# INTRODUCTION

Cardiovascular diseases (CVD) are a major cause of morbidity and mortality in patients with end-stage renal disease (ESRD). The incidence of cardiovascular deaths occurring among dialysis patients is approximately 20 times higher than that in the general population ***(Helal I.etal., 2010)*.**

The high prevalence of cardiovascular disease, either clinically or simply echocardiographically detected, among dialysis patients at the beginning of renal replacement therapysuggests that the pathogenetic mechanisms leading to the development of cardiovascular complications begin to occure very early in the progression of chronic kidney disease (CKD), far before patients reach the need for dialysis (**Locatelli F et al., 2003)**.

This underlines that the prevention of cardiovascular disease in these patients should begin as early as possible during the course of their disease, taking care of the cardiovascular risk factors optimally ***(Locatelli F et al., 2003)***.

CKD-related 'nontraditional' cardiovascular risk factorsinclude haemodynamic overload due to plasma volume expansion and arterio-venous fistula, anemia, disorders of calcium-phosphate metabolism with resulting hyperphosphatemia,

secondary hyperparathyroidism, electrolyte imbalances, chronic inflammation, sympathetic overactivity, increased oxidant stress, hypercatabolism and even uraemia per se ***(Locatelli F et al., 2000).***

Haemodynamic stress due to intra and interdialytic changes in cardiac filling and fluctuations of blood pressure, rapid changes in serum electrolyte levels, bioincompatibility of dialytic membranes and dialysate impurity further contribute to the excess cardiovascular risk of these patients because of the dialytic procedure. ***(Locatelli F et al., 2000).***

Traditionalrisk factors of cardiovascular disease include hypertension, glucose intolerance, dyslipidemia, high serum homocysteine concentrations ***(Gladys Z et al., 2003)***

Mortality of ESRD patients has remained high due to an excessive cardiovascular riskresulting in a very high incidence of coronary artery disease, vascular and valvular calcification, LV hypertrophy and circulatory congestion (***Wang A.2008)***.

Coronary artery disease (CAD) is present in 38% – 40% of patients starting dialysis.Coronary artery calcification (CAC) with a prevalence ranging from 40% to almost 100% in different dialysis cohorts. The prevalence of valvular calcification ranged from 30% to over 50%. (***Wang A.2008)***.

All patients at dialysis initiation should undergo an evaluation for cardiovascular/coronary artery disease. At a minimum, this should involve a baseline electrocardiogram and echocardiogram **(William L et al., 2009)**.

Evaluation for heart disease should also be performed in patients with a change in symptoms and signs, including recurrent hypotension, heart failure that is unresponsive to changes in dry weight, and hypotension that prevents attaining dry weight **(William L et al., 2009).**

SO the understanding and proper management of the determinants of cardiovascular disease in the dialysis population become a challenge of major importance for the nephrologists in the current management of dialysis patients (**Locatelli F et al., 2003)**.

# AIM OF THE ESSAY

- Spot lights on the major cardiovascular risk factors in hemodialysis patients
- Identify assessment and prevention of cardiovascular diseases in hemodialysis patients

# HEMODIALYSIS COMPLICATIONS

Chronic kidney disease (CKD) is a common public health problem, which occurs in many countries with an increasing prevalence, Over 50 million people throughout the world are known to have CKD, and more than 1 million require renal replacement therapies such as dialysis and renal transplantation.

In recent years, the rising incidence of diabetes and hypertension, the most common two causes of CKD, cause an increase in the prevalence of CKD.

## CKD classification/staging

CKD is defined as the presence of kidney damage, manifested by abnormal albumin excretion or decreased kidney function, quantified by measured or estimated glomerular filtration rate (GFR), that persists for more than3 months***(Levin A.et al., 2006)***

Although creatinine clearance can be calculated from urine creatinine concentration measured in a 24-hours urine collection and a concomitant serum creatinine concentration, a more practical approach is to estimate GFR (estimated GFR or eGFR) from the serum creatinine concentration, using either the Cockcroft-Gault or the Modification of Diet in Renal Disease (MDRD) Study estimating equations. Both complications and likelihood of progression to end-stage renal disease requiring renal replacement therapy are more likely to occur in patients

with severe CKD.In addition, early intervention will more commonly reduce serious CKD sequelae and slow CKD progression. To facilitate assessment of CKD severity,the National Kidney Foundation developed criteria as part of its Kidney Disease Outcomes Quality Initiative (NKF K/DOQI) to stratify CKDpatients***(Coresh J, et al.,2003).***

- Stage 1: normal eGFR 90 mL/min per 1.73 m2 and persistent albuminuria
- Stage 2: eGFR between 60 to 89 mL/min per 1.73 m2
- Stage 3: eGFR between 30 to 59 mL/min per 1.73 m2
- Stage 4: eGFR between 15 to 29 mL/min per 1.73 m2
- Stage 5: eGFR ! 15 mL/min per 1.73 m2 or end-stage renal disease (ESRD)

The number of patients being treated for ESRD global was estimated to be 3, 010, 000 at the end of 2012 and with a ~7% growth rate.Approximately 2, 358, 000 were undergoing dialysis treatment (haemodialysis (HD) or peritoneal dialysis (PD)) andaround 652, 000 people were living with kidney transplants (Tx).

Hemodialysis, which is one of the renal replacement therapies, is a life-saving treatment. In the absence of this therapy, more than a million patients worldwide would have died within

weeks, hemodialysis was successfully performed for the first time in 1944 by Willem Kollf in patients with renal failure.hemodialysis is accompanied by several complications. During the first years following the introduction of hemodialysis, complications were common due to the technical drawbacks associated with the dialysis machines and water systems. Currently, the advances in technology,have reduced the complications. However, complications caused by the reasons other than the dialysis machine and water system remain as a significant cause of morbidity and mortality in hemodialysis patients. Cardiovascular complications are currently the most common complication of hemodialysis.It accounts for approximately 45% of the causes of mortality in dialysis patientsand 10-20 fold higher than the general population***(Shastri&Sarnak, 2010).***

Among these complications, the rate of symptomatic intradialytic hypotension ranges between 20% and 50%, and it remains an important problem. Another concern is the hemodialysis-associated arrhythmias, the rate of which was reported to be 5% to 75%. The common and lethal types of arrhythmias include ventricular arrhythmias and ectopies. The rate of hemodialysis-associated complex ventricular arrhythmia is around 35%***(Burton JO et al., 2008).***The second most common type of arrhythmia is the atrial fibrillation, the rate of

which is 27%. Sudden cardiac death accounts for 62% of cardiac-related deaths and it is usually attributed to arrhythmias***(Shastri S, et al., 2010).***

While cramps were observed in 24%-86% of the cases following the introduction of dialysis therapy,it has been shown that only 2% of the patients having ≥2 hemodialysis sessions in a week suffer from cramps**.**Other common complications include nausea, vomiting with a rate of 5%-15%, headache with a rate of 5%-10% and itching with a rate of 5%-10%***(Jesus AC et al., 2009).***

Although cramps, nausea-vomiting, headache and itching do not result in mortality, they substantially deteriorate the quality of life of the patients. Although more common during the first years following the introduction of dialysis, Disequilibrium syndrome and complications associated with dialyser, water systems and dialysis machines are currently uncommon butmay have fatal consequences. It is of great importance to prevent the complications before they occur. The treatment of these complications provides a longer life and a better quality of life for the patients.

***Acute complications of hemodialysis can be classified as follows:***

Complications associated with hemodialysis equipment

-Hemodialysis device-related complications

-Membrane-related complications

-Water system-related complications

-Vascular acces-related complications

The researches allowed a decrease of acute intradialytical complications by improving of ultrafiltration technique, composition of dialysis fluid or by introduction of more biocompatible membranes.

**Acute Cardiovascular complications**

-Hypotension -Hypertension

-Chest pain -Arrhythmias

-Pericardial effusion -Sudden death

**Chronic complications** classified into two categories:

1- Specific complications of ESRD with their modifications by hemodialysis

2- Complications of the primary renal disease which lead to chronic renal failure.

Initiation of hemodialysis increases the incidence and severity of cardiovascular complications by several specific factors***(Murphy Sw and Parfrey PS .,2007)***.

- A voluminous arteriovenous fistula can precipitate or exacerbate congestive heart failure
- Secondary hyperparathyroidism, calcium-containing binders or vitamin D analogues can induce vascular and cardiac calcifications***(Young ew, et al., 2006)***
- Erythropoiesis stimulating agents can exacerbate previous hypertension***(Krapfr, et al., 2009)***
- Hyperhomocysteinemia
- Inadequate intradialysis ultrafiltration
- Rapid electrolyte changes during dialysis session
- Hyperlipidemia and accelerated atherosclerosis of uremic patients

Consequently, there is a clear need for a systematic program of medical intervention. These interventions concern two fields

I) The field of management of already known cardiovascular situation, and

II) The field of reduction and modification of risk factors that lead to cardiovascular complications and adverse clinical events.

Is chronic hemodialysis patient , and patient with renal failure in general , has similar characteristics to those observed in the

general population. a systematic effort has been made to determine the major cardiovascular diseases in patients with chronic renal failure who undergo hemodialysis, as well as the risk factors, and strategies for their prevention and management. However, only a small number of patients with renal failure have been included in epidemiological studies or in long-term randomized clinical trials.epidemiological data show that both heart failure and coronary artery disease are expressed differently in hemodialysis patients than in the general population. a percentage of 30% of hemodialysis patients clinically have ischemic episodes with normal coronary angiograms, because of their small vessel disease, coronary artery calcifications and left ventricular hypertrophy. Furthermore, cardiac dysfunction and failure may not be expressed only through peripheral edemas and dyspnea, but also through episodes of hypotension during hemodialysis***(Foley RN, et al.,1998).***

The main cardiovascular disorders in hemodialysis patients are considered to be

1- Coronary artery disease but it is 4-8 times more frequent than in the general population**.**

2- Left ventricular hypertrophy, because of high frequency and worsening prognosis, is considered to be not only a risk

factor for de novo ischemic cardiomyopathy and de novo cardiac failure, but also increases the mortality of hemodalysis***(Foley RN, et al., 1995).***

3- Heart failure is 8 times more frequent in hemodialysis patients than in the general population and can be the result of coronary artery disease, left ventricular hypertrophy or other factors (e.g. anemia).

Many investigators have shown that cardiac dysfunction and failure are powerful independent prognostic indicators of mortality in hemodialysis patients.

**Management of hemodialysis patients:**

The management of cardiovascular disease is based on primary and secondary prevention:

- Primary prevention includes the modification of risk factors at high and moderate risk patients as well as examination to detect coronary artery disease or left ventricular hypertrophy in low and moderate risk patients without symptoms of cardiovascular disease.

Secondary prevention concerns the management of patients with cardiovascular disease or patients with positive diagnostic tests for ischemia, who are classified as high or moderate risk groups.

In patients at low risk (without cardiovascular disease and diabetes mellitus, with one or no other risk factor) only modification of existent habits is recommended.

- In patients at moderate risk (without cardiovascular disease but with many risk factors or with diabetes mellitus), interventions aim to reduce clinical events and risk factors through suitable pharmaceutical agents and changes in life style. Screening tests are also recommended for detection of asymptomatic cardiovascular disease or in case of major non-cardiovascular surgical procedures.

  However, most hemodialysis patients are classified into the high-risk group (with known history of cardiovascular disease and with more of one risk factors).it is necessary not only to modify their life style but also to investigate pharmaceutical and/or interventional treatment**.**The risk factors for cardiovascular disease in the particular patient population are divided into nonspecific "classic" (which are similar to those of the general population)and specific (which exist only in hemodialysis patients)***( Meyer KB& Levey AS;1998).***

**Classic (Traditional risk factors)**

-Hypertension -Diabetes mellitus -Cigarette smoking

- Hyperlipidemia (High lipoprotein (a) -Hyperhomocysteinemia

**None traditional / uremia-related CV risk factors**

-Hemodynamic overload

-Anemia

-Sympathetic over activation

-Microinflammatory state (C-reactive protein)

-Increased oxidative stress

-Intradialytic changes

-Low blood pressure (intradialytic hypotension)

-Malnutrition (hypoalbuminemia)

-Reduced vascular compliance (arteriosclerosis)

-Secondary hyperparathyroidism

-Hyperphosphatemia

# TRADITIONAL RISK FACTORS

## Hypertension

**Definition**:Predialysis systolic pressure >140mmHg and/or diastolic pressure >90mmHg when the patient is believed to be at so-called "dry weight"

### - Epidemiology and pathophysiology

Hypertension is a common complication in patients with chronic kidney disease. The incidence of hypertension grows along with the decrease in glomerular filtration rate (GFR). It was reported that the incidence of hypertension in patients with GFR less than 60 ml/min was 50%-75%. However, in 69 dialysis units in the United States, almost 86% of MHD patients were suffering from hypertension, and the control rate for their BP was merely 30%***(Agarwal R, et al.,2003).***

Hypertension is a significant risk factor for cardiovascular disease in MHD patients found that with each 10 mm Hg increase of BP in MHD patients, the risk of LVH increased by 48%, ischemic heart disease increased by 39% and congestive cardiac failure increased by 44%.The causes of hypertension in MHD patients are;

-volume overload***(Agarwal R et al., 2009)***