/HDL-C, and TAG/HDL-C were 4.9±1.8, 2.7±1.2, and 6.1±4.2 respectively. Lipid subfraction analyses revealed that, means values for VLDL, IDL-C, and LDL diameter were 36.1±12.6 mg/dl, 52.1±15.4 mg/dL, and 267.7±8 A^0. Mean values for large, intermediate, and small LDL particle sizes were 19.4±8.2 mg/dL, 11.2±7.1 mg/dL, and 5.6±8.4 mg/dL respectively and mean values for large, intermediate, and small HDL particle sizes were 12.5±8.1 mg/dL, 17.4±4.7 mg/dL, and 4.6±2.4 mg/dL respectively.

Studies sugeested a TAG to HDL-C ratio of more than 3.8 as an indicator of "dyslipidemia"[136]. Table **3-4** showed that, of the 116 patients, 74 patients had TAG/HDL-C ratio of more than 3.8 and could be considered as dyslipidemias, 42 had a ratio of less than 3.8 and considered as normal. Dyslipidemia patients had significantly higher TC, TAG and significantly lower HDL-C as compared to those with normal. LDL particle diameters were significantly lower in dyslipidemia patients. Dyslipidemia patients also had significantly higher cholesterol in small and intermediate sized LDL particles and higher cholesterol in large LDL particles. Dyslipidemia patients had significantly less cholesterol in large and intermediate sized HDL particles.

Table **3-5** showed the classification of dyslipidemia (DL) based on ATP (Adult Treatment Panel) III guideline [137], where DL is characterized by the presence of one or more of the following three criteria-i. HDL-C<40mg/dL, ii. LDL-C>100 mg/dL and iii. TAG>150 mg/dL as mixed DL or 'MD', presence of no criteria as normal or 'N', and presence of all three criteria as atherogenic DL or 'AD'. Based on this guideline, 19 patients were 'N' (including 18 type A, 1 Int), 81 were 'MD' (48 Type A, 21 Type B, 12 Int) and 16 patients were 'AD' (2 Type A, 12 Type B and 2 Int). 'AD' patients had significantly higher TC, TAG, VLDL, IDL-C and LDL-C and significantly lower HDL-C and LDL diameters

while compared to 'MD' and 'N' patients. As compared to normal patients, AD patients had 3-fold higher TC, and 2-fold higher LDL-C, 1.5-fold higher TAG and 1.5-fold lower HDL-C. Significantly altered profiles were also apparent in the LDL and HDL sub-fractions. Normal HD patients had significantly less cholesterol in small and intermediate sized LDL particles and small sized HDL particles. Normal HD patients also had significantly more cholesterol in large and intermediate sized HDL particles while compared to both AD and MD patients.

Table **3-6** demonstrated the comparison among patients having LDL phenotype A, B, and Intermediate. Of the 116 patients, 68 patients had LDL phenotype A, 33 had Type B and rest 15 had Intermediate type LDL pattern. Type B patients had significantly higher TC, TAG, VLDL, IDL-C, and LDL-C and significantly lower HDL-C as compared to those with pattern A and significantly higher TAG and Non-HDL-C compared to Intermediate LDL phenotype. LDL particles diameters were significantly lower in both type B and intermediate cases. Type B patients had significantly higher cholesterol in small and intermediate sized LDL particles and lower cholesterol in large LDL particles. Type B patients also had significantly less cholesterol in large and intermediate sized HDL particles and more cholesterol in small sized HDL particles.

Overall, in KFHRI, Table **3-7** showed that, 70% of dialysis patients were MD and 14% were AD. Only 16% of overall study cohort were having a normal (N) lipid profile based on laboratory analyses. Considering LDL-pattern, 59% patients had LDL-phenotype A, 28% had phenotype B, and 13% had intermediate type LDL-pattern. Among AD patients, 75% had LDL phenotype B. Based on TAG/HDL-C ratio, 64% of patients were DL with a ratio of >3.8. Of them, 77% were MD, and 22% were AD. Among 36% patients with a ratio of <3.8, 57% of them had MD, and 43% patients had a normal lipid profile.

Our study, for the first time revealed an approximate picture of dietary intake among Bangladeshi dialysis patients via analyzing a one-day 24-hour diet recall form. At first, one-day 24-hour diet recall data were collected from 112 out of 133 patients in both 2017 and 2018, from which energy, macronutrients and micronutrient intakes were analyzed. From these 112 patients, whose diet data were analyzed, 68 patients were identified as "acceptable reporters" (61%).

Table **3-8** demonstrated that, the mean calorie intake and average dietary energy intake (DEI) were 1434±491 kcal and 23.7±6.6 kcal/kg BW/day. The mean protein intake and average dietary protein intake (DPI) were 54±22 g and 0.9±0.3 g of protein/kg BW/day. Mean phosphorous (P) to protein ratio was 16.3±3.8 mg of phosphorous/ g of protein.

Among other macronutrients, mean carbohydrates intake was 208.5±69.5g, for which the recommendation is relying on body weight, average total fiber intake was 16.7±6.7 g, which is below the recommendation of 20-25g/day, average fat intake was 42.9±20.2, where, major portion, 15.6±9.4 g came from poly unsaturated fatty acids (PUFA), average cholesterol intake was 224±151 mg, which is slightly higher than the recommendation of <200 mg/day.

Average intakes of fat-soluble vitamins- except vit A intake were far below the K/DOQI guideline. Mean intakes for water-soluble vitamins fall mostly within the guidelines provided by K/DOQI for hemodialysis patients. Average intakes of minerals were all within the guideline for HD patients. Only zinc intake was below recommendation.

Table **3-9**. showed findings from the health-related questionnaire that were used in the present study. The mean MIS score among all patients was 6±3, a high score indicating malnutrition [63]. The mean ADAT score was 3.7±1.6, indicating a fair to poor appetite

existing among study cohort. In case of RLS form, "0" point means "no symptom", 1-10 points meaning "mild symptom", 11-20 points meaning "moderate symptom", 21-30 points meaning "severe symptoms", and 31-40 points meaning "very severe symptoms". The mean RLS score for this study cohort was 17.2±8.4 among 63 patients, indicating moderate symptoms of restless leg symptoms prevailed. In case of RLS, patients who reported '0' as response were excluded from the analysis. In case of KD-QoL, the two domain "physical health composite" score was 37.7±11.1 and "mental health composite" score was 44.7±9.9. Here, a lower score indicates malnourished patients. The mean score for the other two components such as-burden of kidney disease and effects of kidney disease were 30±26.4 and 64.3±17.5.

Analyses based on Dialysis Frequency: 2x weekly vs 3x weekly dialysis

Based on dialysis frequency, Table **3-10** showed that, 129 patients' data were analyzed, of which, a total of 81 patients (36 male and 45 female) underwent 2x weekly dialysis and 48 patients (25 male and 23 female) underwent 3x weekly dialysis. Significant difference was observed in terms of dialysis vintage, higher for patients on 3x weekly dialysis 37.5±24.4 months, compared to those on 2x weekly dialysis, 25.5±23.5 months. Causes of developing ESRD showed similar trend in both groups. Significant differences were found in terms of mean MAC and MAMC, which were higher in patients undergoing 3x weekly dialysis.

Table **3-11** demonstrated the average URR % value was higher in patients undergoing 2x weekly dialysis (67%) than in patients on 3x weekly dialysis (63%), whereas the K/DOQI recommendation for URR% is ≥65% to ensure dialysis adequacy[138]. Although, 12 patients

on 2x weekly dialysis had a ferritin value of >2000 ng/ml, mean ferritin value was lower for 2x weekly patients.

Although no significant differences were observed in terms of lipid profile and subfraction between these two groups of patients, those on 3x weekly dialysis had a higher TAG, TC and LDL-C values and a slightly lower HDL-C values compared to their 2x weekly counterparts (Table **3-12**). Based on TAG/HDL-C ratio, 59% patients on 2x weekly dialysis had dyslipidemia, whereas, 74% patients on 3x weekly dialysis had DL. Based on LDL-pattern, 3x weekly patients possess more atherogenic type B and intermediate type LDL compared to their 2x weekly counterparts (Table **3-13**).

Dietary analyses evaluated that, patients who underwent 3x weekly dialysis had a significantly higher intake of protein, water, and potassium, compared to those on 2x weekly dialysis which reflect the fact that, less dietary restriction was imposed on 3x weekly group (Table **3-14**). No statistically significant differences were found in terms of health and nutrition questionnaire between these two groups (Table **3-15**).

Table **3-16** demonstrated the median values of parameters that were statistically significant between 2x weekly vs 3x weekly patients. In overall analyses, significant differences were found in case of dialysis vintage, MAC, MAMC, URR%, Ferritin, Intakes of protein, water, and potassium.

Analyses based on Male vs Female

While analyzing data based on gender, in table **(**Table **S1)**, we found that, mean age for both male and female was same. However, male patient developed ESRD and start on dialysis at an early age compared to their female counterparts. Significant differences were observed in terms of dialysis vintage-higher in case of female, 37.5±24.4 months, than for

male, 25.5±23.5 months. Around 66% of female patients underwent twice weekly dialysis, whereas 58% of male patients did so. Causes of developing ESRD showed similar trend for both groups where HTN was predominant, followed by HTN along with either DN or CGN.

Significant differences were observed between the gender for BMI and mean MAC and TSF which were higher in female while the muscle strength was higher in male. Mean values of sodium and serum albumin were lower in female, and URR (%), and Kt/V were higher in female (Table S**2**) compared to their male counterparts. In case of male patients, average URR% was only 61%.

Lipid and lipoprotein subfraction analyses showed that, TC, TAG, LDL-C, Non-HDL-C and VLDL were significantly higher in case of female patients. In female, higher amount of cholesterol were present in large and intermediate LDL-particles. Based on TAG/HDL-C ratio of more than 3.8, 70% of female patients had dyslipidemia (DL), whereas 58% of male patients had DL (Table S**3**).

Significant differences were observed between gender in terms of calorie, DEI, protein, DPI, P/kg BW, carbohydrates, total fiber, fat and PUFA intakes, all of which were higher in male, Average intakes of vit A, B1, B3, folate and vit C intakes and mean intakes for phosphorous, potassium, zinc, and magnesium were also higher in male (Table **S4**).

No significant differences were found in case of MIS, RLS and ADAT scores, except that, the mean MIS score was a little higher for female than those of male patients. Significant differences were found in case of first two components of KD-QoL score-physical and mental health composite, both were higher in case of male compared to female (Table **S5**).

Analyses based on Dialysis vintage: ≤2 years vs >2 years:

114 patients' data were analyzed, of which, 61 patients were on dialysis for ≤2 years and 53 patients were on dialysis for >2 years. Significant differences were observed between dialysis vintage (less than or equal to two years vs more than two years of dialysis) in case of mean values for age and muscle mass and muscle strength, and TIBC, all of which were higher among patients on >2 years of dialysis (Supp. Table **6** and supp**.** table **7**). No significant differences were observed in terms of lipid profile and subfraction except VLDL which was lower in patients on >2 years of dialysis and small HDL-C, lower in patients on ≤2 years of dialysis (Table **S8**). Based on TAG/HDL-C ratio, 62% patients had dyslipidemia (≤2 years) and 66% patients had dyslipidemia (>2 years). No significant differences were observed in dietary intake as well.

Tables and Figures

Tables.

Table 3-1: Demographics and clinical parameters

	All patients
Age in years (n)	50±13 (133)
Young adult (18-35), n (%)	22 (17%)
Middle-aged adult (36-55), n (%)	60 (45%)
Older adult (>55), n (%)	51 (38%)
Dialysis duration (hr) (n)	3.8±0.4 (119)
Dialysis vintage (mon) (n)	30.0±24.3 (123)
Dialysis frequency, n (%)	
Thrice a week	48 (36%)
Twice a week	81 (61%)
Once a week	1 (1%)
Causes of ESRD, n (%)	
HTN	52 (39%)
HTN and DN	37 (28%)
HTN and CGN	24 (18%)
Others	10 (8%)
Missing data	10 (8%)

Data were collected from the number of patients indicated in parentheses. Values are *Mean ±SD* and n or %.HTN: Hypertension, DN: Diabetic nephropathy, CGN: Chronic glomerulonephritis, Other: 2 APKD, 5 Unknown, 1 postpartum complication; 1 genetic, 1 DN and CGN. ESRD: End-stage renal disease.

Table 3-2: Anthropometric and biochemical parameters

	All patients	Reference value
Height (cm)	159±9 (119)	
Dry weight (Kg)	60.5±12.5 (120)	
BMI (kg/m^2)	24.1±5.2 (119)	
BMI Category, n (%)		
Underweight, <18.5	14 (12%)	
Healthy-weight, 18.6-24.9	62 (52%)	
Overweight, 25-30	28 (24%)	
Obese, >30	15 (13%)	
HGS (Kg)	19.3±7.5 (133)	
MAC (cm)	26.5±5.2 (131)	
TSF (mm)	15.6±8.4 (131)	
MAMC (cm)	21.6±3.6 (131)	
TIBC (mg/dL)	242±64 (89)	300-400 [139]
URR %	65±9 (91)	> 65 [140]
Na (mEq/L)	135.8±4.0 (116)	135-146 [141]
K (mEq/L)	5.0±0.7 (121)	3.5-5.3 [142-144]
P (mg/dl)	4.4±2.2 (108)	
Albumin (g/dL)	3.7±0.6 (105)	3.8-5.0 [145]
Ferritin (ng/ml)	497±443 (74)	5-275 [146]
Ferritin >2000ng/ml (n)	18	
Kt/V	1.3±0.4 (57)	1.2-1.3 [147, 148]

Data were obtained from patient medical records. Values are *Mean* ± *SD* (n). HGS: Hand grip strength, MAMC: Mid-arm muscle circumference. TSF: Triceps skinfold, BMI: Body mass index. URR%: Urea reduction rate. Na: Sodium, K: Potassium, P: Phosphorous.

Table 3-3: Lipid profile and lipid subfraction

	All (116)
TC (mg/dl)	154±40
HDL-C (mg/dl)	35±11
TG (mg/dl)	179±95
LDL-C (mg/dl)	84±31
TC/HDL-C	4.9±1.8
LDL-C/HDL-C	2.7±1.2
Non-HDL-C	120±39
Non-HDL-C/HDL-C	3.9±1.8
TG/HDL-C	6.1±4.2
VLDL (mg/dl)	36±13
IDL (mg/dl)	26±7
Large LDL (mg/dl)	19.4±8.2
Inter. LDL (mg/dl)	11.2±7.1
Small LDL (mg/dl)	5.6±8.4
Mean LDL size (Å)	268±8
Large HDL (mg/dl)	17.4±4.7
Inter. HDL (mg/dl)	12.5±8.1
Small HDL (mg/dl)	4.6±2.4

Data were analyzed for the number of patients indicated in parentheses. Values are *Mean* ± *SD* and n or %. TC: Total Cholesterol, HDL-C: High density lipoprotein, TAG: Triglycerides, LDL-C: Low density lipoprotein. Type A: athero-protective profile, Type B: atherogenic profile, Intermediate: has characteristics of both A and B.

Table 3-4. Distribution of patients based on TAG/HDL-C ratio

	TAG/HDL-C<3.8 (42)	TAG/HDL-C> 3.8 (74)
TC (mg/dL)	143.5±33.3 [a]	160.6±41.9 [a]
TAG (mg/dL)	100.7±30.7 [a]	222.7±91.1 [a]
Non-HDL-C (mg/dL)	99.2±30.4 [a]	131.7±39.2 [a]
VLDL (mg/dL)	30.2±9.7 [a]	39.4±12.9 [a]
IDL-C (mg/dL)	48.0±14.1 [a]	54.4±15.7 [a]
HDL-C (mg/dL)	44.3±10.5 [a]	28.9±6.9 [a]
Large HDL-C (mg/dL)	19.0±8.5 [a]	8.7±4.9 [a]
Intermediate HDL-C (mg/dL)	20.9±3.8 [a]	15.4±3.9 [a]
Small HDL-C (mg/dL)	4.2±2.4	4.8±2.3
LDL-C (mg/dL)	79±28.4	87.2±31.9
Large LDL-C (mg/dL)	21.4±8.9 [a]	18.2±7.5 [a]
Intermediate LDL-C (mg/dL)	7.3±5.8 [a]	13.5±6.8 [a]
Small LDL-C (mg/dL)	0.9±2.3 [a]	8.3±9.3 [a]
LDL diameters (angstroms)	272.7±2.9 [a]	264.6±8.4 [a]
TC/HDL-C	3.3±0.8 [a]	5.7±1.6 [a]
LDL-C/HDL-C	1.9±0.7 [a]	3.1±1.2 [a]
TAG/HDL-C	2.4±0.8 [a]	8.1±3.9 [a]
Non-HDL-C/HDL-C	2.3±0.8 [a]	4.7±1.6 [a]

Data were analyzed for the number of patients indicated in parentheses from 116 patients at Kidney Foundation Hospital and Research Institute. Values are *Mean* ± *SD* (n). TC: Total Cholesterol, HDL-C: High density lipoprotein, TAG: Triacylglycerol/triglycerides, LDL-C: Low density lipoprotein. This table indicates values from both Lipoporint and from enzymatic assays in plasma. TAG/HDL-C>3.8 means dyslipidemia. Mean values sharing a common superscript were significantly different from each other using a one-way ANOVA followed by post-hoc Tukey's test. ($p<0.05$).

Table 3-5. Distribution of patients based on Dyslipidemia (DL) (ATP III Guideline-2013)

	AD [16 (14%)]	MD [81 (70%)]	N [19 (16%)]
TC (mg/dL)	213.9±30.7 [a, b]	145.5±33.2 [a]	142.5±27.4 [b]
TAG (mg/dL)	277.4±98.0 [a, b]	178.0±86.3 [c, a]	97.3±33.7 [b, c]
HDL-C (mg/dL)	30.6±5.2 [b]	31.4±9.2 [c]	50.9±7.7 [b, c]
Non-HDL-C (mg/dL)	183.3±29.6 [a, b]	114.1±29.5 [c, a]	91.6±27.2 [b, c]
VLDL (mg/dL)	52.8±12.7 [a, b]	34.4±10.3 [a]	29.3±9.8 [b]
IDL-C (mg/dL)	73.4±13.7 [a, b]	49.4±12.7 [a]	45.7±12.7 [b]
Large HDL-C (mg/dL)	6.6±2.9 [a, b]	10.8±6.2 [c, a]	24.4±7.0 [b, c]
Inter. HDL-C (mg/dL)	18.0±2.4 [b]	16.1±4.4 [c]	22.5±3.7 [b, c]
Small HDL-C (mg/dL)	5.9±2.6 [b]	4.5±2.3	3.8±2.1 [b]
LDL-C (mg/dL)	127.8±23.4 [a, b]	78.5±26.1 [a]	72.1±24.1 [b]
Large LDL-C (mg/dL)	22±6.2	18.4±7.9	21.0±10.3
Inter. LDL-C (mg/dL)	17.7±5.1 [a, b]	11.2±6.9 [c, a]	6.0±4.8 [b, c]
Small LDL-C (mg/dL)	18.6±11.2 [a, b]	4.3±5.9 [a]	0.5±0.9 [b]
LDL diameters (A^0)	260.3±7.0 [a, b]	267.6±7.8 [c, a]	273.4±2.6 [b, c]
TC/HDL-C	7.2±6.1.5 [a, b]	4.9±1.4 [c, a]	2.8±0.6 [b, c]
LDL-C/HDL-C	4.3±1.1 [a, b]	2.6±1.0 [c, a]	1.5±0.5 [b, c]
TAG/HDL-C	9.4±3.9 [a, b]	6.4±4.0 [c, a]	1.9±0.7 [b, c]
Non-HDL-C/HDL-C	6.2±1.5 [a, b]	3.9±1.4 [c, a]	1.8±0.6 [b, c]

Data were analyzed for the number of patients indicated in parentheses from 116 patients. Values are *Mean* ± *SD* and [n (%)]. TC: Total Cholesterol, HDL-C: High density lipoprotein, TAG: Triacylglycerol/triglycerides, LDL-C: Low density lipoprotein, TAG/HDL-C>3.8 means dyslipidemia/DL. Atherogenic DL (AD): presence of the three condition-HDL-C<40 mg/dl, TAG>150 mg/dl, and LDL-C>100 mg/dl; Mixed DL (MD): presence of one of the three condition-HDL-C<40 mg/dl, TAG>150 mg/dl, and LDL-C>100 mg/dl; Normolipidemic: absence of the three condition-HDL-C<40 mg/dl, TAG>150 mg/dl, and LDL-C>100 mg/dl. Mean values sharing a common superscript were significantly different from each other using a one-way ANOVA followed by post-hoc Tukey's test. This table indicates values from both Lipoporint and from enzymatic assays in plasma. All values are significantly different with a p-value of <0.001 except small HDL-C and small LDL-C which are significantly different with a p-value of <0.05. Only Large LDL-C is not significantly different between the groups

Table 3-6. Distribution of patients based on LDL-pattern

	Type A (68)	Intermediate (15)	Type B (33)
TC (mg/dL)	142.5±32.6 [a]	153.1±29.5	179.6±45.9 [a]
TAG (mg/dL)	139±61.1 [a]	159.0±56.4 [c]	268.8±107.1 [a, c]
LDL-C (mg/dL)	76.3±28.0 [a]	90.5±26.4	97.8±33.4 [a]
Non-HDL-C (mg/dL)	104.1±30.1 [a]	122.3±27.5 [c]	151.6±42.2 [a, c]
VLDL (mg/dL)	31.5±10.0 [a]	37.1±6.8	45.1±14.6 [a]
IDL-C (mg/dL)	48.5±13.2 [a]	51.5±10.1	59.9±18.8 [a]
Large LDL-C (mg/dL)	21.5±8.7 [a]	18.2±6.1	15.5±6.2 [a]
Inter. LDL-C (mg/dL)	8.4±6.4 [a, b]	15.5±5.7 [b]	15.2±6.2 [a]
Small LDL-C (mg/dL)	0.7±1.0 [a, b]	4.2±1.8 [b, c]	16.5±8.5 [a, c]
LDL diameters (A^0)	272.4±2.5 [a, b]	267.0±0.8 [b, c]	257.8±8.0 [a, c]
TC/HDL-C	4.0±1.3 [a, b]	5.2±1.2 [b, c]	6.6±1.6 [a, c]
LDL-C/HDL-C	2.1±1.0 [a, b]	3.1±1.1 [b]	3.6±1.1 [a]
TAG/HDL-C	4.2±2.6 [a]	5.4±1.9 [c]	10.2±4.7 [a, c]
Non-HDL-C/HDL-C	3.0±1.2 [a, b]	4.2±1.2 [b, c]	5.6±1.6 [a, c]
HDL-C (mg/dL)	38.5±11.8 [a, b]	30.7±7.6 [b]	28±7 [a]
Large HDL-C (mg/dL)	16.1±8.3 [a, b]	9.2±4.1 [b]	6.5±4 [a]
Inter. HDL-C (mg/dL)	18.4±4.8 [a]	17.0±4.1	15.6±4.1[a]
Small HDL-C (mg/dL)	3.9±2.1[a]	4.6±2.1	5.9±2.4 [a]

Data were analyzed for the number of patients indicated in parentheses from 116 patients at Kidney Foundation Hospital and Research Institute. Values are *Mean* ± *SD* (n). TC: Total Cholesterol, HDL-C: High density lipoprotein, TAG: Triacylglycerol/triglycerides, LDL-C: Low density lipoprotein. Mean values sharing a common superscript were significantly different from each other using a one-way ANOVA followed by post-hoc Tukey's test. This table indicates values from both Lipoporint and from enzymatic assays in plasma. Type A: atheroprotective, Type B: atherogenic, Intermediate: both. All values are significantly different with a p-value of <0.001 except Intermediate HDL-C which is significantly different with a p-value of <0.05.

Table 3-7. KFHRI patients based on LDL pattern and DL (TAG/HDL-C ratio and ATP III Guideline-2013)

DL-ATP III Guideline, 2013	All, [116 (100%)]	AD, [16 (14%)]	MD, [81 (70%)]	N, [19 (16%)]
LDL-pattern				
Type A	68 (59%)	2 (13%)	48 (59%)	18 (95%)
Type B	33 (28%)	12 (75%)	21 (26%)	0 (0%)
Intermediate	15 (13%)	2 (13%)	12 (15%)	1 (5%)
DL-TAG/HDL-C				
TAG/HDL-C<3.8	42 (36%)	-	24 (57%)	18 (43%)
TAG/HDL-C>3.8	74 (64%)	16 (22%)	57 (77%)	1 (1%)

Data were analyzed for the number of patients indicated in parentheses. Values are n or %. TC: Total Cholesterol, HDL-C: High density lipoprotein, TAG: Triglycerides, LDL-C: Low density lipoprotein. Type A: athero-protective profile, Type B: atherogenic profile, Intermediate: has characteristics of both A and B. TAG/HDL-C>3.8 means dyslipidemia or DL. Atherogenic DL (AD): presence of the three condition-HDL-C<40 mg/dl, TAG>150 mg/dl, and LDL-C>100 mg/dl; Mixed DL (MD): presence of one of the three condition-HDL-C<40 mg/dl, TAG>150 mg/dl, and LDL-C>100 mg/dl; Normolipidemic: absence of the three condition-HDL-C<40 mg/dl, TAG>150 mg/dl, and LDL-C>100 mg/dl.

Table 3-8: Dietary Analysis for Acceptable Reporters (AR)

Parameters	AR (68)	KDOQI Guidelines
Calories (Kcal)	1434±491	Based on BW
DEI/kg BW/day	23.7±6.6	30-35 kcal/kg BW/day
Protein (g)	54±22	Based on BW
DPI/kg BW/day	0.9±0.3	1.2 g/ kg BW/day
P mg/kg BW /day	14.2±5.3	10-17 mg/kg BW /day
Phosphorous: Protein	16.3±3.8	<12 mg/g of protein
Carbohydrates (g)	209±70	Based on BW
Total Fiber (g)	16.7±6.7	20-25 g/day
Fat (g)	43±20	
SFA (g)	8.4±4.3	
MUFA (g)	8.4±4.5	
PUFA (g)	15.6±9.4	
Cholesterol (mg)	224±151	<200 mg/day
omega 6: omega 3	10.8±5.6	4:01
Water (ml)	1417.5±642.3	750-1500 ml/day
Vitamin A-IU	1016±1311	700-900 IU
Vitamin D-IU	47±40	600 IU
Vitamin E-a-Toco (mg)	2.2±1.5	15 mg
Vitamin K (µg)	12.9±32	90-120 µg
Vit B1 (mg)	0.7±0.3	1.1-1.2 mg
Vit B2 (mg)	1.1±1.7	1.1-1.3 mg
Vit B3 (mg)	13.7±5.4	14-16 mg
Vit B6 (mg)	11.8±29.6	13-17 mg
Vit B12 (µg)	1.6±1.6	2.4 µg
Biotin (µg)	10±9.7	30 µg
Folate (µg)	135±184	1000 µg
Vit C (mg)	88±72	75-90 mg/day
Dietary Calcium (mg)	435.4±260	<1000 mg
Iron (mg)	15.4±14.5	Individualized
Dietary Phosphorous (mg)	867.3±422	1000 mg
Potassium (mg)	1411.6±564	Individualized
Dietary Sodium (mg)	2043±924	<2400 mg/day
Zinc (mg)	8±4.5	15 mg
Magnesium (mg)	227±90	200-300 mg/day

The data is reported for all acceptable reporters. Values are as *Mean* ± *SD*. DEI: Dietary energy intake, DPI: Dietary protein intake. SFA: Saturated fat, MUFA: Monounsaturated fat, PUFA: Poly unsaturated fat. IU: International Unit, vit: vitamin, Toco-: tocopherol. AR: Acceptable reporters, BW: Body weight,

Table 3-9. Health and Nutrition Questionnaire

	All patients
MIS Score	6±3 (88)
ADAT Score	3.7±1.6 (57)
RLS Score	17.2±8.4 (63)
KD-QoL	
SF-12 Physical Health Composite	37.7±11.1 (86)
SF-12 Mental Health Composite	44.7±9.9 (86)
Burden of Kidney Disease	30.0±26.4 (89)
Effects of Kidney Disease	64.3±17.5 (79)

Data were collected from the number of patients indicated in parentheses. Values are *Mean* ±*SD* (n). MIS [46]: Malnutrition inflammation score. A score >5 indicates malnourished The MIS has 10 components, each with four levels of severity, from 0 (normal) to 3 (very severe). The sum of all 10 MIS components ranges from 0 (normal) to 30 (severely malnourished); higher score reflects a more severe degree of malnutrition and inflammation. ADAT [124]: Appetite and diet analysis tool. Scale: 1 = very good, 2 = good, 3 = fair, 4 = poor and 5 = very poor. RLS [126]: Restless leg syndrome. medical doctor. Scale: 0, None; 1 – 10, Mild RLS; 11-20, Moderate RLS, 21-30 Severe RLS, 31-40 Very Severe RLS. Patients reporting score '0' were excluded from analysis. KD- QoL[130] Subscale scores range from 0 to 100, with lower scores indicating poor self-reported QOL.

Table 3-10. Demographic and anthropometric parameters: 2x vs 3x weekly dialysis

	2x weekly	**3x weekly**
Gender, M/F (n)	36 / 45 (81)	25 / 23 (48)
Age in years (n)	49±13 (81)	52±13 (48)
Dialysis duration (hr) (n)	3.8±0.4 (76)	3.8±0.3 (43)
Dialysis vintage (mon) (n)	25.5±23.5[a] (77)	37.5±24.4[a] (46)
Causes of ESRD, n (%)		
HTN	33 (41%)	19 (40%)
HTN and DN	22 (27%)	15 (31%)
HTN and CGN	14 (17%)	9 (19%)
Others	7 (9%)	3 (6%)
Missing data	5 (6%)	2 (4%)
Height (cm)	157±9 (76)	161±10 (41)
Dry weight (Kg)	59±12 (77)	63±13 (41)
BMI (kg/m^2)	23.9±4.9 (76)	24.7±5.9 (41)
HGS (Kg)	19.5±8.0 (81)	19.0±7.0 (48)
MAC (cm)	25.8±4.8[a] (79)	28.2±5.6[a] (48)
TSF (mm)	15.0±7.9 (79)	17.3±9.1 (48)
MAMC (cm)	21.1±3.4[a] (79)	22.7±3.7[a] (48)

Data were collected from the number of patients indicated in parentheses. Values are *Mean* ±*SD* (n) and n or %. HGS: Hand grip strength, MAMC: Mid-arm muscle circumference. TSF: Triceps skinfold, BMI: Body mass index. HTN: Hypertension, DN: Diabetic nephropathy, CGN: Chronic glomerulonephritis, Other: APKD, kidney stone, Unknown, postpartum complication; genetic, ESRD: End-stage renal disease. Mean values sharing a common superscript were significantly different from each other using a one-way ANOVA test ($p<0.05$).

Table 3-11. Biochemical parameters: 2x vs 3x weekly dialysis

	2x weekly	3x weekly	Reference value
TIBC (mg/dL)	231±56 (49)	255±71 (40)	300-400 [139]
URR %	67±8[a] (50)	63±9[a] (40)	≥65 [140]
Na (mEq/L)	136±4 (70)	136±4 (45)	135-146 [141]
K (mEq/L)	5.0±0.7 (75)	5.0±0.8 (45)	3.5-5.3 [142-144]
P (mg/dl)	4.5±2 (62)	4.3±2.5 (45)	
Albumin (g/dL)	3.7±0.7 (60)	3.7±0.4 (44)	3.8-5.0 [145]
Ferritin (ng/ml)	376±360[a] (38)	601±476[a] (35)	5-275 [146]
Ferritin >2000ng/mL (n)	12	6	
Kt/V	1.4±0.3 (30)	1.2±0.5 (27)	1.2-1.3 [147, 148]

Data were obtained from patient medical records. Values are *Mean* ± *SD* (n). Mean values sharing a common superscript were significantly different from each other using a one-way ANOVA($p<0.05$). URR% : Urea reduction rate. Na: Sodium, K: Potassium, P: Phosphorous.

Table 3-12. Lipid profile and Lipid subfractions: 2x vs 3x weekly dialysis.

	2x weekly (75)	**3x weekly (39)**
TC (mg/dl)	153±41	160±38
HDL-C (mg/dl)	35±12	34±9
TG (mg/dl)	169±90	198±105
LDL-C (mg/dl)	84±32	86±28
TC/HDL-C	4.9±2.0	4.9±1.4
LDL-C/HDL-C	2.7±1.3	2.7±1.0
Non-HDL-C	118±40	126±38
Non-HDL-C/HDL-C	3.9±2.0	3.9±1.4
TG/HDL-C	6.0±4.5	6.4±3.8
VLDL (mg/dl)	36±13	37±12
IDL (mg/dl)	52±17	53±13
Large LDL (mg/dl)	19.3±8.5	19.3±7.3
Inter. LDL (mg/dl)	10±7	13±7
Small LDL (mg/dl)	4.9±7.8	7.4±9.4
Mean LDL size (Å)	268.0±8.5	266.4±7
Large HDL (mg/dl)	13±8.7	11.4±7
Inter. HDL (mg/dl)	17±5.2	18±3.4
Small HDL (mg/dl)	4.6±2.3	4.7±2.3

Data were analyzed for the number of patients indicated in parentheses. Values are *Mean* ± *SD* and n or %. TC: Total Cholesterol, HDL-C: High density lipoprotein, TAG: Triglycerides, LDL-C: Low density lipoprotein. Type A: athero-protective profile, Type B: atherogenic profile, Intermediate: has characteristics of both A and B. No significant differences were observed between groups using one-way ANOVA

Table 3-13. Dyslipidemia: 2x vs 3x weekly dialysis.

Dyslipidemia (DL)	2x weekly	3x weekly
TAG/HDL-C<3.8	31 (41%)	10 (26%)
TAG/HDL-C>3.8	44 (59%)	29 (74%)
LDL-Pattern		
Type A	50 (67%)	16 (41%)
Type B	20 (27%)	13 (33%)
Intermediate	5 (7%)	10 (26%)

Data were analyzed for the number of patients indicated in parentheses. Values are *Mean* $\pm$ *SD* and n or %. TC: Total Cholesterol, HDL-C: High density lipoprotein, TAG: Triglycerides, LDL-C: Low density lipoprotein. Type A: athero-protective profile, Type B: atherogenic profile, Intermediate: has characteristics of both A and B.

Table 3-14. Dietary analysis for Acceptable Reporters: 2x vs 3x weekly dialysis.

Parameters	2x weekly (41)	3x weekly (27)	KDOQI Guidelines
Calories (Kcal)	1364±393	1540±604	Based on BW
DEI/kg BW/day	23.5±7.5	25.0±7.5	30-35 kcal/kg BW/day
Protein (g)	49±16[a]	61±27[a]	Based on BW
DPI/kg BW/day	0.8±0.3	1.0±0.4	1.2 g/ kg BW/day
P mg/kg BW/day	14.0±4.7	15.0±7.0	10-17 mg/kg BW /day
Phosphorous: Protein	17.0±3.7	15.4±3.7	<12 mg/g of protein
Carbohydrates (g)	201±64	220±76	Based on BW
Total Fiber (g)	16±7	18±6	20-25 g/day
Fat (g)	40±14	47±27	
SFA (g)	7.8±3.5	9.2±5.3	
MUFA (g)	7.9±4.2	9.0±4.8	
PUFA (g)	15.0±7.7	16.7±11.5	
Cholesterol (mg)	233±158	210±140	<200 mg/day
omega 6: omega 3	11.0±5.6	10.4±5.7	4:01
Water (ml)	1288±603[b]	1614±661[a]	750-1500 ml/day
Vitamin A-IU	1036±1424	987±1145	700-900 IU
Vitamin D-IU	52±40	40±38	600 IU
Vitamin E-α-Toco (mg)	2.0±1.1	2.6±2.0	15 mg
Vitamin K (µg)	9.0±19.5	19.0±44.4	90-120 µg
Vit B1 (mg)	0.7±0.2	0.8±0.4	1.1-1.2 mg
Vit B2 (mg)	0.8±0.4	1.4±2.6	1.1-1.3 mg
Vit B3 (mg)	12.4±5.0	15.6±5.4	14-16 mg
Vit B6 (mg)	14±34	8±22	13-17 mg
Vit B12 (µg)	1.6±1.8	1.7±1.4	2.4 µg
Biotin (µg)	9.8±10.6	10.3±8.0	30 µg
Folate (µg)	105±68	179±277	1000 µg
Vit C (mg)	75±71	109±71	75-90 mg/day
Dietary Calcium (mg)	438±276	431±238	<1000 mg
Iron (mg)	16±16	15±13	Individualized
Dietary Phosphorous (mg)	821±277	938±577	1000 mg
Potassium (mg)	1281±447[a]	1610±667[a]	Individualized
Dietary Sodium (mg)	1938±683	2203±1199	<2400 mg/day
Zinc (mg)	7.5±3.4	8.8±5.8	15 mg
Magnesium (mg)	217±60	241±91	200-300 mg/day

The data is reported for all acceptable reporters. Values are as *Mean* ± *SD*. DEI: Dietary energy intake, DPI: Dietary protein intake. SFA: Saturated fat, MUFA: Monounsaturated fat, PUFA: Poly unsaturated fat. IU: International Unit, vit: vitamin, Toco-: tocopherol. Mean values sharing a common superscript were significantly different from each other using a one-way ANOVA ($p<0.05$).

Table **3-15**. Health and Nutrition Questionnaires: 2x vs 3x weekly dialysis

	2x weekly	**3x weekly**
MIS Score	5.8±3.1 (48)	6.0±2.7 (39)
ADAT Score	3.7±1.6 (30)	3.7±1.5 (27)
RLS Score	15.9±8.7 (36)	17.6±7.1 (25)
KD-QoL		
SF-12 Physical Health Composite	37.8±11.3 (47)	37.6±11.1 (39)
SF-12 Mental Health Composite	45.7±8.9 (47)	43.4±11.0 (39)
Burden of Kidney Disease	31.5±27.2 (49)	28.1±25.6 (40)
Effects of Kidney Disease	67.3±16.5 (45)	60.3±18.2 (34)

Data were collected from the number of patients indicated in parentheses. Values are *Mean* ±*SD*.
MIS [46]: Malnutrition inflammation score. A score >5 indicates malnourished The MIS has 10 components, each with four levels of severity, from 0 (normal) to 3 (very severe). The sum of all 10 MIS components ranges from 0 (normal) to 30 (severely malnourished); higher score reflects a more severe degree of malnutrition and inflammation. ADAT [124]: Appetite and diet analysis tool. Scale: 1 = very good, 2 = good, 3 = fair, 4 = poor and 5 = very poor. RLS [126]: Restless leg syndrome. medical doctor. Scale: 0, None; 1 – 10, Mild RLS; 11-20, Moderate RLS, 21-30 Severe RLS, 31-40 Very Severe RLS. Patients reporting score '0' were excluded from analysis. KD- QoL[130] Subscale scores range from 0 to 100, with lower scores indicating poor self-reported QOL.

Table **3-16**: Demographic, Biochemical and Anthropometric differences between 2X and 3X weekly dialysis (IQR for significant differences)

	2x weekly	**3x weekly**
Dialysis Vintage (months)	17 (9-33)	34 (16-51)
(n)		
MAC (cm)	25.1 (22.4-28.9)	27.9 (23.9-30.5)
MAMC (cm)	21.0 (18.2-23.9)	22.6 (19.8-24.9)
URR%	67.5 (61.7-73.6)	63.4 (56.8-68.5)
Ferritin (ng/mL)	288 (138-429)	473 (173-960)
Protein (g)	45 (39-55)	53 (44-76)
Water (ml)	1312 (780-1692)	1473 (1144-1856)
Potassium (mg)	1260 (932-1416)	1579 (1195-1798)

Data was collected for 129 patients at Kidney Foundation Hospital and Research Institute. The data reported is for number of patients for which the parameters were available. Values are Mean + SD (n). MAC: Mid Arm Circumference, MAMC: Mid Arm Muscle Circumference, URR%: Urea Reduction Ratio. Values are reported as Mean ± SD. Statistical analysis was done using one-way ANOVA. All the reported parameters were significantly different between the groups ($p<0.05$). IQR: Interquartile range. Values for the IQR are represented as Median (Quartile 1 – Quartile 3).

CHAPTER 4 SPECIFIC AIM II RESULTS- TO DOCUMENT THE PREVALENCE OF PEW BASED ON ISRNM CRITERIA IN BANGLADESHI HEMODIALYSIS PATIENTS

Results.

Table **4-1** showed that, data for body mass index (BMI) were available for 119 out of 133 patients (89%), of which 58 patients (49%) had a BMI of less than 23 kg/m^2, which is considered as the 1st criteria of PEW diagnosis. Data for mid-arm muscle cirmference (MAMC) were available for 131 out of 133 patients (98%), of which 75 patients (57%) had MAMC value, 10% below the 50th percentile of reference population, and this is considered to be the 2nd criteria for PEW diagnosis.

Data for serum albumin were available for 105 out of 133 patients (79%), of which 64 patients (61%) had serum albumin of less than 3.8, considered to be one of the two option for the 3rd criteria of PEW diagnosis. Data avilable for serum total cholesterol were available for 116 out of 133 patients (87%), of which, only 6 patients (5%) had a value less than 100 mg/dl-2nd option for the 3rd criteria of PEW diagnsis. However, use of serum cholesterol level of <100 mg/dl is rarely found among different studies to be used as a marker of detecting HD patients with malnutrition.

Thus, in Table **4-2**,we found 116 out of these 133 patients (87%) had all three required criteria needed to the analysis of PEW diagnosis, of which 21 patient met 3 criteria (18%)- considered as having PEW. Therefore the prevalence of PEW in this study cohort is 18% without considering dietary intake.

When we included 4th criteria, that is "Dietary energy and protein intake for at least two consecutive months", only one day 24-hour diet recall data were available, from which, considering DEI <25 kcal/kg body weight/day or DPI<0.8 g/kg body weight/day, we found an additional 12 patients met one or both of this criteria. Therefore the prevalence of PEW in

this study cohort is 25% including diet data. Another 26 out of 116 patients met 2 criteria (23%) and are considered at risk of having PEW. Around 36% (40) patients met only one criteria- mild prevalence of malnutrition and 41% patients met no criteria (46). We also found that, 17 out of 133 patients had one or two missing values (13%). Therefore, inspection of data revealed that the number of PEW patients identified was an underestimate and the figure may be as high as 40%.

Based on PEW versus Non-PEW patients-we analyzed our data for 116 patients, of which, 21 PEW and 95 Non-PEW patients. Table **4-3** showed the demographic and clinical parameters between PEW vs Non-PEW, where, 14 out of 21 PEW patients were male (67%), and 41 out of 95 Non-PEW patients were male (43%). PEW patients were younger with mean age of 48±17 years compared to Non-PEW patients with age of 50±12 years. Average dialysis vintage in case of PEW patients, 32±32 months was higher compared to Non-PEW patients, 29±22 months. On an average, 62% of PEW patients and 64% of Non-PEW patients underwent twice weekly dialysis. While causes of ESRD among PEW patients were 38% due to hypertension (HTN) and chronic glomerulonephritis (CGN), 33% due to HTN, 19%-HTN and diabetic nephropathy (DN) and other-5%. Among Non-PEW patients, causes of developing ESRD were reported as HTN 44%, HTN and DM 31%, HTN and CGN 14% and other 9%. HTN and CGN seemed to be the major causes of developing ESRD among patients with PEW.

Table **4-4** demonstrated statistically significant differences in terms of anthropometric and biochemical parameters between PEW vs Non-PEW patients. In case of BMI (20±2.4 kg/m^2 vs 25.2±5.2 kg/m^2), MAC, TSF and MAMC (19.4±2.3 cm vs 22.2±3.8 cm). Only in case of hand grip strength, no significant difference was found. Biochemical evaluations revealed: on an average serum albumin in PEW patients, 3.5±0.6 g/dl vs Non-PEW patients,

3.8±0.5 g/dl. Statistically significant difference was observed only in case of serum albumin. Serum TIBC level was found lower among PEW patients, 228.1±55.4 mg/dL compared to non-PEW patients, 247.7±62.6 mg/dL, and serum Ferritin level was found higher among PEW patients, 724.1±569.1 ng/ml compared to Non-PEW patients, 482±423 ng/ml.

Table **4-5** demonstrated the median values for all anthropometric and biochemical parameters between PEW and Non-PEW groups where we found that, 50% of PEW patients had BMI of 20.2 kg/m^2 with 25% of them had BMI of ≤17.4 kg/m^2 (Quartile 1) and 25% had BMI of ≥22.1 kg/m^2 (Quartile 3), whereas, 50% of Non-PEW group had a BMI of 24.2 kg/m^2 with 25% had BMI of ≤21.2 kg/m^2 in Quartile 1 (a BMI<23 kgm^2 is one of the four criteria for PEW diagnosis) and 25% had BMI of ≥27.5 kg/m^2. For MAMC, median values for PEW patients was lower than their Non-PEW counterparts (18.7 cm vs 22.3 cm) and in case of Non-PEW group, 25% of them were having MAMC of ≤19.6 cm (Quartile 1) which is lower than PEW patients with MAMC of ≥21.4 (Quartile 3). Median value for TIBC in PEW patients was lower than Non-PEW patients (225 mg/dL vs 239 mg/dL), and both were lower compared to the recommended value of 300 to 400 mg/dL. Additionally, 25% of Non-PEW patients had TIBC of ≤212 mg/dL (Quartile 1) which is even lower than the median TIBC value of PEW patients. 25% of both PEW and Non-PEW patients had a median value of URR, lower than 65% (recommendation) and a bit higher for PEW patients than their Non-PEW counterparts (62% vs 59%). Median values for serum albumin between these two groups were 3.7 g/dL vs 3.8 g/dL with 25% of Non-PEW patients having serum albumin of only ≤3.5 g/dL (Quartile 1), lower than the median value for PEW patients. However, median values for Ferritin is higher for PEW patients than Non-PEW group, which further confirm the prevalence of malnutrition and 25% of Non-PEW patients had Ferritin value of 749.3 ng/ml which is higher than the median value of PEW group, 549.5 ng/ml.

In table **4-6**, a statistically significant, moderately strong and positive correlation was found between muscle mass and muscle strength of patients, who met 3 criteria for PEW (n=21), not among Non-PEW group, and a moderately strong and negative correlation between age and grip strength was only seen among Non-PEW group in the present study. Also, a positive association was found between body mass index and muscle strength in both PEW and non-PEW group.

While doing lipid profile and subfraction analyses among study cohort, of the 116 patients, we analyzed the data for 108 patients, in which, 21 PEW patients and 87 Non-PEW patients. Table **4-7** showed that, on average, among PEW patients, LDL and HDL cholesterol of 72±28 and 38±15 mg/dl, and among non-PEW patients, 88±31 and 34±10 mg/dl, respectively. Non-PEW patients had significantly higher TC, TAG and LDL-C as compared to those with PEW patients.

Ratio of TC/HDL-C, LDL-C/HDL-C and TAG/LDL-C all were significantly lower among PEW patients. LDL particles diameters were significantly higher in PEW patients. PEW patients had significantly lower cholesterol in small sized LDL particles and significantly more cholesterol in large sized HDL particles and less cholesterol in small sized HDL particles.

Table **4-8** showed that, dyslipidemia (DL), defined as TAG/HDL-C ratio of >3.8, was prevalent among 43% of PEW patients and 68% of non-PEW patients. DL, defined by ATP III guidelines, no PEW patients had atherogenic DL, (Non-PEW-17%), while almost 76% PEW patients had mixed DL (Non-PEW-68%), with 24% of the PEW patients were normal (Non-PEW-15%). Based on LDL-pattern, 81% PEW and 54% of Non-PEW patients had an LDL phenotype A (atheroprotective), 10% PEW and 31% Non-PEW had type B (atherogenic) and 10% PEW and 15% Non-PEW had intermediate pattern of LDL.

Table **4-9** demonstrated the median values of lipid profile and subfraction between these two groups. Here we found that, 25% of Non-PEW patients had median values which is lower than the median values of 50% of PEW patients in terms of HDL-C, TAG, LDL-C, large and small HDL particles, IDL-C, Large and intermediate LDL particles, mean LDL size and ratios of TAG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and Non-HDL-C/HDL-C, that means these 25% (Quartile 1) had susceptibility to develop malnutrition as well. Based on TAG/HDL-C ratio, 25% of PEW patients had a ratio of ≥6.6 (Quartile 3), which is higher than 3.8 and 25% of Non-PEW patients had a ratio of ≥8.1 (Quartile 3), also higher than 3.8, indicating prevalence of dyslipidemia (DL) in both groups.

Table **4-10** showed that, while comparing nutrient intakes among 66 acceptable reporters, 14 were PEW and 52 patients were Non-PEW patients, it was found that, differences were present between these two groups in terms of calorie intake (1289 kcal vs 1476 kcal), carbohydrates and total fiber intakes, total fat, saturated fat, MUFA, PUFA intakes (lower in PEW patients), vitamin A, E, B1, B2 and folate intakes and dietary calcium intake (lower in PEW patients), but no statistically significant differences were found. In this study, inadequate intakes of calorie and protein were also found among non-PEW patients. Overall, no significant differences in dietary intakes were observed between PEW and Non-PEW patients except dietary calcium intake (lower among PEW patients). However, while compared to K/DOQI guidelines, both PEW and Non-PEW groups showed lower intake in terms of DEI (dietary energy intake), DPI (dietary protein intake), total fiber, fat soluble vitamins (except vitamin A), water soluble vitamins and zinc. Higher phosphorous to protein ratio and omega-6 to omega-3 fatty acid ratios were also observed compared to the reference values in both groups.

Table **4-11** demonstrated median values of both macro and micronutrient intakes between two groups. Here we found that, 25% of our Non-PEW patients' intakes of calorie, protein, phosphorous, carbohydrates, total fiber, fat, water, vitamins and minerals (Quartile 1) were lower than the median values of their PEW counterparts. Median values for DEI and DPI were also lower in Non-PEW patients compared to their PEW counterparts (25 kcal/kg BW/day vs 22 kcal/kg BW/day and 0.9 g vs 0.8 g/kg BW/day). Median values for phosphorous to protein and omega 6 to omega 3 fatty acid ratios were also found higher among non-PEW group. Therefore, we postulated that, both groups were found to be deprived of adequate dietary intake in the present study.

Table **4-12** showed a statistically significant and higher malnutrition inflammation score (MIS) of 7.6 was found among PEW patients compared to a lower score of 5.6 in their non-PEW counterparts. From this point, we can further predict that, the number of PEW patients identified in this study might be an underestimate. No significant differences were observed in terms of ADAT and self-reported RLS score between these two groups. However, while analyzing four components KD-QoL (self-reported) questionnaire, significant differences were observed in terms of 1st two components such as- Physical (43.7±12.5 vs 37.3±10.4) and Mental Health composite score (50.1±7.5 vs 43.9±9.6) between these two groups and PEW group had a higher score, therefore, a low score indicating malnutrition [130]. No significant differences were observed in case of other two components (Burden and Effects of Kidney Disease).

Table **4-13** demonstrated the median values of MIS, ADAT, RLS and KD-QoL between two groups where we found that, 25% of Non-PEW patients had an MIS of ≥7.0 (Quartile 3) which is like the median value for PEW group. Additionally, 25% of Non-PEW patients had KD-QoL score which is higher than the median score for PEW patients, which

further confirms the fact that, prevalence of PEW in this study cohort might be higher than our estimation.

Tables and Figures

Tables.

Table 4-1. Patients with PEW diagnosed based on Anthropometric and biochemical data

Anthropometric Criteria		**Biochemical Criteria**	
1. Body mass index	**n (%)**	**3.a. Sr Albumin (g/dl)**	**n (%)**
BMI data available	119 (89%)	Sr. Albumin data available	105 (79%)
BMI<23 kg/m2	58 (49%)	Sr. albumin<3.8 g/dl	64 (61%)
2. Mid-arm muscle circumference (MAMC)	**n (%)**	**3.b. Sr. Total cholesterol (mg/dl)**	**n (%)**
MAMC data available	131 (98%)	Sr. TC data available	116 (87%)
MAMC 10% below the ref population	75 (57%)	TC<100 mg/dl	6 (5%)

Data were collected from 133 patients. Values are n or percentage (%). ESRD: End stage renal disease. PEW: Protein energy wasting, ISRNM: International society for renal nutrition and metabolism. Anthropometric criteria include, 1. BMI<23 kg/m^2, 2. MAMC below 10^{th}% of the 50^{th} percentile of MAMC for reference US population, Biochemical criteria include-3a. Sr. Albumin<3.8 g/dL or 3b. Sr Total cholesterol<100 mg/dl, which is not considered here.

Table 4-2: Prevalence of PEW based on ISRNM criteria

Matched Criteria for PEW	n (%)
All criteria present	116 (87%)
PEW-3 criteria matched	21 (18%)
At risk PEW-Only 2 criteria matched	26 (23%)
Only 1 criterion matched	40 (36%)
No criteria matched	46 (41%)
Including diet, patients with PEW	33 (25%)

Data were collected from 133 patients at Kidney Foundation Bangladesh. Values are n or percentage (%). ESRD: End-stage renal disease. PEW: Protein energy wasting, ISRNM: International society for renal nutrition and metabolism. Anthropometric criteria include, 1. BMI<23 kg/m^2, 2. MAMC below 10th% of the 50th percentile of MAMC for reference US population, Biochemical criteria include-3a. Sr. Albumin<3.8 g/dL or 3b. Sr Total cholesterol<100 mg/dl. For 3 criteria matched, 116 patients had no missing values for BMI, MAMC and Sr. albumin or total cholesterol. That is why, 116 patients who had all anthropometric and biochemical parameters were considered. In case of diet, 133 patients were considered.

Table 4-3: Demographics and clinical parameters. PEW versus Non-PEW

	All	PEW	Non-PEW
Gender, M/F (n)	55 / 61 (116)	14 / 7 (21)	41 / 54 (95)
Age in years (n)	50±13 (116)	48±17 (21)	50±12 (95)
Dialysis duration (hrs) (n)	3.8±0.4 (110)	3.9±0.3 (19)	3.8±0.4 (91)
Dialysis vintage (mon) (n)	30±24 (115)	32±32 (20)	29±22 (95)
Dialysis frequency, n (%)			
Thrice a week	41 (35%)	7 (33%)	34 (36%)
Twice a week	74 (64%)	13 (62%)	61 (64%)
Once a week	1 (1%)	1 (5%)	0 (0%)
Causes of ESRD, n (%)			
HTN	49 (42%)	7 (33%)	42 (44%)
HTN and DN	33 (28%)	4 (19%)	29 (31%)
HTN and CGN	21 (18%)	8 (38%)	13 (14%)
Others	10 (9%)	1 (5%)	9 (9%)
Missing data	3 (3%)	1 (5%)	2 (2%)

Data were collected from the number of patients indicated in parentheses. Values are *Mean* ±*SD* and n or percentage (%) from 116 patients, of which 21 PEW and 95 non-PEW patients. HTN: Hypertension, DN: Diabetic nephropathy, CGN: Chronic glomerulonephritis, Other: 4 Unknown, 1 postpartum complication; 1 genetic, 2 APKD, 1 DN and CGN. ESRD: End-stage renal disease. PEW: Patients having protein-energy wasting based on ISRNM criteria, Non-PEW: Patients without PEW. No significantly differences were found between groups using a one-way ANOVA test ($p<0.05$).

Table 4-4: Anthropometric and biochemical parameters: PEW versus Non-PEW

	All	PEW	Non-PEW	References
Height (cm)	158.5±9.3 (116)	159.7±8.0 (21)	158.3±9.6 (95)	
Dry weight (kg)	60.6±12.6 (116)	51.0±8.9[a] (21)	62.7±12.3[a] (95)	
BMI (kg/m^2)	24.2±5.2 (116)	19.9±2.4[a] (21)	25.2±5.2[a] (95)	
HGS (kg)	19.8±7.4 (116)	20.2±7.9 (21)	19.7±7.3 (95)	
MAC (cm)	26.6±5.2 (116)	22.3±2.4[a] (21)	27.5±5.2[a] (95)	
TSF (mm)	15.8±8.2 (116)	9.3±3.8[a] (21)	17.2±8.2[a] (95)	
MAMC (cm)	21.7±3.7 (116)	19.4±2.3[a] (21)	22.2±3.8[a] (95)	
TIBC (mg/dL)	244.1±61.5 (81)	228.1±55.4 (15)	247.7±62.6 (66)	300-400 [139]
URR %	65.3±8.8 (83)	66.6±9.7 (16)	65.0±8.6 (67)	$\geq$ 65 [140]
Na (mEq/L)	136.1±3.8 (107)	136.5±2.5 (19)	136.0±4.1 (88)	135-146 [141]
K (mEq/L)	5.0±0.7 (112)	5.1±0.7 (20)	5.0±0.7 (92)	3.5-5.3 [142-144]
P (mg/dl)	4.5±2.2 (100)	4.7±2.6 (18)	4.5±2.1 (82)	
Albumin (g/dl)	3.7±0.6 (97)	3.5±0.6[a] (20)	3.8±0.5[a] (77)	3.8-5.0 [145]
Ferritin (ng/ml)	496.7±442.8 (69)	724.1±569.1 (10)	482.0±423.1 (59)	5-275 [146]
F>2000ng/ml	15	6	9	
Kt/V	1.3±0.4 (55)	1.4±0.4 (11)	1.3±0.4 (44)	1.2-1.3 [147, 148]

Data were collected from 116 patients of which 21 PEW and 95 Non-PEW patients. Biochemical data were obtained from patients' medical record. Values are *Mean* $\pm$ *SD* (n). BMI: Body mass index, HGS: Hand grip strength, MAC: Mid-arm circumference, TSF: Triceps skin fold, MAMC: Mid-arm muscle circumference, TIBC: Total iron binding capacity. F: Ferritin. Mean values sharing a common superscript were significantly different from each other using a one-way ANOVA($p<0.05$). URR %: Urea reduction rate. Na: Sodium, K: Potassium, P: Phosphorous.

Table **4-5:** Anthropometric and biochemical parameters: PEW versus Non-PEW based on Percentile distribution (IQR)

	PEW	Non-PEW	Reference value
Height (cm)	160 (153-165.5)	158 (150165)	
Dry weight (kg)	54 (42.8-57.5) [a]	62 (53-70) [a]	
BMI (kg/m^2)	20.2 (17.4-22.1) [a]	24.2 (21.2-27.5) [a]	
HGS (kg)	20.9 (13.3-24.6)	18.3 (14.3-23.9)	
MAC (cm)	21.5 (21.1-23.5) [a]	27.4 (23.7-30.2) [a]	
TSF (mm)	9.8 (6.5-12.3) [a]	17.3 (10.8-22.5) [a]	
MAMC (cm)	18.7 (17.6-21.4) [a]	22.3 (19.6-24.5) [a]	
TIBC (mg/dL)	225 (172-250)	239 (212-280)	300-400 [139]
URR%	65.5 (61.6-75.3)	65.4 (59.0-70.9)	> 65 [140]
Na (mEq/L)	136 (135-138)	137 (134-139)	135-146 [141]
K (mEq/L)	5.1 (4.8-5.7)	4.9 (4.5-5.4)	3.5-5.3 [142-144]
P (mg/dl)	5.1 (1.9-6.6)	4.8 (2.7-5.9)	
Albumin (g/dl)	3.7 (3.4-3.7) [a]	3.8 (3.5-4.0) [a]	3.8-5.0 [145]
Ferritin (ng/ml)	549.5 (125.1-1400.3)	345.4 (156.0-749.3)	5-275 [146]
F>2000ng/ml	6	9	
Kt/V	1.3 (1.2-1.6)	1.2 (1.1-1.4)	1.2-1.3 [147, 148]

Data is reported for 116 patients of which 21 were PEW and 95 were Non-PEW patients based on ISRNM guidelines. Biochemical data were obtained from patient's medical records. IQR: Interquartile range. Values for IQR are represented as Median (Quartile 1-Quartile 3). BMI: Body mass index, HGS: Hand grip strength, MAC: Mid-arm circumference, TSF: Triceps skin fold, MAMC: Mid-arm muscle circumference, TIBC: Total iron binding capacity. F: Ferritin. URR %: Urea reduction rate. Na: Sodium, K: Potassium, P: Phosphorous. Mean values sharing a common superscript were significantly different from each other using a one-way ANOVA($p<0.05$).

Table 4-6: Correlation of muscle mass with BMI and muscle strength among PEW patients and age with muscle strength and BMI with muscle mass among Non-PEW patients

	MAMC (cm)	Age (years)	BMI (kg/m^2)	HGS (kg)
PEW (21)				
MAMC (cm)	1	0.109	R=0.544*	R=0.648**
Age (years)	0.109	1	0.424	-0.260
BMI (kg/m^2)	R=0.544*	0.424	1	0.357
HGS (kg)	R=0.648**	-0.260	0.357	1
Non-PEW (95)				
MAMC (cm)	1	R=0.235*	R=0.630**	0.154
Age (years)	R=0.235*	1	R=0.286**	R=-0.276**
BMI (kg/m^2)	R=0.630**	R=0.286**	1	-0.107
HGS (kg)	0.154	R=-0.276**	-0.107	1

Data were collected from patients at Kidney Foundation Bangladesh.; values were for 21 PEW and 95 Non-PEW patients; MAMC: Mid-arm muscle circumference, HGS: Hand Grip Strength in Kilograms. *p<0.05 or **p<0.01, R=Pearson Correlation coefficient

Table 4-7: Lipid profile and subfraction analysis: PEW versus Non-PEW

	ALL (108)	PEW (21)	Non-PEW (87)
TC (mg/dl)	155±40	136±34[a]	160±40[a]
HDL-C (mg/dl)	35±11	38±15	34±10
TAG (mg/dl)	177.6±97.4	131.4±50.1[a]	188.7±102.8[a]
LDL-C (mg/dl)	85±31	72±28[a]	88±31[a]
Non-HDL-C	121±40	98±28[a]	126±40.5[a]
TC/HDL-C	4.9±1.8	3.9±1.1[a]	5.1±1.8[a]
Non-HDL-C/HDL-C	3.9±1.8	2.9±1.1	4.1±1.8
LDL-C/HDL-C	2.7±1.2	2.0±0.8 [a]	2.8±1.3[a]
TAG/HDL-C	6.0±4.0	4.2±2.7 [a]	6.4±4.1 [a]
Large HDL (mg/dl)	12.4±8.1	16.4±10.1[a]	11.4±7.3 [a]
Intermediate HDL (mg/dl)	17.5±4.4	18.2±6.0	17.3±4.0
Small HDL (mg/dl)	4.7±2.4	3.3±2.1[a]	5.0±2.3 [a]
VLDL (mg/dl)	36.4±12.8	29.7±10.2 [a]	38.1±12.8 [a]
IDL-C (mg/dl)	52.3±15.2	45.1±11.1 [a]	54±15.5 [a]
Large LDL (mg/dl)	19.4±8.2	19.8±7.0	19.3±8.5
Intermediate LDL (mg/dl)	11.3±7.0	9.3±5.3	11.8±7.3
Small LDL (mg/dl)	5.6±8.4	1.7±2.9 [a]	6.5±9.1 [a]
Mean LDL size (Å)	268±7	271±3 [a]	267±7 [a]

Data were analyzed for the number of patients indicated in parentheses. Values are *Mean* ± *SD* and n or %. TC: Total Cholesterol, HDL-C: High density lipoprotein, TAG: Triacylglycerol/triglycerides, LDL-C: Low density lipoprotein, Type A: athero-protective profile, Type B: atherogenic profile, Intermediate: has characteristics of both A and B. Values sharing same superscripts between the groups were significantly different using one-way ANOVA ($p<0.05$).

Table **4-8:** Dyslipidemia: PEW versus Non-PEW

	All	PEW	Non-PEW
Dyslipidemia (DL)			
TAG/HDL-C ratio<3.0	40 (37%)	12 (57%)	28 (32%)
TAG/HDL-C ratio>3.8	68 (63%)	9 (43%)	59 (68%)
DL-ATP III Guideline, 2013			
Atherogenic DL (AD)	15 (14%)	0	15 (17%)
Mixed DL (MD)	75 (69%)	16 (76%)	59 (68%)
Normolipidemic (N)	18 (17%)	5(24%)	13 (15%)
LDL-Pattern, n (%)			
A	64 (59%)	17 (81%)	47 (54%)
B	29 (27%)	2 (10%)	27 (31%)
Intermediate	15 (14%)	2 (10%)	13 (15%)

Data were analyzed for the number of patients indicated in parentheses. Values are *Mean* $\pm$ *SD* and n or %. TC: Total Cholesterol, HDL-C: High density lipoprotein, TAG: Triacylglycerol/triglycerides, LDL-C: Low density lipoprotein, Type A: athero-protective profile, Type B: atherogenic profile, Intermediate: has characteristics of both A and B. Values sharing same superscripts between the groups were significantly different using one-way ANOVA ($p<0.05$).

Table **4-9:** Lipid profile and Lipid Subfractions between PEW and Non-PEW groups based on Percentile distribution (IQR)

	PEW (21)	**Non-PEW (87)**
TC (mg/dl)	128 (106-158) [a]	154 (133-184) [a]
HDL-C (mg/dl)	34.4 (26.1-47.2)	32 (26-40)
TAG (mg/dl)	129.6 (97.2-183.0) [a]	171.6 (120.1-224.7) [a]
LDL-C (mg/dl)	73.5(51.0-90.2) [a]	83.5 (67.3-103.2) [a]
Non-HDL-C	94 (77-119) [a]	118 (97-150) [a]
TC/HDL-C	3.9 (3.2-4.6) [a]	4.7 (3.8-6.3) [a]
Non-HDL-C/HDL-C	2.9 (2.2-3.6)	3.7 (2.8-5.3)
LDL-C/HDL-C	2.0 (1.6-2.5) [a]	2.5 (1.9-3.5) [a]
TAG/HDL-C	3.4 (2.0-6.6)	5.7 (3.2-8.1)
Large HDL (mg/dl)	14.0 (11.0-20.5) [a]	9.0 (6.0-16.0) [a]
Intermediate HDL (mg/dl)	18.0 (14.0-22.5)	18.0 (14.0-20.0)
Small HDL (mg/dl)	3 (2-5) [a]	5 (3-7) [a]
VLDL (mg/dl)	27 (24-33) [a]	36 (29-45) [a]
IDL-C (mg/dl)	44 (36-55) [a]	50 (43-62) [a]
Large LDL (mg/dl)	18 (14-24)	18 (13-25)
Intermediate LDL (mg/dl)	9.0 (5.5-13.5)	11.0 (6.0-17.0)
Small LDL (mg/dl)	0 (0-2) [a]	2 (0-10) [a]
Mean LDL size (Å)	272[a] (270-273) [a]	268 (263-273) [a]

Data is reported for 108 patients of which 21 were PEW and 87 were Non-PEW patients based on ISRNM guidelines. IQR: Interquartile range. Values for IQR are represented as Median (Quartile 1-Quartile 3). TC: Total Cholesterol, HDL-C: High density lipoprotein, TAG: Triacylglycerol/triglycerides, LDL-C: Low density lipoprotein, Type A: athero protective profile, Type B: atherogenic profile, Intermediate: has characteristics of both A and B. Values sharing same superscripts between the groups were significantly different using one-way ANOVA ($p<0.05$).

Table 4-10. Dietary Analysis for acceptable reporter: PEW and Non-PEW

Parameters	All (66)	PEW (14)	Non-PEW (52)	KDOQI Guidelines
Calories (Kcal)	1436±498	1289±285	1476±537	Based on BW
DEI/kg BW/day	23.7±6.6	24.0±5.3	24.0±7.0	30-35 kcal/kg BW/day
Protein (g)	54.0±22.0	55.0±20.4	53.7±22.4	Based on BW
DPI/kg BW/day	0.9±0.3	1.0±0.3	0.8±0.3	1.2 g/ kg BW/day
P mg/kg BW/day	14.2±5.4	14.5±3.2	14.2±6.0	10-17 mg/kg BW /day
P: Protein	16±4	15±4	17±4	<12 mg/g of protein
Carbohydrates (g)	209±71	188±41	215±76	Based on BW
Total Fiber (g)	17±7	15±4	17±7	20-25 g/day
Fat (g)	43±21	36±13	45±22	
SFA (g)	8.4±4.4	6.6±3.3	8.8±4.5	
MUFA (g)	8.4±4.5	6.8±3.6	8.8±4.7	
PUFA (g)	15.6±9.5	13±7[a]	16.3±10[a]	
Cholesterol (mg)	223±153	177±132	236±157	<200 mg/day
omega 6: omega 3	10.8±5.7	10.0±6.7	11.0±5.5	4:01
Water (ml)	1419±644	1500±704	1395±633	750-1500 ml/day
Vitamin A-IU	1033±1328	835±1106	1087±1386	700-900 IU
Vitamin D-IU	47±40	30±36	51±40	600 IU
Vitamin E (mg)	2.2±1.6	1.9±0.8	2.3±1.7	15 mg
Vitamin K (µg)	13±32	15±19	13±33	90-120 µg
Vit B1 (mg)	0.7±0.3	0.6±0.2	0.8±0.4	1.1-1.2 mg
Vit B2 (mg)	1.1±1.7	0.7±0.2	1.2±2.0	1.1-1.3 mg
Vit B3 (mg)	13.7±5.4	15.0±5.0	13.3±5.5	14-16 mg
Vit B6 (mg)	12.0±30.0	8.0±15.3	13.3±32.8	13-17 mg
Vit B12 (µg)	1.6±1.7	1.5±1.1	1.7±1.8	2.4 µg
Biotin (µg)	10.2±9.7	9.8±8.9	10.3±10.0	30 µg
Folate (µg)	136±187	96±61	147±208	1000 µg
Vit C (mg)	87±72	66±44	94±77	75-90 mg/day
Dietary Ca (mg)	738±263	316±145[a]	471±279[a]	<1000 mg
Iron (mg)	16±15	12±8	17±16	Individualized
Dietary P (mg)	868±428	792±215	888±469	1000 mg
Dietary K (mg)	1412±571	1282±369	1447±612	Individualized
Dietary Na (mg)	2054±929	1876±731	2101±976	<2400 mg
Zinc (mg)	8.1±4.6	7.4±3.0	8.2±4.9	15 mg
Magnesium (mg)	226±92	208±58	232±98	200-300 mg

The data is reported for all acceptable reporters. Values are as *Mean* ± *SD*. DEI: Dietary energy intake, DPI: Dietary protein intake. SFA: Saturated fat, MUFA: Monounsaturated fat, PUFA: Poly unsaturated fat. IU: International Unit, vit: vitamin, Vit E: alpha tocopherol. BW: body weight. Ca: calcium, Na: sodium, K: Potassium, P: Phosphorous. Mean values sharing a common superscript were significantly different from each other using a one-way ANOVA ($p<0.05$).

Table **4-11.** Dietary Analysis for acceptable reporters between PEW and Non-PEW groups based on Percentile distribution (IQR)

	PEW (14)	Non-PEW (52)	KDOQI
Calories (Kcal)	1218 (1078-1488)	1316 (1159-1657)	Based on BW
DEI/kg BW/day	25 (19-28)	22 (19-27)	30-35 kcal/kg BW/day
Protein (g)	46 (42-75)	48 (40-60)	Based on BW
DPI/kg BW/day	0.9 (0.8-1.3)	0.8 (0.6-1.1)	1.2 g/ kg BW/day
P mg/kg BW/day	15 (11.8-16.7)	12.6 (10.0-17.3)	10-17 mg/kg BW /day
P: Protein	14 (11.4-17.8)	16.5 (13.8-19.3)	<12 mg/g of protein
Carbohydrates (g)	186 (148-226)	194 (167-247)	Based on BW
Total Fiber (g)	14 (12-16)	15 (13-21)	20-25 g/day
Fat (g)	37 (25-45)	40 (32-53)	
SFA (g)	6.7 (3.3-10.5)	8.1 (5.7-11.6)	
MUFA (g)	6.6 (3.4-9.8)	7.7 (5.6-11.1)	
PUFA (g)	10.7[a] (7.2-18.4)	14.9[a] (9.3-20.6)	
Cholesterol (mg)	164 (52-292)	196 (136-380)	<200 mg/day
omega 6: omega 3	8.9 (7.4-13.2)	12.0 (8.0-13.8)	4:01
Water (ml)	1563 (959-1777)	1431 (851-1759)	750-1500 ml/day
Vitamin A-IU	527 (166-789)	703 (439-1043)	700-900 IU
Vitamin D-IU	28 (1.2-47)	45 (12-80)	600 IU
Vitamin E (mg)	1.9 (1.3-2.4)	1.9 (1.3-2.8)	15 mg
Vitamin K (µg)	5.2 (2.9-15.3)	5.3 (3.0-9.5)	90-120 µg
Vit B1 (mg)	0.6 (0.5-0.7)	0.7 (0.6-0.9)	1.1-1.2 mg
Vit B2 (mg)	0.7 (0.5-0.8)	0.9 (0.6-1.2)	1.1-1.3 mg
Vit B3 (mg)	14.5 (11.0-19.8)	12 (9.5-15.2)	14-16 mg
Vit B6 (mg)	0.8 (0.5-6.5)	0.8 (0.6-1.2)	13-17 mg
Vit B12 (µg)	1.1 (0.7-2.2)	1.4 (0.9-1.7)	2.4 µg
Biotin (µg)	7 (3.9-11.6)	9.4 (3.9-13.1)	30 µg
Folate (µg)	82.0 (44.0-163.0)	97.3 (74.3-159.6)	1000 µg
Vit C (mg)	53 (32-87)	70 (36-116)	75-90 mg/day
Dietary Ca (mg)	340 (172-431) [a]	418 (246-614) [a]	<1000 mg
Iron (mg)	9 (6-16)	11 (8-16)	Individualized
Dietary P (mg)	728 (632-1022)	774 (644-993)	1000 mg
Dietary K (mg)	1320 (890-1568)	1298 (1018-1734)	Individualized
Dietary Na (mg)	1604 (1227-2675)	1939 (1424-2575)	<2400 mg
Zinc (mg)	7.0 (5.2-8.5)	6.3 (5.2-11.0)	15 mg
Magnesium (mg)	196 (158-250)	208 (176-250)	200-300 mg

The diet data is reported for the acceptable reporters for the two groups. IQR: Interquartile range. Values for IQR are represented as Median (Quartile 1- Quartile 3). DEI: Dietary energy intake, DPI: Dietary protein intake. SFA: Saturated fat, MUFA: Monounsaturated fat, PUFA: Poly unsaturated fat. IU: International Unit, vit: vitamin, Vit E: alpha tocopherol. BW: body weight. Ca: calcium, Na: sodium, K: Potassium, P: Phosphorous. Mean values sharing a common superscript were significantly different from each other using a one-way ANOVA ($p<0.05$).

Table 4-12: Different health and Nutrition related Questionnaire: PEW versus Non-PEW

	PEW	Non-PEW
MIS Score	7.6±3.1 (14) [a]	5.3±2.7 (66) [a]
ADAT Score	3.0±1.1 (10)	3.7±1.6 (43)
RLS Score	14.4±8.1 (10)	17.3±8.1 (46)
KD-QoL		
SF-12 Physical Health Composite	43.7±12.5 (15) [a]	37.3±10.4 (64) [a]
SF-12 Mental Health Composite	50.1±7.5 (15) [a]	43.9±9.6 (64) [a]
Burden of Kidney Disease	35.4±23.5 (15)	28.1±26.9 (66)
Effects of Kidney Disease	72.6±19.1 (13)	63.5±16.2 (18)

Data were collected from the number of patients indicated in parentheses. Values are *Mean* ±*SD* (n). Mean values sharing a common superscript are statistically significant to each other using a one-way ANOVA.
MIS [46]: Malnutrition inflammation score. A score >5 indicates malnourishment. MIS has 10 components, each with four levels of severity, from 0 (normal) to 3 (very severe). The sum of all 10 MIS components ranges from 0 (normal) to 30 (severely malnourished); higher score reflects a more severe degree of malnutrition and inflammation. ADAT [124]: Appetite and diet analysis tool. Scale: 1 = very good, 2 = good, 3 = fair, 4 = poor and 5 = very poor. RLS [126]: Restless leg syndrome. medical doctor. Scale: 0, None; 1 – 10, Mild RLS; 11-20, Moderate RLS, 21-30 Severe RLS, 31-40 Very Severe RLS. Patients reporting score '0' were excluded from analysis. KD- QoL[130] Subscale scores range from 0 to 100, with lower scores indicating poor self-reported QOL.

Table **4-13:** Different health and Nutrition related Questionnaire: PEW versus Non-PEW based on Percentile distribution (IQR)

	PEW	**Non-PEW**
MIS Score	7.0 (5.8 - 9.5) [a]	5.0 (3.0-7.0) [a]
ADAT Score	3.0 (2.0 - 4.0)	3.0 (3.0-4.0)
RLS Score	13.0 (6.8-20.0)	16.5 (10.0-23.5)
KD-QoL		
SF-12 Physical Health Composite	47.7 (27.8-53.6) [a]	36.4 (28.3-44.6) [a]
SF-12 Mental Health Composite	50.1 (43.8-55.0) [a]	44.6 (36.4-51.3) [a]
Burden of Kidney disease	37.5 (18.8-56.3)	18.8 (6.3-45.3)
Effects of Kidney disease	78.1 (51.6-90.6)	64.1 (50.0-75.0)

Data were collected from the number of patients indicated in parentheses. Values are IQR: Interquartile range. Values for the IQR are represented as Median (Quartile 1 – Quartile 3). MIS [46]: Malnutrition inflammation score. A score >5 indicates malnourishment. MIS has 10 components, each with four levels of severity, from 0 (normal) to 3 (very severe). The sum of all 10 MIS components ranges from 0 (normal) to 30 (severely malnourished); higher score reflects a more severe degree of malnutrition and inflammation ADAT [124]: Appetite and diet analysis tool. Scale: 1 = very good, 2 = good, 3 = fair, 4 = poor and 5 = very poor. RLS [126]: Restless leg syndrome. medical doctor. Scale: 0, None; 1 – 10, Mild RLS; 11-20, Moderate RLS, 21-30 Severe RLS, 31-40 Very Severe RLS. KD- QoL[130] Subscale scores range from 0 to 100, with lower scores indicating poor self-reported QOL.

CHAPTER 5 SPECIFIC AIM III RESULTS: TO DEVELOP CULTURALLY ACCEPTABLE RENAL-SPECIFIC NUTRITION INFORMATION AND EVALUATES ITS IMPACT ON PATIENTS' RENAL NUTRITION-RELATED KNOWLEDGE

Results.

At the beginning, a color-coded table was made (Table **5-1**), based on which all 381 foods were separated based on their protein, potassium, phosphorous and phosphorus to protein(mg/g) ratio in 'low', 'medium', 'high', and 'very high level' [85] according to NKF guideline. The ethnic Bangladeshi foods were separately analyzed from different food groups like cereals and their products, pulse, legumes, and their products, vegetables and their products, leafy vegetables, starchy roots, tubers, and their products, nuts, seeds, and their products, spices, condiments, and herbs, fruits, fish, shellfish and their products, meat, poultry, and their products, eggs and their products, milk and milk products, fats and oils, and beverages with their nutrient content which were documented in a recently published 'Food composition table of Bangladesh'[111]. Table **5-2** presented data of some renal-friendly Bangladeshi food stuffs which were analyzed based on protein, phosphorus, phosphorus to protein ratio, potassium, and sodium content in raw food (mostly) that are thought to be the major concern in case of the dietary management of patients having chronic kidney disease.

Then, a phosphorus pyramid in accordance with "International Phosphorous pyramid" was generated with locally acceptable food items which were derived from the former analysis of all 381 food stuffs (Figure **5-1**) and table **5-3** showed the explanation of that newly developed Bangladeshi Phosphorous pyramid.

In table **5-4**. the recommended intakes of energy, protein and phosphorous were calculated for a typical 50 kg, 60 kg and 70 kg adult. A hemodialysis patient requires at least

30 kcal of energy/kg body weight/day, 1.2 g of protein/kg body weight/day and 10-17 mg of phosphorous/kg body weight/day according to NKF/KDOQI guideline[149].

In table **5-5**, foods from meat, egg, fish and legumes were listed based on their phosphorous (P) to protein ratio and separated as 'eat more' if the ratio is <15 mg of P/g of protein and 'eat less' if the ratio is >15 mg of P /g of protein.

Table **5-6** showed the list of food from fruits and vegetables in which potassium is present in low, moderate and high amount based on guideline per 100 g of food. Here we found that, boiling reduces potassium content of some vegetables, such as- boiled radish and cabbage has low potassium compared to raw radish and cabbage. Then in table **5-7**, some tips for reducing potassium content through cooking procedure was provided[150].

Then approximately 150 commonly consumed Bangladeshi dishes were used for recipe construction and analysis of nutrient using Esha Food Processor software (Figure **5-2**). After that, a one-day (1800 kcal for a 60 kg man-30 kcal/kg body weight/day according to NKF K/DOQI Guideline) sample menu (Table **5-8**) and 7-day renal-friendly sample menu was designed/prepared based on this analysis (Table **5-9**), so that it could be used later to design a calorie and protein adjusted "Food plate" for each meal for individual patient. With sample menu, list of local sorted out food items based on potassium content, phosphorous to protein ratio as well as a local 'Phosphorous Pyramid' was provided so that, a patient could select food based on individual need.

Finally all of these information were incorporated in the booklet which basically had two parts-one part includes "translation of necessary nutrition related information and dietary suggestion in "Bengali" and another part includes "analysis of 381 ethnic Bangladeshi food stuffs listed in the "Food composition Table" based on renal-specific nutrients such as-

protein, sodium, potassium, phosphorous, phosphorous to protein ration. English version of that booklet was also prepared and checked by bilingual specialists in this field (Figure **5-3**). The booklet was then verified from the Institute of Nutrition and Food Science (INFS), University of Dhaka for its nutrient analysis part and from KFHRI for its clinical acceptance (Figure **5-4**).

Tables and Figures

Tables

Table **5-1.** Recommended cut-off points of renal-specific nutrients [149].

Nutrient/100 g of Food	**Low**	**Medium**	**High**	**Very High**
Phosphorus to protein ration (mg/g)	< 12 mg/g	12-15 mg/g	>15 mg/g	
Protein (g)	<20 g	(20-50) g	>50 g	
Phosphorus (mg)	<50 mg	50-150 mg	>150 mg	
Potassium (mg)	<100 mg	101-200 mg	201-300 mg	>300 mg

Here, low means desirable, medium means moderately desirable, high means not desirable and very high means detrimental.

Table 5-2. A snapshot of renal-specific nutrient analysis using Food Composition Table, Bangladesh for some renal-friendly Bangladeshi food stuffs [111].

Renal-friendly Food Group	English Name	Protein (g)	P (mg)	P:Pro, (mg/g)	K (mg)	Na (mg)
Beverages	Sugar cane juice	0.7	6.0	8.6	25.0	7.0
Beverages	Jaggery liquid, date palm	0.3	15.0	[b]50.0		
Cereals	Vermicelli, boiled	3.9	38.0	9.7	49.0	4.0
Cereals	Semolina, wheat, raw	10.9	[a]105.0	9.6	[a]158.0	5.0
Cereals	Vermicelli, wheat, raw	8.9	[a]92.0	10.3	[a]140.0	8.0
Cereals	Rice flakes, water soaked	2.0	39.0	[b]19.5	45.0	1.0
Fish	Pangas, w/o bones, raw	15.9	[a]130.0	8.2	[a]169.0	46.0
Fish	Boal, w/o bones, raw	15.4	[a]134.0	8.7	[a]146.0	63.0
Fish	Calbasu, w/o bones, raw	17.0	[a]141.0	8.3	[b]287.0	100.0
Fish	Prawn, raw	18.2	[a]133.0	7.3	[c]355.0	93.0
Fish	Stripped snake-head, raw	17.7	[a]130.0	7.3	[c]362.0	50.0
Fish	Prawn, raw	17.6	[a]132.0	7.5	[c]352.0	92.0
Fish	Prawn, raw	18.8	[a]141.0	7.5	[c]375.0	98.0
Fish	Stone roller, raw	15.3	[a]124.0	8.1	[c]834.0	35.0
Fish	Giant tiger prawn, raw	16.5	[a]141.0	8.5	[c]423.0	117.0
Fruits	Hog plum, raw	1.1	11.0	10.0	[a]175.0	1.0
Fruits	Pineapple, ripe, raw	1.0	9.0	9.0	[a]175.0	13.0
Fruits	Pineapple, ripe, raw	0.8	7.0	8.8	[a]122.0	42.0
Fruits	Pineapple ripe, raw	0.8	7.0	8.8	[a]122.0	42.0
Fruits	Palmyra palm, raw	0.6	20.0	[b]33.3		
Fruits	Bullocks Heart, ripe, raw	1.4	10.0	7.1	[c]495.0	6.0
Greens or leaves	Alligator weed, raw	4.9	46.0	9.4		
Greens or leaves	Amaranth leaves, red, boiled, w/o salt	5.3	34.0	6.4	[a]154.0	53.0
Greens or leaves	Indian spinach, boiled, w/o salt	3.1	37.0	11.9	[a]123.0	69.0
Greens or leaves	Fenugreek leaves, raw	4.4	[a]51.0	11.6	31.0	76.0
Greens or leaves	Agathi, raw	8.4	[a]80.0	9.5		
Greens or leaves	Amaranth leaves, red, raw	4.5	32.0	7.1	[b]261.0	59.0

Greens or leaves	Bottle gourd leaves, raw	2.5	28.0	11.2	[b]276.0	41.0
Greens or leaves	Cassava leaves, raw	4.7	36.0	7.7	[c]303.0	22.0
Greens or leaves	Bengal dayflower, leaves,	2.0	19.0	9.5	[c]473.0	21.0
Greens or leaves	Colocasia leaves, green	4.0	40.0	10.0	[c]764.0	47.0
Milk	Milk, human, colostrum	2.0	14.0	7.0	70.0	47.0
Meat	Lamb/mutton, meat, moderately fat, raw	18.5	[a]150.0	8.1	[a]136.0	41.0
Milk	Milk, human, mature	1.2	15.0	[b]12.5	56.0	16.0
Oils and Seeds	Ghee, vegetables		trace		1.0	1.0
Oils and Seeds	Ghee, cow		trace		1.0	2.0
Pulses	Lentil, boiled, w/o salt	13.6	[a]115.0	8.5	[b]234.0	16.0
Spices	Lemon peel, raw	1.6	12.0	7.5	[a]160.0	6.0
Spices	Coriander leaves, raw	3.3	30.0	9.1	[c]396.0	58.0
Vegetables	Gourd, pointed, raw	2.0	18.0	9.0	[a]148.0	28.0
Vegetables	Gourd, bitter, boiled	2.3	20.0	8.7	[a]141.0	33.0
Vegetables	Gourd, bitter, raw	2.1	20.0	9.5	[a]182.0	36.0
Vegetables	Gourd, pointed, boiled	2.3	18.0	7.8	[a]115.0	26.0
Vegetables	Bean, scarlet, runner	3.9	34.0	8.7	[b]220.0	trace
Vegetables	Plantain, raw	2.0	21.0	10.5	[b]242.0	4.0
Vegetables	Chili green, raw	2.8	30.0	10.7	[b]282.0	12.0
Vegetables	Carrot, boiled, w/o salt	1.1	39.0	[b]35.5	81.0	40.0
Vegetables	Okra, boiled, w/o salt	1.7	21.0	[b]12.4	99.0	24.0
Vegetables	Amaranth, stem, raw	0.9	30.0	[b]33.3		
Vegetables	Pumpkin, boiled, w/o salt	2.2	23.0	10.5	[c]371.0	13.0

Here, the colomn for 'Protein (g)' and 'Sodium or Na (mg)' and all values that have no 'superscript' are in desirable or safe range, superscript [a] indicates 'moderately desirable', [b] indicates 'not desirable' and [c] indicates 'detrimental'. P: Phosphorous, K: Potassium, Na: Sodium, Pro: Protein.

Table **5-3.** Explanation of Bangladeshi Phosphorus pyramid

	Foods to be eaten from different Food groups
Level#1.	Whole grain cereals and oil seeds: roti, bhaat, suji, semai, porota, polao, khichuri, pawruti, soybean oil, palm oil, sesame oil, olive oil, ghee (vegetable/cow).
Level#2.	Vegetables: leafy vegetables such as, lal shak, pui shak, lau shak, methi shak, and vegetables like, pointed gourd, plantain, bitter gourd, teasle gourd, beans, pumpkin, okra, green and boiled tomato.
Level#3.	Plant protein: lentil, grass pea, pea, green gram
Level#4.	Animal protein: Different types of fish such as- ayre, shorputi, pangas, boal, white rupchada, mrigel, ilish, chital, rui, katla, magur, shol (no small fish) and egg white, chicken, beef, mutton, goat meat.
Level#5.	Fruits and beverages: pineapple, lichi, lemon, black berry, bel, amra, papaya, mango (langra), pears, guava, sugarcane juice, soymilk, licker tea.
Level#6.	Use sparingly: dairy products, spices, too much oily or greasy foods, nuts, hard cheese, egg yolk, fast food or restaurant food, street food, foods with preservatives such as pickles, sauce and all types of processed foods.

Explanation of Bangladeshi Phosphorous Pyramid. Boil foods to reduce their mineral content, including phosphorus (then discard the water). According to one study, boiling reduces phosphorus by 51% for vegetables, 48% for legumes, and 38% for meats [91].

Table 5-4: Nutrient Requirement of a Hemodialysis Patient according to NKF K/DOQI Guideline[151]

	Energy (Kcal)	**Protein (g)**	**Phosphorus (mg)**							
KDOQI Recommendation (g/kg BW/Day)	30	1.2	10	11	12	13	14	15	16	17
For 50 kg BW	1500	60	500	550	600	650	700	750	800	850
For 60 kg BW	1800	72	600	660	720	780	840	900	960	1020
For 70 kg BW	2100	84	700	770	840	910	980	1050	1120	1190
Phosphorous: Protein (mg/g)			8.3	9.3	10	10.8	11.7	12.5	13.3	14.2

NKF: National Kidney Foundation, KDOQI: Kidney Disease Outcomes and Quality Initiatives. BW: Body weight.

Table **5-5.** List of fish, meat and legumes based on Phosphorous to Protein (P: Pro) Ratio (mg of P per g of Pro)[111]

	Eat More (P:Pro of <15)	**Eat Less (P:Pro>15)**
Fish	Ayre, Pangas, Rohu, White Rupchanda, Hilsha, *(Prawn, Shol, tatkini, Kalibaush, Shorputi, Boal, Poa, Thai Koi, Vetki, Lakkha, Silver carp, dried fish, Chital, narkeli chela, magur, katla, Gulsha, Bagda and Golda chingri)	Black Rupchanda, Kanchki, Mola, Kholisha, Kajuli, *(Mrigel, Pabda, tilapia, Shing, Local Koi, Bacha, Bele, Foli, Taki, Parshe, Meni, Kakila, Puti, Chapila, Horina chingri)
Meat and egg	Chicken egg and meat, mutton, pork, *(goat meat, beef, buffalo meat, pork, duck meat, pigeon meat)	Egg from Farm chicken, Duck egg, cheese, whole cow's milk, sweet yogurt, powdered milk, condensed milk, whey
Pulse and legumes	Lentil, green gram, peas, grass peas	Chickpea/Bengal gram, Black gram

(*) means-foods high in potassium content and it can be reduced by boiling and proper cooking method[111]

Table 5-6. Amount of potassium per 100 g of Fruits and vegetables[111]

	Less (0-100 mg)	**Moderate (101-200 mg)**	**More (Above 201 mg)**
Vegetables	Radish (boil), green papaya (boil), cabbage (boil), okra (boil), carrot (boil)	Cucumber, pointed gourd (boil), green papaya, radish, eggplant (boil), snake gourd, ash gourd, bottle gourd, sponge gourd, cabbage, bitter gourd (boil), teasle gourd, pointed gourd, carrot, plantain (boil), green and ripe tomato, black bean, eggplant, sweet potato (boil)	Onion, green chili, cauliflower boil, broad bean, plantain, peas, drumsticks, pumpkin, beet, cowpea, garlic, sweet potato, potato, colocassia, taro, edd
Greens/leaves	Fenugreek/methi	Indian spinach, red amaranth (boil), green amaranth leaves (boil)	Water spinach, water cress, red amaranth, bottle gourd leaves, potato leaves, raddish leaves, spinach, colocassia leaves
Fruits	Apple (w/o skin)	Jamrul, apple, water-melon, pineapple, Carambola, pear, muskmelon, lichi, orange, pomegranate, black berry, mango (langar), ripe papaya, grape, malta	Mango (fazli), melon, embelic, pomelo, jujube, wood apple, elephant apple, tamarind, dates, banana, jackfruit, custard apple, palmyra palm

Raw vegetables high in potassium content can be reduced through proper cooking method[111]

Table 5-7. How to Leach Potassium from tuberous Root Vegetables[150]

	Cooking procedure
#1	Wash and peel the vegetables and slice the vegetables into thin slices
#2	Place the sliced vegetables in room temperature water. Use two times the amount of water to the amount of vegetable.
#3	Bring the water to a boil and drain off the water and add fresh, room temperature water.
#4	Use two times the amount of water to the amount of vegetables, bring the water to a boil again and cook until the vegetable is soft and tender.

Excess mineral content can be reduced following this cooking procedure[150]

Table 5-8. One-day Sample menu for a typical 60 kg dialysis patient containing 1800 kcal of energy and 72 g of protein

	Food item	**Amount**
Breakfast	Roti	3 pieces (30g/pc)
	Cooked mixed vegetables	1 cup (150g/cup)
	Egg boil (no yolk)	2 pcs
Morning snacks	Any fruit	1/3 cup (50 g)
Lunch	Bhaat	2.5 plate or medium bowl (160g/plate or medium bowl)
	Fried leafy vegetable	2/3 cup (100g)
	Fish curry	2 pcs (1 pc=1 match box=30g)
	Dshi thin daal(lentil)	½ cup (75g)
Afternoon Snacks	Licker tea	1 cup (150 ml)
	Vegetable pakora/pancake/shemi/suji/noodles	2 to 3 pcs or 0.5 cup
Dinner	Roti	5 pcs (30g/pc)
	Chicken/Fish curry	2 pcs (30g/pc)
	Cooked mixed/single vegetable	0.5 cup (75g)
Before bed	Yogurt/skim milk	0.5 cup (75 ml)

This sample menu was prepared based on NKF K/DOQI recommendation for a 60 kg HD patient using local food stuffs and along with this chart, a local 'Phosphorous Pyramid' as well as 'list of local food stuffs sorted out based on renal-specific nutrient content' were also given to patients so that they ca choose food item and plan their meal according to individual need.

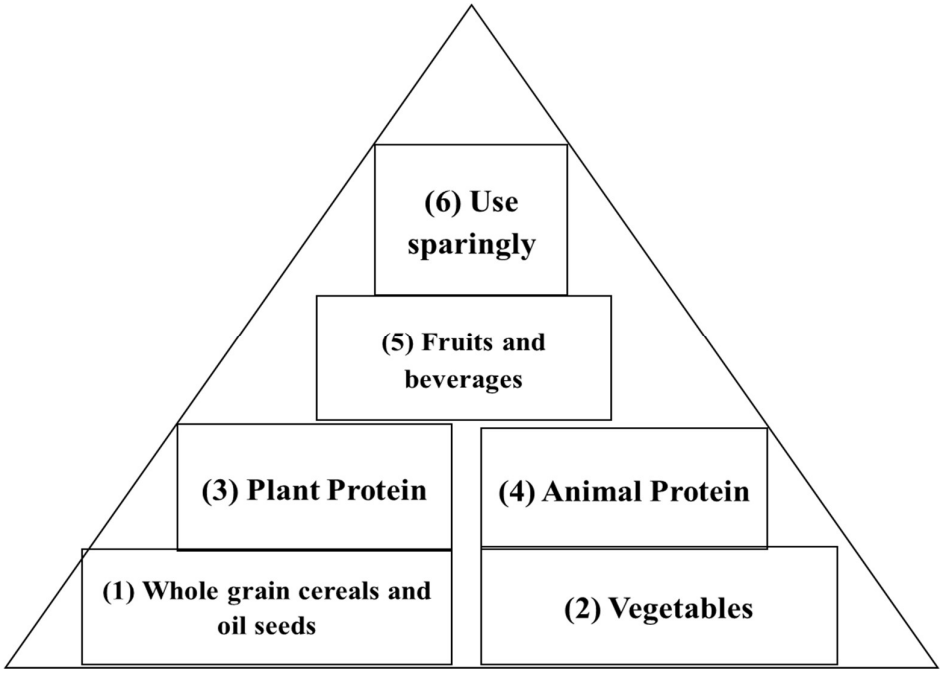
Table 5-9. Seven-day Sample menu for dialysis patient

Days	Breakfast	Snacks	Lunch	Snacks	Dinner
Sat	Roti, vegetable, boiled egg (no yolk)	Any fruit	Rice, greens, fish with veg	Licker tea, vegetable pakora	Roti, chicken curry
Sun	Porota, suji halwa/daal curry, egg boil (no yolk)	Any fruit	Rice, greens, fish curry, dal	Licker tea, pancake	Roti, fish with vegetable
Mon	Pawruti, butter, licker tea, egg boil	Any fruit	Rice, mash veg, fish curry, daal	Licker tea, shemi jorda	Roti, meat curry
Tues	Rice, egg fry/chicken curry	Any fruit	Roti, vegetable curry	Licker tea, noodles(egg/veg)	Roti, egg/daal bhuna
Wed	Roti, vegetable, egg boil (no yolk)	Any fruit	Vegetable khichuri, egg or meat curry	Licker tea, rice jorda	Roti, vegetable, daal
Thurs	Khichuri, chicken/egg curry	Any fruit	Rice, vegetable, fish curry, daal	Licker tea, flattened rice with yogurt/soymilk	Roti, fish with vegetable, egg curry
Fri	Porota, vegetable, egg boil, licker tea	Any fruit	Polao, fried vegetable, Hilsha fish or chicken curry	Licker tea, suji with soymilk	Roti/porota, vegetable curry

NB: Patient can decide which food to select in his daily menu planning based on his taste, wish and physical condition

Figures.

Figure 5-1. The Phosphorous Pyramid for Bangladeshi Dialysis Patients.



Here, box#1 and box#2 indicate 'eat more', box#3 and box#4 indicate 'eat moderately', box#5 indicates 'eat less' and box#6 indicates 'eat with limit'. It consists of 6 levels: Level 1 (low phosphorous) to level 6 (high phosphorous).

Figure 5-2. Commonly consumed Bangladeshi Dishes

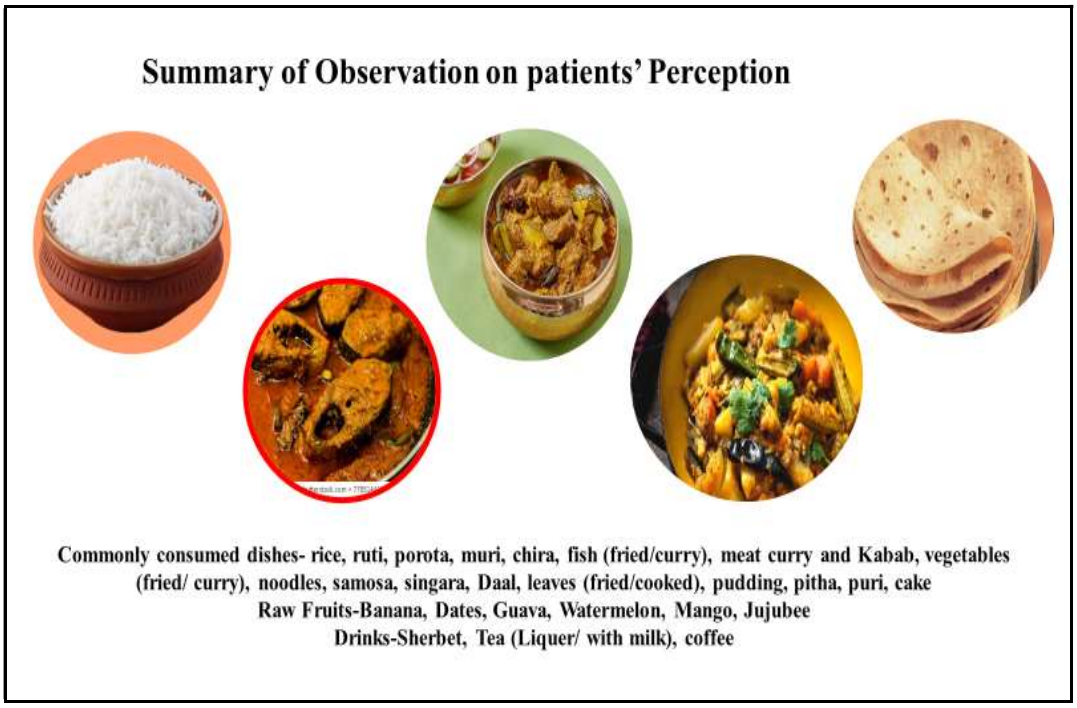


Figure 5-3. Nutrition Booklet, *"Necessary Nutrition Information for the better heath of Bangladeshi Dialysis Patients"*

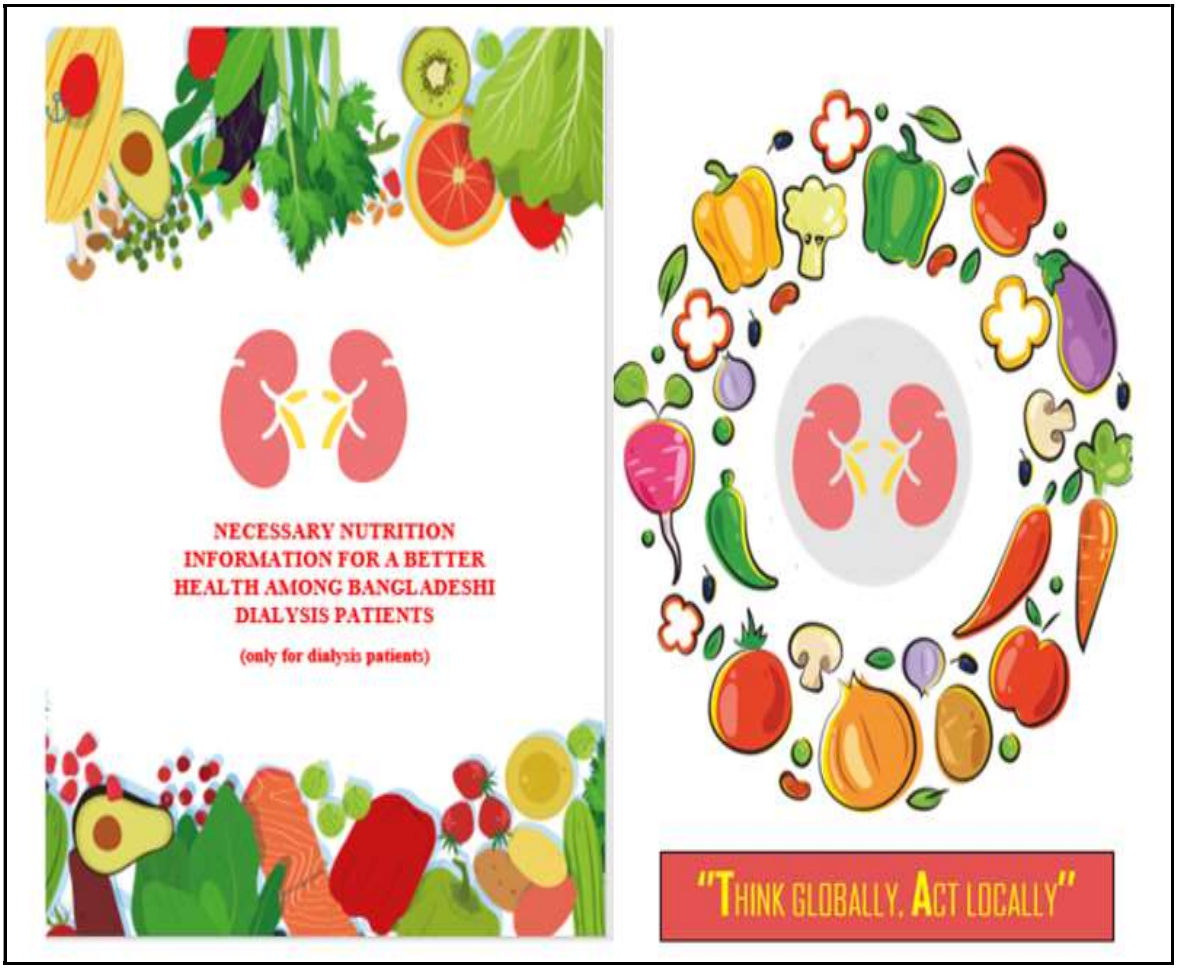
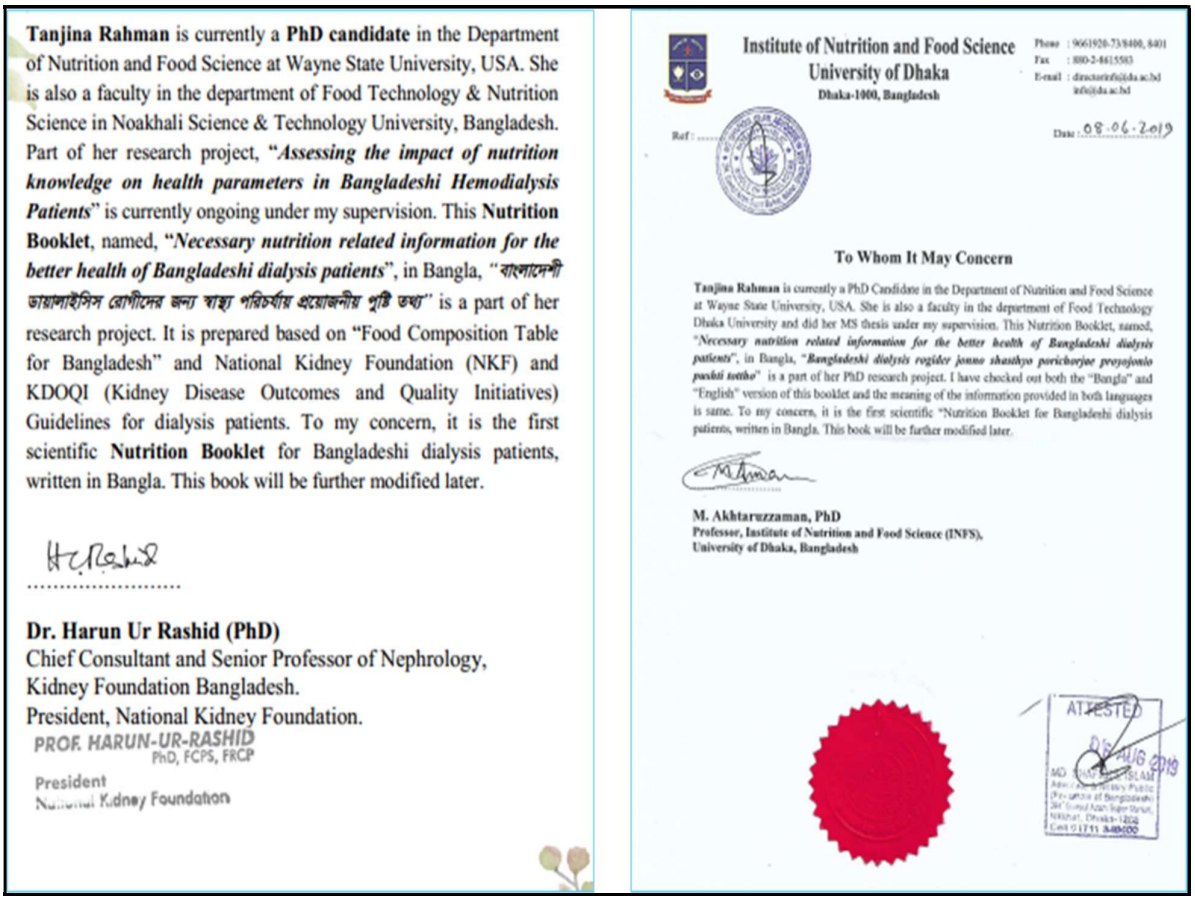


Figure 5-4. Booklet Endorsed by Kidney Foundation, Bangladesh and University of Dhaka.



Tanjina Rahman is currently a **PhD candidate** in the Department of Nutrition and Food Science at Wayne State University, USA. She is also a faculty in the department of Food Technology & Nutrition Science in Noakhali Science & Technology University, Bangladesh. Part of her research project, "***Assessing the impact of nutrition knowledge on health parameters in Bangladeshi Hemodialysis Patients***" is currently ongoing under my supervision. This **Nutrition Booklet**, named, "***Necessary nutrition related information for the better health of Bangladeshi dialysis patients***", in Bangla, "*বাংলাদেশী ডায়ালাইসিস রোগীদের জন্য স্বাস্থ্য পরিচর্যায় প্রয়োজনীয় পুষ্টি তথ্য*" is a part of her research project. It is prepared based on "Food Composition Table for Bangladesh" and National Kidney Foundation (NKF) and KDOQI (Kidney Disease Outcomes and Quality Initiatives) Guidelines for dialysis patients. To my concern, it is the first scientific **Nutrition Booklet** for Bangladeshi dialysis patients, written in Bangla. This book will be further modified later.

Dr. Harun Ur Rashid (PhD)
Chief Consultant and Senior Professor of Nephrology,
Kidney Foundation Bangladesh.
President, National Kidney Foundation.
PROF. HARUN-UR-RASHID
PhD, FCPS, FRCP
President
National Kidney Foundation

Institute of Nutrition and Food Science
University of Dhaka
Dhaka-1000, Bangladesh

Phone : 9661920-73/8400, 8401
Fax : 880-2-8615583
E-mail : directorinfs@du.ac.bd
info@du.ac.bd

Ref : .....
Date : 08-06-2019

To Whom It May Concern

Tanjina Rahman is currently a PhD Candidate in the Department of Nutrition and Food Science at Wayne State University, USA. She is also a faculty in the department of Food Technology Dhaka University and did her MS thesis under my supervision. This Nutrition Booklet, named, "*Necessary nutrition related information for the better health of Bangladeshi dialysis patients*", in Bangla, "*Bangladeshi dialysis rogider jonno shasthya porichorjae proyojonio pushti totho*" is a part of her PhD research project. I have checked out both the "Bangla" and "English" version of this booklet and the meaning of the information provided in both languages is same. To my concern, it is the first scientific "Nutrition Booklet for Bangladeshi dialysis patients, written in Bangla. This book will be further modified later.

M. Akhtaruzzaman, PhD
Professor, Institute of Nutrition and Food Science (INFS),
University of Dhaka, Bangladesh

ATTESTED
08 AUG 2019

CHAPTER 6 DISCUSSION

Specific Aim I

Methods to identify patients at risk for ESRD are a high priority in Bangladesh, where kidney transplants or dialysis options are limited and costly. Evidence from epidemiological studies showed that, anthropometric, biochemical, clinical, and dietary data together will help to get a better picture of health status among this population group. Nutrition intervention to delay the progression to ESRD is a promising and affordable strategy. However, data on nutritional status of Bangladeshi renal patients is limited and is not adequately documented. Very few studies conducted in Bangladesh among MHD patients did a nutritional screening following internationally accepted standard protocols and to the best of our knowledge, ours is a very first attempt in this context. This may also serve as a useful reference for future work in this field. Here we examine current health and nutritional status of hemodialysis (HD) patients.

In present study, we evaluated demographics, anthropometric, biochemical, dietary and laboratory parameters in a group of patients on MHD in a specialized renal hospital as a representative of Bangladeshi MHD population. Then, we did subgroup of our patients based on gender, dialysis frequency, lipid biochemistry and dialysis vintage and explored our results.

The *most notable findings* that evolve from our study is that, there is high prevalence of both mixed and atherogenic dyslipidemia (AD) among Bangladeshi patients on MHD. Dyslipidemia in CKD is related to high TG, low HDL-C and abnormal lipoprotein composition such as low cholesterol level predisposed to atherosclerosis and cardiovascular events-one of the leading causes of death among ESRD patients [152]. However, one study

conducted in India among 159 CKD patients showed that, CKD patients had a significantly lower level of HDL-C and higher level of TC, TAG, VLDL and LDL-C compared to healthy subjects of same age [153]. Another study showed that, abnormal lipid metabolism was common in MHD patients in India that may contribute to high CVD morbidity and mortality [154]. There was little information on the prevalence of dyslipidemia in Bangladeshi MHD patients. In the present study, 70% patients had mixed dyslipidemia and 14% had atherogenic dyslipidemia. European Best Practice Guidelines (EBPG) as well as K/DOQI recommended appropriate treatment of dyslipidemia for CKD patients with drugs and lifestyle modification as it triggers the risk of CVD among them [152, 155]. Data are needed to establish the prevalence of such patterns in a much larger cohort and establish criteria, if any, for patient management in Bangladesh.

Previous studies showed that, CKD patients tend to develop CVD much higher than the general population due to the development of rapid atherosclerosis [156]. Dyslipidemia is a significant risk factor for CVD and is common among CKD patients, due to lowering HDL-C and rising of TAG level and often improves after transplantation with increasing HDL-C level and lowering TAG level, shown in a study conducted on 60 patients[157]. We had also found a low HDL-C and a high TAG level in our study population. However, recent studies showed that, quality of HDL-C is more important rather than its quantity and a very high concentration of HDL-C could also triggers CVD risk [158]. A paradoxical association between high serum HDC-C concentration over time and high mortality rate in hemodialysis patients was found in one study, where it was demonstrated that both too low and too high HDL-C level could be the reason for CV mortality[159].

In our study, we did a subfraction analysis to see the actual disturbance in lipoprotein metabolism among Bangladeshi hemodialysis patients, where we found that, patients with

LDL phenotype A (considered as atheroprotective, being larger and more buoyant) [160] had increased amount of cholesterol in their large HDL particles whether those with LDL phenotype B (considered as atherogenic, small, and denser) had small amount of cholesterol in their large HDL particles [161]. One study showed that, small LDL-particle size is an early sign of uremic dyslipidemia [162]. In our study, LDL-particle size is significantly small for patients with type B LDL compared to patients with LDL phenotype A. 'Intermediate' LDL-pattern is the least described of three patterns, which carries the criteria of both A and B and often termed as [AB] and could be easily shifted to either A or B[163]. In our study, patients with phenotype [AB] also had a significantly small LDL-particle size compared to phenotype A. Thus, LDL pattern analysis could be clinically important for CKD patients and patients with LDL phenotype B need attention to reduce CVD events.

Analysis of HDL particle size may also be considered clinically important to predict CVD risk in patients in general. In HD patients, large HDL is more abundant whereas in normal persons, small HDL is more abundant, which may be responsible for high risk of atherosclerosis among this patients[164]. In one study, it was found that, presence of more small HDL particle is associated with high risk of CVD mortality [165]. However, in some study, it was found that, the small but dense protein-rich HDL-C is thought to carry antioxidant and anti-inflammatory cardioprotective benefits, compared to the large buoyant HDL with large amount of cholesterol[166]. In our study, significantly large amount of cholesterol was found in the small HDL particle for patients with LDL phenotype B. Additionally, with a decline in kidney function, there is also evidence in changing the protein composition of HDL particle as a metabolic derangement[167].

Another *important finding* that was evolved from our study is that, majority of our patients failed to meet the recommendation provided by NKF K/DOQI for energy, protein as

well as other macro and micronutrients for hemodialysis patients. In this study, we assessed a one-day 24-hour diet recall and consider the results from 61% of acceptable reporters to analyze their nutrient intakes. About 39% of our study patients were under-reporters, which is a common scenario among HD patients, especially in women and in those with a high BMI [168]. Previously, there was little documentation regarding a proper nutrient intake analysis of this specific population in Bangladesh. This is one of the very first attempts that has been made in Bangladesh. In the present study, it was observed that, most of the respondents were not aware of specific renal diet, their average calorie and protein consumption showed lower values than that is recommended by K/DOQI [149]. These values were below the recommendation provided by NKF/KDOQI for hemodialysis patients, where it was stated that, for hemodialysis patients, DEI should be 30-35 kcal/kg body weight/day and DPI should be 1.2 g/kg body weight/day [89, 149]. Studies showed that, both low protein intake and inflammation reduce the synthesis of albumin in body and further deteriorate the health status of patients[169].

Inadequate intakes of important vitamins and minerals were also found which indicates that, the patients are deprived of adequate amount of anti-oxidant and anti-inflammatory food intake, and are more prone to develop hypokalemia, anemia and electrolyte imbalance [170]. A significant number of dietary restrictions are imposed traditionally and consistently on MHD patients, whereas there is very little data to support their benefits. Recent studies indicate that dietary restrictions of phosphorus may lead to poor survival and nutritional status. Restricting dietary potassium may deprive dialysis patients of heart-healthy diets such as fruits and vegetables and thus lead to intake of more atherogenic diets [71, 171]. Zn deficiency can lead to perturbance in taste and smell that may often cause poor intake of dialysis patients [172]. In contrast, toxicities in dialysis patients may include

aluminum and possibly copper [173]. However, it is important to note that in dialysis patients, there is a high prevalence of antioxidant deficiency due to inadequate ingestion of antioxidant vitamins such as vitamins E, C, and carotenoids [97].

Resnicow et al. in their paper, "Validation of Three Food Frequency Questionnaires and 24-Hour Recalls with Serum Carotenoid Levels in a Sample of African-American Adults" mentioned about the pros and cons of three different methods [174], that are used to determine food intake pattern among a group of people. These include, 24-hour recall method and food diaries (3 to 7 days diet record) for short-term diet information, and traditional FFQ (Food frequency questionnaire) for long-term diet information. Of them, 24-hours diet recall is easy, quick and convenient, though, it possesses some demerits such as, day-to day variability in nutrient intake, the importance of obtaining multiple recalls to estimate the usual intake in a reliable way, burden of patients, and literacy of the participants for correctly estimating the portion size. Literacy of the participants is more important in case of using Food Dairies [175]. In case of using FFQ, the amount of exact daily nutrient intake is only based on assumption and is also difficult to record [176], especially for elderly patients. And it must be accustomed for cross-culture applications [177].

Dietary intake evaluation is an important tool for dialysis patients which provides an insight of their nutrient intake and helps in the assessment of both nutritional adequacy and toxicity. Estimating dietary intake is challenging in patients with chronic diseases [178]. Through a proper dietary assessment, both nutritional adequacy and toxicity of a patient could be determined [179]. When less staffs and time is available in a clinical setting, it is difficult to conduct more formal assessment of nutritional intake analysis, a 24-hour recall method might be used as a substitution in this situation for dietary interviews [177].

In the United States and Canada there are significant restrictions for eating during hemodialysis treatment in dialysis clinics. Possible reasons reported include postprandial hypotension, aspiration risk, infection control and hygiene, dialysis staff burden, diabetes and phosphorus control, and financial constraints. However, in other countries such as Germany, Japan and many other Europeans and Asians nations, meal trays are regularly prepared and served during each hemodialysis treatment session. Palmer et al. proposed approaches to help patient learn and incorporate with individualized dietary restriction, such as-improving patient's education, motivation, and identifying ways that help patient in adapting the dietary recommendation positively[180]. In Bangladesh, although, patients are allowed in taking food during dialysis, no emphasis has been put on the type and quality of food consumed. In such condition, provision of high-protein meals during hemodialysis could be a feasible, inexpensive, and patient-friendly, and an economically feasible strategy [181].

An additional finding observed in this study was that, we got an opportunity to explore our results based on dialysis frequency as more than half of our patient pool underwent 2x weekly dialysis which is not common in USA and Malaysia. Approximately 62% of patients underwent 2x weekly dialysis and remaining 38% underwent 3x weekly dialysis in our patient pool. Minor differences were present between patients undergoing 2x weekly versus 3x weekly dialysis. A study conducted on 74 patients in Taiwan showed that, if patients on 2x weekly dialysis have sufficient urinary output, they maintain better dialysis adequacy and exhibit better preservation of their residual renal function (RRF), compared to those on 3x weekly dialysis [182]. Although we found that, patients undergoing thrice weekly dialysis were more prone to both atherogenic and mixed dyslipidemia in our study, this become contrary to another study conducted in Bangladesh, where it was found that, twice weekly dialysis patients develop dyslipidemia more than thrice weekly dialysis patients[54].

Dietary analyses evaluated that, patients who underwent 3x weekly dialysis had a significantly higher intake of protein, water, and potassium, compared to those on 2x weekly dialysis which reflect the fact that, less dietary restriction was imposed on 3x weekly group. However, a cross-sectional study conducted among 142 patients in Thailand showed that, there was no significant differences in terms of dietary intake between 2x weekly vs 3x weekly patients [183].

In Bangladesh, hemodialysis prescription is empiric, which may lead to under-dialysis and other related complications. A lot of patients go on a "need to go" basis of dialysis. In some clinics, due to high volume of patients, dialysis times are cut down to accommodate more patients. In some places rather than KFHRI, there is lack of trained manpower in dialysis unit, some dialysis facilities also do not have water treatment facilities, which was also common in Pakistan dialysis facilities[184]. Another important issue is the assessment of dialysis adequacy for patients who are on dialysis either 2x or 3x weekly. In India, only 20% of patients underwent 3x weekly dialysis with a Kt/V<1 for most patients [185]. Kt/V is a number that is used to calculate dialysis adequacy, where 'K' stands for dialyzer clearance of urea, 't' stands for dialysis time and 'V' stands for volume of urea distribution that is approximately equal to a patient's total body water. In Bangladesh, same problem existed as a patient may missed the regular dialysis schedule due to shifts running late, late arrival due to transportation issue, time of dialysis each day that was not recorded properly, missing sessions etc. Increasing dialysis session from 2x weekly to 3x weekly is not always an option due to increasing number of patients and inadequate number of dialysis machines. Although the yearly expenses of HD are much lower in developing countries (such as- 30 times lower in India compared to the US), patients often do not have enough money to bear the costs, which is also not covered by health insurance or Government policy [186]. Patients'

educational and understanding level and financial condition is often critical that they cannot afford 3x weekly dialysis. Most patients live far away from dialysis centers and they had to travel a long distance by spending extra money from their already broken economic status, that makes them even missing their regular dialysis session for at least once a month, if otherwise feeling better. Overall, insufficient number of Kidney disease care hospitals result in overcrowding and long awaiting time for patients, and lack of access to dialysis treatment results in premature death of patients. Cumulative approach along with health care system reform and research as well as necessary steps from Government level could play a crucial role to improve the overall situation.

In most developed countries, frequency of hemodialysis was anchored to thrice-weekly regimens. Health policy in developed countries like the USA and UK usually covers the cost of renal replacement therapy and thus makes patients choose the best treatment option once they were diagnosed to have ESRD [187]. But this situation is not practical for developing countries where it is a matter of scarce facilities and poor socioeconomic status of majority of inhabitants. Patients were getting limited and no treatment support from the Government [16]. In developing countries, approximately three-fourths of ESRD patients undergo twice weekly dialysis [183]. In India, most patients undergo twice weekly dialysis and only 20% of patients undergo thrice weekly dialysis. Although, increasing the frequency of dialysis improves the quality of life (QoL), it is not an option here due to pressure from too many patients and inadequate numbers of dialysis machines [188]. Though, some recent data suggests that, frequent hemodialysis accelerates residual renal function decline, and infrequent regimens may provide better preservation of native kidney function. In this study- 62% of patients undergo twice a week dialysis and 38% performed thrice a week dialysis. In Lithuania, a study with 2063 HD patients demonstrated that patients on once- and twice-

weekly therapy had a two-fold higher risk in mortality compared to those on thrice weekly dialysis [189]. However, in a subgroup analysis of the HEMO study, women experienced a survival benefit with higher dialysis dose whereas men did not[190]. Thus, prescribing specific dialysis frequency using an approach instead of a "one size fits all" strategy, and assessing its effects across Bangladeshi renal populations could be an emerging field for future research.

The effects of kidney damage cause problems in all organ system [191]. Previous studies suggest that, in Bangladesh, 40% of ESRD is due to glomerulonephritis 31% due to diabetic nephropathy, and 15% due to hypertension [5]. A recent study showed that, prevalence of CKD is alarmingly high in hypertensive patents and is a hidden cause of developing glomerular diseases[192]. CGN is another common cause of ESRD around the world and is associated with high rates of inflammation[193]. Diabetic nephropathy (DN)-another leading cause of ESRD and is also a well-known complication of diabetes mellitus (DM). It may arises from uncontrolled hypertension, dyslipidemia, hyperglycemia, smoking as well as family history of DM [194]. If we look at our neighboring countries, we found that, DN, followed by CKD of unknown cause and CGN were common causes of developing ESRD in India. On the other hand, obstructive uropathy (22%), followed by reflux nephropathy (13%) and CGN (11%) were the common causes in Pakistan[184]. In this study, major causes of developing ESRD was reported to be hypertension following HTN along with either diabetic nephropathy or chronic glomerulonephritis.

Overnutrition is a major problem in the general population and a serious risk of metabolic syndrome, cardiovascular disease with an increase in death risk. However, in malnourished CKD patients, this relationship is different, especially in those who undergo maintenance dialysis treatment. This is known as "Obesity paradox" or "Reverse

epidemiology" [195-197], where, survival rates among patients improve if they have a higher BMI [198-200]. In present study, the average BMI of patients was reported to be 24.1±5.2 kg/m^2, however, 12% with less than 18.5 kg/m^2 and 13% of them were having a BMI of >30 kg/m^2. Kalantar-Zadeh et al. also demonstrated that, a U-shaped BMI between <25 kg/m^2 and ≥35 kg/m^2 is associated with poor outcomes in CKD patients[201].

Mid arm muscle circumference (MAMC) is another important measure as low muscle mass is related to poor survival, reflecting poor nutritional status, and inflammation [202]. Average MAMC in this study was reported to be 21.6±3.6 cm which is also similar to the value reported by Tashkandi et al. in HD patients from Saudi Arabia[120]. Studies in the general population showed that, muscle strength is inversely related with inflammation and oxidative stress [203]. Currently, there are no standardized tables of grip strength for HD population. And the reference HGS value in kg for a 55-year old right-handed male is 21.7[204, 205], which is not appropriate for dialysis patients. However, the mean age and HGS in Kg of the study population were 50 years and 19 Kg, which shows similar, but a lower trend compared to what was found among healthy adult population. The value is also similar to HGS among hemodialysis population of comparable age in Saudi Arabia reported by Tashkandi et al. [120]. Stenvinkel et al. showed a negative association between hand grip strength (HGS) (surrogate of muscle strength) and age of the respondents [206].

Serum transferrin could be measured by using serum TIBC (total iron binding capacity) and is considered as a marker of malnutrition in patients on MHD. One study showed that, MHD patients with a serum TIBC of >250 mg/dL had a high BMI and low serum ferritin level and thus a low risk of inflammation and death compared to patients with a low TIBC level[207]. In this study, mean TIBC was 242±64 mg/dL. [138]. Hypokalemia is defined as a potassium level of less than 3.5 mmol/L and hyperkalemia is defined as a

potassium level of more than 5.0 mmol/L (our study). Moderate to severe hyperkalemia is defined as a potassium level of more than 5.5 mmol/L[144]. Studies showed that, high serum ferritin level of more than 250 ng/ml is associated with high risk of mortality among patients with CKD[208]. 74 of our study patients had a ferritin level of 496.7±442.8 ng/ml and 18 patients had a ferritin of >2000 ng/ml. In order to measure dialysis adequacy, URR% is the most used tool along with Kt/V. However, both has its own limitation and is not applicable to all dialysis facilities. URR (%) reflected dialysis adequacy. If the URR% is more than 65 (recommended by Kidney Disease Outcome and Quality Initiative, K/DOQI) , then it is thought that, dialysis was adequate [138, 148]. In our data, URR% was approximately 65% on an average. Standard Kt/V can also be used as an important tool to modify twice weekly dialysis sessions and to provide better quality of life to the patients in India where patients live far away from dialysis centers and had to spend additional money to travel to these centers [185]. One study conducted among 25 HD patients in Turkey showed that, both URR% and single-pool Kt/V reduced if the patients were given food during dialysis[147].

ADAT form has a five-point scale, where, “1=very good’, “2=good’, “3=fair’, “4=poor’, and “5=very poor’. One study showed that, malnourished patient tends to develop poor appetite during the course of disease progression [123]. In our study, it was found ‘fair’ to ‘poor’. KD-QoL is an easy to use tool that can be use in the outcome assessment programs for dialysis patients [129]. It is also a clinically adequate and inexpensive method that gives a balanced estimation of nutritional status in dialysis patients [131]. Studies showed that, low health-related quality of life among patients with CKD is more associated with CVD events than with disease progression [209].

Specific Aim II

We found that, majority of our patient had a nutrient intake below the K/DOQI recommendation for hemodialysis patients. Additionally, poor muscle mass and muscle strength as well as abnormal biochemical parameters lead us to further analyze our data to diagnose patients having malnutrition or protein energy wasting (PEW). PEW in hemodialysis patients is prevalent worldwide, so as in Bangladesh, affecting their morbidity and mortality. Despite having numerous important consequences of PEW to CKD patients such as-a negative impact on patients' prognosis, complications, management, quality of life as well as in health economics, it is not being considered as a clinical priority in many parts of the world and is often undetected and untreated. Increased awareness of PEW in CKD begins with identifying the prevalence of PEW among CKD patients. In 2018, a review paper was published by ISRNM, where malnutrition-inflammation score (MIS) cut-off point of ≥5 was used to identify the prevalence of PEW in overall CKD population worldwide and proposed that, 28% to 54% of MHD patients have PEW globally [63] where no data was available for Bangladesh. Data on nutritional status of Bangladeshi dialysis patients (specifically those with PEW) is limited to the best of our knowledge. Therefore, an appropriate, cost-effective and reliable detection method is highly warranted in order to assess the prevalence of this comorbid condition among Bangladeshi MHD patients. In this study, we found the prevalence of PEW among MHD patients was 18% using criteria provided by ISRNM for PEW diagnosis, which is one of the very first studies conducted in Bangladesh.

A recent study in Bangladesh [25], which was conducted in Kushtia district stated that, 57% of their study population had a BMI <23 kg/m^2, which correlates with the result from this study. In the current study population, 49% had a BMI less than 23 kg/m^2.

Additionally, 57% patients showed lower MAMC compared to the values that are 10% below the 50th percentile reference population and 61% had a serum albumin of <3.8 g/dL. Similarly a recent study conducted in Indonesia among HD patients showed that, 66% of patients had a lower MAMC and serum albumin of <3.8 g/dL [106] that correlates with our observation. There are several reasons why low muscle mass is related to poor survival., such as, lower muscle mass may reflect poor nutritional status, and a level of inflammation [202]. Honda *et al*. showed a significant increase of inflammation (CRP≥10 mg/l) in HD patients with low lean-body mass determined by DEXA[210]. Again, muscle mass is the compartment in the body where uremic toxins are distributed in HD patients. Gotch *et al*. stated that, total body water and muscle mass are strongly correlated, and muscle mass is the main location of intracellular water. Therefore, patients with lower muscle mass indicates a high level of uremic toxins [211]. Thus, presence of muscle-wasting, inflammation and comorbidities contribute to an additional burden of physiological derangement in this group of patients.

Sarcopenia is a disease that is found among elderly population who have loss of muscle mass and strength [212]· Studies also showed that, in patients with chronic disease, there is hormonal changes, increment of proinflammatory factors, and accumulation of reactive oxygen species, which lead to muscle atrophy at even younger age [213]. Studies on general population showed that, muscle strength is inversely related with inflammation and oxidative stress[203], but no study was done among renal population. Though a statistically significant, moderately strong and positive correlation was found between muscle mass and hand grip strength of PEW patients in the present study, which indicates that, with the severity of malnutrition, patients experienced frailty- loss of muscle mass and strength, thus a diminished physiological function [214, 215]. No previous study found in Bangladesh have data related to muscle mass and muscle strength of HD patients.

Hypoalbuminaemia is another diagnostic criteria to determine the prevalence of malnutrition and half of dialysis patients having a serum albumin level of less than 3.8 g/dl, show a two fold increase in mortality rate [39]. Although serum albumin is reduced due to inadequate dietary protein intake, inflammation is mainly responsible for its reduction due to a decrease in synthesis and transfer to extravascular space [216]. Low serum albumin is one of the strongest forecaster of mortality in HD patients[217]. In our study, the average serum albumin levels for PEW and Non-PEW patients were 3.5±0.6 g/dL and 3.8±0.5 g/dl respectively, indicating that, majority of our patients were suffering from hypoalbuminemia. However, measurement of serum albumin is not a routine biochemical procedure in most of the renal clinic in Bangladesh and we speculate that, if it is made as a mandatory assessment along with necessary anthropometric assessment following standardized protocol in all HD clinic in Bangladesh, it could be easier to capture the true picture of the prevalence of PEW in these population.

Both low TIBC and high Ferritin values found in this study indicates the prevalence of malnutrition and inflammation with a higher death risk in this PEW cohort and also among Non-PEW cohort [207, 218]. Increased metabolic and regulatory derangements such as-acidosis, inflammation, hormonal and electrolyte imbalance take place in patients with ESRD. All these lead to the development of hyper catabolism and negative nitrogen balance and at this point, patient experience anorexia, poor appetite and other gastrointestinal disorders which decrease their food intake and increase their loss of muscle protein. Presence of other comorbidities like hypertension, diabetes and often CVD significantly increased their mortality risk and thus make their condition worst [219].

TC, TAG, LDL-C, all are lower in PEW patients-attributed to malnutrition and increased inflammation. However, inflammation is also very common in malnourished HD

patients[220] and a synergistic relationship between malnutrition, inflammation and oxidative stress is responsible for rapid development of atherosclerosis in ESRD patients [221]. Approximately, 76% of PEW patients were suffering from mixed dyslipidemia and 43% PEW patients were having dyslipidemia based on TAG/HDL-C ratio, which suggest that, both PEW and dyslipidemia were prevalence side by side in MHD patients in this specialized renal hospital.

Close monitoring of a patient's nutritional status, dietary modification and counselling based on his physiological condition could be one of the preventive strategies to preserve health in malnourished dialysis patients[222]. A prospective cohort study was conducted among 809 patients who participated in NIED study [223] (Nutritional and Inflammatory Evaluation in Dialysis) for 63 months where it was found that, the MIS is correlated with nutritional status, quality of life, inflammation and mortality prediction among chronic HD patients and improving the MIS may improve their clinical outcomes [224].

Based on, 4th diagnostic criteria for PEW by ISRNM, theoretically, an HD patient with a dietary energy intake (DEI) below 25 kcal/kg body wt./day and a dietary protein intake (DPI) below 0.8 g/kg body wt./day for at least 2 consecutive months need to be considered. In this study, a one-day 24-hour diet recall data were analyzed for 112 patients, of which 68 patients were considered as acceptable reporters (61%). Considering one occasion of dietary information (that has been done in present study), 38 patients (56%) had a dietary energy intake (DEI) below 25 kcal/kg body wt./day and 30 patients (46%) had dietary protein intake (DPI) below 0.8 g/kg body wt./day. More data are required to validate this result. However, average dietary energy intake (DEI) was 24 kcal/day and dietary protein intake (DPI) was 1.0g/day in case of PEW patients which were below the recommended intakes of 30-35 kcal/day of DEI and 1.2g/day of protein for hemodialysis patients according to National

Kidney Foundation (NKF)/Kidney Disease Outcome and Quality Initiative (KDOQI) guidelines [151, 225]. Amongst all patients (PEW and Non-PEW) protein intakes of 54±22 g/day and energy intakes of 1436±498 kcal/day were noted. Although we did not assess diet intake in normal non-dialysis patients in this study, previous data from a normal urban population in Bangladesh revealed protein intake estimates of 68-78 g/day, with energy intake estimates of 2142 to 2394 kcal/day [226]. Studies showed that, compromised dietary energy and protein intake among hemodialysis patients leads to the development of malnutrition along with duration of dialysis [227, 228].

No significant differences were observed in other components of health-related questionnaires, (which might be due to the small number of PEW patients) with the exception of MIS score and two components of KD-QoL (PCS and MCS) between PEW and non-PEW patients (Both had higher values for PEW patients). However, an MIS score of $\geq$ 5 is considered as an indicator of the prevalence of malnutrition in many studies and a higher score of KD-QoL indicates malnutrition. From this point of view, we can further predict that, the number of PEW patients identified in this study might be an underestimate.

PEW is the consequence of various mechanisms intrinsic to CKD, including undernutrition, systemic inflammation, comorbidities, hormonal imbalances, the dialysis practice, and magnitudes of uremic toxicity. It may instigate infection, cardiac events, frailty, and depression, but these impediments may also upsurge the extent of PEW [59].

Sabatino et al. in 2016, proposed the following "Nutrition approach" for HD patients having PEW[222]:

1. Early nutrition intervention should be targeted for PEW patients when their energy intake is less than 30 kcal/kg body weight/day and protein intake is less than 1g/kg

body weight/day up to 35 kcal/kg body weight/day and 1.1 g/kg body weight/day- in order to make up accelerated muscle catabolism.

2. Individualized nutrition counseling is needed at a regular basis in order to provide them with correct dietary information, assessing and reassessing their eating habits, helping them to increase their food intake with adjustment in excess phosphorous, potassium and sodium intake at the same time, and
3. Help patients to avoid unnecessary fasting during acute illness or hospitalization and due to dialysis schedule.

However, if the causes of developing PEW in CKD patients is not linked to poor dietary intake but to poor clinical condition, then the patients may not respond to the dietary therapy, that is high calorie and protein intake [70].

For now, we conclude that, based on ISRNM criteria as gold-standard, prevalence of PEW in this specialized renal hospital is 18% and the number could be more or up to 40% if all data were available at this point. If this is the scenario in an Urban renal-specialized hospital in Bangladesh, it is obvious that, many more hemodialysis patients were also suffering from PEW all over the country. In summary, our nutrition assessment protocol and PEW diagnosis criteria from ISRNM are comparatively easy, quick, inexpensive and reliable which enables malnourished or PEW hemodialysis patients to be identified and put on nutrition intervention trials. If PEW remains undiagnosed, it will make the situation of Bangladeshi MHD patients even worst. Now, it is high time to plan and implement the strategies to diagnose PEW patients undergoing hemodialysis and recommend additional care for them to improve their health status, which will ultimately impact on a better survival of Bangladeshi hemodialysis patients.

Specific Aim III

In order to understand the impact of the provision of targeted renal-specific nutrition information among a group of disadvantageous dialysis population as well as to support diet counseling among Bangladeshi dialysis patients, the culturally acceptable 'Nutrition Booklet' was developed. For educating MHD patients, a renal-friendly food pyramid and more particularly a phosphorus pyramid was prepared as an educational tool and incorporated in the 'Booklet' as because most Bangladeshi people are not aware of the existence of a renal food pyramid and to the best of our knowledge, there is no food pyramid as well as phosphorus pyramid available for renal patients in Bangladesh. Attempts had also been taken in order to improve Patients' knowledge regarding proper dialysis diet and nutrition. Thorough analysis of Bangladeshi common food list [111] was done to address the gap in knowledge between the patients and nutritionist in field level.

Studies previously done in this field showed that effective renal-specific knowledge among patients could reduce the deterioration of renal function among patients at early stages of renal disease [69], and also reduce the incidence of diet related comorbidities such as hypertension, hyperphosphatemia, hypo and hyperkalemia among chronic kidney disease patients[67, 94]. Studies also showed that, patients with chronic disease having nutrition counseling were shown to have a positive outcomes, compared to patients who did not receive any counseling by analyzing height, weight, recent laboratory data, past medical history, 24-hour diet recall both before and after nutrition counseling [68].

In some study, it was found that, interactive educational intervention could improve patients' knowledge about disease, self-management, and clinical outcomes of patients with CKD[44].

Only big city hospitals have dietitians in Bangladesh who provide nutrition and food related advise to all patients in general. There is mostly no renal dietitian to the best of our knowledge. Patients often seemed confused on what food to select among wide varieties of local foods and ends up selecting the wrong one or none. Thus, their food intake became inappropriate, that lead them to the vicious cycle of malnutrition and further complicate their health. For this study, the renal-specific nutrition booklet was only developed for Bangladeshi MHD patients and made feasible to use in practice as an educational tool to improve their selection of food items as well as adherence towards renal-specific diet practice. Future research is needed to observe the impact of this booklet in a large group of Bangladeshi hemodialysis patients.

Limitation of the study

This study has several limitations, which are highlighted to facilitate future studies by other groups. Firstly, data were collected from one hospital in Dhaka, and likely may not be representative of the country. Secondly, only a 24hr diet recall was captured, limitations of which have been discussed by others. Third, home-cooking involved numerous recipes, all of which may not have been captured by the patients. Fourth, while Bangladesh Food composition tables were used, these are not exhaustive, and no software captures this information. Fifth, diet data were not collected for dialysis day and may not reflect the usual intake of patients. Sixth, logistic support for such studies are hampered by lack of trained support staff, renal dietitians, and a general lack of nutritional knowledge of patients and hospital staff. Seventh, causality could not be determined due to cross-sectional nature of the study.

Our study though has several strengths. First, we were able to capture anthropometric, dietary, and biochemical parameters from the same set of patients, which is one of the first from Bangladeshi ESRD patients to the best of our knowledge. Second, a coordinated training effort across Malaysia, Bangladesh and US ensured uniform protocols for diet and anthropometric assessment. The latter were modeled on the protocols of ISAK. Third, the presence of overseas personnel to supervise and train local staff in data collection helped facilitate logistic support. Fourth, the fact that, the hospital had patients whose typical care included twice or thrice weekly dialysis, allowed us to detect some initial data on individuals receiving twice/thrice weekly dialysis. Fifth, our lipid analyses extended beyond serum measures of TC, TG and LDL to capture data on lipoprotein particle size and distribution.

CHAPTER 7 ADDITIONAL TASK AS A PILOT SKIM TO EDUCATE AND TRAIN RENAL NUTRITION SUPPORT PERSONNEL IN A RESOURCE-POOR FACILITY

Individuals with expertise in renal nutrition and associated aptitude in nutrition assessment are scarce in resource-poor countries. In order to disseminate detailed renal-specific nutrition education to each dialysis patients and their family members, and later, throughout Bangladesh, involvement of properly trained and skilled manpower with a background of renal nutrition-related research turns out to be an important part of the study. Taking necessary permission from the appropriate authorities, students in nutrition background from one of the reputed government STEM universities in Bangladesh were involved at this point. A renowned specialized Bangladeshi renal hospital and the department of Nutrition and Food Science, Wayne State University, USA were also involved and actively cooperate to resolve this issue. Attempts were made to generate trained manpower in order to facilitate research work in renal nutrition field in a resource-poor country, like Bangladesh. The purpose was to educate and train a group of graduate students (in nutrition) with basic skills to assist renal staff in nutrition and anthropometric assessments in a hospital providing dialysis services in Dhaka, Bangladesh, who could be utilized to help out improving the health and nutritional status of Bangladeshi dialysis patients in near future. A total of 50 graduate students (in Nutrition) from a research University, “Noakhali Science and Technology University” participated in a pilot training program from November 2018 till March 2019 that involves 3 phases.

First stage involved online lectures via Skype from the USA on selected topics. Lectures totaled 6-8 hours of contact time and allowed for interactive exchanges. There is an 11 hours of differnce in local time schedule between USA and Bangladesh, for which in USA, the training schedule was from 6.30 AM till 10 A.M and in Bangladesh, it was from 5.30 PM till 9.0 PM from November, 27 through November, 29, 2018. A couple of lecture

materials were also provided to the participants regarding an overview of the basic information on kidney disease, complication related to CKD and its possible management, anthropometric and dietary assessment, malnutrition among CKD patients, use of different health related questionnaire to detrmine health outcomes, lipid metabolism in CKD or ESRD patients as well as the precess of doing nutrition related reseach among dialysis patients.

In the second phase, half of the participants were divided into five groups and each group rotated in KFHRI in Dhaka providing renal services to make them understanding of how to work in a clinical setting for a 7-10 days period from January to February, 2019. KFHRI is a perfect clinical settingfor Bangladesh perspective. It is a specilized renal hospital with both laboratory and dialysis facilities at the same place as well as facilities for renal transplant. Admitted patients were provided cooked food over there as because it has its oen kitchen and canteen facilities. At the same time, this hospital is also served as a research and training institute on chronic kidney disease and has collaboration with renowned hospitals and universities throughout the world. In one word, students got an opportunity to see the whole picture related to renal disease treatment and research in one single place. Students were provided real-life exposures to patients, medical staff and dietitians as well as the opportunity to work and view nutritional services in the cafeteria. They observed different units of the whole hospital, took pictures of different packed foods, sold in the canteen, measured and document the weight od both raw and cooked food ingredients from the kitchen in a scientific way, performed self-reported 24-hour diet recall practice, learnt how to collect anthropometric data and attended “ward round” with the doctors for two days of their foundation training period and observed how dialysis patients were being treated based on their different signs and symptoms, both biochemical and clinical. They also observed how to use a formal case report form for research purpose.

In the third stage, seven students who had completed both online and on-site rotation, and upon recommendations from the hospital director, were selected to receive additional training. Then they were given additional *2-days of hand-on training* by the **Experts** in this field on March, 2019.

Through the whole process, students learnt research ethics, techniques of interviewing patients and completion of food diaries. They collected photographs and videos of cooking procedure as well as foods prepared and served in the cafeteria to create recipes, standardized serving sizes and prepared nutrition information for hospital staff. Students were trained in anthropometric assessments from ISAK certified personnel, nutritional assessment by Dietitians with accreditations from Australia, Malaysia and USA. Students were also trained to analyze data using "NutriPro" software. which was done for the 1st time in Bangladesh to analyze dietary data to the best of our knowledge. Based on successful performance, 7 students were "certified" and co-opted to assist in an ongoing clinical research study where they subsequently assisted the lead researchers with data collection. From an initial pool of 50 students-7 (14%) were successfully trained to assist researchers in an ongoing clinical trial.

This pilot training program also helped increase awareness of renal nutrition amongst students, hospital staff and patients. While mechanisms are developed between Universities and renal facilities to expand this program in Dhaka and formalize certification process, this simple model may be a cost-effective way to increase pool of trained "technicians" in renal research in resource-poor settings. It has successfully developed qualified health research supporting personnel in renal nutrition research field and the perceived impact of this pilot program had created a positive impact among experts in renal nutrition as well as corresponding hospital authorities. Further training programs should be initiated in order to

increase the number of qualified research personnel in renal nutrition field, especially in low income developing countries like Bangladesh in order to conduct quality research in future in this field.

There are gaps in research, care, and policy that severely compromised our ability to improve the outcomes of patients with CKD worldwide. The goal of ISN (International Society of Nephrology) for the community is-at least 30% of all people with CKD should be involved in relevant clinical trials by 2030 which might greatly improve secondary prevention and treatment of CKD [229]. There are high demand in capacity building training programs in the field of dissemination and implementation research, which had been found based on a NIH (National Institute of Health) workshop in 2013[230]. The development of renal registries in resource-poor countries could be an important step forward in documenting current disease burden and changes. Therefore, it is high time to close gaps and reduce the burden of CKD worldwide. If such pilot training could be arranged in future, research personnel who got certificates from such program (International Accreditation) could be further utilize for successful initiation and completion of multinational clinical trial focusing on CKD prevention strategies.

CHAPTER 8 CONCLUSION AND RECOMMENDATION

To summarize, in the first study (specific aim **I**), the purpose was to examine current health and nutritional status of hemodialysis (HD) patients in a specialized renal hospital in Dhaka, Bangladesh. Methods to identify patients at risk for ESRD are a high priority in Bangladesh, where kidney transplants/dialysis options are limited and costly. Nutrition intervention to delay progression to ESRD is a promising and affordable strategy. However, data on nutritional status of Bangladeshi dialysis patients is limited and is not adequately documented. We assessed 133 patients (49% male) at the Kidney Foundation Hospital and Research Institute (in 2017 and 2018) based on different anthropometric, biochemical, and clinical parameters. Lipid profiles and subfractions were analyzed and patients with DL were characterized using ATP (Adult Treatment Panel) III guideline. Malnourished patients were identified using criteria from the International Society of Renal Nutrition and Metabolism (ISRNM). Results revealed patient characteristics: Age 50±13 years, dialysis vintage 30± 24 months, 62% twice weekly dialysis, with causes of ESRD- hypertension (HTN) 42%, HTN and diabetes 28%, HTN and chronic glomerulonephritis 19%. Anthropometric and biochemical evaluations revealed; BMI 24.1± 5.2 kg/m^2, mid-arm muscle circumference 21.6± 3.6 cm, serum albumin 3.7± 0.6 g/dL. Laboratory analyses revealed: low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) of 84.2±30.8 and 34.5±11.2 mg/dL, respectively, with 59% of the patients having LDL phenotype A, 28% -LDL phenotype B. Type B patients had significantly higher total cholesterol, triglycerides (TG), and LDL-C and significantly lower HDL-C as compared to those with pattern A. Type B patients also had significantly less cholesterol in large and intermediate sized HDL particles and more cholesterol in small sized HDL particles. Based

on TG to HDL-C ratio>3.8, ~64% patients were DL, while based on ATP III guideline, ~70% patients had mixed DL and ~14% patients had atherogenic DL.

In the second study, PEW was assessed by the presence of 3 out of 4 standard criteria (as per the ISRNM) and was found prevalent in 21 patients (18%). Another 23% of patients were considered at risk for PEW (presence of 2 criteria). The figures may be underestimates as only one clinic was evaluated. Although these are some of the first measurements reported from Dhaka, additional data from a cross section of dialysis patients in Bangladesh are needed, prior to formulating strategies for nutrition and life-style interventions.

In the third pilot study for specific aim **III**, attempts were taken to develop an educational tool for improving renal-specific nutrition knowledge among Bangladeshi dialysis patients in the form of a "Nutrition booklet". Provision of renal-specific nutrition knowledge may help renal patients make more informed food choices. This may be especially important in resource-poor settings where nutritional support is a low-priority amongst health-care providers. The booklet was certified by Kidney Foundation Hospital and Research Institute, Dhaka (for its clinical content) and the INFS for its nutrition information, and was developed only for Bangladeshi dialysis patients and made feasible to use in practice as an educational tool to improve their selection of food items as well as adherence towards renal-specific diet practice.

As an additional task as a pilot scheme, attempts were made to educate and train a group of graduate students (in nutrition) with basic skills to assist renal staff in nutrition and anthropometric assessments in a hospital providing dialysis services in Dhaka, Bangladesh. Individuals with expertise in renal nutrition and associated aptitude in nutrition assessment are scarce in resource-poor countries. Students learnt research ethics, techniques of interviewing patients and completion of food diaries. They collected photographs and videos

of cooking procedure as well as foods prepared and served in the cafeteria to create recipes, standardized serving sizes and prepared nutrition information for hospital staff. Students were trained in anthropometric assessments from personnel certified by the International Society for Anthropometrics and Kinantiometry, nutritional assessment by Dietitians with accreditations from Malaysia and USA. Students were trained to analyze data using "NutriPro" software. From an initial pool of 50 students-7 (14%) were successfully trained to assist researchers in an ongoing clinical trial. This pilot training program also helped increase awareness of renal nutrition amongst students, hospital staff and patients. While mechanisms are developed between Universities and renal facilities to expand this program in Dhaka and formalize certification process, this simple model may be a cost-effective way to increase pool of trained "technicians" in renal research in resource-poor settings in near future.

Due to epidemiological transition, existing disease pattern changed from communicable and infectious diseases to non-communicable and chronic diseases in Bangladesh and CKD contributes to the later a lot. There is a rising trend in the incidence and prevalence of kidney diseases in Bangladesh. Besides the well-known risk factors like hypertension, diabetes, obesity, glomerular diseases, genetic and other unknown emerging risk factors might play a role in the initiation and progression of this disease. Though numerous researches are ongoing worldwide based on CKD, Bangladesh is still far behind. In context of Bangladesh, lots of information is still missing. Despite some efforts, reliable and consistent data concerning various aspects of CKD is unknown.

Besides these, large-scale, countrywide survey and epidemiological and clinical research should be conducted to determine different aspects of CKD in Bangladesh so that we can combat the widespread of CKD more efficiently in future. CKD prevention should be integrated with primary health care and kidney health promotion should be part of health

education program that is currently taken into consideration in developed countries [231]. Mass media can play role to build up awareness about CKD. Approaches like screening for hypertension, diabetes, malnutrition or protein-energy wasting and dyslipidemia should be made feasible to general people. Formulation of appropriate policy and emphasis on preventive strategies could help to combat CKD in our country.

Additionally, a 3 Day Diet Record should be collected from different renal hospitals (both public and private) and analyzed to grasp a better picture of CKD Diet intake pattern in Bangladesh. Promotion of healthy lifestyles such as-moderation in salt use, cessation of smoking/tobacco use, limit intakes of high sugar or fatty food, processed and fast foods should be taken place in every parts of the country. Food labelling should be introduced to help consumers choose what they should buy. Food adulteration should be monitored more strictly. Moreover, collaborative research with international organization should be undertaken to explore still unidentified risk factors unique to develop CKD. Formation of a Bangladeshi FFQ (Food frequency questionnaire), specific for renal patients would also be considered as a noble approach in future.

APPENDIX A. SUPPLIMENTARY TABLES

Table S1. Demographic and clinical parameters (Male vs Female)

	Male	Female
Age in years (n)	50±14 (65)	50±12 (68)
Young adult (18-35), n (%)	12 (18%)	10 (15%)
Middle-aged adult (36-55), n (%)	30 (46%)	30 (44%)
Older adult (>55), n (%)	23 (35%)	28 (41%)
Dialysis duration (hr) (n)	3.8±0.4 (76)	3.8±0.3 (43)
Dialysis vintage (mon) (n)	25.5±23.5a (77)	37.5±24.4a (46)
Dialysis frequency, n (%)		
Thrice a week	25 (40%)	23 (34%)
Twice a week	36 (58%)	45 (66%)
Once a week	1 (2%)	0
Causes of ESRD, n (%)		
HTN	26 (40%)	26 (38%)
HTN and DN	14 (22%)	23 (34%)
HTN and CGN	12 (18%)	12 (18%)
Others	4 (6%)	6 (9%)
Missing data	9 (14%)	1 (1%)

Data were collected from the number of patients indicated in parentheses. Values are *Mean* ±*SD* and n or %. HTN: Hypertension, DN: Diabetic nephropathy, CGN: Chronic glomerulonephritis, Other: 2 APKD, 5 Unknown, 1 postpartum complication; 1 genetic, 1 DN and CGN. ESRD: End-stage renal disease. Mean values sharing a common superscript were significantly different from each other using a one-way ANOVA test ($p<0.05$).

Table S2. Anthropometric and biochemical parameters (Male vs Female)

	Male	Female	Reference value
Height (cm)	166±7 [a] (56)	152±6 [a] (63)	
Dry weight (Kg)	62.4±10.5 (58)	58.5±13.9 (63)	
BMI (kg/m^2)	22.7±3.3 [a] (56)	25.4±6.2 [a] (63)	
Underweight, <18.5, n (%)	6 (11%)	8 (13%)	
Healthy-weight, 18.6-24.9, n (%)	37 (66%)	25 (40%)	
Overweight, 25-30, n (%)	12 (21%)	16 (25%)	
Obese, >30, n (%)	1 (2%)	14 (22%)	
HGS (Kg)	23.6±7.6 [a] (65)	15.3±4.6 [a] (68)	
MAC (cm)	25.3±4.1 [a] (65)	27.7±5.9 [a] (66)	
TSF (mm)	11.5±5.8 [a] (65)	19.7±8.7 [a] (66)	
MAMC (cm)	21.7±3.0 (65)	21.6±4.0 (66)	
TIBC (mg/dL)	252.8±67.1 (40)	233.4±60.5 (49)	300-400 [139]
URR %	61±8 [a] (41)	68±8 [a] (50)	> 65 [140]
Na (mEq/L)	137±3.4 [a] (56)	134.8±4.3 [a] (60)	135-146 [141]
K (mEq/L)	5±0.6 (56)	4.9±0.8 (65)	3.5-5.3 [142-144]
P (mg/dl)	4.3±2.2 (49)	4.5±2.3 (59)	
Albumin (g/dL)	3.8±0.6 [a] (48)	3.6±0.5 [a] (57)	3.8-5.0 [145]
Ferritin (ng/ml)	550.9±441.6 (33)	453.1±444.3	5-275 [146]
Ferritin >2000ng/mL (n)	8	10	
Kt/V	1.1±0.2 [a] (28)	1.5±0.5 [a] (29)	1.2-1.3 [147, 148]

Data were obtained from patient medical records. Values are *Mean* ± *SD*. Mean values sharing a common superscript were significantly different from each other using a one-way ANOVA($p<0.05$). HGS: Hand grip strength, MAMC: Mid-arm muscle circumference. TSF: Triceps skinfold, BMI: Body mass index. URR%: Urea reduction rate. Na: Sodium, K: Potassium, P: Phosphorous.

Table S3. Lipid profile and Lipid subfractions (Male vs Female)

	Male (56)	Female (60)
TC (mg/dl)	139±32 [a]	169±41 [a]
HDL-C (mg/dl)	33±11	36±11
TG (mg/dl)	158±86 [a]	197±100 [a]
LDL-C (mg/dl)	75±25 [a]	93±33 [a]
TC/HDL-C	4.7±1.7	5.0±1.8
LDL-C/HDL-C	2.3±1.1	2.9±1.4
Non-HDL-C	106±32 [a]	133±41 [a]
Non-HDL-C/HDL-C	3.7±1.7	4.0±1.8
TG/HDL-C	5.9±4.7	6.2±3.7
VLDL (mg/dl)	32±11 [a]	40±13 [a]
IDL (mg/dl)	23±6 [a]	28±8 [a]
Large LDL (mg/dl)	17.3±8.2 [a]	21.2±7.7 [a]
Inter. LDL (mg/dl)	9.8±5.7 [a]	12.6±8.0 [a]
Small LDL (mg/dl)	4.5±5.9	6.7±10.1
Mean LDL size (Å)	267±9	268±7
Large HDL (mg/dl)	11.1±7.6	13.7±8.4
Inter. HDL (mg/dl)	16.8±4.7	17.9±4.6
Small HDL (mg/dl)	4.8±2.3	4.4±2.4
Dyslipidemia (DL)		
TAG/HDL-C<3.8	24 (43%)	18 (30%)
TAG/HDL-C>3.8	32 (57%)	42 (70%)
LDL-Pattern		
Type A	34 (61%)	34 (57%)
Type B	16 (29%)	17 (28%)
Intermediate	6 (11%)	9 (15%)

Data were analyzed for the number of patients indicated in parentheses. Values are *Mean* ± *SD*. TC: Total Cholesterol, HDL-C: High density lipoprotein, TAG: Triglycerides, LDL-C: Low density lipoprotein. Type A: athero-protective profile, Type B: atherogenic profile, Intermediate: has characteristics of both A and B. Mean values sharing a common superscript were significantly different from each other using a one-way ANOVA test ($p<0.05$).

Table S4. Dietary analysis for Acceptable Reporters (Male vs Female)

Parameters	Male (39)	Female (29)	KDOQI Guidelines
Calories (Kcal)	1594±577 [a]	1218.6±204 [a]	Based on BW
DEI/kg BW/day	25.2±7.6 [a]	21.7±4.2 [a]	30-35 Kcal/kg BW/day
Protein (g)	60±24.7 [a]	46.2±13.1 [a]	Based on BW
DPI/kg BW/day	0.9±0.3 [a]	0.8±0.2 [a]	1.2 g/ kg BW/day
P mg/kg body wt. /day	15.3±6.4 [a]	13±3 [a]	10-17 mg/kg BW/day
Phosphorous: Protein	16.4±4	16.1±3.6	<12 mg/g of protein
Carbohydrates (g)	233±79 [a]	175±33 [a]	Based on BW
Total Fiber (g)	19.2±7.7 [a]	13.4±2.8 [a]	20-25 g/day
Fat (g)	47.5±24.2 [a]	36.7±10.6 [a]	
SFA (g)	9±4.7	7.5±3.7	
MUFA (g)	9.2±4.5	7.3±4.2	
PUFA (g)	18±11 [a]	12.6±5.2 [a]	
Cholesterol (mg)	232±157.2	213.2±143.3	<200 mg/day
omega 6: omega 3	11.5±6.1	9.8±4.8	4:01
Water (ml)	1506.5±643.5	1298±632	750-1500 ml/day
Vitamin A-IU	1290.7±1605.7 [a]	647.3±607.7 [a]	700-900 IU
Vitamin D-IU	47±37.8	47±42.5	600 IU
Vitamin E-a-Toco (mg)	2.4±1.2	2±1.9	15 mg
Vitamin K (µg)	23.3±38	14±20.1	90-120 µg
Vit B1 (mg)	0.9±0.3 [a]	0.6±0.2 [a]	1.1-1.2 mg
Vit B2 (mg)	1.3±2.2	0.8±0.3	1.1-1.3 mg
Vit B3 (mg)	15.6±6 [a]	11.2±2.7 [a]	14-16 mg
Vit B6 (mg)	8.9±24.4	15.6±35.7	13-17 mg
Vit B12 (µg)	1.7±1.2	1.6±2.1	2.4 µg
Biotin (µg)	12±11.6	7.3±5.4	30 µg
Folate (µg)	175±234.2 [a]	80.5±40 [a]	1000 µg
Vit C (mg)	104±79.8 [a]	67±55 [a]	75-90 mg/day
Dietary Calcium (mg)	414.4±236.2	463.2±290.5	<1000 mg
Iron (mg)	15.4±11.9	15.6±17.6	Individualized
Dietary Phosphorous (mg)	978±519.6 [a]	718.3±140.7 [a]	1000 mg
Potassium (mg)	1556.7±678 [a]	1216±262 [a]	Individualized
Dietary Sodium (mg)	2168±1094	1876±606	<2400 mg/day
Zinc (mg)	9±5.1 [a]	6.7±3 [a]	15 mg
Magnesium (mg)	251±108 [a]	195±43 [a]	200-300 mg/day

The data is reported for all acceptable reporters. Values are as *Mean* ± *SD*. DEI: Dietary energy intake, DPI: Dietary protein intake. SFA: Saturated fat, MUFA: Monounsaturated fat, PUFA: Poly unsaturated fat. IU: International Unit, vit: vitamin, Toco-: tocopherol. BW: Body weight. Mean values sharing a common superscript were significantly different from each other using a one-way ANOVA ($p<0.05$).

Table S5. Health and Nutrition Questionnaires (Male vs Female)

	Male	Female
MIS Score	5.8±2.9 (40)	6.2±3.0 (48)
ADAT Score	3.4±1.4 (28)	4.0±1.7 (29)
RLS Score	15.0±8.3 (24)	18.5±8.3 (39)
KD-QoL		
SF-12 Physical Health Composite	42.9±10.2 (39)[a]	33.4±10.1 (47)[a]
SF-12 Mental Health Composite	47.3±9.6 (39)[a]	42.5±9.7 (47)[a]
Burden of Kidney Disease	32.5±25.6 (40)	27.9±27.2 (49)
Burden of Kidney Disease	67.8±18.6 (34)	61.6±16.3 (45)

Data were collected from the number of patients indicated in parentheses. Values are *Mean* ±*SD* (n). Mean values sharing a common superscript are statistically significant using a one-way ANOVA ($p<0.05$).
MIS [46]: Malnutrition inflammation score. A score >5 indicates malnourished The MIS has 10 components, each with four levels of severity, from 0 (normal) to 3 (very severe). The sum of all 10 MIS components ranges from 0 (normal) to 30 (severely malnourished); higher score reflects a more severe degree of malnutrition and inflammation. ADAT [124]: Appetite and diet analysis tool. Scale: 1 = very good, 2 = good, 3 = fair, 4 = poor and 5 = very poor. RLS [126]: Restless leg syndrome. medical doctor. Scale: 0, None; 1 – 10, Mild RLS; 11-20, Moderate RLS, 21-30 Severe RLS, 31-40 Very Severe RLS. Patients reporting score '0' were excluded from analysis. KD- QoL[130] Subscale scores range from 0 to 100, with lower scores indicating poor self-reported QOL.

Table S6. Demographic and anthropometric parameters (≤ 2 years vs >2 years dialysis)

	≤ 2 years (65)	**>2 years (59)**
Age in years (n)	51.8±12.5 [a] (65)	47.3±12.6 [a] (59)
Dialysis duration (hrs) (n)	3.7±0.4 (63)	3.8±0.3 (56)
Height (cm)	158.4±8.8 (62)	158.6±10.1 (56)
Dry weight (Kg)	60±12.4 (62)	60.9±12.8 (56)
BMI (kg/m^2)	24±5.2 (62)	24.3±5.3 (56)
HGS (Kg)	18±6.9 [a] (65)	21±7.9 [a] (59)
MAC (cm)	26.1±5.3 (64)	27.4±5.2 (58)
TSF (mm)	16.8±8.6 (64)	15.3±8.5 (58)
MAMC (cm)	20.8±3.6 [a] (64)	22.6±3.5 [a] (58)

Data were collected from 124 patients (65 patients with dialysis vintage of less than or equal to 2 years and 59 patients with more than 2 years). Values are *Mean* ± *SD* (n). Mean values sharing a common superscript were significantly different from each other using a one-way ANOVA($p<0.05$). HGS: Hand grip strength, MAMC: Mid-arm muscle circumference. TSF: Triceps skinfold, BMI: Body mass index.

Table S7. Biochemical parameters (≤ 2 years vs >2 years dialysis)

	≤ 2 years (65)	>2 years (59)	Reference value
TIBC (mg/dL)	219.7±50.8 [a] (36)	257.4±67.7 [a] (53)	300-400 [139]
URR %	64.2±11.4 (38)	64.8±9.6 (54)	>65 [140]
Na (mEq/L)	136±3.6 (60)	135.5±4.4 (56)	135-146 [141]
K (mEq/L)	5.1±0.7 (64)	4.9±0.8 (57)	3.5-5.3 [142-144]
P (mg/dl)	4.1±2.4 (51)	4.7±2 (57)	
Albumin (g/dl)	3.6±0.7 (49)	3.7±0.4 (56)	3.8-5.0 [145]
Ferritin (ng/ml)	503.7±383.7 (29)	492.2±481.1 (45)	5-275 [146]
Kt/V	1.2±0.3 (18)	1.4±0.4 (39)	1.2-1.3 [147, 148]

Data were obtained from patient medical records. Values are *Mean* ± *SD*. Mean values sharing a common superscript were significantly different from each other using a one-way ANOVA($p<0.05$). TIBC: Total Iron binding capacity. URR%: Urea reduction ratio. Na: Sodium, K: Potassium, P: Phosphorous.

Table S8. Lipid profile and subfraction (≤ 2 years vs >2 years dialysis)

	≤ 2 years (61)	>2 years (53)
TC (mg/dl)	158.5±42	152±35.9
HDL-C (mg/dl)	36.7±12.2 [a]	32.6±8.9 [a]
TG (mg/dl)	180±105.8	175.3±83.9
LDL-C (mg/dl)	85.8±31	84.3±29.8
TC/HDL-C (*4.0)	4.7±1.9	4.9±1.6
LDL-C/HDL-C	2.6±1.2	2.8±1.2
Non-HDL-C (mg/dl)	121.8±42.8	119.4±35.3
Non-HDL-C/HDL-C	3.7±1.9	3.9±1.6
TG/HDL-C	5.9±4.4	5.9±3.3
VLDL (mg/dl)	38.9±13.7 [a]	33.4±10.6 [a]
IDL (mg/dl)	53±15.7	52.3±14.1
Large LDL (mg/dl)	18.4±7.1	20.8±9
Intermediate LDL (mg/dl)	10.7±6.7	12.2±7.5
Small LDL (mg/dl)	5.8±8.6	5.4±8.1
Mean LDL size (Å)	267.9±6.8	267.9±6.6
Large HDL (mg/dl)	13.7±9.1	11.1±6.7
Intermediate HDL (mg/dl)	18.5±4.5 [a]	16.6±4 [a]
Small HDL (mg/dl)	4.4±2.3	5±2.3

Data were collected from the number of patients indicated in parentheses. Values are *Mean ±SD*. TC: Total Cholesterol, HDL-C: High density lipoprotein, TAG: Triglycerides, LDL-C: Low density lipoprotein. Mean values sharing a common superscript were significantly different from each other using a one-way ANOVA test ($p<0.05$).

APPENDIX-B INFORMED CONSENT FORM

KIDNEY FOUNDATION HOSPITAL AND RESEARCH INSTITUTE

WAYNE STATE UNIVERSITY, USA

Name of the respondent: ---------- Date: ----/----/ -----

I am **Tanjina Rahman,** a PhD student of Nutrition and Food Science, Wayne State University, USA. As a course requirement I am doing research on "**Nutrition and Health Status of Hemodialysis Patients in Dhaka, Bangladesh".**

I hereby would expect necessary information from you to complete the questionnaires. I would also like to assure that this data will be used only for the study purpose. If you feel any inconvenience you can stop the interview at any time. Your participation will not directly benefit you and will be volunteered. I would also like to mention that an additional 20ml blood will be taken from your routine blood draw for this research purpose if you participate in this study.

I would appreciate your cooperation. If you agree to join the study, please sign at the space indicate below.

All information will be kept confidential.

Investigators signature & Date **Volunteer signature & Date**

Witness signature / Thumb impression & Date

APPENDIX-C CASE REPORT FORM (CRF)

Effects of Supplementing Palm Tocotrionls in Chronic Hemodialysis (PATCH)

IRB#123314MP4F

BASELINE CRF Checklist

	Date Completed	Initials
Personal Details & Medical History	_____	_____
Hemodialysis Regimen	_____	_____
Anthropometry, Body Comp & Muscle Strength	_____	_____
Biochemical Data	_____	_____
24 Hour Recall	_____	_____
Appetite and Diet Assessment Tool (ADAT)	_____	_____
Restless Legs Syndrome Rating Scale	_____	_____
KDQOL	_____	_____

Subject Number:

Center Information

Kidney Foundation Hospital and Research Institute.

CONTENT

Effects of Supplementing Palm Tocotrionls in Chronic Hemodialysis (PATCH)

Investigators:

1. **Dr Harun Ur Rashid (PI)**
2. **Dr. Tasnuva Kashem**
3. **Dr. Nura Afza Salma Nupur**

All information contained therein is strictly confidential and cannot be shared without the joint approval of the investigators.

INCLUSION CRITERIA

1. Patient is willing and able to give informed consent for participation in the trial
2. Male or Female, aged 18 years and above. Undergoing chronic hemodialysis treatment for more than 3 months (life expectancy > 1 year).
3. Able and willing to comply with all trial requirements.
4. Willing to allow his or her /Physician/Nephrologist/General Practitioner and consultant, if appropriate, to be notified of participation in the trial.

If the answer to any of the questions above is no, the participant is not eligible.

EXCLUSION CRITERIA

1. Participants who have participated in another research trial involving an investigational product in the past 12 weeks
2. History of functional kidney transplant 6 months before study entry; anticipated live donor kidney transplant over the study duration;
3. Participants who are taking vitamin E- containing supplements >60 IU/d during the past 30 days
4. History of poor adherence to hemodialysis or medical regimen
5. Participants who are currently on active treatment for cancer, excluding basal cell carcinoma of the skin
6. Participants who have been diagnosed as HIV/AIDS and/or on the anti-HIV therapy. (HIV seropositivity is not an exclusion criterion)
7. Patients taking anti-inflammatory medication, except aspirin<325 mg/d, over the past 30 days
8. Female participant who is pregnant, lactating or planning pregnancy during the course of the trial
9. Participants who are receiving nutritional support (i.e. enteral and intra-venous route)
10. Patients using a temporary catheter for dialysis access at baseline or patients receiving a graft/fistula within the 6-month study period
11. More than two hospitalizations within the last 90 days or one hospitalization within the 30 days preceding enrollment
12. Any other significant disease or disorder which, in the opinion of their nephrologist, may either put the participants at risk because of participation in the trial, or may influence the result of the trial, or the participant's ability to participate in the trial.

If the answer to any of the questions above is yes, the participant is not eligible.

PERSONAL DETAILS

Dialysis Shift:

Time of Dialysis Shift: _____am/pm; Duration: _____ hrs.

Gender: M/F Age: _____ years old.

Date of Birth (dd/mm/yy): _____

Ethnicity: Caucasian African American Hispanic/Latino

Asian Other: _____

MEDICAL HISTORY

What is the cause of kidney failure?

Unknown Nephronophthisis

Diabetes Mellitus APKD (Adult Polycystic Kidney Disease)

Hypertension Gout Nephropathy

HIV-Nephropathy Toxic Nephropathy

Kidney Stone SLE (Systemic Lupus Erythematosus)

Glomerulonephritis Other: _____

Start Date of HD: (mm/yy) _____

Kidney Transplantation? Yes No

Parathyroid Gland removed? Yes No

Current Diagnoses: Diabetes? Yes No

Tobacco Use? Yes No

Hepatitis C? Yes No

HEMODIALYSIS PRESCRIPTION

Is the dialyzer reused? Yes, How often? _____Times No

Type of dialyzer membrane: Polysulfone Cellulose triacetate Other: _____

Types of vascular graft being used: Arterio venous fistula

Arteriovenous graft (AVG) Venous Catheter

Type of dialysate buffer: Acetate

Low calcium

Normal Calcium High Calcium Bicarbonate

APPETITE AND DIET ASSESSMENT TOOL (ADAT)

1. During the past wee (7 days), how would you rate your appetite?

1= Very Good

2=Good

3=Fair

4=Poor

5=Very Poor

2. Have you had a change of appetite in the past week (7 days?)

0=no

1=Yes

3. If you answered 'yes' to #2, how has your appetite changed?

1=Increased

2=Remained the same

3=Decreased

ANTHROPOMETRIC DATA

Measurements	**Date**
Target Weight (kg)	
Height (cm)	
Post dialysis weight (dry weight)	
Body Mass index (kg/m^2)	
Average IDWG	
Average UFR	
Average BP	

MUSCLE STRENGTH

Hand Grip Dynamometer

Hand Grip Strength (kg)							
Left (L) or Right (R) hand	**Dominant Hand**	**Avg**	**SD**	**CV**	**Test #1**	**Test #2**	**Test #3**

BODY COMPOSITION -- MUSCLE MASS MEASUREMENTS

	1st measure	**2nd measure**	**Mean**
Mid-arm circumference (cm)			
Triceps skinfolds (mm)			

BIOCHEMICAL DATA

Renal Profile (Pre-Dialysis)	**Date**	**Test Result**	**Normal Range**
Pre BUN (mg/dL)			
Post BUN (mg/dL)			
Creatinine (mg/dL)			
Sodium (mEq/L)			
Potassium (mEq/L)			
Corrected Calcium (mg/dL)			
Phosphorus (mg/dL)			
Serum Albumin (g/dL)			
Total Cholesterol (mg/dL			
Triglycerides (mg/dL)			
HDL-C (mg/dL)			
LDL-C (mg/dL)			
Glucose (mg/dL)			
HgbA1C (g/dL)			
Hemoglobin (g/dL)			
Hematocrit (%)			
Serum Fe (µg/dL)			
Serum TIBC (µg/dL)			
TSAT (%)			
Ferritin (ng/mL)			
Kt/V			
URR			
nPCR (g/kg/day)			
hsCRP (mg/L)			
PTH			

24-hour dietary recall			Dialysis Day or Non-Dialysis day		
Meal	**Home (H)/Outs ide of Home (O)**	**Food Eaten**	**Quantity (c, tsp. oz., g)**	**Preparation Method (fried, grilled, roasted, stewed)**	**Source of food (fresh, frozen, canned, etc.)**

MALNUTRITION INFLAMMATION SCORE (M.I.S.)			
(A) Patients' related medical history			
1. Change in end dialysis dry weight (overall change in past 3-6 months):			
0	1	2	3
No decrease in dry weight or weight loss <0.5 kg	Minor weight loss (≥0.5 kg but < 1 kg)	Weight loss more than 1 kg but <5%	Weight loss> 5%
2. Dietary intake:			
0	1	2	3
Good appetite and no deterioration of the dietary intake pattern	Somewhat sub-optimal solid diet intake	Moderate overall decrease to full liquid diet	Hypo-caloric liquid to starvation
3. Gastrointestinal (GI) symptoms:			
0	1	2	3
No symptoms with good appetite	Mild symptoms, poor appetite or nauseated occasionally	Occasional vomiting or moderate GI symptoms	Frequent diarrhea or vomiting or severe anorexia
4. Functional capacity (nutritionally related functional impairment):			
0	1	2	3
Normal to improved functional capacity, feeling fine	Occasional difficulty with baseline ambulation, or feeling tired frequently	Difficulty with otherwise independent activities (e.g. going to bathroom)	Bed/chair-ridden, or little to no physical activity
5. Co-morbidity including number of years on Dialysis:			
0	1	2	3
On dialysis less than one year and healthy otherwise	Dialyzed for 1-4 years, or mild co-morbidity (excluding MCC*)	Dialyzed > 4years, or moderate co-morbidity (including one MCC*)	Any severe, multiple co-morbidity (2 or more MCC*)
(B) Physical Exam (according to SGA criteria)			
6. Decreased fat stores or loss of subcutaneous fat (below eyes, triceps, biceps, chest):			
0	1	2	3
Normal	Mild	Moderate	Severe
7. Signs of muscle wasting (temple, clavicle, scapula, ribs, quadriceps, knee, interosseous):			
0	1	2	3
Normal	Mild	Moderate	Severe
(C) Body mass index:			
8. Body mass index: BMI = Wt (kg)/Ht^2 (m)			
0	1	2	3
BMI ≥ 20 kg/m^2	BMI: 18 - 19.99 kg/m^2	BMI: 16 – 17.99 kg/m^2	BMI ≤ 16 kg/m^2
(D) Laboratory Parameters:			
9. Serum albumin:			
0	1	2	3
Albumin ≥ 4.0 g/dL	Albumin: 3.5 -3.9 g/dL	Albumin: 3.0 – 3.4 g/dL	Albumin ≤ 3.0 g/dL
10. Serum TIBC (total Iron Binding Capacity):			
0	1	2	3
TIBC ≥ 250 mg/dL	TIBC: 200 - 249 mg/dL	TIBC: 150 - 199 mg/dL	TIBC ≤ 150 mg/dL
Total Score = sum of above 10 components (0-30):			

RESTLESS LEG SYNDROME RATING SCALE

Have the patient rate his/her symptoms for the following ten questions. The patient and not the examiner should make the ratings, but the examiner should be available to clarify any misunderstandings the patient may have about the questions. Either the examiner or the patient may mark the answers on the form.

1. How would you rate the RLS discomfort in your legs or arms?

   (4) Very Severe
   (3) Severe
   (2) Moderate
   (1) Mild
   (0) None

2. Overall, how would you rate the need to move around because of your RLS symptoms?

   (4) Very Severe
   (3) Severe
   (2) Moderate
   (1) Mild
   (0) None

3. Overall, how much relief of your RLS arm or leg discomfort do you get from moving around?

   (4) No relief
   (3) Slight relief
   (2) Moderate relief
   (1) Either complete or almost complete relief
   (0) No RLS symptoms and therefore question does not apply.

4. Overall, how severe is your sleep disturbance from your RLS symptoms?

   (4) Very Severe
   (3) Severe
   (2) Moderate
   (1) Mild
   (0) None

5. How severe is your tiredness or sleepiness from your RLS symptoms?

   (4) Very Severe
   (3) Severe
   (2) Moderate
   (1) Mild
   (0) None

6. Overall, how severe is your RLS as a whole?

   (4) Very Severe
   (3) Severe
   (2) Moderate
   (1) Mild
   (0) None

7. How often do you get RLS symptoms?

   (4) Very Severe (This means 6 to 7 days a week)
   (3) Severe (This means 4 to 5 days a week)
   (2) Moderate (This means 2 to 3 days a week)
   (1) Mild (One day a week or less)
   (0) None

8. When you have RLS symptoms, how severe are they on an average day?

   (4) Very Severe (This means 8 hours per 24 hours a day or more)
   (3) Severe (This means 3 to 8 hours per 24 hour a day)
   (2) Moderate (This means 1 to 3 hours per 24 hour a day
   (1) Mild (One hour per 24 hour a day)
   (0) None

9. Overall, how severe is the impact of your RLS symptoms on your ability to carry out your daily affairs, for example, carrying out a satisfactory family, home, social, school, or work life?

   (4) Very Severe
   (3) Severe
   (2) Moderate
   (1) Mild
   (0) None

10. How severe is your mood disturbance from your RLS symptoms-for example angry, depressed, sad, anxious, or irritable?

(4) Very Severe
(3) Severe
(2) Moderate
(1) Mild
(0) None

Very Severe=31-40 points
Severe=21-30 points
Moderate=11-20 points
Mild=1-10 points
None=0

Your Health

– *and* –

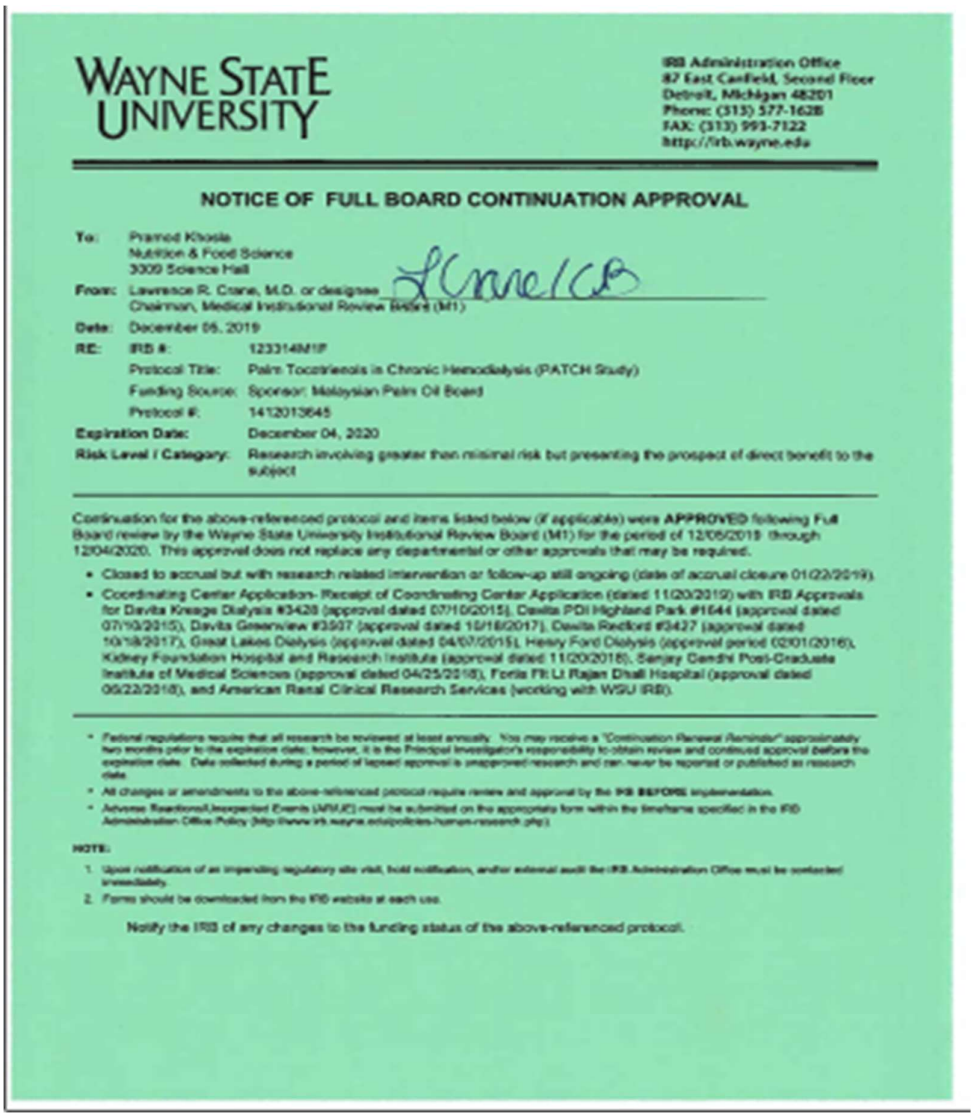
Well-Being

Kidney Disease and Quality of Life (KDQOL™-36)

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

Thank you for completing these questions!

APPENDIX-D IRB APPROVAL-WAYNE STATE UNIVERSITY



WAYNE STATE UNIVERSITY

IRB Administration Office
87 East Canfield, Second Floor
Detroit, Michigan 48201
Phone: (313) 577-1628
FAX: (313) 993-7122
http://irb.wayne.edu

NOTICE OF FULL BOARD CONTINUATION APPROVAL

To: Pramod Khosla
Nutrition & Food Science
3009 Science Hall

From: Lawrence R. Crane, M.D. or designee
Chairman, Medical Institutional Review Board (M1)

Date: December 05, 2019

RE:
IRB #: 123314M1F
Protocol Title: Palm Tocotrienols in Chronic Hemodialysis (PATCH Study)
Funding Source: Sponsor: Malaysian Palm Oil Board
Protocol #: 1412013645

Expiration Date: December 04, 2020

Risk Level / Category: Research involving greater than minimal risk but presenting the prospect of direct benefit to the subject

Continuation for the above-referenced protocol and items listed below (if applicable) were **APPROVED** following Full Board review by the Wayne State University Institutional Review Board (M1) for the period of 12/05/2019 through 12/04/2020. This approval does not replace any departmental or other approvals that may be required.

- Closed to accrual but with research related intervention or follow-up still ongoing (date of accrual closure 01/22/2019).
- Coordinating Center Application- Receipt of Coordinating Center Application (dated 11/20/2019) with IRB Approvals for Davita Kreage Dialysis #3428 (approval dated 07/10/2015), Davita PDI Highland Park #1644 (approval dated 07/10/2015), Davita Greenview #3937 (approval dated 10/18/2017), Davita Redford #3427 (approval dated 10/18/2017), Great Lakes Dialysis (approval dated 04/07/2015), Henry Ford Dialysis (approval period 02/01/2016), Kidney Foundation Hospital and Research Institute (approval dated 11/20/2018), Sanjay Gandhi Post-Graduate Institute of Medical Sciences (approval dated 04/25/2018), Fortis Flt Lt Rajan Dhall Hospital (approval dated 05/22/2018), and American Renal Clinical Research Services (working with WSU IRB).

- Federal regulations require that all research be reviewed at least annually. You may receive a "Continuation Renewal Reminder" approximately two months prior to the expiration date; however, it is the Principal Investigator's responsibility to obtain review and continued approval before the expiration date. Data collected during a period of lapsed approval is unapproved research and can never be reported or published as research data.
- All changes or amendments to the above-referenced protocol require review and approval by the IRB **BEFORE** implementation.
- Adverse Reactions/Unexpected Events (AR/UE) must be submitted on the appropriate form within the timeframe specified in the IRB Administration Office Policy (http://www.irb.wayne.edu/policies-human-research.php).

NOTE:

1. Upon notification of an impending regulatory site visit, audit notification, and/or external audit the IRB Administration Office must be contacted immediately.
2. Forms should be downloaded from the IRB website at each use.

Notify the IRB of any changes to the funding status of the above-referenced protocol.

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ABSTRACT

NUTRITION AND HEALTH STATUS OF HEMODIALYSIS PATIENTS IN DHAKA, BANGLADESH

by

TANJINA RAHMAN

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Advisor: Dr. Pramod Khosla

Major: Nutrition and Food Science

Degree: Doctor of Philosophy

Methods to identify patients at risk for ESRD are a high priority in Bangladesh, where kidney transplants/dialysis options are limited and costly. Every year, 35,000 to 40,000 people reach ESRD in Bangladesh, but currently available facilities can hardly accommodate only 9000 to 10,000 new patients with twice weekly dialysis and the remaining 66% have no access to any kind of renal replacement therapy (RRT) in the form of dialysis or transplantation. Nutrition is an important factor in maintaining good health of hemodialysis patients. However, data on nutritional status of Bangladeshi dialysis patients is limited and is not adequately documented. The purpose of the first study (specific aim I and II) was to assess current health and nutritional status of hemodialysis (HD) patients in a specialized renal hospital in Dhaka, Bangladesh. We assessed 133 patients (49% male) at the Kidney Foundation Hospital and Research Institute (in 2017 and 2018) based on different anthropometric, biochemical, and clinical parameters. Lipid profiles and subfractions were analyzed and patients with dyslipidemia (DL) were characterized using ATP (Adult

Treatment Panel) III guideline. Patients were also analyzed based on 2x weekly versus 3x weekly dialysis in order to see if there were any significant differences between these two groups. Patients with protein-energy wasting (PEW) were identified using criteria from the International Society of Renal Nutrition and Metabolism (ISRNM). Therefore, we conclude that, in this specialized renal hospital, no significant differences were found based on dialysis frequency. However, both mixed and atherogenic DL were prevalent and 64% of patients were having DL based on TAG/HDL-C ratio. Prevalence of PEW was 18%, thus both DL and PEW were common among the study cohort. The figures may be underestimates as only one clinic was evaluated. If this is the scenario in an Urban renal-specialized hospital in Bangladesh, it is obvious that, many more hemodialysis patients were also suffering from DL and PEW all over the country. For specific aim III, we took an attempt to develop an educational tool for improving renal-specific nutrition knowledge among Bangladeshi dialysis patients in the form of a "Nutrition booklet" based on robust analysis of local Food compoition table and then incorporated key observations based on scientific basis into the booklet. Provision of renal-specific nutrition knowledge may help renal patients make more informed food choices. This may be especially important in resource-poor settings where nutritional support is a low-priority amongst health-care providers. The renal-specific nutrition booklet was developed only for Bangladeshi dialysis patients and made feasible to use in practice as an educational tool to improve their selection of food items as well as adherence towards renal-specific diet practice through this study. Additionally, we took initiative to educate and train a group of graduate students (in nutrition) with basic skills to assist renal staff in nutrition and anthropometric assessments in a hospital providing dialysis services in Dhaka, Bangladesh. The outcomes for both attempts were hopeful. Individuals with expertise in renal nutrition and associated aptitude in nutrition assessment are scarce in

resource-poor countries which limit the opportunity to conduct research in this field in order to find the hidden truth behind the occurrence and severity of disease. Therefore, attempts should be made to generate trained manpower in order to facilitate research work in renal nutrition field in such region.

AUTOBIOGRAPHICAL STATEMENT

Tanjina Rahman received her Bachelor of Science (2008) and Master of Science degree (2010) in Nutrition and Food Science from Institute of Nutrition and Food Science, University of Dhaka, Bangladesh. She got a government fellowship from NSICT (National Science, Information, and Communication Technology) from 2009-2010 for her thesis work. In 2015, she completed her Master of Public Health (MPH) degree from "North South University, Bangladesh". She started her PhD program from August 2015 to till date in the department of Nutrition and Food Science, at Wayne State University, Michigan, USA. In 2017, she was certified by the ISAK global for completing Level 1 ISAK course requirement and she is now a member of International Society for Anthropology and Kinanthropometry (ISAK) for next four years. She is also an active member in BMANA (Bangladesh Medical Association of North America) and UTAB (University Teachers Association of Bangladesh) from 2017 to till date. Back in Bangladesh, she is an "Assistant Professor" in the department of "Food Technology and Nutrition Science" in one of the renowned public university "Noakhali Science and Technology University". After pursuing her PhD degree, she is willing to devote her life in the field of renal nutrition to make a positive change for Bangladeshi patients with chronic kidney disease.