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Faculty of Graduate Studies

Evaluation of Prescribing Pattern and Compliance to Treatment Guidelines in Hemodialysis Patients in Hebron Governmental Hospital

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Dedication

To my lovely parents

To my sister and brothers

To Ahmad and Bayan

To my grandfather

To all whom I love

Acknowledgement

وَمَا تَوْفِيقِي إِلَّا بِاللَّهِ عَلَيْهِ تَوَكَّلْتُ وَإِلَيْهِ أُنِيبُ هود- 88

Greeting goes to my supervisor Dr. Rowa' AL-Ramahi for her sincere encouragement, helpful, and close supervision which has been invaluable for me throughout all stages of this study. Thanks go to my family with all my love, specially my mother, father, sister, and brothers, who provided me with psychological support and encouragement.

الإقرار

أنا الموقعة ادناه، مقدمة الرسالة التي تحمل العنوان:

Evaluation of Prescribing Pattern and Compliance to Treatment Guidelines in Hemodialysis Patients in Hebron Governmental Hospital

تقييم نمط الأدوية الموصوفة ومدى الالتزام بالخطط العلاجية لدى مرضى الغسيل الكلوي في مستشفى الخليل الحكومي

أقر بأن ما اشتملت عليه هذه الرسالة إنما هو نتاج جهدي الخاص، باستثناء ما تمت الإشارة إليه حيثما ورد، و أن هذه الرسالة كاملة، أو أي جزء منها لم يقدم من قبل لنيل أي درجة أو لقب علمي أو بحثي لدى أي مؤسسة تعليمية أو بحثية أخرى

Declaration

The work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

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Abbreviations

Abbreviations	Meaning
ACE-I	Angiotensin Converting Enzyme Inhibitor
ARB	Angiotensin II receptor blocker
BUN	Blood Urea Nitrogen
CG	Cockcroft Galt
CKD	Chronic Kidney Disease
CVD	Cardiovascular Disease
DOPPS	The Dialysis Outcomes and Practice Patterns
ESA	Erythropoietin Stimulating Agent
ESRD	End Stage Renal Disease
GFR	Glomerular Filtration Rate
Hb	Hemoglobin
HD	Hemodialysis
Hb A1c	Hemoglobin A1c
IV	Intavenous
KDIGO	Kidney Disease: Improving Global Outcomes
MDRD	The Modification of Diet in Renal Disease
MOH	Ministry of Health
NKF/DOQI	National Kidney Foundation kidney Dialysis Outcome and Quality Initiative
PD	Peritoneal Dialysis
PTH	Parathyroid Hormone
ROD	Renal Osteodystrophy
SC	Subcutanous
SCr	Serum Creatinin
URR	Urea Reduction Ratio

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Evaluation of Prescribing Pattern and Compliance to Treatment Guidelines in Hemodialysis Patients in Hebron Governmental Hospital

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Abstract

Background: Chronic kidney disease (CKD) including end-stage renal disease (ESRD) is a growing epidemic. Hemodialysis (HD) is the most commonly used renal replacement therapy in addition to the management of diabetes, hypertension, dyslipidemia, anemia, and bone mineral disorder in hemodialysis patients.

Objectives: The objectives of this study were to asses prescribing pattern and to evaluate compliance to treatment guidelines in hemodialysis patients.

Method: This study was an observational retrospective cohort study, it was conducted at Hebron governmental hospital / Palestine between March and April 2014. All adult on chronic HD there were included. All information were collected from governmental electronic health record (AviCenna HIS program), and patients were asked to answer some questions when data was not found in the system. Statistical analysis was performed by using Statistical Package for Social Sciences (SPSS) program.

Results: During the study period 158 HD patients were prescribed 1567 medication orders of 103 different medications, 49 medications for the management of chronic illness, and 54 medications for acute illness. The

patients were taking a minimum of 2 and a maximum of 18 medications, with a mean of 9.92±2.94. The most commonly prescribed medications were calcium carbonate (91.8%), followed by alfacalcidol (84.8%), then iron/folic acid (69.6 %). About (36.7%) of the patients had diabetes, and hemoglobin A1c (HbA1c) test which reflect average blood sugar level for the past 2-3 months was not performed for these patients. Insulin mixtard, insulin actrapid, and glibenclamide were used to control diabetes . A majority of the patients (72.2%) had Hypertension. The target predialysis blood pressure of <140/90 mmHg were achieved in 77.2% of the patients (70.5% of the males vs 87.3% of the females; P- value =0.014) , and post dialysis blood pressure of < 130/80 were achieved 57.6% of the patients. Target predialysis correlate with postdialysis blood pressure (r=0.236, P-value =0.003) and amlodipine was the most commonly used drug for the management of hypertension which is differ from what the guidelines advise. Atorvastatin was the most prescribe medication for dyslipidemia (39.9%). Patients with total cholesterol levels of < 200 mg/dl were 78.3% patients. Regarding triglycerides levels, 96.2% had levels of < 500 mg/dl. There was an association between the control of the total cholesterol and triglycerides as 80.1% of the patients had total cholesterol of < 200 mg/dl (P- value =0.006). In the management of anemia, patients who reached goal hemoglobin (Hb) of 11-12 mg/dl according to the national kidney foundation (NKF) guidelines were 8.9% patients only. If kidney disease improving global outcome (KDIGO) guidelines are used, these guidelines accept a Hb level between 9-11.5 mg/dl but not to exceed 13 mg/dl, the

patients in this range was 43.0% cases. Transferrin levels were not measured. Iron was used by 69.9% of the patients, and erythropoietin stimulating agents (ESA) by 5.1% of the patients as it was not available in the hospital, and very expensive to purchased by the patient's own accounts. No data was available for calcium, and parathyroid hormone levels to manage bone mineral disorder, Target phosphorus level was obtained in 12% of the patients according to the NKF guidelines. If serum phosphorus normal range of 2.5–4.5 mg/dl is used according to KDIGO guidelines, this target was achieved in 4.4% patients only. Calcium carbonate was used by 91.8%, sevelamir by 15.8%, and alfacalcidol by 84.8% of the HD patients.

Conclusion: The results reflect a poor compliance to treatment guidelines according to NKF and KDIGO guidelines for diabetes, hypertension, dyslipidemia, anemia, and bone mineral disorder. The target levels for treatment are not achieved in many HD patients. The medications are not prescribed optimally to the patients and many investigations and laboratory tests are not performed.

Chapter One

Introduction

Chapter One
Introduction

1.1 Background

Kidneys play very important role in human body, they are a pair of bean shaped, brown organs, each kidney is about the size of the fist, which measures 10-12 cm long, about 150 grams weight, it is covered by the renal capsule, which is a tough capsule of fibrous connective tissue. It consists of three major regions; cortex, medulla and pelvis (Drake *et al*, 2009).

The most important function of the kidneys is regulation of plasma ionic composition by their amount excreted such as sodium, potassium, calcium, magnesium, chloride, bicarbonate, and phosphates. The kidneys regulate plasma osmolarity by having direct control over how many ions and how much water are excreted and plasma volume regulation by controlling how much water a person excretes, which has a direct effect on blood pressure (Guyton and Hall, 2006).

Kidneys also regulate hydrogen ion concentration (pH) by maintaining the blood pH mainly by excreting hydrogen ions and reabsorbing bicarbonate ions as needed, In addition to the removal of metabolic waste products from the plasma such as ammonia, creatinine and uric acid. Kidneys secrete hormones as renin and erythropoietin which stimulates red blood cell production. Vitamin D which promotes calcium absorption from the digestive tract is activated by the kidneys (Guyton and Hall, 2006).

Kidneys receive about 22 percent of the cardiac output, or 1100 ml/min. Renal blood flow enters the glomerulus via the afferent arterioles and leaves via efferent arterioles where the renal blood flow is regulated by norepinephrin and angiotensin II (constriction which causes reduction of flow), dopamine and acetylcholine (vasodilation which increases flow), and prostaglandins (which causes dilation in the renal cortex and constriction in the renal medulla) (Barrett et al., 2010).

Nephron is the basic structural and functional unit of the kidney, and each kidney in the human contains about 1 million nephrons. The kidney cannot regenerate new nephrons. After age 40, the number of functioning nephrons usually decreases about 10 percent every 10 years; thus, at age 80, many people have 40 percent fewer functioning nephrons than they did at age 40. This loss is not life threatening because adaptive changes in the remaining nephrons occur. Nephron consists of an individual renal tubule and its glomerulus. Each tubule has several segments, beginning with the proximal tubule, followed by the loop of Henle, the distal convoluted tubule, the connecting tubule, and the collecting duct (Guyton and Hall, 2006).

When plasma enters the kidneys it will be filtered in the glomerulus. As the filtrate passes down the nephron and through the tubules, its volume is reduced and water and solutes are removed (tubular reabsorption) and waste products are secreted (tubular secretion) (Ganong and Barrett, 2005). The normal filtration rate is around 125 ml/min. The diagnostic test of

kidney function is the glomerular filtration rate (GFR). A decreased GFR may be a sign of renal failure (Guyton and Hall, 2006).

GFR can be measured by a substance that is freely filtered and neither reabsorbed nor secreted in the tubules, nontoxic, and is not metabolized by the body. Inulin meets these criteria and was used to measure GFR in the past (Barrett et al., 2010). The Modification of Diet in Renal Disease (MDRD) formula and a modified version of the Cockcroft-Gault (CG) formula adjusting for body surface area are widely used these days (Bookstaver *et al.*, 2008).

Diseases of the kidneys are among the most important causes of death and disability. Renal failure can be divided into two main categories: acute and chronic renal failure. In acute renal failure, the kidneys abruptly stop working entirely or almost entirely but may eventually recover nearly normal function. This can be prerenal, intrarenal and postrenal. The other type is chronic renal failure, in which there is progressive loss of function of nephrons that gradually decreases overall kidney function (Guyton and Hall, 2006).

1.2 Chronic kidney disease

1.2.1 Definition

Chronic kidney disease (CKD) is a growing epidemic worldwide (Afsar, 2013), and is defined as either kidney damage or decreased kidney function for ≥ 3 months (Cavanaugh *et al.*, 2007). It is associated with a

poor prognosis, the development of premature cardiovascular disease and increased mortality (Hemmelgarn, 2007). The attention being paid globally to CKD due to many factors; the rapid increase in its prevalence, the enormous cost of treatment, recent data indicating that overt disease is the tip of an iceberg of covert disease, its major role in increasing the risk of cardiovascular disease, and the discovery of effective measures to prevent its progression (National Kidney Foundation, 2002). In 2004, more than 20 million adults in the United State were estimated to have CKD (Hall and Guyton, 2010).

1.2.2 Classification

National Kidney Foundation's Kidney Dialysis Outcomes and Quality Initiative (K/DOQI) classified CKD by the level of kidney function, based on GFR, into stages 1 to 5, with each increasing number indicating a more advanced stage of the disease, as defined by a declining GFR. This classification system accounts for structural evidence of kidney damage also (Wells *et al.*, 2012).

Table (1.1): Classification of CKD (National Kidney Foundation, 2002).

Stage	GFR (ml/ min/ 1.73 m^2)	Description
Stage 1	≥ 90	Kidney damage with normal or increase GFR
Stage 2	60-89	Kidney damage with mild decrease GFR
Stage 3	30-59	Moderately decrease GFR
Stage 4	15-29	Severely decrease GFR
Stage 5	<15	Kidney failure

1.2.3 Risk factors

- Susceptibility factors

These factors increase susceptibility to kidney damage such as older age, family history to CKD, reduction of kidney mass, low birth weight, racial or ethnic minority status, low income, and education (levey *et al*., 2005).

- Initiation factors

These factors directly initiate kidney damage as diabetes, high blood pressure, autoimmune disease, systemic infection, urinary tract infection, urinary stone, lower urinary tract obstruction, drug toxicity, and hereditary diseases (Chisholm-Burns *et al*., 2008).

- Progression factors

These factors cause worsening kidney damage and faster decline in kidney function after initiation of kidney damage, such as higher level of proteinuria, higher blood pressure level, poor glycemic control in diabetes, possibly dyslipidemia, and smoking (levey *et al.,* 2005).

1.2.4 Clinical presentation

CKD development and progression is insidious. Patients with stage 1 or 2 CKD usually do not have symptoms or metabolic derangements seen with stages 3 to 5, such as anemia, secondary hyperparathyroidism, cardiovascular disease, malnutrition, and fluid and electrolyte abnormalities

that are more common as kidney function deteriorates. Uremic symptoms (fatigue, weakness, shortness of breath, mental confusion, nausea, vomiting, bleeding, and anorexia) are generally absent in stages 1 and 2, minimal during stages 3 and 4, and common in patients with stage 5 CKD who may also experience itching, cold intolerance, weight gain, and peripheral neuropathies (Wells *et al.*, 2012), and in which preparations for dialysis and transplantation are required (MacGregor *et al.*, 2006).

1.2.5 Treatment

Treatment of CKD aims to slow progression to end-stage renal disease (ESRD) and to prepare for it. Therapy is usually started at an asymptomatic condition detected only by laboratory testing (Turner *et al.*, 2011).

- Nonpharmacologic and supportive therapy

Although the benefit of a low-protein diet (0.6 to 0.75 g/kg/day) is relatively small. They can delay progression of CKD in patients with or without diabetes. All of dietary protein restriction, lipid-lowering medications, smoking cessation, and anemia management may help slow the rate of CKD progression (Wells *et al.*, 2012).

- Pharmacologic therapy

Patients with type 1 and type 2diabetes should be intensively treated to reduce microvascular complications, including nephropathy. Intensive

therapy can include insulin or oral drugs and including blood sugar testing three times daily (Wells *et al.*, 2012).

Adequate blood pressure control can reduce the rate of decline in GFR and albuminuria in patients with or without diabetes, so antihypertensive therapy should be initiated in diabetic or nondiabetic CKD patients with an angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin II receptor blocker (ARB). A second line Nondihydropyridine calcium channel blockers are generally used as antiproteinuric drugs when ACEIs or ARBs are not suitable. The progression of CKD can be limited by optimal control of hyperglycemia and hypertension (Wells *et al.*, 2012).

1.3 End stage renal disease

1.3.1 Definition

ESRD is a clinical condition where kidneys lose their ability of filtering metabolites and waste products from the body (Bellazzi *et al.*, 2012). The population with ESRD is increasing, expanding at a rate of 7% per year worldwide (Huang *et al.*, 2013). The increase in ESRD incidence could be due to the increase of patients with CKD and the rate of their disease progression, decreases in competing mortality, and/or increasing treatment availability (Coresh *et al.*, 2005). The leading cause of ESRD is diabetes (30%) followed by renal vascular disease, including hypertension (20%) (Kappel *et al.*, 2002).

1.3.2 Treatment

The maintenance therapy for ESRD is by renal replacement therapy, through dialysis or kidney transplant. A study in 2004 showed that there were 1783000 people worldwide who needed treatment for ESRD, 77% were on dialysis treatment, and 23% were living with functioning renal transplant (Grassmann *et al.*, 2005). Clinical management of dialysis patients often involves treatment of multiple comorbid conditions, in which dialysis patients are prescribed on average 9-10 oral medications and 2-3 parenteral medications (Weinhandl *et al.*, 2013 and Manley *et al.*, 2005).

Hemodialysis (HD) is the most commonly used renal replacement therapy (Kara, 2013), because it achieves a good quality of life and quality of service for ESRD patients (Chen, 2013). In the United States, more than 350000 patients with ESRD are being treated by dialysis with about 92% receiving HD and about 8% on continuous ambulatory peritoneal dialysis. HD, is usually performed 3 times per week, uremic nitrogenous waste, potassium, phosphate, and magnesium move from blood into the dialysate down the concentration gradient, and calcium and bicarbonate move into the circulation. HD also corrects the fluid overload (Venkat *et al.,* 2006). Mortality rates remain > 20% per year with the use of dialysis, with more than half of the deaths related to cardiovascular diseases (Go *et al*., 2004). Many factors contributed to the high risk of death, including: cardiovascular disorders, diabetes, hypertension, inflammation, dyslipidemia, and bone mineral disorders (Setiani Agus *et al.,* 2013).

1.3.3 Complications of ESRD and their management

1.3.3.1 Fluid and electrolyte abnormalities

Patients with advanced kidney dysfunction exhibit signs of sodium and fluid retention. Expansion of blood volume, if not controlled, can cause peripheral edema, heart failure, and pulmonary edema. To control this most patients with advanced kidney disease need sodium restriction (<2.4 g/day) and fluid restriction (1 to 2 L/day). These restrictions will depend on the current dietary intake, extent of volume overload, and urine output and should be altered according to the special needs of the patient. Loop diuretics increase urine volume and renal sodium excretion. Although thiazide diuretics are ineffective when creatinine clearance is less than 30 mL/min, adding them to loop diuretics can enhance excretion of sodium and water (Alldredge *et al.*, 2013).

1.3.3.2 Potassium homeostasis

Serum potassium concentration starts to increase when the GFR is < 20 mL/min/1.73m^2. The definitive treatment of severe hyperkalemia in ESRD is hemodialysis. Temporary measures include calcium gluconate, insulin and glucose, nebulized albuterol, and sodium polystyrene sulfonate (Wells *et al.*, 2012).

1.3.3.3 Anemia

The primary cause of anemia in patients with CKD or ESRD is erythropoietin deficiency. Other factors include decreased lifespan of red

blood cells, blood loss, and iron deficiency. Iron supplementation is necessary to replete iron stores. Parenteral iron therapy improves response to erythropoietic therapy and reduces the dose required. In contrast, oral therapy is often inadequate. Sodium ferric gluconate and iron sucrose have better safety records than iron dextran. Iron dextran requires a test dose to reduce the risk of anaphylactic reactions (Wells *et al.*, 2012).

Iron indices (transferrin saturation; ferritin) should be evaluated before initiating an erythropoietic agent. For monitoring purposes, hemoglobin is preferred to hematocrit because the latter fluctuates with volume status (Alldredge *et al.*, 2013).

1.3.3.4 Secondary hyperparathyroidism and renal osteodystrophy

Calcium–phosphorus balance is mediated through a complex interplay of hormones and their effects on bone, GI tract, kidney, and parathyroid gland. As renal function declines, serum calcium balance can be maintained only at the expense of increased bone resorption, ultimately resulting in renal osteodystrophy (ROD). Secondary hyperparathyroidism can cause altered lipid metabolism, altered insulin secretion, resistance to erythropoietic therapy, impaired neurologic and immune functions, and increased mortality. ROD progresses insidiously for several years before the onset of symptoms such as bone pain and fractures (Wells *et al.*, 2012). Most patients require a combination of phosphate-binding agents calcium- and non calcium-containing products (e.g., sevelamer HCL, lanthanum carbonate), vitamin D (Calcitriol, 1,25-dihydroxyvitamin D3), and

calcimimetic therapy (Cinacalcet) to achieve target concentration (Alldredge *et al*., 2013).

1.3.3.5 Metabolic acidosis

Reduced bicarbonate reabsorption and impaired production of ammonia by the kidneys are the major factors responsible for development of metabolic acidosis in advanced kidney disease. Metabolic acidosis can contribute to bone disease by promoting bone resorption, and it may also influence nutritional status by decreasing albumin synthesis and promoting a negative nitrogen balance. Oral alkalinizing salts can be used in patients with stage 4 or 5 CKD. Metabolic acidosis in patients undergoing dialysis can often be managed by using higher concentrations of bicarbonate or acetate in the dialysate (Lederer *et al.*, 2007; Alldredge *et al*., 2013).

1.3.3.6 Hypertension

Hypertension is common in patients with CKD with a prevalence that varies depending on the cause of CKD and residual kidney function. Multiple factors are involved in the development of hypertension in the CKD population, including extracellular volume expansion from salt and water retention and activation of the renin angiotensin aldosterone system (Alldredge *et al.,* 2013).

Most patients with ESRD require three or more antihypertensive agents to achieve target blood pressure. As with less advanced CKD, angiotensin converting enzyme inhibitors (ACEI), angiotensin receptor

blockers (ARB), and dihydropyridine calcium channel blockers are the preferred agents, and salt (2 to 3 g/day) and fluid intake should be restricted (Wells *et al.*, 2012).

1.3.3.7 Hyperlipidemia

The prevalence of hyperlipidemia increases as renal function declines. Hyperlipidemia should be managed aggressively in patients with ESRD. Statins are the drugs of first choice in patients with ESRD, and lipid profile should be reassessed at least annually and 2 to 3 months after changing treatment (Wells *et al.*, 2012).

1.3.3.8 Infection

Infection is a serious complication of HD, and infection arising from the percutaneous vascular access necessary to accomplish HD is the most common source of infection occurring in these patients. Previous studies have established that infection risk is lowest when vascular access occurs through ateriovenous graft and highest through central venous catheter . Other identified risk factors for infection include diabetes, Staphylococcus aureus nasal carriage, patient hygiene, iron overload, hypoalbuminenia, and use of bioincompatible membranes (Taylor *et al.*, 2004).

1.4 Problem statement

To the best of our knowledge the prescribing pattern and adherence to treatment guidelines in HD patients were not study wells, and limited information about this population was available.

1.5 Objectives

1.5.1 General objective

The aims of this study are to asses prescribing pattern and to evaluate compliance to treatment guidelines in hemodialysis patients in Hebron governmental hospital.

1.5.2 Specific objectives

1. To find the prescribed medications and the percentages of HD patients using them.
2. To evaluate compliance to treatment guidelines for anemia, bone disease, diabetes mellitus, hypertension and dyslipidemia.
3. To evaluate if the outcomes of treatment (e.g target hemoglobin, calcium, phosphorus, HB A1c, blood pressure (BP), etc) meet the recommended goals.
4. To find possible relationship between compliance to treatment guidelines in HD patients, and socio-demographic and clinical factors.

1.6 Significance of the study

To the best of our knowledge, there are limited data about HD patients in our country . Therefore, this study will give baseline data and information about prescribing pattern and compliance to treatment guidelines in HD patients, and this study is the first of its type in Palestine, and one of the few in the Middle East.

These information are highly required in our country to optimize the service provided. This study will help in improving HD patients' quality of life by controlling their illness according to the treatment guideline. Findings can help in developing educational programs and interventions to improve compliance with international treatment guidelines in HD patients.

Chapter Two
Literature Review

Chapter Two
Literature Review

2.1 The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) and Kidney Disease: Improving Global Outcomes (KDIGO) guidelines in HD patients

No national guidelines for treatment of ESRD could be found. Around the world, several international guidelines are present.

The most famous are the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) guidelines for all stages of CKD and related complications. Recognized throughout the world for improving the diagnosis and treatment of kidney disease, the KDOQI Guidelines have changed the practices of numerous specialties and disciplines and improved the lives of thousands of kidney patients (National Kidney Foundation, 2014).

Guidelines by the NKF-KDOQI and Kidney Disease: Improving Global Outcomes (KDIGO) provide information to assist healthcare providers in clinical decisions and the design of appropriate therapy to manage CKD progression and the associated complications worldwide (Wells et al., 2012). KDOQI and KDIGO work in concert to expand the scope of guidelines relevant to the care of patients with CKD and improve the care of these patients worldwide. The treatment of HD patients in this study will be compared to these guidelines. Here is a summary of these guidelines (table 3.2).

2.1.1 Guidelines for diabetes in HD patients

The National Kidney Foundation (NKF) released guidelines related to diabetes in 2007 and these guidelines were updated in 2012.

There is evidence that Hb A1C is not as representative of glycemic control in patients on HD or peritoneal dialysis (PD). The precise target of HbA1c that is associated with the best outcome in dialysis patients has not been clearly established (National Kidney Foundation, 2005). In the updated guidelines, a target HbA1c of around 7.0% to prevent or delay progression of the microvascular complications of diabetes is recommended. However, it is recommend not treating to an HbA1c target of <7.0% in patients at risk of hypoglycemia and that target HbA1c be extended above 7.0% in individuals with co-morbidities or limited life expectancy and risk of hypoglycemia (National Kidney Foundation, 2012).

Patient on dialysis can use the newer insulin regimens and insulin preparations with other oral hypoglycemic agents that should be used with caution (e.g. glyburide, glipizide, and glimepride). Metformin is contraindicated (National Kidney Foundation, 2007).

2.1.2 Guidelines for hypertension in HD patients

The NKF released guidelines related to hypertension in 2005 and KDIGO released guidelines in 2012; the KDIGO guidelines concentrate mainly on hypertension during early stages of CKD.

It is noteworthy that 60% to 90% of maintenance HD patients have hypertension. Despite the use of multiple medications, hypertension in these patients often is poorly controlled (National Kidney Foundation, 2006).

Guidelines for hypertension treatment in HD patients require both management of fluid status, and adjustment of antihypertensive medications, the target predialysis and postdialysis blood pressure should be <140/90 mm Hg and <130/80 mmHg, respectively (National Kidney Foundation, 2005).

Excessive fluid accumulation between dialysis sessions should be managed with education and regular counseling by dietitians, low sodium intake (2-3 g/day sodium intake), increased ultrafiltration, longer dialysis, more than 3 dialysis treatments per week, and drugs that reduce salt appetite. Management of hypertension with drugs in dialysis patients by ACE-Is or ARBs should be preferred because they cause greater regression of left ventricular hypertrophy, reduce sympathetic nerve activity and may reduce oxidative stress. Antihypertensive drugs should be given preferentially at night, to reduce the nocturnal surge of blood pressure and minimize intradialytic hypotension, which may occur when drugs are taken before a dialysis session (National Kidney Foundation, 2005).

2.1.3 Guidelines for dyslipidemia in HD patients

The NKF released guidelines related to dyslipidemia in 2003 and the KDIGO released guidelines in 2013.

There is association between cholesterol levels and cardiovascular disease in HD patients. So management of dyslipidemia is important (National Kidney Foundation, 2005). According to the old NKF guidelines from 2003, for adults with stage 5 CKD and fasting triglycerides ≥500 mg/d, treatment with therapeutic lifestyle changes and a triglyceride-lowering agent should be considered and for adults with stage 5 CKD and LDL ≥100 mg/dL, treatment should be considered to reduce LDL to <100 mg/dL usually with statins (National Kidney Foundation, 2003).

In the new KDIGO guidelines, they suggest that in patients already receiving statins or statin/ezetimibe combination at the time of dialysis initiation, these agents should be continued. However, in adults with dialysis-dependent CKD, they suggest that statins or statin/ezetimibe combination not to be initiated, as initiation of statin treatment is not recommended for most prevalent HD patients. However, patients might reasonably choose statin treatment if they are interested in a relatively small, uncertain reduction in cardiovascular events (Kidney Disease: Improving Global Outcomes Lipid work group, 2013).

2.1.4 Guidelines for anemia in HD patients

The NKF released guidelines related to anemia in 2006 and they were updated in 2007, the KDIGO released guidelines in 2012.

In general, the anemia of CKD is normochromic and normocytic; that is, morphologically indistinguishable from the anemia of chronic disease. The CBC provides information about the severity of anemia,

adequacy of nutrients including folate, vitamin B12, and iron (serum ferritin to assess iron stores, serum transferin or content of hemoglobin (Hb) in reticulocytes to assess adequacy of iron for erythropoiesis, also adequacy of bone marrow function. In patients with HD interdialytic weight gain contributes to a dilutional decrease in Hb level, whereas intradialytic ultrafiltration promotes a contractional increase in Hb level. Therefore, sampling for Hb determination should be performed before dialysis without specific reference to dialysis day. The K/DOQI guidelines updates in 2007 for treatment of anemia recommend target Hb level 11-12 g/dl, observational evidence showed that mortality rates were lower in HD patients with Hb values close to this range and showed an association between anemia and left ventricular hypertrophy (National Kidney Foundation, 2007). Target serum ferritin level > 200 ng/mL, and transferin > 20%, by using erythropoietin stimulating agent (ESA) and iron are recommended (National Kidney Foundation, 2006).

ESAs are critical components in managing the anemia of CKD, the frequency of Hb monitoring in patients treated with ESAs should be at least monthly. Among HD patients either SC or intravenous IV administration is possible, but IV administration is preferred (National Kidney Foundation, 2006).

These patients require effective use of iron agents, guided by appropriate testing of iron status. The goal is to achieve and maintain a target-range Hb level. Iron agents may serve as adjuvant therapy for those also undergoing treatment with an ESA, in which iron agents prevent iron

deficiency and serve to minimize the dose of ESA needed. Iron status tests should be performed at least every 3 months during stable ESA treatment or in patients with HD-CKD not treated with an ESA. To guide iron therapy the results of iron status tests, Hb, and ESA dose should be interpreted together. In HD patients the preferred route of administration is IV. Patients on HD are more likely to need blood transfusions because of the HD procedure itself. However, aggressive iron replacement has largely eliminated the need for red blood cell transfusions (National Kidney Foundation, 2006).

The new KDIGO are less aggressive in treatment of anemia, they still define anemia as Hb concentration is < 13.0 g/dl in males and <12.0 g/dl in females. However, for adult HD patients, they suggest that ESA therapy be used to avoid having the Hb concentration fall below 9.0 g/dl by starting ESA therapy when the hemoglobin is between 9.0–10.0 g/dl and that ESAs not be used to maintain Hb concentration above 11.5 g/dl in adult patients with CKD (Kidney Disease: Improving Global Outcomes Anemia work group, 2012).

2.1.5 Guidelines for bone mineral disorder in HD patients

The NKF released guidelines bone mineral disorders in 2003 and the KDIGO released guidelines in 2009.

Serum levels of calcium, phosphorus, and intact plasma parathyroid hormone (PTH) should be measured in all patients with CKD and GFR<60 mL/min/1.73m^2 (National Kidney Foundation, 2003).

The serum levels of phosphorus should be maintained between 3.5 to 5.5 mg/dL in HD patients. Dietary phosphorus should be restricted to 800 to 1,000 mg/day when the serum phosphorus levels are elevated >5.5 mg/dL and also when the plasma levels of intact PTH are elevated above target range. Both calcium-based phosphate binders and other non calcium-phosphate-binding agents (e.g. sevelamer HCl) are effective in lowering serum phosphorus levels and either may be used as the primary therapy. In dialysis patients who have serum phosphorus >5.5 mg/dL despite the use of either calcium-based phosphate binders or other agents, a combination of both should be used. The total dose of elemental calcium provided by the calcium-based phosphate binders should not exceed 1,500 mg/day, and the total intake of elemental calcium (including dietary calcium) should not exceed 2,000 mg/day. Non calcium-containing phosphate binders are preferred in dialysis patients with severe vascular and/or other soft-tissue calcifications (National Kidney Foundation, 2003).

Serum levels of corrected total calcium should be maintained within the normal range for the laboratory used, preferably toward the lower end (8.4 to 9.5 mg/dl). The treatment of hypocalcemia should include calcium salts such as calcium carbonate and/or oral vitamin D sterols (National Kidney Foundation, 2003).

HD patients with serum levels of intact PTH levels >300 pg/mL should receive an active vitamin D sterol (such as calcitriol, alfacalcidol, paricalcitol, or doxercalciferol) to reduce the serum levels of PTH to a target range of 150 to 300 pg/mL. The intermittent, intravenous

administration of calcitriol is more effective than daily oral calcitriol in lowering serum PTH levels. Serum levels of calcium and phosphorus should be monitored at least every 2 weeks for 1 month and then monthly thereafter. The plasma PTH should be measured monthly for at least 3 months and then every 3 months once target levels of PTH are achieved (National Kidney Foundation, 2003).

The new KDIGO guidelines recommend measuring PTH and alkaline phosphatase every 3-6 months and calcium and phosphorus every 1-3 months for HD patients. Regarding the goals, they suggest maintaining serum phosphorus and calcium in the normal range (2.5–4.5 mg/dl and 8.5–10.0 or 10.5 mg/dl respectively) and maintaining iPTH levels in the range of approximately two to nine times the upper normal limit for the assay (Kidney Disease: Improving Global Outcomes CKD BMD, 2009).

2.2 Studies related to prescribing pattern in HD patients

To the best of our knowledge limited number of studies that evaluate prescribing patterns in HD patients could be found. In a study by Manley et al in America to evaluate medication prescribing patterns in ambulatory HD patients, they showed that there were 128477 medication orders for 10474 patients. Patients were prescribed 12.3±5.0 (median 12) different medications, and patient with diabetes were prescribed more medication than non diabetics (Manley *et al.*, 2004).

Another study conducted at the nephrology unit in a Malaysian hospital showed that, the total number of medications prescribed for the

600 patients was 5795. During the pre-intervention phase, the 300 patients were prescribed 2814 medication orders of 176 different medications and during the intervention phase there were 2981 prescriptions of 158 medications. Calcium carbonate was the most commonly prescribed medication, followed by a combination of folic acid and vitamin B complex. The third commonly prescribed medication was metoprolol (Al Ramahi, 2009).

In a study from India, a total 111 prescriptions were included in the study. Average number of drugs per prescription was 9.47. Out of total prescribed drugs (1052), most commonly prescribed were vitamins and minerals (24.71%), cardiovascular drugs, (22.14%), and hematopoietic agents (20.15%). Considering individual drugs, five most commonly prescribed drugs were multivitamins (14.82%), iron (8.65%), folic acid (8.55%), calcium carbonate (8.17%), and calcitriol (5.60%). A total of 11.02% of prescribed drug were phosphate binders (PBs). Among PBs, calcium carbonate was the most frequently prescribed and sevelamer was the least prescribed PB. No patient was prescribed lanthanum carbonate (Bajait et al., 2014).

In DOPP (The Dialysis Outcome and Practice Pattern) study in America to evaluate analgesic prescription patterns among HD patients, NSAIDs were the major type of non narcotic analgesics prescribed for dialysis patients (ibuprofen), while in patients taking narcotic analgesics, most were prescribed propoxyphene alone or in a combination product with

acetaminophen (Bailie *et al.*, 2004). Japanese study found that the mean number medications in HD patients was larger 7.2. The three most prescribed drug types in HD patients were those related to calcium and phosphate metabolism (88%), antihypertensive agents (71%), and erythropoietin (60%) (Tozawa et al., 2002).

2.3 Studies related to diabetes, hypertension, dyslipidemia, anemia, and bone mineral disorder in HD patients

Abe et al study showed that HbA1c level is not an ideal index for assessing glycemic control in diabetic dialysis patients. Therefore, glycated albumin, which is unaffected by the changes in the survival time of erythrocytes, has been suggested as a better indicator of glycemic control. However, there is no clear consensus on the target HbA1c and glycated albumin levels for a good prognosis of diabetic dialysis patients (Abe et al., 2011).

A study in 2005, mentioned that normal to low predialysis blood pressure values were associated with significantly increased mortality, while the lowest mortality was associated with predialysis systolic pressure value of 160 to 189 mm Hg (Kalantar-Zadeh *et al.*, 2005). Also another study showed that greater intradialytic systolic blood pressure variability is associated independently with increased all-cause and cardiovascular mortality (Flythe *et al.*, 2013).

Statin use in uremic patients undergoing HD in Huang et al study was associated with a decreased risk of developing future ischemic stroke,

hospitalization for unstable angina ,cardiovascular mortality, deep vein thrombosis and all-cause mortality (Huang *et al.*, 2013).

Many studies were related to anemia management, in 2004 a DOPP study (The Dialysis Outcome and Practice Pattern) in France, Italy, Spain, and the UK found that higher morbidity and mortality were associated with lower hemoglobin concentrations (Locatelli *et al.*, 2004). Anemia and mortality in HD patient study estimated that 95% of HD patients receive treatment for anemia (Robinson *et al.*, 2005), While a 2- years cohort study in 2006 found that, a hemoglobin level between 12 - 13 g/dl was associated with the lowest all-cause and cardiovascular death risks (Regidor *et al.*, 2006).

Renal data from the Arab World showed that control of anemia, was not satisfactory as 50% of study patients had hemoglobin levels below 10 g/dl in 103 HD patients in Libya, in the same study the target serum level of intact parathyroid hormone (PTH) was reached in 17.4% of the patients. Only 30% of the patients achieved target serum calcium (8.4-9.5 mg/dl), and 34.5% had calcium-phosphate products higher than 55 (Buargub *et al.*, 2006).

Abnormal mineral metabolism was associated with all-cause mortality in HD patients with secondary hyperparathyroidism, even after accounting for the effects of mineral and bone disorder treatments on that association (Fukagawa *et al.*, 2014).

In a study from Sudan, four randomly selected HD units were included in the study. They found that rate of implementation of the HD vascular access guidelines was 54.8%, adequacy guidelines 57%, anemia of CKD 68.8%, nutrition 58.4%, cardiovascular risk assessment 57%, and hepatitis B and C infection control guidelines was 79.2%. They concluded that there is a need of great improvements regarding adherence to protocols (Abdelwahab *et al.*, 2013).

In Palestine, limited number of studies was found in nephrology branch. One study to evaluate major risk factors that lead to onset ESRD in Northern West Bank was found; it showed that main risk factors that lead to ESRD in Palestine are chronic diseases such as diabetes mellitus, hypertension, cardiovascular disease, in addition to urinary tract infection. Also some wrong habits such as taking medication without prescription, polycystic kidney disease, and certain types of cancer played a role in leading to ESRD such as bladder cancer and prostate cancer (Basheer, 2011).

In Jenin district the three most common causes of chronic renal failure were diabetes mellitus (33.32%), hypertension (16.7%), and chronic glomerulonephritis (13.1%). In addition to inherited kidney diseases (17.85%). These results differ from what is found in most developing countries including many Arab countries where the principal causes of chronic renal failure are chronic glomerulonephritis and interstitial nephritis (Abumwais, 2012).

Prevalence of patients with ESRD on dialysis in the West Bank, Palestine study demonstrated that the highest prevalence was seen in Jericho city. There were 57.7% males and 42.4% females in the study. The majority of patients (62.3%) were living in villages, while 28.8% were living in cites and 8.9% were living in refugee camps. Most of the patients (45%) aged between 45 and 64 years. The vast majority of patients were either diabetic (2.5%) or hypertensive (1.1%) or both at the same time (10.6%). There were a considerable number of patients in whom the cause was undetermined (27.6%). The majority of recorded cases of congenital causes were from the Hebron, Jenin and Tubas districts. The prevalence of ESRD noted is comparable with other regional countries but far below the rate recorded in industrialized countries (Khader *et al.*, 2013).

A study in a Palestinian hospital to asses adequacy of HD dose mentioned that only 25 (39.1%) patients achieved the Kt/V goal of $\geq$1.2 and only 22 (34.4%) had target urea reduction ratio (URR) of $\geq$65%, and most patients were inadequately dialyzed. Patients who attained pre-dialysis blood pressure goals of <140/90 mm Hg were 33 (51.6%) and postdialysis goal of < 130/80 mm Hg were 31 (48.4%) (Adas *et al*., 2014).

Chapter Three

Methodology

Chapter Three
Methodology

3.1 Study design

The study was an observational retrospective cohort study.

3.2 Study setting

The study was carried out at Hebron governmental hospital/ Palestine between the first of March 2014 and the end of April 2014. Hebron governmental hospital is one of the major hospitals in Palestine, it contain about 280 beds, and provide services to about 662,452 people in the province. According to the ministry of health report in 2013, there were 26 HD machines were available in the dialysis unit in this hospital where 18165 dialysis sessions were performed for the patients during that year (table 3.1).

Palestinian Ministry of Health (MOH) is the main health care provider for the ESRD management in Palestine, where the different treatments of ESRD are given free to the patients. According to the Palestinian Ministry of health report in 2013 there are 800 patients on HD in the West Bank hospitals with 141 dialysis machines distributed among 10 hemodialysis units. Details are presented in Table 1.2 (Palestinian ministry of health, 2013).

Table (3.1): Distribution of Heamodialysis in MOH Hospitals by Hospital, West Bank, Palestine (annual report for 2013)

Hospital	Total dialysis	No. of patients	No. of machines	Total deaths
Jenin	11825	106	12	31
Tullkrm	9311	69	12	21
Nablus	23332	154	28	22
Qalqiliya	7570	46	9	5
Salfit	3014	22	7	0
Jerico	2996	24	7	5
Beit Jala	10338	79	12	19
Hebron	18165	155	26	0
Yata	4105	33	9	8
Ramallah	15498	112	19	0

3.3 Population of the study

All HD patients who have their HD sessions in Hebron governmental hospital during the study period and meet the inclusion criteria were asked to participate in the study.

Inclusion criteria: all adult patients who are on chronic HD during data collection period.

Exclusion criteria: patients who were younger than 18 years of age or patients who required HD for acute renal failure were excluded.

3.4 Sample size

All HD patients whom met the inclusion criteria in Hebron governmental hospital (the number was 158 patients during data collection period) were asked to participate in this study. All of them accepted to be involved.

3.5 Data collection

Data collection form was prepared after literature review of guidelines and previous studies (Appendix 1). All information were collected from the governmental electronic health records of Hebron governmental hospital (AviCenna HIS program), which was used to identify chronic HD patients. Oral consent was obtained from the patients. All of them accepted to be involved in the study. The file for every patient was reviewed; baseline demographics, comorbid conditions, vital signs, laboratory data, and information about the medications were collected. Regarding the medications, the last medication order was reported and for the laboratory tests the last reading in the file was documented. Also, patients were asked to answer some questions about sociodemoghraphic factors and medications purchased on his own accounts when data were not found in (AviCenna HIS program).

The study protocol was authorized by the Institutional Review Boards (IRB) of An Najah National University (Appendix 2) and the Ministry of Health (Appendix 3) before initiation of this study.

As we do not have our own national guidelines for treatment of ESRD patients, guidelines by the National Kidney Foundation Kidney Disease/Dialysis Outcomes Quality Initiative (NKF-KDOQI) and Kidney Disease: Improving Global Outcomes (KDIGO) were used to compare the practice (medications and target goals) in this study with these guidelines. These guidelines are very well-known and are being followed in many

countries. The secondary complications of CKD that are addressed in the currently available KDOQI guidelines include anemia of CKD, bone metabolism and disease, CVD in dialysis patients, dyslipidemias, hypertension, and nutrition. KDIGO clinical practice guidelines pertinent to CKD address evaluation and management of CKD, blood pressure, bone metabolism and disease, anemia, lipid management, hepatitis C in CKD, and glomerulonephritis (National Kidney Foundation, 2014). Nutrition and hepatitis C guidelines were not evaluated in this study, so the practice related to diabetes, hypertension, dyslipidemia, anemia and bone disease was included.

Table (3.2): Summary of KDOQI and KDIGO clinical practice guidelines

Recommended medications	Goals	Reference
Diabetes		
Insulin regimens Oral hypoglycemic agents should be used with caution (e.g. glyburide, glipizide, and glimepride) Metformin is contraindicated	HbA1c of around 7.0%	NKF, 2007 NKF, 2012
Hypertension		
ACE inhibitors or ARBs should be preferred	Predialysis BP <140/90mmHg Postdialysis BP <130/80mmHg	NKF, 2005
Dyslipidemia		
Statins are preferred Statins or statin/ezetimibe combination not to be initiated after HD if they were not used before	LDL cholesterol < 100 mg/dL Triglycerides < 500 mg/d	NKF, 2005 KDIGO, 2012
Anemia		
Erythropoietin stimulating (ESA) agent and iron	Hb level 11-12 g/dl Serum ferritin level > 200 ng/mL Transferin > 20% Hb level 9-11.5 g/dl Serum ferritin level > 500 ng/mL Transferin > 30%	NKF, 2007 NKF, 2006 KDIGO, 2012
Bone metabolism and disease		
Calcium-based phosphate binders and non calcium-, containing phosphate-binding agents (such as sevelamer HCl) Active vitamin D	Phosphorus 3.5 - 5.5 mg/dL Corrected total calcium 8.4 - 9.5 mg/dL PTH 150 - 300 pg/mL. Serum phosphorus and calcium in the normal range iPTH levels in the range of approximately 2-9 times the upper normal limit for the assay	NKF, 2003 KDIGO, 2009

3.6 Statistical Analysis

Statistical analysis was performed by using Statistical Package for Social Sciences (SPSS version 16.0) program. Descriptive statistics were carried out for all variables. Mean ± standard deviation was computed for continuous data. Frequencies (percentages) were calculated for categorical variables. Categorical variables were compared using Chi-square. When categorical and continuous variables were compared; independent student T test or Mann-Whitney test according to the normality were used. Association between continuous variables were assessed with pearsons or spearman according to the normality. kolmogrove smirnove test were used for normality. A p-value of less than 0.05 was considered to be statistically significant for all analyses.

Chapter Four

Results

Chapter Four
Results

4.1 Socio-demographic characteristics

The number of HD patients was 158 patients; 95 males (60.1%) and 63 females (39.9%). Age was between 18-92 years, the mean age was 49.6±18.0 years. The mean weights before and after dialysis were 72.87±20.0 kg, and 70.60±19.5 kg respectively, and the mean height was 166±8.9 cm. All the patients were from Hebron region, 75 (47.5%) of them were from the city, 82 (51.9%) were from the villages, and only one patient was (0.6%) from a camp. The highest percentage of participants had a middle school degree (39.2%). Most of HD patients (90.5%) were not working, and (17.7%) were still smoking. Socio-demographic characteristics of the patients are presented in (Table 4.1).

Table (4.1): Socio-demographic characteristics of the 158 patients

Characteristics	**Mean**	
Age	49±18 years	
Weight before dialysis	72.87±20 Kg	
Weight after dialysis	70.60±19.5 Kg	
Height	166±8.9 cm	
Characteristics	**Frequency**	**Percentage**
Patients' gender		
Male	95	60.1%
Female	63	39.9%
Living place		
City	75	47.5%
Village	82	51.9%
Camp	1	0.6%
Educational level		
Primary and illiterate	36	22.8%
Middle school	62	39.2%
High school	31	19.6%
University graduate	26	15.6%
Postgraduate	3	1.9%
working		
Yes	15	9.5%
No	143	90.5%
Smoking		
Smoker	28	17.7%
Not smoker	130	82.3%

4.2 Prescribing pattern for HD patients

During the study period 158 HD patients were prescribed 1567 medication orders of 103 different medications, 49 medications for the management of chronic illness, and 54 medications for acute illness. The patients were taking a minimum of 2 and a maximum of 18 medications, with a mean of 9.92±2.94 (Figure 4.1). The most commonly prescribed medications were calcium carbonate (91.8%), followed by alfacalcidol (84.8%), then iron/folic acid (69.6 %).

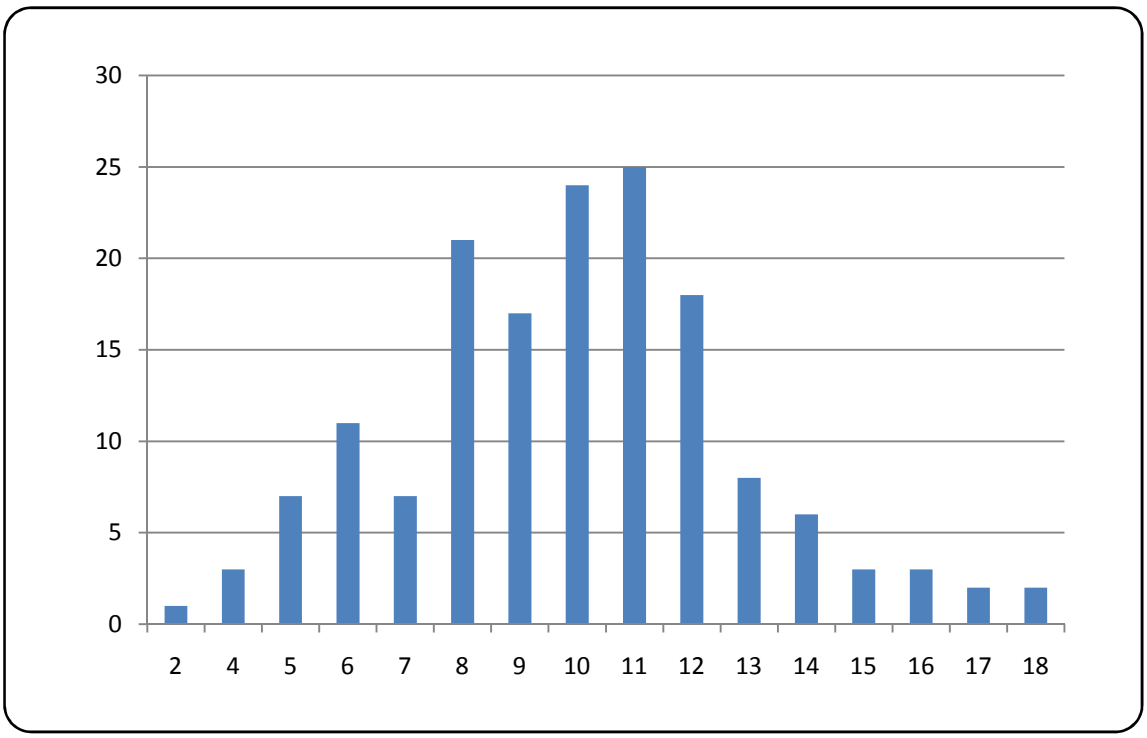

Figure (4.1): Number of medications used by the patients

The top twenty commonly used medications were calcium carbonate (oral), alfacalcidol (oral), iron/folic acid (oral), amlodipine (oral), paracetamol (oral), aspirin (oral), folic acid (oral), atorvastatin (oral), ranitidine (oral), insulin mixtard (SC), omeprazole (oral), furosemide (oral), diclofenac sodium (oral+IV), allopurinol (oral), ceftriaxone (IV), atenolol (oral), amoxycilline+clavulonic acid (oral), sevelamir (oral), chlorpheniramine (oral), and isosorbid-5-mononitrate (oral). There was a drug related problems as metformin was prescribed for 2 patients. All medications prescribed for HD patients are presented in (Table 4.2) for chronic illness, and in (Table 4.3) for acute illness.

Table (4.2): Prescribing pattern for chronic illness in 158 HD patients

NO.	Medication	Frequency	Percentage (%)
1	Calcium Carbonate	145	91.8%
2	Alfacalcidol	134	84.8%
3	Iron/ folic acid	110	69.6%
4	Amlodipine	105	66.5%
5	Aspirin	70	44.3%
6	Folic Acid	67	42.4%
7	Atorvastatin	63	39.9%
8	Insulin Mixtard	54	34.2%
9	Furosemide	43	27.2%
10	Allopurinol	32	20.3%
11	Atenolol	27	17.1%
12	Sevelamir	25	15.8%
13	Isosorbide-5-Mononitrate	22	13.9%
14	Carvidilol	18	11.4%
15	Clopidogrel	18	11.4%
16	Methyl Dopa	12	7.6%
17	Enalapril	11	7.0%
18	Isosorbid Dinitrate Sublingual	10	6.3%
19	Nifedipine	10	6.3%
20	Levothyroxine	8	5.1%
21	Erythropoitein	8	5.1%
22	Colchicine	6	3.8%
23	Doxazosin	6	3.8%
24	Mycophenolate Mofetile	6	3.8%
25	Budesonide	5	3.2%
26	Losartan	5	3.2%
27	Glibenclamide	4	2.5%
28	Cyclosporine	3	1.9%
29	Insulin Actrapid	3	1.9%
30	Tacrolimus	3	1.9%
31	Propranolol	3	1.9%
32	Valsartan	3	1.9%
33	Bisoprolol	2	1.3%
34	Digoxin	2	1.3%
35	Diltiazm	2	1.3%
36	Hydrochlorothiazide	2	1.3%
37	Metformin	2	1.3%
38	Sodium Bicarbonate	2	1.3%
39	Warfarin	2	1.3%

NO.	Medication	Frequency	Percentage (%)
40	Amiodarone	1	0.6%
41	Bezafibrate	1	0.6%
42	Capecitabine	1	0.6%
43	Cinacalcit	1	0.6%
44	Goserelin	1	0.6%
45	Methotrexate	1	0.6%
46	Propylthiouracil	1	0.6%
47	Rosvastatin	1	0.6%
48	Thalidomide	1	0.6%
49	Theophylline	1	0.6%

Table (4.3): Prescribing pattern for acute illness in 158 HD patients

NO.	Medication	Frequency	Percentage (%)
1	Paracetamol	76	48.1%
2	Ranitidine	61	38.6%
3	Omeprazole	50	31.6%
4	Diclofenac Sodium	37	23.4%
5	Ceftriaxone	32	20.3%
6	Amoxycillin/Clavulanic Acid	25	15.8%
7	Chlorpheniramine	24	15.2%
8	Bisacolyl	16	10.1%
9	Dexamethasone	15	9.5%
10	Cefuroxime	14	8.9%
11	Metronidazole	13	8.2%
12	Azithromycin	10	6.3%
13	Prednisolone	10	6.3%
14	Ciprofloxacin	9	5.7%
15	Loratidine	9	5.7%
16	Cephalexin	8	5.1%
17	Carbamazepine	7	4.4%
18	Teicoplanin	7	4.4%
19	Amoxycillin	6	3.8%
20	Metoclopramide	6	3.8%
21	Hyoscine N-Butyl Bromide	5	3.2%
22	Salbutamol	5	3.2%
23	Promethazine	4	2.5%
24	Sodium Polysterne sulphonate	4	2.5%
25	Betahistine	4	2.5%
26	Anti-Acid Suspension	3	1.9%
27	Betamethasone Cream	3	1.9%
28	Enoxaparin	3	1.9%
29	Fucidic Acid Cream	3	1.9%
30	Meropenem	3	1.9%
31	Human Albumin	2	1.3%
32	Ceftazidim	2	1.3%
33	Clobetasol cream	2	1.3%
34	Esomeprazole	2	1.3%
35	Lactulose	2	1.3%
36	Miconazole cream	2	1.3%
37	Vitamin B12	2	1.3%
38	Acyclovir	1	0.6%
39	Amitriptyline	1	0.6%

NO.	Medication	Frequency	Percentage (%)
40	Anti-Hemorroid	1	0.6%
41	Chloramphenicol ointment	1	0.6%
42	Clonazepam	1	0.6%
43	Codiene	1	0.6%
44	Fluconazole	1	0.6%
45	Indomethacine	1	0.6%
46	Mebendazole	1	0.6%
47	Meloxicam	1	0.6%
48	Miconazole Vaginal Tab	1	0.6%
49	Noirethisterone	1	0.6%
50	Nystain	1	0.6%
51	Phytomenadione	1	0.6%
52	Sodium Valproate	1	0.6%
53	Tramadol	1	0.6%
54	Vitamin E	1	0.6%

4.3 ESRD causes and comorbid conditions

Many causes can lead to the ESRD, for which HD should be initiated. A high number of HD patients in this study had no known cause of ESRD; 44 (27.8%), followed by diabetes in 36 (22.8%) cases, then hypertension in 21(13.3%) cases (Table 4.4).

Table (4.4): Causes of ESRD in the 158 HD patients

No.	Causes of ESRD	Frequency	Percentage (%)
1	Unknown	44	27.8
2	Diabetes	36	22.8
3	Hypertension	21	13.3
4	Small Kidney	15	9.5
5	Nephrotic Syndrome	9	5.7
6	Urinary Reflux	9	5.7
7	Kidney Stone	6	3.8
8	IV- Contrast	4	2.5
9	Familial Mediterranean Fever	3	1.9
10	Preeclampsia	3	1.9
11	Urinary Tract Infection	3	1.9
12	Polycystic Kidney Disease	2	1.3
13	Systemic Lupus Erythromatous	2	1.3
14	Rheumatoid Arthritis	1	0.6

Only 27 (17.1%) HD patients did not have other comorbid conditions. The majority of the patients 55 (34.8%) had one comorbid condition, while 41 (25.9%) had two comorbid conditions, 27 (17.1%) had three comorbid conditions, and 8 (5.1%) had four comorbid conditions.

Hypertension, diabetes, coronary heart disease, and heart failure respectively, were the most commonly comorbid conditions present in the HD patients, with different combination between these conditions in each patient. Among patients, 114 (72.2% had hypertension, 58 (36.7%) had diabetes and 29 (18.4%) had coronary heart disease (Figure 4.2).

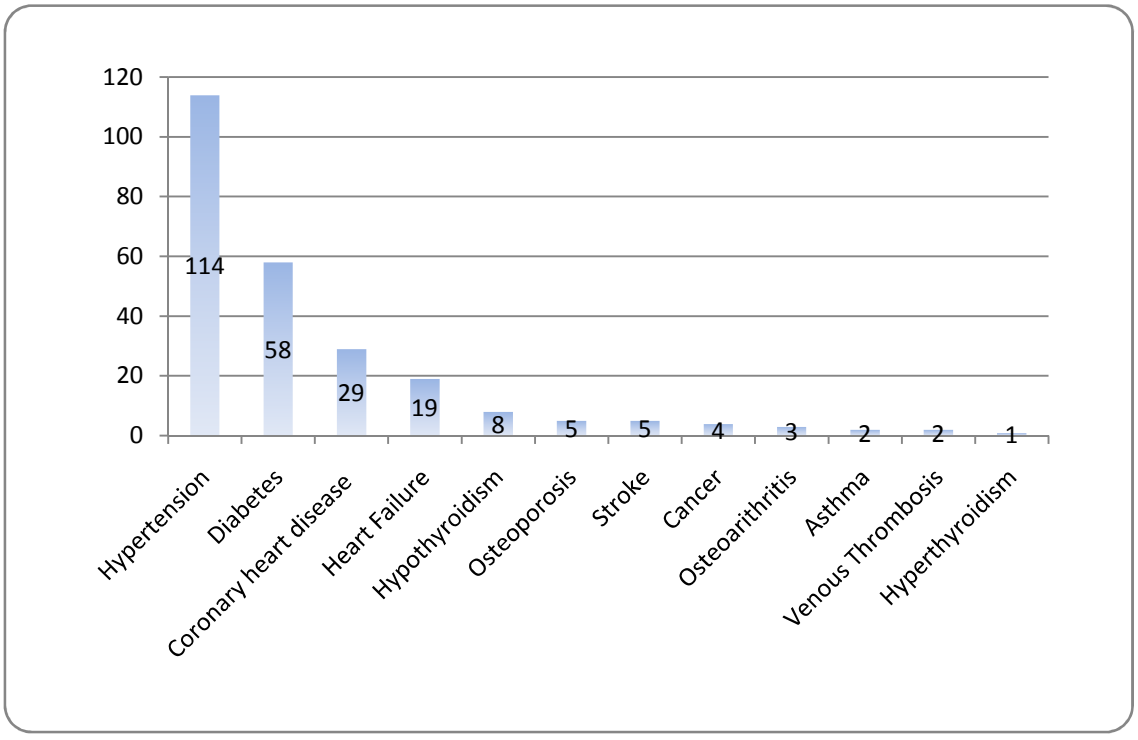

Figure (4.2): Comorbid conditions in HD patients (N=158)

4.4 Dialysis data

In this study there was one patient who spent 21 years on HD. One month was the minimum duration, and 252 months was the maximum. The

length of each dialysis session was 180 minute in most patients, other options were 210, or 240 minutes (Table 4.5), and the number of dialysis session per week were 1, 2, 3, and 4. Most of the patients had 3 sessions (Figure 4.3).

In HD patients, potassium level was measured for only 68 patients with a mean of 5.08±0.97 mg/dl and range (2.4-7.1 mg/dl). Blood urea nitrogen (BUN) and serum creatinine were measured for all patients and the mean was 67.65±24.31mg/dl (range 7.8-169 mg/dl) and 7.7±2.68 mg/dl (1.3-14.8 mg/dl) respectively.

Table (4.5): The length of each dialysis session

Length	Frequency	Percentage
180 minute	152	96.2%
210 minute	4	2.5%
240 minute	2	1.3%

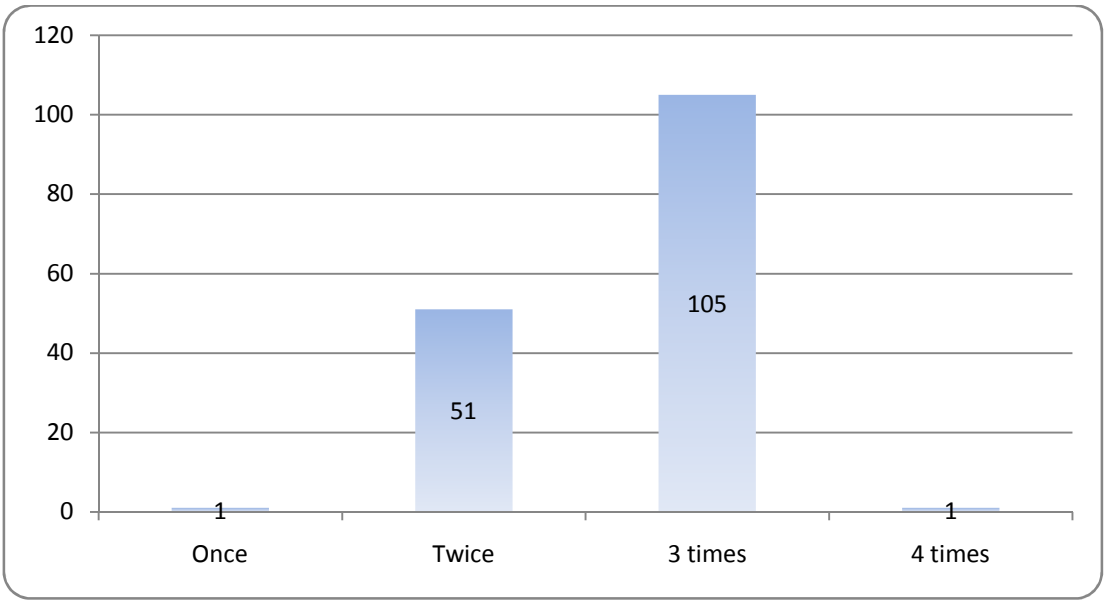

Figure (4.3): Number of dialysis sessions per week (N=158)

4.5 Compliance to treatment guidelines for diabetes

Fifty eight (36.7%) patients were found to have diabetes. Insulin mixtard was used by 54 of the patients, four were taking glibenclamide, three were taking insulin actrapid and two of them were on oral metformin. HgA1c was not performed in the hospital, and data about it was missing and there was no follow up for it.

Fasting blood sugar levels was tested for all HD patients who had or had not diabetes and random was tested for 41 patients, only 21 of them were diabetic. Among the 58 patients with diabetes, 25 (43.1%) patients had fasting blood sugar test < 130mg/dl, while random blood sugar test was performed for 21 diabetic patients, and 9 (42.8%) of them had their readings below 180mg/dl. No statistically significant association between diabetes control and any other related variable was found.

4.6 Compliance to treatment guidelines for hypertension

There were 114 (72.2%) HD patients who had hypertension. Many drugs were used by the HD patients, which controlled blood pressure and others comorbid conditions such as enalapril, losartan, valsartan, amlodipine, nifedipine, diltiazm, atenolol, bisoprolol, carvidilol, propranolol, methyldopa, doxazocin, hydrochlorothiazide, and furosemide. Amlodipine was the most commonly antihypertensive medication used by 105 (66.5%) of the patients.

The target predialysis blood pressure of less than 140/90 mmHg was achieved in 122 (77.2%) patients (70.5% of the males vs 87.3% of the

females; P- value = 0.014). On the other hand, postdialysis blood pressure of less than 130/80 mmHg was achieved in 91 (57.6%) patients only. There was no statistically significant association between postdialysis blood preessur and socio-demographic and clinical variables. Continuous variables of target predialysis blood pressure correlated with postdialysis blood pressure as pearsons test is significance (r = 0.236, p value = 0.003).

4.7 Compliance to treatment guidelines for dyslipidemia

Among the 158 patients, atorvastatin was used by 63 (39.9%), and rosvastatin, bezafibrate were used in one patient only. Total cholesterol and triglyceride were tested for the patients. The mean total cholesterol was 164±50.24 mg/dl ranging from 65 to 364 mg/dl. Patients with total cholesterol levels of less than 200 mg/dl were 123 (78.3%) patients from 157 for whom total cholesterol was measured. Regarding triglycerides levels, they ranged from 43 to 622 mg/dl. The majority of the patients 96.2% had triglycerides levels of <500 mg/dl. There was an association between the control of total cholesterol and triglycerides as 80.1% of the patients had total cholesterol of < 200 mg/dl (chi-sequr, p value = 0.006).

4.8 Compliance to treatment guidelines for anemia

Iron was used by 110 (69.9%) patients, and erythropoietin by 8 (5.1%) patients only. Mean hemoglobin level was 8.84±1.52 mg/dl with a range (5.8-14.4 mg/dl), Patients who reached goal Hb of 11-12 mg/dl according to the NKF guidelines were 14 (8.9%) patients only. If KDIGO guidelines are used, these guidelines accept a Hb level between 9-11.5

mg/dl but not to exceed 13 mg/dl, the patients in this range reach 68 (43.0%) cases.

Target ferittin level of > 200 ng/ml according to NKF guidelines was achieved in 91 (57.6%) patients. Target ferittin level of > 500 ng/ml according to KDIGO guidelines was achieved in 74 (46.8%) cases. There were no data available about ferittin level for 51 (32.3%) patients. Transferin test was not performed for all the patients.

No statistically significant association between anemia control and socio-demographic or clinical factors was found.

4.9 Compliance to treatment guidelines for bone mineral disorder

There was no data available for calcium, or PTH levels in HD patients. Only phosphorus level was measured but not for all the patients. Calcium carbonate was used by 145 (91.8%) patients, sevelamir by 25 (15.8%) patients, and alfacalcidol by 134 (84.8%) patients. Phosphorus target level of 3.5-5.5 mg/dl according to the NKF guidelines was achieved in only 19 (12.0%) patients, 128 (81.0%) had phosphorus levels out of the target, and 11 (7.0%) of the patients had no data. If serum phosphorus normal range of 2.5–4.5 mg/dl is used according to KDIGO guidelines, this target was achieved in 7 (4.4%) patients only.

Chapter Five

Discussion

Chapter Five
Discussion

5.1 Prescribing pattern for HD patients

In this study, the 158 HD patients were prescribed 1567 medications of 103 different drugs with a mean of 9.92±2.94. The number of medications in this study is close to other studies that included CKD and ESRD patients where the mean was around 9 medications. (Al Ramahi, 2009; Bajait *et al*., 2014). However, this is lower than other study where the mean of medications prescribed for HD patient reached 12.3 ±0.5 medications (Manley *et al.*, 2004), and higher than other study where the mean was 7.2 medications (Tozawa et al., 2002). Polypharmacy is common and expected among HD patients, this increases the possibility of drug-related problems, and the need for extra counseling and monitoring. For example metformin which is contraindicated for HD patients is still used.

The most commonly prescribed medications for HD patients in this study were calcium carbonate (91.8%), followed by alfacalcidol (84.8%), then iron/folic acid (69.6 %). This is expected based on the complications of the disease. A study conducted at a nephrology unit in a Malaysian hospital showed that calcium carbonate was the most commonly prescribed medication also, followed by a combination of folic acid and vitamin B complex, and the third commonly prescribed medication was metoprolol (Al Ramahi, 2009). In a study from India, the five most commonly prescribed drugs were multivitamins, iron, folic acid, calcium carbonate, and calcitriol (Bajait et al., 2014).

5.2 ESRD causes and comorbid conditions

In Palestine, one study to evaluate major risk factors that lead to End-Stage Renal Disease in Northern West Bank was found; it showed that main risk factors that lead to ESRD were chronic diseases such as diabetes mellitus, hypertension, cardiovascular disease, in addition to urinary tract infections. It showed that 46.4% of ESRD patients had diabetes mellitus, 50.8% had hypertension, 31% had cardiovascular disease, 16.7 % had kidney stone, 11.9% had congenital abnormality and 25.6% had urinary tract infection (Basheer, 2011). In this study, the same chronic diseases were very common among patients where 114 (72.2%) had hypertension, 58 (36.7%) had diabetes and 29 (18.4%) had coronary heart disease. Regarding the documented causes of ESRD, unknown causes accounted for (27.8%) of the cases, followed by diabetes (22.8%), hypertension (13.9%), and small kidney (9.5%). These are well known causes of ESRD worldwide, that is why it is important to control diabetes and hypertension to prevent the progress of CKD.

5.3 Compliance to treatment guidelines for diabetes

In this study, 58 (36.7%) patients had diabetes, among them, 54 were on mixtard insulin, 4 were on glibenclamide, 3 were on actrapid insulin and 2 were on metformin. According to the NKF guidelines insulin and glibenclamide are accepted choices to be used. First generation sulfonylureas (e.g., chlorpropamide, tolazamide, and tolbutamide) should be avoided in patients with CKD because they have increased half-lives

and the risk of hypoglycemia. Glipizide is the preferred second-generation sulfonylureas as it does not have active metabolites and does not increase the risk of hypoglycemia in patients with CKD (National Kidney Foundation, 2012).

Regarding metformin is cleared by the kidneys, so its use in CKD is restricted. Black-box warning was mandated by the FDA regarding the risk of lactic acidosis. The label indicates that metformin should not be used in men with a SCr of 1.5 mg/dL or in women with a SCr of 1.4 mg/dl (National Kidney Foundation, 2012), two patients in this study were prescribed this medication.

The guidelines evaluate diabetes control according to Hb A1c test. In this study no HbA1c values were available in the files and these tests were not performed for diabetic hemodialysis patients. Fasting and random blood glucose levels were the only available tests. Fasting blood glucose test was done for all HD patients once every month, it is recommended to test blood glucose frequently for diabetic patients. However, measuring glucose levels in patients without diabetes with this frequency might not be needed. Among the 58 patients with diabetes, 25 (43.1%) patients had fasting blood sugar test < 130mg/dl, while random blood sugar test was performed for 21 diabetic patients, and 9 (42.8%) of them had their readings below 180mg/dl. The American Diabetes Association recommends preprandial plasma glucose of < 130 mg/dl and postprandial levels of < 180 mg/dl for diabetic patients in general (Wells *et al.*, 2012). It can be noticed here that more than half of diabetic patients did not achieve

these levels. Treatment of diabetes in HD patients needs to be improved, monitoring of Hb A1c is needed to guide treatment.

5.4 Compliance to treatment guidelines for hypertension

In this study 114 (72.2%) of HD patients had hypertension, this is expected and similar to other parts of the world where 60% to 90% of maintenance HD patients have hypertension. Hypertension in these patients often is poorly controlled despite the use of multiple medications (National Kidney Foundation, 2006).

In this study many drugs were used, to controlled blood pressure and others comorbid conditions such as enalapril, losartan, valsartan, amlodipine, nifedipine, diltiazm, atenolol, bisoprolol, carvidilol, propranolol, methyldopa, doxazocin, hydrochlorothiazide, and furosemide. Amlodipine was the most commonly antihypertensive medication used by 105 (66.5%) of the patients, 11 (7%) were on enalapril, 5 (3.2%) were on losartan, and 3 (1.9%) were on valsartan. This low use of ACE inhibitors and ARBs is not in agreement with the NKF recommendations in which drugs that inhibit the renin angiotensin system are preferred for the management of hypertension in HD patients to decrease cardiovascular risk (National Kidney Foundation, 2005). In a review by Enam et al in 2014, they consider beta-Blockers, CCBs, ACE inhibitors, and ARBs as appropriate primary choices for HD patients.

The target predialysis blood pressure of < 140/90 mmHg was achieved in 123 (77.8%) patients, while postdialysis blood pressure of <

130/80 mmHg was achieved in 91 (57.6%) patients only. This is better than recent results from Tulkarem HD unit where 33 (51.6%) patients attained predialysis blood pressure goals of <140/90 mm Hg and 31 (48.4%) reached the postdialysis goal of < 130/80 mm Hg. (Adas et al., 2014). However, there is a room for improvement. To control blood pressure, not only medications are important, restrictions in sodium and fluids are recommended.

According to the NKF control of blood pressure is a worldwide problem. For example, among the first 1,238 maintenance HD patients enrolled in the HEMO Study, less than 30% had blood pressures that were considered normotensive. In another study of 2,535 clinically stable adult HD patients, 86% were found to be hypertensive. Within this hypertensive group, only 30% had their blood pressure under adequate control, 58% were inadequately treated, and 12% were not treated at all (National Kidney Foundation, 2006).

Predialysis and postdialysis blood pressure goals were not achieved in a high percentage of patients. This may be related to inadequate hemodialysis, inadequate antihypertensive medications or non-compliance with the restrictions of sodium and fluid intake. Hypertension increases cardiovascular risk in hemodialysis patients; therefore, it is very important to control it (Adas et al., 2014).

Fluid accumulation between dialysis sessions can be managed with education and counseling, low sodium intake, increased ultrafiltration,

longer dialysis and > 3 dialysis treatments per week (National Kidney Foundation, 2005). Postdialysis blood pressure correlated with predialysis values, so if it is possible to control BP between sessions, the control will improve after dialysis also.

5.5 Compliance to treatment guidelines for dyslipidemia

According to the NKF, LDL cholesterol levels should be below 100 mg/dL, and statin can be used to achieve this target. In this study LDL levels were not tested, instead, total cholesterol and triglycerides were measured, atorvastatin was used by (39.9%), and rosvastatin, bezafibrate were used in one patient only. The mean total cholesterol was 164±50.24 mg/dl ranging from 65 to 364 mg/dl. Patients with total cholesterol levels of < 200 mg/dl were 123 (78.3%). Regarding triglycerides levels, they ranged from 43 to 622 mg/dl. The majority of the patients 151 out of 157 (96.2%) had triglycerides levels of <500 mg/dl. Dyslipidemia may increase risk of ischemic stroke and cardiovascular mortality. The control of dyslipidemia in this study is better than other conditions and complications as most of the patients have accepted levels of total cholesterol and triglycerides, however, it is recommended to test LDL cholesterol and concentrate on dietary counseling.

5.6 Compliance to treatment guidelines for anemia

In this study complete blood count was done periodically once a month, and (91.1%) of the HD patients had anemia defined as Hb levels < 11mg/dl according to the National Kidney Foundation guidelines (2007)

and even If KDIGO guidelines are used, these guidelines accept a Hb level between 9-11.5 mg/dl but not to exceed 13 mg/dl, the patients in this range were 68 (43.0%) cases which means that many patients in the study are anemic. Renal data from the Arab World, showed that control of anemia, was not satisfactory as 50% of study patients had Hb levels < 10 g/dl in 103 HD patients in Libya (Buargub *et al.*, 2006). Anemia and mortality in HD patient study estimated that 95% of HD patients receive treatment for anemia (Robinson *et al.*, 2005).

According to NKF the ESAs are critical components in managing the anemia of CKD, where IV administration is preferred, and effective use of iron agents, guided by appropriate testing of iron status is recommended. Iron was used in (69.9%) of the patients, but erythropoietin IV route was used by 8 (5.1%) out of 158 patients only, as it was not available during study period in the hospital due to financial problems in the MOH, this medication is very expensive to be purchased by the patients. Target ferittin level of > 200 ng/ml according to NKF guidelines was achieved in 91 (57.6%) patients. Target ferittin level of > 500 ng/ml according to KDIGO guidelines was achieved in 74 (46.8%) cases. There were no data available about ferittin level for 51 (32.3%) patients. Transferin test was not performed for all the patients. It is clear that better treatment for anemia is recommended and more investigations are needed.

5.7 Compliance to treatment guidelines for bone mineral disorders

According to NKF Serum levels of calcium, phosphorus, and PTH should be measured in all patients with CKD and GFR<60 mL/min/1.73m^2.

A study in Libya in 2006 found that the target serum level of intact parathyroid hormone (PTH) was reached in 17.4% of the patients, and only 30% of the patients achieved target serum calcium (8.4-9.5 mg/dl) (Buargub *et al.*, 2006). But in this study calcium and parathyroid hormone serum level were not measured for the patients, because they are not available in the hospital's laboratory, and are very expensive to be done out in private laboratories. During this study period only one patient did these tests on his own account. Almost all the patients (91.8%) were taking calcium carbonate, in addition to (84.8%) were taking alfacalcidol to reduce the serum levels of PTH to a target range of 150 to 300 pg/mL as recommended by NKF. Target phosphorus level of (3.5-5.5 mg/dl) was reached in (12%) of the HD patients, and according to KDIGO guidelines, this target was achieved in 7 (4.4%) patient. Only 25% of the HD patients were taking phosphate binder sevelamir. Management of chronic kidney disease mineral and bone disorder requires interdisciplinary team interventions that include dietary modification, medications, and adequate dialysis therapy. Optimizing adherence to diet and medications requires an educated and motivated patient, and patient support system (McCann and Hoefs, 2014).

In summary, compliance to treatment guidelines was low. However, there is a room for improvement. The clinical pharmacist can play an important role in this field to increase awareness, participate in the therapeutic process, and pharmaceutical policies to improve HD patient's quality of life, and to decrease morbidity and mortality.

5.8 Limitations and strength

The first limitation of this study is that the answers reported by the respondents cannot be validated, but this cannot be avoided. Another limitation is the study was performed in dialysis center in Hebron Governmental Hospital so it might not be representative to the practice in other dialysis centers in other hospitals. Third limitation is the unavailability of many medications, and laboratory tests which are important to measure compliance to treatment guidelines. The last limitation was the unavailability of national guidelines to compare with and the presence of different international guidelines.

This study is the first of its type in Palestine, and in the Arab world. Also it is one of the few in the world. However, these results can give a baseline data that can be useful in designing and implementing suitable interventions, educational programs and performing other related studies.

5.9 Conclusions

This study shows a poor level of compliance to treatment guidelines according to NKF and KDIGO guidelines for diabetes, hypertension, dyslipidemia, anemia, and bone mineral disorder, where target levels for treatment are not achieved in many HD patients. The medications are not prescribed optimally to the patients and many required investigations and laboratory tests are not performed.

5.10 Recommendations

To achieve a good compliance to treatment guidelines in HD patients, cooperation between patients, doctors, dietitians and clinical pharmacists is needed. In each HD department a nephrologist, and a clinical pharmacist should be available to follow up the patients. All the laboratory test, and medications to control diabetes, hypertension, dyslipidemia, anemia (especially ESA), and bone mineral disorder should be available, which is the responsibility of the ministry of health. Based on this study, the following points are recommended;

For diabetes mellitus, it is recommended to have HbA1c or glycated albumin tests for all diabetic HD patients as recommended. However, there is no need to measure glucose levels in patients without diabetes with this frequency.

For hypertension, it is recommended to increase the use of ACE-I and ARBs in HD patients due to their advantages as cardioprotective agents. Patients may need better counseling on sodium and fluids intake, longer HD sessions or more antihypertensive medications to reach the recommended blood pressure goals.

For dyslipidemia, it is recommended to test LDL cholesterol and concentrate on dietary counseling.

For anemia, it is recommended to increase the use of ESA and make it available because it is an important medication for anemia in HD

patients. It is also recommended to optimize the required tests to guide the suitable treatment.

For bone mineral disorders, it is recommended to test PTH, calcium and phosphorus for all patients to guide the suitable treatment.

It is highly recommended to add a clinical pharmacist to the healthcare team for HD patients because these patients use a large number of medications and require frequent counseling and investigations.

It is recommended to review the international guidelines in this field and develop our national guidelines to be followed by all our HD units.

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Appendices

Appendix (1) Data collection form

This study was designed to evaluate prescribing pattern and compliance to treatment guidelines in HD patients, with the knowledge that this information will be used for the purposes of scientific research and will be treated strictly confidential.

Serial Number:

File Number:

Personal Data:

1- Sex: _ Male _ Female

2- Age:

3-Weight:

4-Hight:

5- work:_ Yes _ No

6- -Living place: _City _ Village _ Camp

7- Are you a smoker: _ No _ Yes

8-Educational level: □ Primary and illiterate □ middle school □ high school □ graduate □ post graduate

Laboratory Blood Test of the Patient:

Test	Level	Test	Level
9-Hemoglobin level		17-SrCr level	
10-Ferittin level		18-Cholesterol level	
11-Transferin level		19-Triglyceride level	
12-Potassium level		20-Fasting blood sugar	
13-Calcium level		21-Random blood sugar	
14-Phosphorus level		22-HgA1C	
15-PTH level		23-Perdialysis blood pressure	
16-BUN level		24-Postdialysis blood pressure	

Medical History of the Patient:

25-Cause of ESRD (If Known):

26-Other comorbid conditions:

A.	C.	E.
B.	D.	F.

27-The duration of dialysis (months):

28-Number of dialysis session in a week:

29-The length of each dialysis session (minutes):

30- List of all medication taken by the patient:

	Medication	Strength	Dose & Frequency
A.			
B.			
C.			
D.			
E.			
F.			
G.			
H.			
I.			
J.			
K.			
L.			
M.			
N.			
O.			
P.			
Q.			
R.			

Appendix (2) IRB Approval letter

بسم الله الرحمن الرحيم

An - Najah National University
Faculty of Medicine & Health Sciences
Department of Graduate Studies

جامعة النجاح الوطنية
كلية الطب وعلوم الصحة
دائرة الدراسات العليا

IRB Approval letter

Study title:
Evaluation of Prescribing Pattern and Compliance to Treatment Guidelines in Hemodialysis Patients in Hebron Governmental Hospital

Submitted by:
Bayan Jamal Al-Deen Nammourah

Date Reviewed:
Jan 30 , 2014

Date approved:
Feb 9, 2014

Your study titled: **"Evaluation of Prescribing Pattern and Compliance to Treatment Guidelines in Hemodialysis Patients in Hebron Governmental Hospital"** Was reviewed by An-Najah National University IRB committee & approved on Feb 9, 2014.

Samar Musmar,MD, FAAFP

IRB Committee Chairman,
An-Najah National University

IRB

نابلس - ص.ب 7 أو 707 هاتف 14/8/7/4/2342902(09)(970)، فاكسميل 2342910 (09) (970)
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Appendix (3) MOH Approval letter

State of Palestine
Ministry of Health - Nablus
General Directorate of Higher & Continuing Education

دولة فلسطين
وزارة الصحة- نابلس
الإدارة العامة للتعليم الصحي

Ref.: .....
Date:.....

الرقم: ٢٠١٤/٨٧٨/١٦٠٤
التاريخ: ٢٠١٤/٤/١٣

الأخ مدير عام الادارة العامة للمستشفيات المحترم،،،

تحية واحترام،،

الموضوع: تسهيل مهمة طلاب كلية الصيدلة – جامعة النجاح

تماشياً مع سياسة وزارة الصحة المتعلقة بتعزيز التعاون مع الجامعات والمؤسسات الأكاديمية بإتاحة فرص التدريب أمام الطلبة والخريجين والباحثين في المؤسسات الوطنية وإسهاماً في تنمية قدراتهم.

يرجى تسهيل مهمة الطالبة بيان جمال الدين نمورة – تخصص صيدلة– كلية الطب وعلوم الصحة / جامعة النجاح، في عمل بحث بعنوان " Evaluation of Prescription Pattern and Compliance to Treatment Guidelines in Hemodialysis Patients in Hebron Governmental Hospital" وذلك من خلال السماح للطالبة بمراجعة ملفات المرضى لتجميع معلومات عن ادويتهم وفحوصاتهم وقد تحتاج الطلب منهم الاجابة على استبانة بسيطة عن بعض المعلومات التي يحتاجها لانجاز البحث. علما بانه سيتم الالتزام بمعايير البحث العلمي والحفاظ على سرية المعلومات. وذلك في مستشفى الخليل الحكومي.

مع الاحترام،،

د. أمل أبو عوض
ق. أ. مدير عام التعليم الصحي

نسخة: مدير دائرة الصيدلة المحترم/ جامعة النجاح

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جامعة النجاح الوطنية
كلية الدراسات العليا

تقييم نمط الأدوية الموصوفة ومدى الالتزام بالخطط العلاجية لدى مرضى الغسيل الكلوي في مستشفى الخليل الحكومي

إعداد
بيان جمال الدين نمورة

إشراف
د. رواء الرمحي

قدمت هذه الأطروحة استكمالا لمتطلبات الحصول على درجة الماجستير في الصيدلة السريرية بكلية الدراسات العليا في جامعة النجاح الوطنية في نابلس، فلسطين.
2015م

تقييم نمط الأدوية الموصوفة ومدى الالتزام بالخطط العلاجية لدى مرضى الغسيل الكلوي في مستشفى الخليل الحكومي

إعداد

بيان جمال الدين نمورة

إشراف

د. رواء الرمحي

الملخص

تعتبر أمراض الكلى المزمنة بما فيه الفشل الكلوي من الأوبئة المتنامية، حيث يعد غسيل الكلى هو العلاج الأكثر شيوعا بالإضافة إلى علاج الأمراض المترافقة معه كمرض السكري وارتفاع ضغط الدم، خلل دهنيات الدم، وفقر الدم، واضطراب المعادن في العظام. وتبرز أهمية هذه الدراسة في تقييم نمط الأدوية الموصوفة ومدى الالتزام بالخطط العلاجية لدى مرضى غسيل الكلى.

هذه الدراسة هي عبارة عن دراسة وصفية تم تطبيقها في مستشفى الخليل الحكومي / فلسطين، خلال الفترة منذ بداية شهر آذار حتى نهاية شهر نيسان 2014، واشتملت على جميع مرضى الغسيل الكلوي خلال فترة جمع المعلومات التي تمت من خلال استخدام السجل الصحي الإلكتروني الحكومي (برنامج ابن سينا HIS)، وطلب من المرضى الإجابة على بعض الأسئلة عندما لم يتم العثور على البيانات في النظام، وتم تحليل البيانات بواسطة البرنامج الاحصائي SPSS.

اشملت الدراسة على 158 مريض غسيل كلوي وصفت لهم 1567 وصفة علاجية ل 103 صنف من الأدوية المختلفة، حيث بلغ عدد الأدوية التي يتناولها المريض بما لا يقل عن 2 ولا يزيد عن 18 نوع ، بمتوسط 2.94 ± 9.92. وكانت الأدوية الموصوفة الأكثر شيوعا كربونات الكالسيوم (91.8٪)، تليها الالفاكلسيدول (84.8)٪، ثم الحديد / حمض الفوليك (69.6٪). كانت نسبة المرضى المصابين بمرض السكري حوالي (36.7)، ولم يتم تنفيذ اختبار HbA1c لهؤلاء المرضى التي تعكس متوسط نسبة السكر في الدم خلال الثلاثة شهور الماضية.

وبلغت نسبة الاصابة بمرض ارتفاع ضغط الدم لدى المرضى (72.2٪)، وكان دواء الاملوديبين هو اكثر الادوية الموصوفة لمريض الغسيل الكلوي المصاب بارتفاع ضغط الدم، وتحقق ضغط الدم المرجو قبل وبعد عملية الغسيل لدى (77.2٪) و (57.6٪) من المرضى على التوالي، كان ضغط الدم المرجو قبل الغسيل افضل لدى الاناث منه لدى الذكور. وكان هنالك علاقة بين ضغط الدم المرجو قبل وبعد عملية الغسيل (r=0.236,P-value=0.003). استخدم دواء الاتورفاستاتين لعلاج (39.9%) من المرضى وتحقق مستوى الكوليسترول المرجو لدى (78.3٪) من المرضى والدهنيات الثلاثية لدى (96.2%) منهم، ووجد ان هنالك علاقة ايجابية ما بين تنظيم مستوى الكوليسترول وتنظيم مستوى الدهنيات الثلاثية لدى هؤلاء المرضى. ان مستوى الهيموغلوبين المطلوب لدى مرضى الغسيل الكلوي > 11 ملغ/ ديسيليتر حسب تصنيف NKF تحقق لدى (8.9٪) من المرضى واكثر من 9 ملغ/ ديسيليتر حسب تصنيف KDIGO في (43%) من الحالات. استخدم دواء الحديد/ الفوليك اسيد لدى (69.9%) من المرضى، بينما استخدم دواء المحفز لتصنيع الايريثروبوتن عند (5.1%) من المرضى لعدم توفيره من قبل وزارة الصحة الفلسطينية وصعوبة شراؤه من قبل المريض لارتفاع أسعاره. لا توجد بيانات متاحة عن مستوى الكالسيوم، وهرمون الغدة الدرقية لإدارة اضطراب المعادن في العظام، لكن مستوى الفوسفور المستهدف تحقق لدى (12٪) من المرضى حسب تقسيم NKF ولدى (4.4%) من المرضى حسب تقسيم KDIGO. واستخدم الكالسيوم كاربونات لدى 91.8%، السيفيلامير لدى 15.8%، ودواء الالفاكالسيدول لدى 84.8% من مرضى الغسيل الكلوي.

إن هذه النتائج تعكس سوء الامتثال للمبادئ العلاجية لدى مرضى الغسيل الكلوي المصحوب بأمراض أخرى كمرض السكري، وارتفاع ضغط الدم، خلل دهنيات الدم، فقر الدم، واضطراب المعادن في العظام بالمقارنة مع المبادئ العلاجية ل NKF و KDIGO ، حيث تحققت المستويات المستهدفة للعلاج في أعداد صغيرة من مرضى الغسيل الكلوي وكانت الأدوية لا توصف على النحو الأمثل للمرضى والعديد من الاختبارات والفحوص المخبرية غير موجودة ولا يتم تنفيذها.