IMPACT OF PATIENT EDUCATION BY CLINICAL PHARMACIST ON MEDICATION ADHERENCE AND QUALITY OF LIFE IN HEMODIALYSIS PATIENTS

Dissertation submitted to Kerala University of Health Sciences

in partial fulfil

DOCTOR OF PHARMACY

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MAY 2023

ABSTRACT

INTRODUCTION

Chronic kidney disease (CKD) is a growing health problem in India, and it is estimated that more than 17% of the adult population in India has some form of kidney disease. It is an irreversible progressive condition with high morbidity and mortality by means of an increase in incidence and prevalence, poor outcomes along with high cost. Lifelong treatment and lifestyle modifications are difficult to adapt, which significantly impairs treatment adherence and quality of life (QOL).

Hemodialysis is a viable, safe, efficient method for the maintenance of patient with CKD progressing to end stage renal disease (ESRD). The patients are dialysed twice or three times per week for approximately 4 hour per session. Failure of adherence in Hemodialysis can lead to increased morbidity, mortality, cost, and burden on health care system. As kidney disease advances, dangerous levels of waste can rapidly build up inside the body. Treatment aims to stop or slow the progression of kidney dysfunction by controlling the underlying cause. ESRD patients are usually on complex drug regimens, with about 8-10 medications daily, many of which require multiple doses per day. Due to polypharmacy, medically unstable nature of the disease and restricted lifestyle, dialysis patients are at increased risk of non-adherence and drug-related problems. Education and counselling programs are mandatory in ESRD population for their better QOL and to improve the treatment adherence.

AIM

To assess the impact of patient education by clinical pharmacist on medication adherence and quality of life in hemodialysis patients.

OBJECTIVES

- To assess the medication adherence in hemodialysis patients using specially designed and validated questionnaire.
- To assess the quality of life of patients on hemodialysis using KDQOL SF 36 version 1.3.

- To correlate medication adherence with quality of life.
- To document the pharmacological management of complications in CKD patients undergoing hemodialysis.

METHODOLOGY

STUDY DESIGN

- A prospective, observational, comparative single centered study.

STUDY PERIOD

- A six-month study was designed using prospective data.

STUDY SETTING

This study was carried out in Lourde's Hospital, Post Graduate Institute of Medical Science and Research, Ernakulam - 682 012, Kerala, India, which is a 500 bedded multi-specialty tertiary care hospital with a wide range of amenities. The institution is equipped with 7 super specialty department and 22 other departments with facilities comprising 12 operation theatres, 10 intensive care units and a computerized Lourdes Mediware system. Clinical laboratories with ISO standards. It is one of the top most hospitals in Kerala.

STUDY SAMPLE

The sample size was calculated by the formula,

$$n = (z^2 \times pq) \div m^2$$

Were,

z - statistic corresponding to the level of confidence 1.96

P - expected prevalence = 19.71

q- 100-p

m- allowable error=10

The minimum sample size required was found to be 61.

METHOD OF SELECTION

Patients was selected based on inclusion and exclusion criteria

Inclusion criteria

- CKD patients of either gender aged above 18 years.
- Patients undergoing hemodialysis at least twice weekly.

Exclusion criteria

- CKD patients with psychiatric illness.
- Patients with multiple organ failure, malignancies, memory impairment, unconscious, severely disabled.
- Patients with reported hearing problem and blindness.

DATA COLLECTION METHOD

- Lourdes mediware system.
- Specially designed data collection form.
- Patients medical record.
- Specially designed medication adherence questionnaire.
- KDQOL-SF™ (Kidney Disease And Quality Of Life™ Short Form Version 1.3).

STUDY METHOD

- A prospective, observational, comparative single centered study.
- The study population consisted patients undergoing hemodialysis from the Nephrology department of Lourdes Hospital, Ernakulam.
- The study period was from November 2022 to April 2023 which include pre and post analysis on medication adherence and quality of life.
- Patients were selected based on inclusion and exclusion criteria after obtaining written consent of the patient.
- Medication adherence of the hemodialysis patients was evaluated by specially designed and validated questionnaire and quality of life was evaluated by KDQOL SF 36.

- Patients were given additional information related to medications with the help of specially designed patient information leaflet.
- Follow up was done after three months to assess medication adherence and quality of life.

RESULT AND DISCUSSION

We included a total of 74 patients who met the inclusion criteria for the study. The mean age of the study population was 58.95±10.09 years, with male patients dominating with 67.6%. About 81.1% of patients were undergoing dialysis twice a week. The dominating comorbidity was Hypertension (25.7%), followed by Hypertension and Cardiovascular disease (24.3%) and Hypertension, Diabetes and Cardiovascular disease (13.5%)

During pre-test there were only 39.2% patients showing high adherence to medications and it was increased to 91.9% after patient education by clinical pharmacist. There were 48.6% patients in the medium adherence level during pre-test. It was decreased to 8.1% during post-test. Though there were 12.2% patients with poor medication adherence in the pre-test, there were no patients in the study group with poor adherence in the post test.

There were no patients showing good quality of life in the pre-test. It was increased to 43.2% after patient education by clinical pharmacist. There were 41.9% patients showing average quality of life during pre-test. It was increased to 56.8% during post-test. However, there was 58.1% patients with poor quality of life in the pre-test, but there were no patients in the study group with poor quality of life in the post test.

The study revealed remarkable difference in the scores (mean ± standard deviation) of medication adherence, overall quality of life and 3 components of KDQOL. The scores after patient education were improved as medication adherence (8.8±1.41), Overall quality of life (2467.4±268.72) and 3 components of KDQOL (PCS-448.6±108.61, MCS-546.1±125.16, KDCS-1472.6±123.94) and was proved using paired-t test.

Among the three dimensions of QOL, i.e., physical component summary, mental component summary and kidney disease component summary, the respondents had higher score for kidney disease component summary in compare to that of mental component summary and Physical Component summary

Pearson correlation coefficient shows a significant positive correlation between medication adherence and quality of life (0.230) ie, as medication adherence increases, quality of life is also increasing. The components of QOL also shows positive correlation with the adherence pattern

Chronic kidney disease patients on hemodialysis receive multiple medications on long-term basis. On assessing the pharmacological management of complications in CKD patients, most of the patients in our study site were having Hypertension as the complication and it was mainly managed by Nifedipine and Clonidine. Patients with cardiovascular disease and Hypertension were managed mainly with aspirin and clopidogrel along with nifedipine, clonidine combination. Diuretics were not effective in controlling hypertension but it was used in patients with fluid retention. Hyperphosphatemia is associated with vascular calcification and bone mineral disorders and is a major concern of patients with chronic kidney disease. In our study site hyperphosphatemia were managed by using the first line agent calcium acetate and then the combination of calcium acetate with non-calcium based phosphate binders and mineral bone disorders with calcitriol. Anemia was the next common clinical problem in the CKD patient, in our study site and it was mainly managed by using Inj Erythropoetin.

The main therapy objective for CKD patients is to increase patient compliance and QOL. The treatment adherence and overall QOL of ESRD patients are significantly impacted by patient education. Clinical pharmacist activities improved the patients drug/disease knowledge, adherence to drug dosage regimen. This improvements in both medication adherence as well as overall quality of life might be due to the additional care given by the clinical pharmacists as it was the only additional care given to the study sample during this study period.

CONCLUSION

The impact of additional care by clinical pharmacist have resulted in improvement of medication adherence and overall quality of life of the patients with a positive correlation between them. Due to heavy patient load doctors may not get enough time to explain in detail about each drugs and importance of adherence to treatment to manage concomitant diseases and complications of chronic kidney disease. This gap can be filled by the clinical pharmacists as there is improvement in medication adherence and in each components of quality of life of patients due to the additional education imparted by the clinical pharmacists. Combination therapy was preferred to manage complications such as hypertension, electrolyte abnormalities and Anemia.

INTRODUCTION

Chronic kidney disease can be defined as the structural or functional irregularities of the Kidney which is present for > 3 months with implications for health and which are classified based on cause, glomerular filtration rate (GFR) and albuminuria[1]. It is an irreversible progressive condition with high morbidity and mortality by means of an increase in incidence and prevalence, poor outcomes along with high cost[2].

Chronic kidney disease (CKD) is a growing health problem in India, and it is estimated that more than 17% of the adult population in India has some form of kidney disease. According to a report by the Indian Society of Nephrology, the prevalence of CKD in India is increasing rapidly, and it is projected that there will be around 17.2 million cases of CKD in India by 2025.The last two years have been the most challenging and trying period for all of us in healthcare. The Covid pandemic took centre stage many a time at the cost of non-Covid care including the care of patients with chronic kidney disease and its treatment in the form of dialysis and transplantation[3]. Hemodialysis is a viable, safe, and efficient method to maintain patients with chronic kidney disease who progress to end-stage renal disease (ESRD). Patients undergo dialysis two to three times a week for approximately four hours each[1].

Lifelong treatment and lifestyle modifications are difficult to adapt, which significantly impairs treatment adherence and quality of life (QOL). ESRD patients are usually on complex drug regimens, with about 8-10 medications daily, many of which require multiple doses per day[2].

World health organization (WHO) defines medication adherence as, the degree to which the persons behaviour corresponds with the agreed recommendations from a heath care provider. Adherence is the key link between therapy and outcome in medical care[4]. Due to polypharmacy, medically unstable nature of the disease and restricted lifestyle, dialysis patients are at increased risk of non-adherence and drug-related problems[5].

Education and counselling programs are mandatory in ESRD population for their better QOL and to improve the treatment adherence. As the diet and fluid restrictions should be strictly

adhered to, thus ideally the diet should be salt-free, low in potassium and phosphorus content, and the protein uptake should be in accordance with the patient's condition[6,7].

Chronic Kidney Disease causes sudden changes in the daily lives of patients and creates a great impact on their quality of life. Failure of adherence in Hemodialysis can lead to increased morbidity, mortality, cost, and burden on health care system. In the early stages there are often no symptoms, but it can cause high blood pressure and swelling due to fluid retention. In the later stages, it can lead to kidney failure. As kidney disease advances, dangerous levels of waste can rapidly build up inside the body. Treatment aims to stop or slow the progression of kidney dysfunction by controlling the underlying cause[8].

COMPLICATIONS

- Anemia is a common complication in CKD and its mechanism may include a decrease in endogenous erythropoietin (EPO) production, absolute and/or functional iron deficiency, and inflammation with increased hepcidin levels.
- Sodium and water retention: In CKD stages 4-5 and possibly in stage 3 there is a loss of defence against both sodium excess and sodium depletion. Excess sodium and fluid not only contribute to edema, which may negatively impact the quality of life, but also to hypertension and thereby cardiovascular disease.
- Metabolic acidosis and electrolytes disorders: Metabolic acidosis is common in CKD and is caused when acid intake and generation exceed renal acid excretion. Chronic metabolic acidosis contributes to skeletal muscle catabolism, insensitivity to endocrine hormones, and bone disease.
- Uremic symptoms include symptoms like anorexia, fatigue, cachexia, pruritus, nausea, restless leg syndrome, sleep disturbances, and sexual dysfunction. Pruritus is common and can adversely impact the quality of life.
- Gout: This is a type of arthritis caused by build-up of uric acid in joints. Uric acid is filtered through the kidneys, linking the two conditions.
- Heart disease: Elevated cardiovascular risk manifesting as heart failure, arrhythmia and sudden cardiac death[9].

Kidney disease also increases the risk of having heart and blood vessel disease. These problems may happen slowly over a long time. Early detection and treatment can often keep chronic kidney

disease from getting worse. When kidney disease progresses, it may eventually lead to kidney failure, which requires dialysis or a kidney transplant to maintain life[10].

Diabetes and high blood pressure, or hypertension, are responsible for two-thirds of chronic kidney disease cases.

Diabetes: Diabetes occurs when blood sugar remains too high. Over time, unmanaged blood sugar can cause damage to many organs, including the kidneys and heart and blood vessels, nerves, and eyes.

High blood pressure: High blood pressure occurs when blood pressure against the walls of blood vessels increases. If uncontrolled or poorly controlled, high blood pressure can be a leading cause of heart attacks, strokes, and chronic kidney disease. Also, chronic kidney disease can cause high blood pressure.

There are a few other conditions or circumstances that can cause kidney disease.

- Glomerulonephritis: Glomerulonephritis is a group of diseases that cause inflammation and damage the kidney's filtering units. These disorders are the third most common type of kidney disease.
- Inherited diseases: Polycystic kidney disease, or PKD, is a common inherited disease that causes large cysts to form in the kidneys and damage the surrounding tissue.
- Kidney and urinary tract abnormalities before birth: Malformations that occur as a baby develops in its mother's womb
- Autoimmune diseases: When the body's defense system, the immune system, turns against the body, it's called an autoimmune disease. Lupus nephritis is one such autoimmune disease that results in inflammation of the small blood vessels that filter wastes in kidney.
- Other causes: Obstructions caused by kidney stones or tumors can cause kidney damage. An enlarged prostate gland in men or repeated urinary infections can also cause kidney damage[11].

NUTRITIONAL CONSIDERATIONS

Many ESRD patients are malnourished, putting them at increased mortality risk. Appetite loss, when present, is often multifactorial and may be due to accumulation of toxins, chronic inflammation, comorbid conditions, gastrointestinal dysfunction, acidotic state, as well as the actual dialysis procedure. Socioeconomic factors can also play a role, as patients may be

depressed, unable to purchase their own food, unable to obtain good-quality food, or lacking in social support.

- Weight Maintenance and Protein Requirements

Protein needs are higher in patients with ESRD due to losses that occur during dialysis. The daily recommended dietary protein intake for clinically stable maintenance hemodialysis patients is 1.2 g/kg body weight. ESRD patients on dialysis may spontaneously reduce protein and calorie intake as a result of uremic toxins, elevations in leptin and other cytokines, and delayed gastric emptying.

To prevent malnutrition-related morbidity and mortality, ESRD patients on dialysis should have individualized, frequent nutrition assessments and counselling.

- Sodium and Potassium Balance

ESRD patients should avoid high-sodium foods. Hypertension in dialysis patients is largely attributed to positive sodium balance and volume expansion. While many patients on dialysis can effectively control blood pressure without drugs on a low-sodium (2 g) diet and a low-sodium (130 mmol) dialysate, current practice is such that a significant percentage of dialysis patients require the addition of antihypertensive medications. Although many patients may not achieve a therapeutic degree of sodium restriction, those who do can effectively control blood pressure and reverse left ventricular hypertrophy.

For most people, a high-potassium diet is desirable to control blood pressure and reduce risk for stroke. Individuals with ESRD on hemodialysis cannot excrete potassium. Therefore, ESRD patients should be educated regarding high-potassium foods, which include many "heart healthy" fruits, vegetables, legumes, and grains and given guidelines to include moderate amounts of these foods while avoiding other sources of dietary potassium. Evidence indicates that the vast majority of patients comply with potassium restriction. In patients on peritoneal dialysis, hyperkalemia is significantly less likely, and hypokalemia has been reported in some patients, at times requiring an increase in potassium-containing foods and even potassium supplementation.

- Fluid Restriction

It is essential that ESRD patients restrict their fluid intake. Without adherence to a specified fluid allowance, patients are more likely to have poorly controlled blood pressure and risk congestive heart failure. The typical fluid allowance for patients on dialysis is 700-1000 mL/day, plus urine output.

- Phosphorus

Elevated blood phosphorus concentrations are associated with increased mortality in ESRD patients and increase the risk for cardiovascular events, at least in part by contributing to vascular calcification. Excess phosphorus also causes secondary hyperparathyroidism, triggering the release of calcium from the bone matrix, and osteodystrophy.

Management of hyperphosphatemia and renal osteodystrophy has improved with phosphate binders, particularly sevelamer hydrochloride which also helps prevent hypercalcemia-related vascular calcification.

- Saturated Fat and Cholesterol

Dialysis patients should follow a diet low in saturated fat and cholesterol. These patients are at very high risk for coronary artery disease. They often have increases in serum triglycerides and low HDL cholesterol.

The relationship between total cholesterol and cardiovascular mortality is clearly evident in ESRD patients, although this relationship may be obscured in those with elevated markers of inflammation or malnutrition, pre-existing cardiovascular disease, diabetes, or advanced age[12].

STAGES OF CKD

The GFR shows how well a person's kidney is filtering waste. A person's GFR can depend on their body size, sex, and age. A person's GFR can be determined by testing the levels of creatinine in their blood. Creatinine is a waste product of creatine, which is an acid that helps supply energy to muscle cells. When the kidneys are working correctly, they filter a relatively constant amount of creatinine from the blood. Changes in blood creatinine levels can indicate that a person has a problem with their kidneys. A change in a person's GFR can be used to classify CKD into stages, as follows.

Stage 1

Stage 1 CKD means that a person's GFR is at least 90 millilitres per minute (ml/min) per 1.73 meters squared (m2). This is normal kidney function but with evidence of kidney damage. Some signs of kidney damage in stage 1 CKD can include protein in a person's urine or physical damage.

Stage 2

If a person has stage 2 CKD, their GFR is 60–89 ml/min per 1.73 m2. A GFR in this range usually means that a person's kidneys are working well. However, this GFR indicates that a person with stage 2 CKD has additional signs of kidney damage. These signs can include physical damage to the kidney or protein in a person's urine. A person with stage 1 or 2 CKD can speak with a doctor about medications that can help protect their kidneys.

Stage 3

At stage 3 CKD, a person's GFR is 30–59 ml/min per 1.73 m2. This range indicates that a person has some damage to the kidneys. A person's kidneys are not working as well as they should at stage 3 CKD.

Stage 3 CKD can be separated into two subcategories:

Stage 3a: Stage 3a means that a person has a GFR of 45–59 ml/min per 1.73 m2.

Stage 3b: Stage 3b means that a person has a GFR of 30–44 ml/min per 1.73 m2.

Although most people with stage 3 CKD do not have symptoms, some may experience:

- swelling in the hands and feet
- back pain
- more frequent urination
- anemia
- high blood pressure
- bone disease

A person with stage 1–3 CKD may be able to slow the damage to their kidneys by:

- controlling their blood sugar, if they have diabetes
- controlling their blood pressure
- eating a healthy diet
- not smoking or using tobacco
- being active for 30 minutes per day on 5 days per week
- maintaining a moderate weight

A person with stage 3 CKD should follow a healthy diet and use medications can lower blood pressure that may help prevent CKD from worsening.

Stage 4

By stage 4 CKD, a person's GFR is 15–29 ml/min per 1.73 m2. At this stage, a person's kidneys are moderately to severely damaged. Stage 4 CKD is a serious condition and the last stage before a person develops kidney failure. A person with stage 4 CKD is more likely to experience symptoms such as swollen hands and feet, back pain, and more frequent urination. Complications such as anemia or bone disease are also more likely.

Stage 5

A person with stage 5 CKD has a GFR of 15 ml/min per 1.73 m2 or less. At this stage, a person's kidneys have either failed or are close to failing[8].

SYMPTOMS OF CKD CAN INCLUDE:

- Hypertension,
- Anemia
- Edema, or swollen feet, hands, and ankles
- fatigue, or tiredness
- decreased urine output
- bloody urine, in some cases
- dark urine, in some cases
- decreased mental alertness, when the condition is severe
- a loss of appetite
- persistent itchy skin, when the condition is severe
- more frequent urination, especially at night, in some cases[8].

PHARMACOLOGICAL MANAGEMENT OF COMPLICATIONS OF CKD

Kidney damage brought on by CKD is typically irreversible. However, some treatments can aid in symptom management, lower the risk of complications, and halt the disease's course. The following are a few conditions that CKD can lead to and which need to be treated.

High blood pressure

High blood pressure is a leading cause of CKD. Lowering blood pressure is important to protect the kidneys and subsequently slow down the progression of CKD.A person with high blood pressure may need to take certain medications. Additionally, making lifestyle changes such as eating healthy and getting regular exercise can help reduce a person's blood pressure.

Over time, high blood pressure can damage blood vessels throughout body. This can reduce the blood supply to important organs like the kidneys. High blood pressure also damages the tiny filtering units in kidneys. As a result, the kidneys may stop removing wastes and extra fluid from blood. The extra fluid in blood vessels may build up and raise blood pressure even more.

High blood pressure can also be a complication of CKD. kidneys play a key role in keeping blood pressure in a healthy range. Diseased kidneys are less able to help regulate blood pressure. As a result, blood pressure increases.

Control of hypertension is important in those with CKD as it leads to slowing of disease progression as well as reduced CVD risk. Non-pharmacological interventions are useful in reducing BP in CKD but are rarely sufficient to control BP adequately. Patients with CKD and hypertension will often require a combination of antihypertensive medications to achieve target BP. Certain pharmacological therapies provide additional BP-independent renoprotective and/or cardioprotective action and this must be considered when instituting therapy.

Choice of antihypertensive medications.

Patient heterogeneity and scarcity of comparative evidence preclude recommending any one medication class over another for all patients. Antihypertensive medications considered first-line in the general population (e.g., angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, and calcium channel blockers) can also be considered first-line to lower BP in patients receiving dialysis. It is reasonable to choose medications based on patient characteristics, cardiovascular indications, and availability.[13]

Diabetes Mellitus

Diabetes mellitus is a growing epidemic and is the most common cause of chronic kidney disease (CKD) and kidney failure. Diabetic nephropathy affects approximately 20–40 % of individuals who have diabetes, making it one of the most common complications related to diabetes. Screening for diabetic nephropathy along with early intervention is fundamental to delaying its progression in conjunction with providing proper glycemic control[14].

Glycemic control is essential to delay or prevent the onset of diabetic kidney disease. There are a number of glucose-lowering medications available but only a fraction of them can be used safely in chronic kidney disease and many of them need an adjustment in dosing. The ideal target hemoglobin A1c is approximately 7 % but this target is adjusted based on the needs of the patient. Diabetes control should be optimized for each individual patient, with measures to reduce diabetes-related complications and minimize adverse events. Overall care of diabetes necessitates attention to multiple aspects, including reducing the risk of cardiovascular disease, and often, multidisciplinary care is needed[15].

Diabetic nephropathy can be detected by the measurement of urine albumin or serum creatinine, and both tests should be performed at minimum annually. The first stage of nephropathy is usually the onset of elevated urine albumin which predicts the development of CKD and a gradual decline in glomerular filtration rate (GFR). Some individuals with CKD, however, do not develop elevated urine albumin initially. It is therefore important that individuals have both blood and urine screening tests performed. Glycemic control is essential to delay or possibly prevent nephropathy[14].

Lower A1c levels are associated with higher risk of hypoglycemia which necessitates tailored A1c targets for different individuals. Consequences of hypoglycemia, which in turn can cause injury, myocardial infarction, seizure, stroke or death, are greatest in those who are frail and elderly, with erratic eating habits, on insulin and sulfonylureas, and with CKD. Higher A1c targets should be considered for those with shortened life expectancies, a known history of severe hypoglycemia or hypoglycemia unawareness, CKD, as well as in children. Individuals with diabetes and CKD are at risk for acute diabetes-related complications such as hypoglycemia and diabetic ketoacidosis; long-term complications such as retinopathy, neuropathy, and foot complications; the risk of kidney failure with a need for dialysis or transplantation; and in

particular, the risk of cardiovascular complications, including ischemia, arrhythmia, and heart failure. Comprehensive diabetes care, therefore, includes regular screening for these complications and management of the many cardiovascular risk factors in addition to hyperglycemia, such as hypertension, dyslipidemia, obesity, and lifestyle factors, including diet, smoking, and physical activity[16].

Anemia

Anemia is a common complication of chronic kidney disease (CKD) that can lead to poor outcomes. The treatment of anemia in CKD is directed towards improving renal function and increasing red blood cell production. Erythropoiesis-stimulating agents (ESAs) along with iron supplementation are the preferred treatment options for anemia in CKD. Injections of erythropoiesis-stimulating agents (ESAs) are the most common treatment for CKD and anemia. ESAs mimic the protein erythropoietin, which is secreted by the kidneys to stimulate red blood cell production.

Blood transfusions may be used in severe cases. Patients with CKD are at an increased risk of iron deficiency due to impaired dietary iron absorption, chronic bleeding, frequent phlebotomy, and blood trapping in the dialysis apparatus. Therefore, iron supplementation is an essential part of the treatment of anemia in CKD.

Multiple oral supplements are available for the treatment of iron deficiency. Many multivitamins contain iron, typically providing ~18 mg of elemental iron per unit dose. Iron-only supplements usually consist of ferrous salts. The one most commonly used in patients with CKD patients is ferrous sulfate, which contains 20% elemental iron per tablet. Other ferrous salts include ferrous gluconate (12% elemental iron), ferrous fumarate (33% elemental iron), ferrous succinate (35% elemental iron), and iron polymaltose (28% elemental iron). Oral iron supplements frequently cause gastrointestinal adverse effects in 35% to 60% of patients particularly with administration of ≥ 45 mg elemental iron per day, limiting the ability to replete iron using high doses of oral formulations alone.

The hepcidin-induced blockade of iron absorption in the gut explains the reduced efficacy of oral iron replacement in patients with CKD, often necessitating iron repletion therapies that bypass the gastrointestinal tract in patients with CKD. Chronically elevated circulating concentrations of hepcidin limit gastrointestinal absorption of iron, hampering the efficacy of oral iron supplements in patients with CKD. Because of this, iv. iron infusion is a mainstay in the treatment of iron

deficiency in CKD. Oral and iv. iron formulations are both safe and effective in treating iron deficiency in patients with CKD, concomitantly erythropoiesis-stimulating agents are also used[17].

Phosphate balance

Hyperphosphatemia is a common complication in patients with chronic dialysis treatment. It can lead to vascular calcification and increased cardiovascular risk. Hyperphosphatemia in dialysis patients is routinely attributed to nonadherence to diet, prescribed phosphate binders, or both, but the role of individual patient variability in other determinants of phosphate control is not widely recognized. The bodies of people with kidney disease may not be able to eliminate phosphate correctly. Treatment involves a person reducing their intake of nutritional phosphate and proper intake of phosphate binders[18].

Skin itching

Itching is a common problem for people in the advanced stages of CKD or who have kidney failure and are receiving dialysis.

It can be difficult to control itching, and a person may find that they have difficulty sleeping. A person can try speaking with a dermatologist about their itchy skin. The dermatologist may provide a person with medication or moisturizers to help reduce itching.

Vitamin D deficiency

There is a considerable risk of vitamin D insufficiency in people with CKD. Vitamin D is essential for healthy bones. The kidneys activate the vitamin D obtained from the sun or food before the body can use it. Low levels of vitamin D can lead to a loss of bone density, which can lead to osteoporosis or fractures.

People with vitamin D deficiency may require supplementation. However, the evidence on its effectiveness is limited, so doctors typically decide based on the individual's needs and health status.

Fluid retention

People with chronic kidney disease should watch their fluid intake and limit their salt intake. When the kidneys are not working properly, fluid retention and congestion are more likely.

Eating too much salt can cause your body to retain more water. Fluid retention lead to hypertension, which can lead to the progression of kidney disease and serious heart problems[8].

PATIENT COUNSELLING

The World Health Organization (WHO) defines patient counselling as a process in which a healthcare professional, usually a pharmacist, provides information and advice to a patient or caregiver about a medication or a medical condition. The purpose of patient counselling is to ensure that the patient understands the medication, how to take it, its benefits and risks, and how to manage any potential side effects or adverse reactions. The goal is to improve patient outcomes and quality of life by promoting medication adherence and proper use. In addition empower patients to actively participate in their care, make informed decisions about their treatment, and manage their symptoms and lifestyle changes related to their condition.

Patient counselling may cover a range of topics, including:

1.Dialysis treatment options: Patients should be informed about the different types of dialysis treatments available, including hemodialysis, peritoneal dialysis, and home hemodialysis, and the pros and cons of each option.

2.Dietary and fluid restrictions: Dialysis patients typically need to follow a special diet and limit their fluid intake to help manage their condition. Patients should be given guidance on what foods and fluids to avoid and how to maintain a healthy diet.

3.Medication management: Many dialysis patients require medications to manage their symptoms and complications related to their condition. Patients should be informed about the medications they are taking, their dosages, and potential side effects.

4.Lifestyle changes: Dialysis treatment can require significant lifestyle changes, such as changes in work schedule or travel plans. Patients should be given support and guidance on how to manage these changes and maintain a good quality of life.

5.Emotional support: Living with ESRD and undergoing dialysis treatment can be emotionally challenging. Patients should be given access to counselling and other support services to help them cope with the emotional aspects of their condition.

Patients undergoing dialysis have limited mobility, deranged family and social life and decreased financial autonomy, all of which affect their quality of life. Overall, patient counselling for dialysis patients should be tailored to meet the individual needs and preferences of each patient, and should be provided by a multidisciplinary team that includes doctors, nurses, dietitians, and social workers. Patient counselling will be an effective way to improve the multi-dimensional concept, health related quality of life (HRQOL) of hemodialysis patients by increasing the knowledge and awareness about the disease and its management[19].

MEDICATION ADHERENCE

The World Health Organization (WHO) defines medication adherence as "the degree to which the person's behaviour corresponds with the agreed recommendations from a healthcare provider." This includes taking the medication at the right time, in the right dose, and in the right way. High levels of medication adherence are essential for the effectiveness of treatments and the prevention of health complications.

Providing adequate information about medications to patients helps them to understand the importance of medications and improves their adherence behaviour, which helps in achieving the desired therapeutic goals.

Patients may not believe that the medication is necessary, may never begin taking it, or may take more or less than prescribed; they may even prematurely stop taking it. To effectively increase patient medication adherence, pharmacists must adjust their approach based on the cause and type of nonadherence and on patient-specific needs. Tailored patient counselling that targets the underlying causes of nonadherence is one method of helping patients increase their medication-taking behaviours. Patients have specifically identified the pharmacist as a source of medication education. Therefore, pharmacists have a key opportunity to address medication nonadherence through patient communication. The use of behavioural theory in patient education and counselling can inform and improve medication adherence.

Several factors are said to influence medication of the information provided by the health care providers adherence in chronic disease patients. Patients' lack of are forgotten immediately and 50% of the information knowledge amongst other factors, contributes to medication nonadherence

1. Knowledge about the name, indication (purpose of the medication), dosage, frequency and side effects of the medications are considered basic essential information that patients must know about their medications

2. The medication knowledge of the patient is approximated based on the extent of patient's ability to recall these basic essential information.

Patient counselling by clinical pharmacists can improve the medication adherence by improving awareness about medication which in turn helps them to achieve a better quality of life[20].

QUALITY OF LIFE

WHO defines quality of life as the extent to which patients are able to enjoy their life and achieve their goals, taking into account their physical, psychological, and social well-being. This includes factors such as symptom burden, functional status, social support, emotional well-being, and overall satisfaction with life.

The WHO highlights the importance of measuring and monitoring quality of life in dialysis patients to identify areas for improvement and to help healthcare providers optimize care to enhance patients' overall well-being.

Quality of life refers to an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns. Quality of life is highly subjective and can refer to the experience an individual has of their own life and to the living conditions in which individuals find themselves. It can be measured using various methods, including subjective views of the patient, and is relevant in clinical settings such as hospice and palliative care[21].

FACTORS AFFECTING QUALITY OF LIFE

1.SLEEP DISTURBANCES

Sleep complaints are very common in patients with end-stage renal disease (ESRD) and contribute to their impaired quality of life. Both obstructive and central sleep apnea syndromes are reported more often in patients on dialysis than in the general population. Impaired daytime functioning, sleepiness, and fatigue, as well as cognitive problems, are well known in patients with sleep apnea. Increasing evidence supports the pathophysiological role of sleep apnea in cardiovascular disorders, which are the leading cause of death in ESRD patients[22].

Subjective sleep complaints that are reported sleep apnoea syndrome, restless legs syndrome, and periodic limb movement disorder are much more prevalent than in the general population. Excessive daytime sleepiness is also an important problem. These sleep abnormalities appear to have significant negative effects on quality of life and functional health status

Sleep apnea can be defined as consecutive reduction (hypopnea) or cessation (apnea) of breathing during sleep with consequent hypoxemia. The number of episodes of apneas and hypopneas during sleep are quantified by the apnea-hypopnea index (AHI), which classifies the sleep apnea into mild (between 5 and 15 episodes per hour (/hr) of sleep), moderate (between 15 and 30 episodes/hr of sleep) and severe (more than 30 episodes/hr of sleep). There are primarily two types of sleep apnea namely obstructive sleep apnea (OSA) and central sleep apnea (CSA)[23].

Sleep-disordered breathing refers to a wide spectrum of sleep-related breathing abnormalities; those related to an increase in upper airway resistance include snoring, upper airway resistance syndrome, and obstructive sleep apnea–hypopnea syndrome. It is also possible that sleep apnea accelerates the deterioration of kidney function in patients with CKD either indirectly by increasing systemic BP, inflammatory cytokines and sympathetic nervous system activity all of which have been proposed to reduce kidney function or directly through the effect of hypoxia on the kidney. Severe hypoxic events in obstructive sleep apnea (OSA) might lead to kidney damage.

Sleep disorders tend to be under-recognized by renal healthcare providers. Polysomnography remains the gold standard for diagnosing sleep-disordered breathing. Monitoring should be done in conjunction with a comprehensive sleep medicine evaluation. Portable monitoring can be performed in a patient who cannot be safely transported for laboratory polysomnogram.

Appropriate management of sleep disorders could improve the quality of life and possibly even impact upon survival of renal patients[24].

2.BREATHING DIFFICULTIES AND HYPOXEMIA

Hypoxemia during haemodialysis has been well recognized since the early days of haemodialysis with studies reporting it to be as common as 10% in end stage renal disease patients on haemodialysis. During haemodialysis, the PaO2 may fall by 10–20 mmHg and this drop can be detrimental to patients with underlying chronic lung disease or chronic heart failure. There have been several mechanisms proposed, however the causes remains unclear. Some studies have attributed hypoxemia during haemodialysis to the type of dialysate used, type of membrane used or a combination of both. Other factors contributing to this include anaemia, chronic volume overload and compromised pulmonary function[25].

Renal injury is not only a localized disease, eventually leading to a progressive and irreversible loss of nephron mass and functions, but also a syndrome affecting multiple organ systems. Among those, CKD and KRT options, such as hemodialysis and peritoneal dialysis, severely affect the respiratory system. Specifically, their effects are (a) acute: causing infections, pleural effusions, and ARDS and (b) chronic: leading to calcification of the lung parenchyma and finally respiratory impairment.

Hypoxemia during hemodialysis has variously been attributed to worsening ventilation-perfusion (VA/Q) relationships, alveolar hypoventilation combined with a reduced respiratory quotient, increased right-to-left shunting, and diffusion impairment. The hypoxemia observed during hemodialysis is primarily due to a decrease in alveolar ventilation and respiratory quotient associated with removal of metabolic CO2 in the dialyzer. Secondary factors affecting arterial PO2 were the slight improvement in ventilation-perfusion relationships tending to increase it, and the decrease in cardiac output tending to decrease it. No evidence for diffusion impairment because the measured VA/Q inequality accounted for the degree of hypoxemia[26].

3.FLUID AND FOOD RESTRICTIONS

Nonadherence to the prescribed diet and fluid restrictions is a severe health problem that limits the benefits of routine therapies. It can cause electrolyte imbalance, fluid overload, exacerbation of symptoms, poor quality of life, repeated hospitalization, higher health care costs, and high

mortality. The prevalence of nonadherence to diet and fluid restriction is highly incoherent and variable across studies in patients undergoing HD. In HD patients, strict adherence to dietary and fluid recommendations is known to minimize the deterioration of nephron function and lower the risk of morbidity and mortality.

Patient's noncompliance dietary and fluids intake can lead to a build-up of toxic fluids and metabolic end-products in the blood stream which may result in an increased morbidity and premature death. The successful treatment of patients with end stage renal failure requires adherence to complex, whole of lifestyle changes, and lack of compliance with diet and fluid restrictions may lead to accumulation of metabolic by products and excess fluid in the circulatory system, leading to increased morbidity and mortality for renal failure patients.

Salt free diet, low potassium containing foods and limited fluid intake are possible interventions, and even though protein adds up to uremia, ESRD patients have to consume a high protein diet (i.e., 1-1.2gm/kg/day) so as to meet the extra needs for body repair functions and immunity.

Following recommended treatments (diet and fluid restriction) by the patient is one of the most important issues in the health care programs. Intake of the correct amount of fluids on a daily basis is crucial to stabilizing your kidney patient and reducing potential symptoms associated with fluid overload including shortness of breath, headaches, abdominal bloating, hypertension, heart failure, and edema. Limiting fluid consumption is a complex part of the renal diet as there are many factors that play into patient acceptance of this restriction

Life in end stage renal disease (ESRD) is miserable, food and fluid restrictions are mandatory for the patients due to hyperkalemia high blood pressure and fluid retention[27].

4.SMOKING

Smoking may be a significant mediator of not only BP but also of chronic fluid overload in ESRD patients. Smoking represents a superimposed, additional layer of risk and been found to be a major cause of mortality in the dialysis population by others.

Smoking seems to exert its deleterious effects through the acceleration of atherosclerotic disease. It is highly controversial whether hypertension as defined by high pre-HD blood pressure readings is an independent risk factor for mortality in HD patients – in fact, low pre-HD may be associated with higher mortality.

patients with ESRD have a high rate of cardiovascular disease, as do smokers with normal kidney function, we hypothesized that ESRD patients who smoke would be at extraordinarily high risk of cardiovascular disease and subsequent mortality[28].

5.XEROSIS AND PRURITIS

Dry skin is a common problem in dialysis patients which could be a contributing factor for decreased quality of life. Xerosis and pruritus are common chronic Dermatological disorders among patients undergoing maintenance renal dialysis and in diabetic patients. Several underlying causes have been proposed, including skin dryness, hypervitaminosis A, mast cell accumulation (increase in histamine release), disturbance in tryptase and chymase activity (pH increase in the stratum corneum), uremic toxins, allergic sensitization related to dialysis, imbalance in divalent ions, peripheral neuropathy, and opioid system involvement. Xerosis, called uremic xerosis in these patients, is not the primary cause of pruritus. Pruritus, or as normal people call it, itching, is a common problem that afflicts patients with kidney failure or dialysis patients. It is one of those complications of advanced kidney disease that is hard to understand and perhaps harder to treat. But in the presence of pruritus, dry skin may have an exacerbating effect by reducing the threshold for itch. Furthermore uremic pruritus is a predictor of poor sleep and profoundly impacts the quality of life.

Xerosis is one of the commonly observed cutaneous manifestations of diabetic patients. Management of diabetes mellitus-related skin conditions, in addition to improving patient quality of life, can avoid serious complications, such as diabetic foot development. It results in a higher risk of chronic wounds and infection Xerosis in diabetes mellitus is often associated with pruritus, mostly localized to the scalp, ankles, feet, trunk, or genitalia.

Therefore, management of these skin conditions in dialysis and diabetic patients is important for patient skin-related quality of life as it allows bothersome symptoms and even serious complications to be avoided. Unfortunately, these conditions are frequently underdiagnosed and usually neglected, although dermo-cosmetic management can be beneficial. Indeed, skincare can be able to overcome and even prevent skin alterations in dialysis and diabetes mellitus, especially by improving skin hydration[29].

Uraemic xerosis often affects the entire surface of the body, and may be more intense in some areas. It is a permanent syndrome, with a clinical picture comprising a dry skin appearance,

marked scaling and roughness, and poor skin turgor. Associated signs are premature skin ageing (elastosis) and pruritus. Severe involvement of certain areas, such as the hands and feet, leads to possible functional impairment. Because the cutaneous barrier function is reduced, the skin is more easily exposed to external attacks and aggression, such as wind, cold, sun and reduced air humidity. As in some other severe xerotic conditions, a greater susceptibility to irritation caused by chemical factors (eg. soaps and detergents) may be observed. Irritative clothes must often be replaced by smoother fabrics (eg. cotton). In some patients, uraemic xerosis is associated with diminished sweating and poor wound healing. The cause of uraemic xerosis is unknown[30].

Dry and itchy skin can be treated with antihistamines, like Benadryl or diphenhydramine, or another medication which is similar called hydroxyzine. Loratadine is a non-sedating alternative.

Other medications that have been tried include gabapentin, pregabalin, and antidepressants including sertraline. For patients who get no relief even with these drugs, phototherapy with ultraviolet B light, UV therapy, acupuncture, might help. In addition, itching and dry skin are common in patients with high calcium levels, as indicated by high calcium and phosphorus products or elevated PTH levels. Therefore, it is necessary to reduce the concentration of calcium, phosphorus and PTH. It is also recommended to use body moisturizers and skin lubricants.

Some causes of dry skin and itchy skin during dialysis include:

Limited fluid intake: Dialysis treatment removes a lot of water from the body, as fluids are lost Traveling a lot can lead to dry and itchy skin;

Uncontrolled phosphorus: When blood phosphorus levels are high, it binds to calcium and leads to an itchy sensation. During hemodialysis, the doctor will give phosphate binders and use them as directed to improve the condition; Allergies: Some people may be allergic to the dialysis membrane or dialysis line[31].

6.CHANGES IN APPEARANCE

Pedal edema in HD patients was associated with common cardiovascular risk factors such as older age, overweight or obesity, and left ventricular hypertrophy. The independent determinants of edema were BMI, age, and LVM[32].

Skin hyperpigmentation is a common clinical finding in ESRD patients undergoing dialysis and can lead to cosmetic and psychological concerns. Retention of middle-molecular-weight molecules, such as urochromic pigments, carotenoids and α- and β-melanocyte-stimulating hormone, has been implicated in the pathogenesis of diffuse pigmentation in ESRD patients[33].

7.MUSCLE CRAMPS

Muscle cramps are the most prevalent intradialytic complication and an important difficulty for patients. The frequency of muscle cramps is about 35-86% during haemodialysis. Excessive ultrafiltration, intradialytic hypotension, electrolyte-mineral disturbances, hypoosmolality are the most frequent causes. Muscle cramps can be treated by isotonic-hypertonic saline or hypertonic dextrose solutions. Also, preventing hypotension, profiling sodium, vitamin E and C can be used to prevent.

Elevated PTH levels can cause muscle spasms in HD patients. L-carnitine is a quaternary amine known to transfer long chain fatty acids from cytoplasm into the mitochondrial matrix to be oxidized. Carnitine production is greatly reduced in patients with end-stage renal disease and significantly reduced in HD patients.

L-carnitine is largely cleared from the dialyzer during a single dialysis session. Treatment with chronic hemodialysis has been shown to be associated with decreased plasma and tissue L-carnitine concentrations and accumulation of acylcarnitines.

There are many new advances to treat and prevent this common clinical problem such as minimizing interdialytic weight gain, prolonging dialysis session time to reduce ultrafiltration rate, using sodium modelling, and avoiding hypotension may reduce cramps during dialysis. They may be treated with bolus hypertonic saline or dextrose and local heating and massage of the cramped muscle. Prevention of cramps may include a trial of vitamin[34].

8. FOOT ULCERATION

Dialysis patients experience high rates of foot ulceration. Although risk factors for ulceration have been extensively studied in patients with diabetes, there is limited high-quality, longitudinal evidence in the dialysis population.

Neuropathy and previous ulceration are major risk factors for foot ulceration in dialysis patients. Risk factors differ between those with and without prior ulceration. The risk factors identified will help to reduce the incidence of ulceration and its associated complications[35].

9.GASTROINTESTINAL COMPLICATIONS

The most common non-renal complaints in end-stage renal disease (ESRD) patients are gastrointestinal symptoms such as heartburn, constipation, diarrhea and dyspepsia . Dyspepsia is highly prevalent and characterized by upper abdominal pain, nausea, vomiting, upper abdominal bloating, and early satiety. The prevalence of dyspepsia among HD patients varies between 48% and 70%. In the general population, dyspepsia has been shown to impair quality of life. Nevertheless, dyspeptic symptoms are not widely investigated among patients treated by HD, as is usually the case in relation to cardiovascular disease, osteodystrophy and nutritional status.

Like in the general population, functional dyspepsia is the most frequent among ESRD patients. There are reports of the possible role of gastric emptying delay as a cause of dyspeptic symptoms in HD patients. Gastrointestinal symptoms are widespread in patients undergoing maintenance hemodialysis and are a major cause of morbidity. These symptoms are more common in older adults because of changes associated with aging, comorbidities such as diabetes, and medications they have to take. Delayed motility, decrease in gastric secretion, and decreased absorption in the elderly may be responsible for gastrointestinal symptoms

The increased concentration of gastrointestinal hormones, and changes of intestines due to uremia may be linked to gastrointestinal symptoms. Changes of diet, gastroparesis and prolonged gastric emptying also influence these symptoms in elderly adults. Old patients on hemodialysis have more comorbidities such as diabetes, heart disease and hypertension[36].

10.FINANCE

The worldwide incidence of kidney failure is on the rise and treatment is costly; thus, the global burden of illness is growing. Kidney failure patients require either a kidney transplant or dialysis to maintain life.

Patients with chronic kidney disease (CKD) spend substantial money on hemodialysis (HD) treatment. The growing intersection between socioeconomic status and financial burden

represents an emerging challenge to the CKD community. The financial burden was associated with employment status, salary, and income class among HD patients.

Age, gender, education, type of financing, family income, stress, frequency of hemodialysis, level of physical dependence, comorbidity, and social group affect the quality of life of hemodialysis patients.

11.DEPRESSION

Diagnosis of depression has been especially problematic in patients with end-stage renal disease (ESRD). Patients on hemodialysis may manifest various psychiatric problems like affective disorders, dementia and personality disorders. Amongst all psychiatric disorders depression is the most important and common in patients with ESRD. Depression in dialysis patients not only effect mortality but increased rate of hospitalizations and dialysis withdrawal is also very common.

Depression is characterized by both cognitive and somatic features. The somatic characteristic of depression is similar to symptoms of uremia like anorexia, sleep disturbance, fatigue, gastrointestinal disorders and pain. Due to this overlap of symptoms of uremia with depression it is usually neglected, under diagnosed and remain untreated. Majority of patients undergoing hemodialysis were depressed. Major risk factors for depression were illiteracy, socioeconomic factors, marital status, number of children, financial support, gender, hypertension and hypoalbuminemia. Patients with anemia and hyponatremia have suicidal tendency. Patients with hepatitis C and disturbed liver function have strong correlation with psychological parameters[37].

NEED FOR THE STUDY

End stage renal disease patients are on polypharmacy and adherence to the medications is very important to improve their quality of life. Additional care given by clinical pharmacists may improve the medication adherence and quality of life of these patients. No such studies have been conducted in our study site.

AIM AND OBJECTIVE

AIM

To assess the impact of patient education by clinical pharmacist on medication adherence and quality of life in hemodialysis patients

OBJECTIVE

- To assess the medication adherence in hemodialysis patients using specially designed and validated questionnaire.
- To assess the quality of life of patients on hemodialysis using KDQOL SF 36 version 1.3.
- To correlate medication adherence with quality of life.
- To document the pharmacological management of complications in CKD patients undergoing hemodialysis