

A Review on Chronic Kidney Disease

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ABSTRACT:- Chronic kidney disease means long term kidney renal failure, which also define presence of abnormalities in kidney structure or function. 72% cases found in India among Indian population of CKD. For the determination of CKD, the rate of glomerular filtration rate, albuminuria, proteinuria is required. Classification of CKD divided according to their stages. Creatinine is generally found in serum, urine and it is excreted by glomerular filtration rate. Creatinine clearance (Crcl) is a more accurate measurement of renal function than serum creatinine. Most common symptoms of chronic kidney disease are fatigue, itching, irritability, anxiety and nausea. Chronic kidney disease is a syndrome characterised by progressive and irreversible deterioration of renal function due to slow destruction of renal parenchyma. Diabetics, hypertension and anaemia are the main causes of CKD. For the detection and confirmation of CKD kidney biopsy test is used. In the end stage of CKD patient goes to the dialysis and kidney transplantation. Where dialysis means artificial replacement of kidney functioning, in which ultrafiltration and diffusion done. Kidney transplantation is the part of organ transplantation. In which transplantation of kidney is done by healthy person to the renal failure patient.

Keywords:- Chronic Kidney Disease, ESRD, Dialysis, Etiopathogenesis, Human Kidney Transplantation.

I. INTRODUCTION

Chronic kidney disease means long term disease of kidney renal failure. Chronic kidney disease cases found in India as 17.2% with stage 1,2,3,4,5. 43.1% group of people with same age had Hypertension and 18.8% had diabetes of Indian people (Varma. P. P. et al. 2015).

Chronic kidney disease is defined as the presence of an abnormalities in kidney structure or function persisting for more than 3 months. Which includes, Glomerular Filtration Rate less than 60 ml/min / 1.73 m². Albuminuria, urine albumin >_30

mg per 24 hours or urine albumin to creatinine ration (ACR) >30 mg/g. Renal tubular disorder. History of kidney transplantation (Teresa K. Chen. et al. 2019).

As the kidney comprises many independent function and nephrons. Glomerular filtration rate follows equation $GFR (total) = GFR (single-nephron) \times \text{no of nephron}$. This equation used to check how well kidney are working and estimate how much blood passes through the glomeruli each time. A normal GFR approximately 130 ml/min ⁻¹ in male and female (Paola Romagnani. et al. 2017).

Excretory, endocrine and metabolic function decline together in most chronic kidney diseases. GFR is generally accepted as the best overall index of kidney function. We refer to a GFR 60 ml/min/ 1.73 m² as kidney failure. AKI may occur in patients with CKD and hasten the progression to kidney failure (Evan A, Sandilands. et al. 2013).

Role of Proteinuria, Albuminuria in CKD Proteinuria

Proteinuria is strongly associated with the risk of CKD progression in both non diabetic and diabetic patients. Proteinuria is general term for the presence of increases amounts of protein in the urine. Proteinuria may reflect abnormal loss of plasma protein due to. Increased glomerular permeability to large molecular weight proteins (albuminuria or glomerular proteinuria), incomplete tubular reabsorption of normally filtered low molecular weight proteins (tubular proteinuria), increased plasma concentration of low molecular weight proteins (overproduction proteinuria, such as immunoglobulin light chains). Proteinuria up to 2g/24 hour are non-specific and may occur in any type of renal disease (Ahmed SS. et al. 2013).

Albuminuria

Abnormal loss of albumin in the urine is called albuminuria. Albumin is one type of plasma protein found in the urine in normal subjects and in larger quantity in patients with kidney disease. Small amounts of albumin in the urine between 30 and 300 mg per day were previously thought to be clinically insignificant. Menstrual bleeding, urinary

tract infection, exercise, and other factors may affect the urinary albumin/creatinine ratio. Values for albuminuria and proteinuria are generally expressed as the urinary loss rate. The urinary loss rate of albumin and protein has commonly been referred to as albumin excretion rate and protein excretion rate, respectively.

Classification of CKD

Stage	Description	GFR ml/min/1.73m ²	Terms
1	Kidney damage with normal GFR	>90	Albuminuria, proteinuria
2	Kidney damage with mild GFR	60-89	Albuminuria proteinuria
3	Moderate GFR	30-59	Chronic renal insufficiency, early renal insufficiency
4	Severe GFR	15-29	Chronic renal insufficiency, late renal insufficiency, pre-ESRD
5	Kidney failure	<15 or dialysis	Renal failure, uraemia, end stage renal disease (Levey AS. et al. 2005)

Creatinine

Creatinine is a non-protein nitrogenous compound that is produced by the breakdown of creatine in a muscle. Creatinine is generally found in serum, plasma and urine and it is excreted by glomerular filtration rate. Serum creatinine is the most commonly used endogenous glomerular filtration in clinical practice (Evan A Sandilands. et al 2013). The use of serum creatinine as a substitute for GFR. Serum creatinine is increased by deficient glomerular filtration, also increased by necrosis or atrophy of skeletal muscle, hyperthyroidism, infection, burns or fractures (Washington IM. et al.).

Creatinine clearance (CrCl) is a more accurate measurement of renal function than serum creatinine. Major factor affects serum creatinine is muscle mass. As people age increases their muscle mass decreases. Serum creatinine falls as muscle mass decrease, this renal function decline appears as normal serum creatinine but with abnormal creatinine clearance (Jignesh Shah. et al. 2013)

Creatinine clearance formula, Cockcroft Gault equation.

Creatinine

$$\text{Creatinine clearance} = \frac{\{140 - \text{age (in years)}\} \times \text{ideal body weight (in kg)}}{72 \times \text{serum creatinine} \left(\frac{\text{mg}}{\text{dl}}\right)}$$

Ideal body weight (IBW) for men = 51.65kg Height greater than 5 feet.

Ideal body weight (IBW) for women = 48.67kg Height greater than 5 feet.

Symptoms of chronic kidney disease

Most common symptoms of chronic kidney disease are fatigue, itching, irritability, anxiety and nausea. Early stages of CKD are 1,2,3 shown symptoms are bone/joint pain, feeling irritable, muscle cramp, swelling of arms and leg. Difficulty in sleeping, difficulty breathing, weight loss, loss of appetite. Difficulty in keeping legs still and feeling irritable are highest prevalent symptoms of stage 5 and on dialysis. Bone/joint pain is most common symptom and loss libido is the most severe symptom (Sameera Senayka. et al. 2017).

Etiopathogenesis of chronic kidney disease

Chronic kidney disease is a syndrome characterised by progressive and irreversible deterioration of renal function due to slow destruction of renal parenchyma. Finally

terminating in death when sufficient number of nephrons have been damaged. All chronic nephropathies can lead to chronic kidney disease. Chronic kidney disease can generally be classified into two major groups.

1. Disease causing glomerular pathology: - Glomerular disease associated with chronic kidney disease have their pathogenesis in immune mechanism. Glomerular destruction results in change in filtration process leads to development of the nephrotic syndrome characterised by proteinuria., hypalbuminaemia. The important example of chronic glomerular disease-causing chronic kidney disease is covered under two headings primary glomerular pathology and systemic glomerular pathology.
2. Disease causing tubulointerstitial pathology: - Damage to tubulointerstitial tissues result in reabsorption and secretion important constituents leading to excretion of large volume of dilute urine. Tubulointerstitial disease can be categorised according to initiating etiology into four groups: vascular, infectious, toxic and obstructive.
 - a. Vascular cause: - long standing primary hypertension produces characteristics changes in renal arteries and arterioles referred to as nephrosclerosis. Nephrosclerosis cause progressive renal vascular occlusion terminating in ischemia and necrosis of renal tissue.
 - b. Infectious cause: - chronic renal infection causing chronic kidney disease in chronic pyelonephritis. Pyelonephritis is a bacterial infection which can lead to urinary obstruction and inflammation on kidney.
 - c. Toxic cause: - some toxic substance induces slow tubular injury lead up to chronic kidney disease. The most common example is intake high dose of analgesics such as phenacetin, aspirin and acetaminophen. Other substances that can cause chronic kidney disease after prolonged exposure are lead, cadmium and uranium.
 - d. Obstructive cause: - Chronic obstruction in the urinary tract leads to progressive damage to the nephron due to fluid back pressure. The example of this type of chronic injury are stones, blood clots, tumours, strictures(Harsh Mohan. 2015).

Causes of chronic kidney disease

Diabetics: -

Nephrons are millions of small filters that make up each kidney. Diabetes can damage blood arteries in the kidneys and nephrons over time, causing them to stop working as well they should. High blood pressure is common among diabetics, and can harm the kidneys as well. In addition to hypertension, chronic diabetic mellitus hyperglycaemia is believed to be one of the main causes of chronic kidney disease (CKD). It is characterised as anomalies in renal structure or function that have been present for more than three months and have health concern. The severity of CKD is determined by the kind of kidney disease, the glomerular filtration rate category and the category of albuminuria (CGA). The effects of CKD include not only progression to renal failure, but also decreased complication of renal function and increased risk of cardiovascular disease and overall mortality from all cause(Nazzal, Z. et al. 2020)

Diabetes is a still the leading cause of end stage renal disease (ESRD).New medication called sodium-glucose cotransporter-2 (SGLT2) inhibitors have been approved to treat CKD patient(Merlin C. et al. 2020).

In type 1 diabetes, the prevalence of CKD is lower than in type 2 diabetes over the course of their lives, about one-third of all patients with type 1 diabetes are expected to acquire CKD. This difference is mostly because subjects with type 1 diabetes are generally younger, healthier at diagnosis and carry fewer co-morbid conditions than with type 2 diabetes (Chen y. et al. 2020).

Hypertension: -

Hypertension is a major risk factor for chronic kidney disease.Hypertension means high blood pressure. It is the condition when the pressure of the blood caused by the pumping of the heart goes much beyond normal values from the top of the head to the bottom of the feet, the heart pumps blood into the arteries with great effort in order to push blood to distant organs. Blood pressure is the force that blood exerts on the artery walls as it flows through the body. Blood pressure is highest when it leaves the heart via the aorta and gradually drops as it passes via smaller and smaller blood arteries(Mohd Tariq Salman. et al. 2015).

Factors that may cause hypertension in chronic kidney disease impaired sodium excretion which expansion of extracellular fluid volume.

Activation of renin-angiotensin system which direct vasoconstriction sympathetic activation. Sympathetic activation which direct vasoconstriction stimulation of renin release. Imbalance in prostaglandins or kinins which vasoconstriction. Endothelin which direct vasoconstriction renal injury. Reduced nitric oxide which loss of vasodilator effect(Tedla FM. et al. 2011).

Patient's characteristic risk factor for hypertension in chronic kidney disease are older age, high baseline BP, obesity, obstructive sleep apnea, ethnic minorities, diabetes, excessive dietary salt ingestion, heavy alcohol consumption, smoking and vascular atherosclerosis(Hamrahan. et al. 2016).

Anaemia: -

Anaemia is caused mainly by decreased production of erythropoietin by peritubular cells, and bone marrow unresponsiveness to erythropoietin, indicating systemic inflammation, increased hepcidin production by the liver and decreased iron availability for erythropoiesis. In haemodialysis patients, clinical decision-making should balance risks and benefits, erythrocyte stimulating agents' administration is frequently preferred. Haemoglobin concentration are monitored during dialysis. Lowers the quality of life and necessitates the use of a blood transfusion. More frequently than those early stages of chronic kidney disease(Andrew S. Levey. et al. 2012).

Comorbid disease such hyperparathyroidism and high calcium/phosphorus product are common in ckd patients, which can lead to myocardial fibrosis and calcium deposition. Anaemia's effects on myocardial remodelling may be exacerbated in this situation, leading to more server left ventricular hypertrophy and less reversible disease. In consequence, left ventricular hypertrophy can lead to heart failure or exacerbate ischemic heart disease (IHD). Its unclear if milder forms of anaemia or anaemia caused by other factors create more subtle changes in heart remodelling(AREMA A. PEREIRE. et al. 2003).

Kidney biopsy: -

In the diagnosis and treatment of many disorders, a kidney biopsy is the gold standard. A kidney biopsy is an invasive surgery that can be dangerous. When kidney tissue is needed to obtain a clear diagnosis that could change treatment or provide information regarding disease progression or prognosis, a kidney biopsy should be

recommended. When the possible risk to the patient out weights the likely benefit of obtaining kidney tissue, a biopsy should be avoided(Jonathan. J. Hogan. et al. 2016).

If the following criteria are met, a kidney biopsy is an advised as an invasive diagnostic test:

- a. A kidney biopsy is necessary to obtain a diagnosis or to gather information that will help guide treatment.
- b. The natural history of suspected disease is linked to high morbidity and/ or mortality.
- c. With treatment the natural history of these disease can improved(if the natural history of these disorders could not be altered, then a biopsy would not be performed).
- d. Treatments for these disorders vary depending on the diagnosis obtained by a kidney biopsy (one therapy does not exist for all renal diseases for which a diagnosis has been made)(Randy L. Luciano. et al. 2019).

Indication for kidney biopsy of chronic kidney disease are rapid elevation in serum creatinine level or new onset haematuria and proteinuria. Contraindication to kidney biopsy is bleeding risk, hypertension, infection anticoagulation concerns and solitary kidney(S K. Agarwal. et al. 2013).

Dialysis: -

Dialysis is done in chronic kidney diseases when the glomerular filtration rate falls below 15 ml/min/1.73m². The process of removal of waste and extra water from blood is called dialysis. It is an artificial replacement of kidney functioning, especially in renal failure case. Dialysis cannot completely perform lost kidney function, but, to some extent, manages its activities by means diffusion and ultrafiltration. This stage is also called end stage renal disease (ESRD). Dialysis is performed in chronic kidney disease patients to remove accumulated toxins from the body(SabithaVadakedath. etal. 2017).

Haemodialysis: -

Haemodialysis as a treatment for irreversible kidney failure described WillemKolff and Belding Scribner, who together received the 2002 Albert Lasker Clinical Medical Research Award for this accomplishment(Jonathan Himmelfarb.Etal. 2020). When enough nephrons are destroyed for the retention of salt, water and non-volatile metabolic waste products to be potentially lethal, this condition is known as end stage kidney disease. End stage renal disease is less

frequent than illnesses like ischemic heart disease, cancer and chronic obstructive renal disease but when it does, it quickly results in mortality. Without beginning renal replacement treatment (RRT). The available therapies are expensive difficult, and lifelong (NP. Mallick. etal. 1999).

Haemodialysis procedure: -

During haemodialysis, metabolic waste products are removed from the body and body buffers are replenished as a result of solute diffusion between the blood and a dialysis solution. A plastic dialyzer is used to filter heparinized blood at flow rates of dialysate flows in at rate of 300 to 500 ml per minute. Inverse direction at a rate of 500 to 800 ml per minute in order to eliminate waste products. Resulting urea clearance rates of 200 to 350 ml per minute effect a 65 to 70 percent reduction in blood urea nitrogen concentration during a three-to-four-hour treatment session, the urea clearance rate also depends on the surface area of dialyzer and the permeability of the membrane. By means of adjustments in the transmembrane pressure across the dialyzer remove of the fluid from the plasma into dialysate can be accurately controlled (STEPHEN PASTAN. etal. 1998).

Dialyzer: -

The first commercial dialyzers were in the form of coiled cellulose tubing. Later developments were of large, flat polypropylene plates sandwiching a blood compartment of copper-

cellulose sheet, then compact, factory made, flat plate filters. They consist of small units made up of bundles of finely extruded hollow fibres. Platelet aggregates and leucocytes coat cellulose-based membrane during hem dialysate in varying degrees. Combination activation cytokine release, as well as, have been observed. Another employ biocompatible synthetic membrane as an alternative avoids attracting cell aggregation. Dialyzer surface area for adults varies from 1.0 m² to more than 1.8 m² (N P Mallick. etal. 1999).

Dialysate: -

Dialysate, an electrolyte solution at body temperature, is prepared by the system. Dialysis takes place in the dialysate compartment of the dialyzer, through which the dialysate flows. Blood from the patient is pumped through the extracorporeal circulation system, into the dialyzer's blood compartment, and then returned to the patient. The dialysate circuit and the blood circuit are the two main categories to watch.

The arterial and venous blood tubing sets, the blood side of the dialyzer, the intravenous (IV) normal saline and administration line, and the heparin syringe and infusion line make up the blood circuit. The blood and dialysate are separate circuits that interface at the dialyzer membrane. The machine design must involve extensive monitoring of both circuits. Specific warning alarms must be initiated when the machine pre-set limit are exceeded and/or an unsafe condition exist (Joanne D. Pittard. etal.).

Comparison of Normal Blood Values and Dialysate Composition

Electrolyte	Dialysate Level Range	Normal Blood Value Range
Sodium	135-145 mEq/L	135-145 mEq/L
Potassium	0-4 mEq/L	3.5-5.5 mEq/L
Calcium	2.25-3.0 mEq/L	4.5-5.5 mEq/L
Magnesium	0.5-1.0 mEq/L	1.5-2.5 mEq/L
Chloride	100-115 mEq/L	95-105 mEq/L
Bicarbonate	30-40 mEq/L	22-28 mEq/L
Non-electrolyte		
Dextrose	0-200 mg/dL	80-120 mEq/L

Peritoneal dialysis: -

Peritoneal dialysis is now established form of therapy in the management of end-stage renal failure (ESRF), but more than a century of painstaking work and research was needed to

establish it. In 1959, Maxwell and colleagues described a simplified method of intermittent irrigation of the peritoneal cavity, which used a single, disposable catheter and commercially prepared dialysis solutions (R Gokal. etal. 1999).

In peritoneal dialysis, the peritoneal membrane, which is made up of a vascular wall, the interstitium, and the mesothelium, allows for exchange of solutes and fluids between the peritoneal capillary blood and the dialysis solution in the peritoneal cavity. The peritoneal dialysis solution addition of the proper osmotic agents cause osmosis, which is what cause fluid changes. Solute mobility is governed by the physical rules of diffusion and convective transport. The peritoneal blood flow, the highly vascular membrane, and the flow rate and volume of the peritoneal dialysis solutions are the critical elements of the peritoneal dialysis system. The only variable that can be changed to achieve maximum solute and fluid elimination is the flow rate because peritoneal blood flow and the membranes vascularity cannot be altered (R Gokal. et al. 1999).

Continuous ambulatory peritoneal dialysis (CAPD). This concept discovered by Popovich, by the uses of the smallest volume of dialysate. The lowest dialysate flow rate to prevent uraemia. Using a double pool (the body as one pool and fluid in the peritoneal cavity as the other) model, they showed that the accumulation of a metabolite in the body is equal to the generation rate, minus combined effect of the residual renal function and overall dialysate clearance.

Human Kidney Transplantation

Organ transplantation is the best therapy for transplantation is the best therapy for terminal and irreversible organ failure. Kidney transplantation introduced in the 1950s was the pioneer solid organ transplant to treat patient with end stage renal disease (ESRD) in an era when renal replacement therapies were in their first step. From the distinct alternatives for the treatment of end stage renal disease, renal transplantation may also be the first therapeutic option of renal replacement theory to avoid dialysis. Pre-emptive renal transplantation (PRT) may reduce the comorbidities associated with dialysis enhance quality of life, and improve transplant outcomes (Josep M. 2013).

Criteria for exclusion of kidney donor

1. Age less than 18 Years or Greater than 55 years.
2. Hypertension:- Patients whose systolic pressure is consistently above 140 mm Hg and whose diastolic pressure is consistently above 90 mm Hg or patient who require antihypertensive drugs to normalize blood

pressure are usually excluded from consideration as donors.

3. Diabetes: - glucose tolerance is assessed by measuring haemoglobin A1C and by measuring fasting blood glucose levels on two separate occasions. If finding is normal, we consider the patient to be nondiabetic.
4. History of kidney stone or Evidence of Kidney Stone on Roentgenogram.
5. Abnormal Glomerular Filtration Rate:- This rate estimated from the measurement of serum creatinine concentration and the relating of that level to body size. The normal range of serum creatinine concentration in an adult is 0.6 to 1.3 mg/dL.
6. Unexplained Microscopic Haematuria:- when high frequency erythrocyte found in urine sediment. Use of these criteria to indicate normal values would include patients with significant renal disease.
7. Abnormal Proteinuria.
8. Any Urologic Abnormality in a Donor Kidney That Could Pose a Future Risk to Either Donor or Recipient.
9. History of Systemic Disorder That Has Impaired or Might Impair General Health.
10. Obesity: - Generally, Potential donors who are more than 15% above ideal body weight are advised to lose the excess weight before the kidney transplantation is scheduled (WILLIAM H. BAY, et al, 2018).

Indication for renal transplantation

Once a patient meets the medical requirements for major surgery and long-term immunosuppression, they are classified as having stage 5 Chronic Kidney Disease (eGFR 15 ml/min/1.73 m²). In rare cases patients with an eGFR >15 ml/min/1.73 m² may also be given the option of transplantation if they are experiencing severe uraemic side effects. Depending on the type of cancer and how severe it is, the guidelines recommend delaying surgery recommend delaying surgery for 2-5 years in individuals who had a prior malignancy (excluding non-melanoma skin cancer). Although age-related comorbidity is a key factor in the decision to move forward with the transplant, the age of the recipient is not a restriction on the decision to transplant (Adam D Barlow. 2014).

Sources of kidney for transplantation

Kidney donation divided into two types.

1. Living donor: - Living related donor, Living unrelated donor, Altruistic (non- directed) donor.

2. Decreased donor: - Donation after brain death (DBD) and Donation after circulatory death (DCD). In DCD they are controlled and uncontrolled (Adam D Barlow. 2014).

Clinical practice guideline for the post-operative care of the kidney transplant recipient (KTR).

Guideline 1.1: - KTR clinic infrastructure.

- A consultant- level health care professional should be available for every transplant clinic.
- KTRs should be reviewed in a dedicated outpatient area.
- The results of blood tests (including drug level if possible) should be available within 24hr.
- There should be access to a multidisciplinary renal team including pharmacist, dietician, social worker and psychologist.
- Patient care should be planned along principles set out in the National Service Framework and Kidney Health Delivering Excellence.

Guideline 1.2: - KTR clinic frequency

- 2- 3 times weekly for the first month after transplantation.
- 1-2 times weekly for months 2-3.
- Every 2-4 weeks for months 4-6.
- Every 4-6 weeks for 6-12.
- 3-6 monthly thereafter.

Guideline 1.3: - KTR patient access

- All patients should have the option of on-line access to their results via the patient view service.
- All patient should have open access to the renal transplant outpatient service and have an established point of contact enquiries.
- Patient information should be available in both written and electronic formats.

Guideline 1.4: - KTR chronic transplant care review.

- A process should exist for patient review on an annual basis in a different format of clinic according to the care plan model.
- This should be patient – centred clinic, facilitated by a health care professional.
- It should address concern in medical, social psychological and sexual domains.
- Access to a renal dietician, social worker, specialist renal pharmacist and psychologist should be readily available from this clinic.
- This process should proceed in parallel with formal medical review (Richard J. Baker, et al. 2017).

II. CONCLUSION

This review focuses on the chronic kidney disease. Chronic kidney disease means long term kidney disease, presence of abnormalities in kidney structure or functioning persisting for more than 3 months. There is presence of excess amount of protein and albumin in urine called proteinuria and albuminuria in CKD patients. Classification of chronic kidney disease is divided according to their stages. CKD also includes Etiopathogenesis and its causes. For detection of CKD kidney biopsy test is used. At the end stage of chronic kidney disease patient must undergoes dialysis and kidney transplantation. At the time kidney transplantation patient should follow pre and post guidelines directed by physician.

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