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**NATIONAL PROTOCOL FOR THE  
PREVENTION AND MANAGEMENT OF  
CHRONIC KIDNEY DISEASE**

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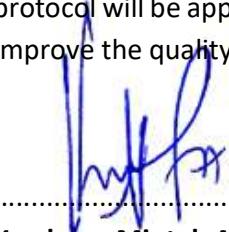
## **FOREWORD**

The global incidence and prevalence of chronic kidney disease (CKD) is on the rise and is estimated to be between 10% and 13%. CKD has now emerged as a significant public health challenge in Sub-Saharan Africa, with a reported prevalence of 13.9% in a recent meta-analysis. In Ghana, the prevalence of CKD has been shown to be 13.3%. The prevalence of CKD is much higher (28.5%) among patients with both diabetes mellitus and hypertension. It has been reported to be 26.3% among patients with hypertension and 16.1% among those with diabetes mellitus. CKD is also associated with increasing morbidity and mortality with significant financial burden on health systems.

The negative impact and catastrophic financial burden on patients cannot be over-emphasized, with an average monthly cost of approximately GHS 3,467 for CKD patients on dialysis which is five times higher than costs for patients with CKD who do not require dialysis. Unfortunately, very low levels of CKD awareness exist in Ghana and Africa in general with awareness estimated at 6% in the general population and 10% amongst high-risk populations. Ghana has very few trained nephrologists who are only available in tertiary facilities. This emphasizes the importance of investing in kidney health promotion and prevention of kidney disease.

The Ministry of Health has rolled out policies aimed to curb the rising burden of non-communicable diseases. CKD and other non-communicable diseases (NCD) impose significant economic burden on healthcare systems resulting in loss of productivity, ultimately impacting economic and health indicators negatively. This protocol is, therefore, timely and will provide solutions to the challenges around CKD in Ghana

The Ministry of Health expresses its sincere appreciation to all individuals and stakeholders involved in developing this ground-breaking protocol. It is our hope that the provisions in the protocol will be applied to reduce morbidity and mortality associated with CKD and ultimately improve the quality of life of persons living with CKD in Ghana.



.....  
**Kwabena Mintah Akandoh (MP)**

Minister of Health  
Ghana

March 2025



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- Director Public Health GHS
- Director Institutional Care Division GHS
- The NCD Control Programme
- The Ghana Kidney Association
- AstraZeneca
- PATH

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## ABBREVIATIONS & ACRONYMS

ABGs	Arterial Blood Gases
ACEi	Angiotensin-Converting Enzyme inhibitors
ACR	Albumin Creatinine Ratio
AER	Albumin Excretion Rate
AGI	Alpha-Glucosidase Inhibitor
aHUS	Atypical Hemolytic Uremic Syndrome
AKI	Acute Kidney Injury
ARBs	Angiotensin Receptor Blockers
ASCVD	Atherosclerotic Cardiovascular Disease
AV Fistula	Arteriovenous Fistula
BMI	Body Mass Index
CAKUT	Congenital Abnormalities of the Kidney and Urinary Tract
C-ANCA	Cytoplasmic Anti-neutrophil Cytoplasmic Antibody
CCB	Calcium Channel Blocker
CCC	Comprehensive Conservative Care
CGA	Cause, GFR category and Albuminuria category
CGM	Continuous glucose monitoring
CKD	Chronic Kidney Disease
MDB	Mineral and Bone disorder
CMP	Calcium, Magnesium and Phosphate
CT-scan	Computed Tomography Scan
CVD	Cardiovascular Disease
DKD	Diabetic Kidney Disease
DM	Diabetes Mellitus
DN	Diabetic Kidney Disease
DPP-4i	Dipeptidyl Peptidase-4 inhibitor
ECG	Electrocardiogram
EGFR	Estimate Glomerular Filtration Rate
ESKD	End Stage Kidney Disease
FSGS	Focal segmental glomerulosclerosis
FTT	Failure to Thrive
GBM	Glomerular basement membrane
GFR	Glomerular filtration rate
GLP-1	Glucagon-Like Peptide-1 Receptor Agonist
HB	Haemoglobin
HbA1C	Glycated Haemoglobin
HD	Haemodialysis
HELLP	Haemolysis, Elevated Liver Enzymes, And Low Platelets
HIV	Human Immunodeficiency Virus
HPF	Microscope High-Power Field
HUS	Haemolytic Uraemic Syndrome
ISN-GKHA	International Society of Nephrology: Global Kidney Health Atlas
KDOQI	Kidney Disease Outcomes Quality Initiative
KRT	Kidney Replacement Therapy
LDL	Low Density Lipoprotein
MCHC	Mean Corpuscular Haemoglobin Concentration
MCV	Mean Corpuscular Volume
MBD	Mineral and Bone Disorder
MNT	Medical Nutrition Therapy



MRI	Magnetic Resonance Imaging
MSG	Monosodium Glutamate
NFK	National Kidney Foundation
NICE	National Institute for Health and Care Excellence
NSAIDs	Non Steroidal Anti-inflammatory Drugs
NsMRA	Non-Steroidal Mineralocorticoid Receptor Antagonist
P-ANCA	Perinuclear Pattern Antineutrophil Cytoplasmic Antibody
PCSK-9	Proprotein Convertase Subtilisin/Kexin Type 9
PD	Peritoneal Dialysis
PTH	Parathyroid Hormone
PUJ	Pelvic Ureteric Junction
PUV	Posterior Urethral Valves
RAASi	Renin Angiotensin aldosterone System inhibitors
RBC	Red blood cell
SBP	Systolic blood pressure
SGLT2i	Sodium-Glucose Cotransporter-2 inhibitor
SLE	Systemic Lupus Erythematosus
SMBG	Self-Monitoring of Blood Glucose
SU	Sulfonylurea
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
TSAT	Transferrin Saturation
TPP	Thrombotic Thrombocytopenic Purpura
TZD	Thiazolidinedione
UACR	Urine Albumin Creatinine Ratio



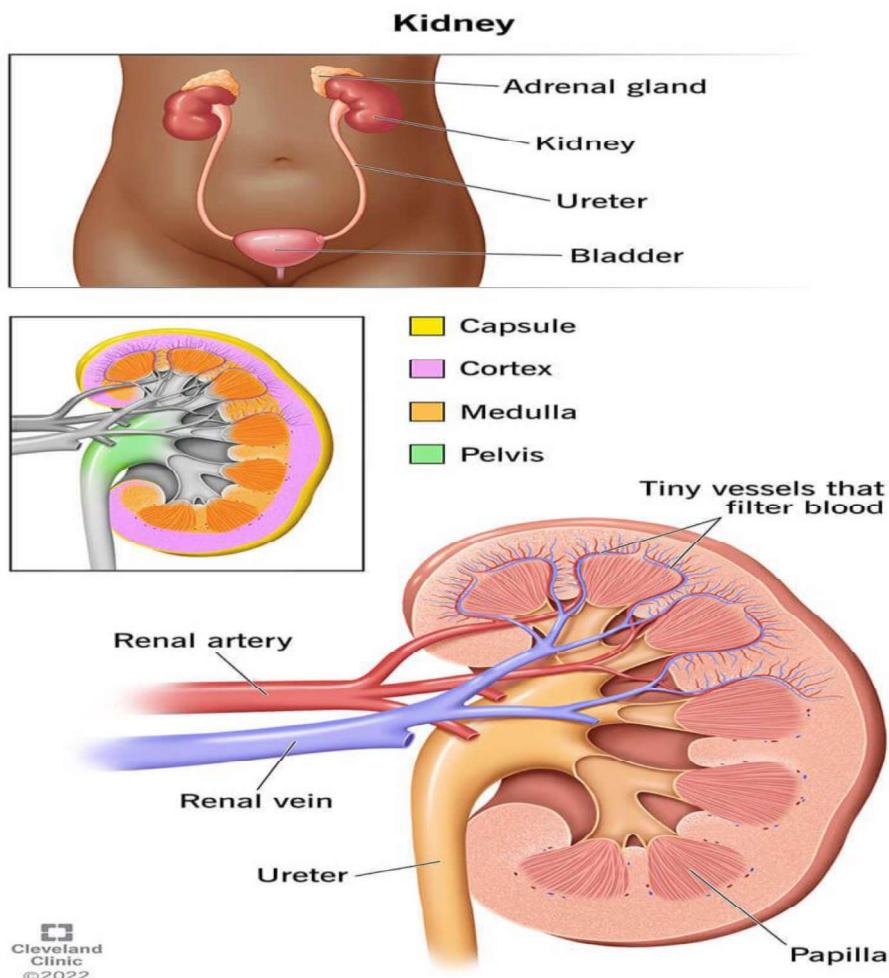
# MODULE 1: UNDERSTANDING CKD

## Objectives

1. Understand basic anatomy and physiology of the kidney.
2. Define chronic kidney disease (CKD)
3. Assess kidney function.
4. Provide an overview of CKD epidemiology globally and in Ghana.

## Anatomy of the kidneys

The kidneys are paired organs, located in the flanks below the diaphragm and retroperitoneally. The right kidney is usually slightly lower than the left due to the concomitant presence of the liver. Figure 1 below depicts the anatomy of the kidney.



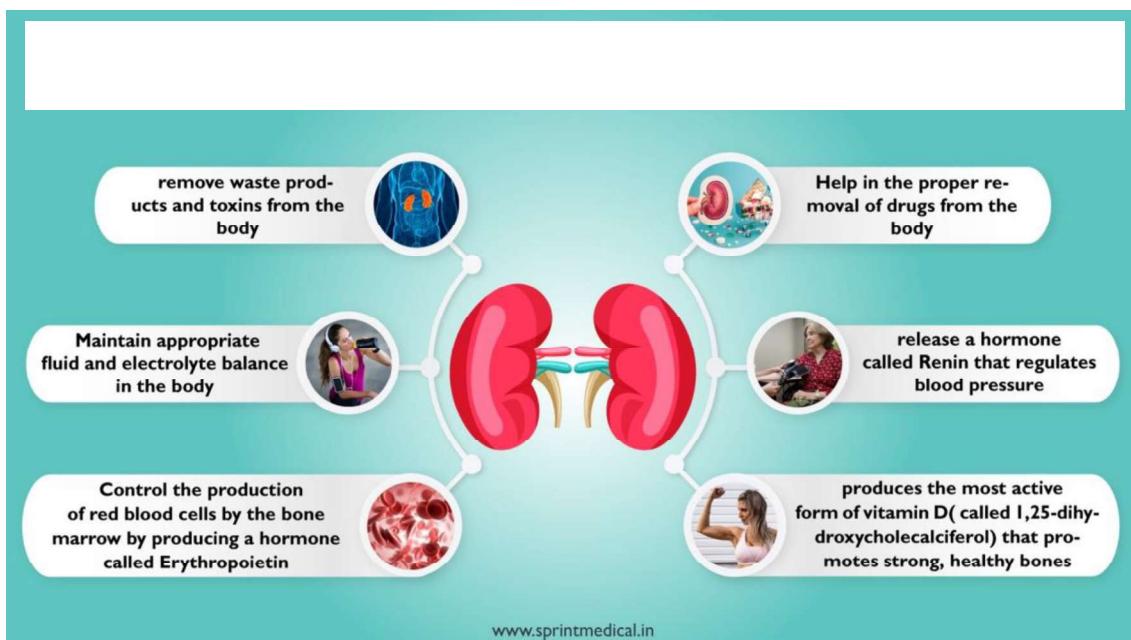
**Figure 1:** Anatomy of the kidneys



Each kidney normally weighs between 125g to 170g in adult males and 115 to 155g in adult females, and measures approximately 10 to 12cm long. They individually receive their blood supply from a single renal artery which take their origin from the abdominal aorta, although one or more accessory renal arteries may be present.

On the cut surface of a bisected kidney, two main regions are visible: a granular outer cortex and a striated inner medulla. The cortex and medulla contain the basic functional units of the kidney, the nephrons. On average, each kidney contains 1 million nephrons. It is important to note that by virtue of the many critical functions the kidney performs, it receives 20-25% of the blood pumped into the systemic circulation by the heart (cardiac output) and is considered a vital organ.

## Functions of the kidney



**Figure 2: Functions of the kidneys**

Generally, the functions of the kidneys are as follows:

1. Maintenance of normal body fluid balance.
2. Excretion of waste products of metabolism and excretion of foreign substances.
3. Regulation of blood pressure.
4. Production of hormones
  - a. Erythropoietin which is needed for the production of blood
  - b. Vitamin D needed for calcium and phosphate balance.



## Definition and assessment of kidney function

Chronic Kidney Disease (CKD) is defined as abnormalities of **kidney structure or function** present for > 3 months with implications for health.

One of the most frequently used measures of kidney function is the **estimated Glomerular Filtration Rate (eGFR)**: which is a mathematical approximation of the measured or true Glomerular Filtration Rate (GFR). This term refers to the excretory function of the kidney and can be used to stage the degree of kidney dysfunction, as will be seen in subsequent sections of this manual. The excretory function is largely described as but not limited to the ability of the kidney to excrete toxic waste substances produced from the body's metabolic processes in the form of urine.

The second marker of kidney function that is routinely assessed to determine abnormal kidney function is **albuminuria**. The gold standard for determining albuminuria is the 24-hour urine albumin collection. This test is associated with significant inconvenience to the patient as it requires collection of urine over a 24-hour period. The spot urine albumin to creatinine ratio has been found to be a reliable marker of the different grades of albuminuria which are suggestive of abnormal kidney function. However, a positive urine dipstick (regardless of the degree of positivity) is indicative of possible kidney dysfunction, warranting further evaluation if persistent.

Structural abnormalities of the kidneys are most conveniently assessed by ultrasound imaging and may include shrunken kidneys, polycystic kidneys or evidence of urine outflow obstruction.

It is also important to note that to arrive at a diagnosis of CKD, one or a combination of these features lasting for a period of more than 3 months may be used. This concept will be further explained subsequently.

## Epidemiology of CKD

The global prevalence of CKD is estimated at 9.1% with the 2023 ISN-GKHA revealing that, from the approximately 850 million people affected by CKD worldwide, people of every age and race are affected, with people from disadvantaged populations being at a higher risk. It has been reported that 78% of people affected globally reside in low- and middle-income countries<sup>1,2</sup>. The average prevalence in sub-Saharan Africa is 13.9% with the prevalence in Ghana shown to be 13.3%<sup>3</sup>. The number of deaths caused by CKD has doubled, from 0.6 million deaths in 1990 to 1.2 million deaths in 2016; CKD was the 18th leading cause of death in 1990 and ascended to the 11th leading cause of death in 2016. The World Health Organization projects CKD to become the 5th most common chronic disease in 2040. The increased burden of CKD is driven in large part by the increased global epidemic of diabetes and hypertension<sup>4</sup>.



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# MODULE 2: CLASSIFICATION OF CKD

## Objectives

1. Discuss the classification of CKD
2. Understand the rationale for CKD classification and staging.

## Staging and classification of CKD

The staging system for CKD is intended to aid clinicians in:

- determining the degree of kidney dysfunction
- identifying those at greatest risk for progression and complications.
- management of patients with CKD.

Chronic Kidney Disease is classified based on **Cause, GFR category and Albuminuria category** abbreviated as CGA. CGA staging allows for a more complete description of risk for the major adverse outcomes of CKD<sup>1,2</sup>.

**Classification by Cause of disease** — Identifying the cause of kidney disease enables specific therapy directed at preventing further injury which has implications for the rate of progression and the risk of complications. It can sometimes be difficult to ascertain the cause of CKD. Table 1 shows classification of CKD according to cause of disease.

CAUSES	EXAMPLES
<b>Glomerular diseases</b>	Diabetes mellitus Systemic infections such as HIV Systemic autoimmune diseases (eg SLE) Medications such as non-steroidal anti-inflammatory drugs (NSAIDs) Focal segmental glomerulosclerosis (FSGS) Minimal change disease
<b>Tubulo-interstitial diseases</b>	Urinary tract infections, stones, obstruction Systemic infections Sarcoidosis Medication (eg. NSAIDs, Omeprazole) Environmental toxins (eg lead, Mercury, Arsenic, unlicensed herbal medications) Neoplasia (eg myeloma)
<b>Vascular diseases</b>	Atherosclerosis Hypertension Cholesterol emboli Systemic vasculitis
<b>Cystic and congenital diseases</b>	Polycystic kidney disease Congenital Abnormalities of the Kidney and Urinary Tract (CAKUT) Alport's syndrome

*Table 1: Classification of CKD according to Cause of disease<sup>1,2</sup>.*



### Classification by Glomerular filtration rate (GFR) category:

GFR stages follow the original CKD classification scheme<sup>3</sup> as in Table 2 below.

GFR Category	GFR (ml/min per 1.73m <sup>2</sup> )	Terms
G1	≥90	Normal or high*
G2	60-89	Mildly decreased*
G3a	45-59	Mildly to moderately decreased
G3b	30-44	Moderately to severely decreased
G4	15-29	Severely decreased
G5	< 15	Kidney failure

\*In the absence of evidence of kidney damage, neither G1 nor G2 fulfill the criteria for CKD.

**Table 2: GFR categories in CKD**

**Classification by Albuminuria category** — The three albuminuria stages follow familiar definitions of normal, moderately increased (formerly called "microalbuminuria"), and severely increased (formerly called "macroalbuminuria" and nephrotic range) albuminuria as in table 3 below.

Category	AER (mg/24 hours)	ACR (approx. equivalent)		Terms
		(mg/mmol)	(mg/g)	
A1	<30	<3	<30	Normal to mildly increased
A2	30-300	3-30	30-300	Moderately increased*
A3	>300	>30	>300	Severely increased†

\* Relative to young adult level. † Including nephrotic syndrome (albumin excretion usually >2200 mg/24hours [ACR >2200 mg/g; >220 mg/mmol]). AER, albumin excretion rate, ACR, albumin-to-creatinine ratio. (KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease)

**Table 3: Albuminuria categories in CKD.**

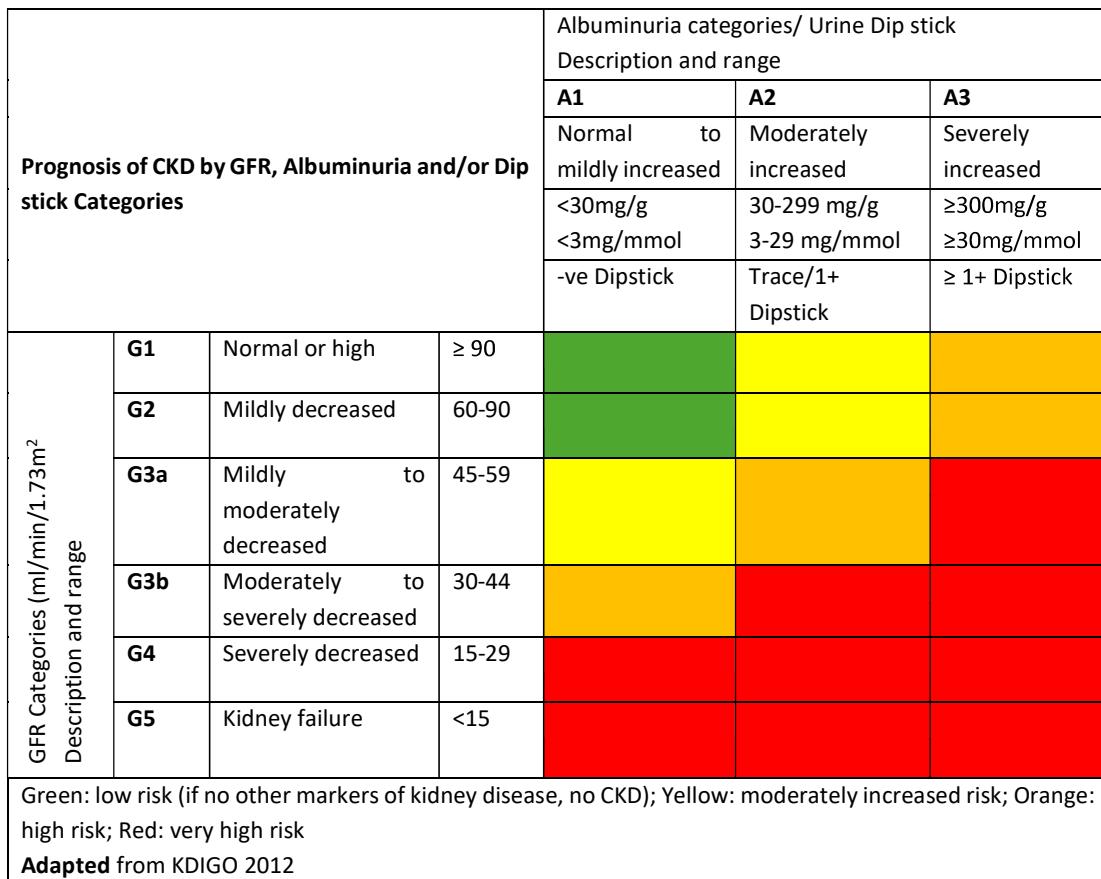
**In the absence of a urine ACR, a positive urine dipstick may give an idea of the level of albuminuria (Refer to urine dipsticks in module 4).**

Albuminuria staging has been added because of the graded increase in risk for mortality, progression of CKD, and ESKD at higher levels of albuminuria, independent of eGFR. Based on the above classification, a "heat map" can be constructed that groups patients with CKD into the following four (4) broad risk categories based upon the likelihood of developing future kidney and cardiovascular complications (eg, ESKD, cardiovascular death). The risk categories are as follow:



- |                              |                                  |
|------------------------------|----------------------------------|
| <b>1. Low risk (green)</b>   | <b>2. Moderate risk (yellow)</b> |
| <b>3. High risk (orange)</b> | <b>4. Very high risk (red)</b>   |

These four (4) broad risks categories may help clinicians decide whether or not to refer their patients to a nephrologist or specialist with expertise in caring for patients with CKD, and to develop a clinical action plan. The classification of CKD based on GFR and Albuminuria is shown in figure 3 below.



**Figure 3: Classification of CKD Based on GFR and Albuminuria Categories: "Heat Map"<sup>2</sup>**

Risk stratification is used as a guide to inform appropriate treatments and the intensity of monitoring and patient education<sup>4</sup>.



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# MODULE 3: CKD RISK FACTORS AND CAUSES

## Objectives

The objective of this module is to highlight the common risk factors and causes for CKD.

## Risk factors for CKD

CKD risk factors are attributes, characteristics or exposures that increase the likelihood of a person developing CKD. Several risk factors for CKD have been identified<sup>1</sup>. These risk factors may be classified as susceptibility, initiation and progression factors (See Table 4). Early detection and management of these CKD risk factors will help prevent and/or slow the progression of CKD<sup>2</sup>.

Risk factors	Examples
<b>Susceptibility factors</b> - Factors that predispose to CKD	Black race, genetic and familial predisposition Maternal-fetal factors (low birth weight, malnutrition in utero) Age (elderly) Gender (male) Structural urinary tract disease Recurrent kidney calculi Prior acute kidney injury (AKI)
<b>Initiation factors</b> - Factors that directly trigger kidney damage	Diabetes mellitus Hypertension Cardiovascular disease Dyslipidemia Obesity Hyperuricemia Nephrotoxin exposure (eg NSAIDs, unlicensed herbal medication)
<b>Progression factors</b> - Factors associated with worsening of already established kidney damage	Poor blood sugar control Poor blood pressure control Cardiovascular disease Proteinuria Nephrotoxin exposure (eg NSAIDs and unlicensed herbal medication use) Acute kidney injury

*Table 4: Categories of risk factors for CKD<sup>2</sup>.*



A history of diabetes, hypertension, or cardiovascular disease confers the highest risk for developing CKD, and individuals who have such a history should be evaluated for CKD. Table 5 below summarizes the common risk factors for CKD encountered in clinical practice.

## Common Risk Factors for CKD

CATEGORY OF RISK FACTOR	CONDITIONS
Common risk factors	Hypertension Diabetes Cardiovascular disease (including heart failure) Prior AKI
Genitourinary disorders	Structural urinary tract disease Recurrent kidney calculi Gestational conditions (eg pre-eclampsia)
Multisystem diseases	Systemic lupus erythematosus Gout HIV Preeclampsia/eclampsia Chronic Viral Hepatitis B and C Sickle cell disease
Occupational exposures	Cadmium, lead, and mercury exposure Polycyclic hydrocarbons Pesticide
Nephrotoxins	Chronic NSAID use Lithium Unlicensed Herbal preparations
Others	Obesity Tobacco smoking

**Table 5: Common CKD risk factors<sup>3,4</sup>.**



## Modifiable and Non - Modifiable Risk Factors

There are severable modifiable risk factors and a few non-modifiable risk factors for CKD<sup>3,4</sup> as shown in table 6 below.

### Modifiable and Non-Modifiable Risk factors

*Table 6. Modifiable and Non-modifiable risk factors*

Modifiable risk factors	Non-modifiable Risk Fcators
Diabetes mellitus	Genetic factors (eg high risk APOL1(G1 and G2)
Hypertension, PreEclampsia/Eclampsia	Family history
Obesity	Gender (Male)
Physical inactivity	Black race
Excessive salt intake	Advancing age
Excessive alcohol intake	Low birth weight
Cigarette smoking or tobacco use	
Nephrotoxins (NSAIDs, Herbs abuse)	
History of acute kidney injury	
Systemic conditions such as SLE	
Human Immunodeficiency Virus (HIV)	
Urinary tract abnormalities	

## Causes of CKD in Ghana

The most common causes of CKD in Ghana<sup>5</sup> are:

- Hypertension
- Diabetic mellitus
- Glomerular diseases
- CKD of uncertain cause

Other causes include:

- Cystic kidney disease such as polycystic kidney disease
- Chronic urinary tract obstruction
- Sickle cell disease
- Systemic Lupus Erythemathosus (SLE)
- HIV infection
- NSAIDs and unlicensed herbal medications use.



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# MODULE 4: SCREENING AND DIAGNOSIS OF CKD

## Objectives

1. Assess patient history relevant to CKD.
2. Identify signs and symptoms of CKD.
3. Identify high risk patients for screening.
4. Screen patients appropriately for CKD.
5. Make an accurate diagnosis of CKD.
6. Outline relevant investigations in patients with CKD.

## History taking in a patient with CKD

- A detailed medical history will help to establish the presence of symptoms of CKD and possible cause(s) of CKD.
- Patients with CKD stages 1-3 are largely asymptomatic and most are diagnosed with routine laboratory screening.
- Some forms of CKD such as glomerular diseases may present with symptoms in the early stages.
- A patient with CKD may present with the following symptoms<sup>1</sup>:
  - Generalized swelling of the body (legs, early morning facial swelling, abdominal swelling etc.)
  - Frothy or foamy urine
  - Haematuria (blood in urine)
  - Difficulty in breathing on exertion or at rest
  - Unexplained fatigue
  - Frequent urination at night
  - Reduced urine output
  - Gastrointestinal symptoms such as loss of appetite, abdominal pain, nausea, vomiting, and weight loss
  - Generalized body itch
  - Metallic taste in the mouth
  - Muscle cramps and twitches
  - Headache
  - Restless leg syndrome
  - Convulsions
  - Reduced level of consciousness



- Look out for a history of any of the following:
  - Diabetes mellitus (duration and history of poor control)
  - Hypertension (duration and history of blood pressure control)
  - Sickle cell disease
  - Autosomal dominant polycystic kidney disease
  - Previous acute kidney injury (AKI)
  - Recurrent or longstanding proteinuria, haematuria, edema, etc.
  - Autoimmune diseases that often involve the kidney (e.g. SLE, mixed connective tissue disease, Sjogren syndrome etc.)
  - Heart failure
  - Liver failure
  - Peripheral vascular or cerebrovascular disease
  - Obesity
  - Cigarette smoking or tobacco use
  - Multiple myeloma or monoclonal gammopathy.
  - Nephrotoxic medications exposure (NSAIDS, cancer chemotherapy drugs, unlicensed herbal medications, recreational drug use).
  - Environmental toxin exposure (E.g. arsenic and mercury etc. from galamsey mining)
  - Family history of kidney disease
  - Recurrent and complicated urinary tract infections
  - Lower urinary tract obstruction (prostate disease, urethral stricture, kidney stones etc.)
  - Prior, known or suspected urologic, pelvic, and retroperitoneal malignancy.
  - Known infection with HIV, Hepatitis B and Hepatitis C infection.
- A targeted cause-specific history should also be sought to find the possible cause of the CKD (Table 7).

Disease condition	History
Diabetes mellitus	History of longstanding diabetes mellitus Poor glycemic control Poor or worsening vision History of other long-term complications of diabetes mellitus eg. Neuropathy, amputation
Hypertension	History of longstanding hypertension Poor blood pressure control Episodes of malignant hypertension (DBP > 120mmHg with fresh retinal bleed ± papilloedema) history of other complications of hypertension eg. Stroke, heart failure, AKI
Urinary tract	Lower urinary tract obstructive symptoms



obstruction	<ul style="list-style-type: none"> <li>• Reduced urine output</li> <li>• Straining at micturition</li> <li>• Hesitancy</li> <li>• Incomplete emptying of bladder</li> </ul>
Systemic Lupus erythematosus	<p>Skin rash (butterfly rash on face)</p> <p>Joint pains</p> <p>Hair loss</p> <p>Mouth ulcers</p>
Multiple myeloma	<p>Symptoms of anemia</p> <p>Bone pains</p> <p>Weight loss</p> <p>Frequent infections</p>
Polycystic kidney disease	<p>Positive family history</p> <p>Recurrent urinary tract infection</p> <p>Flank pain</p> <p>Abdominal distension</p>

**Table 7: Summary of relevant history on presentation of common causes of CKD**

- Another aspect of the history taking is to attempt to distinguish acute kidney injury from chronic kidney disease, especially in patients who present for the first time with abnormal kidney function. Further evaluation may be needed (See Module 6.

## Physical examination in chronic kidney disease

Physical examination in CKD will help to identify signs as well as a possible cause of CKD.

A patient with CKD may present with any of the following signs<sup>1,2</sup>:

### General examination

- Pallor
- Uremic frost
- Fluid retention (generalized body swelling, facial puffiness, bipedal edema)
- Skin changes (pigmentation, rashes, palpable purpura, scratch marks from body itch, nail changes)
- Fundoscopic examination showing retinopathy from hypertension or diabetes mellitus.
- Body mass index (>25kg/m<sup>2</sup>)



### **Cardiorespiratory system examination**

- Elevated blood pressure
- Pericardial rub due to uremic pericarditis
- Displaced apex beat suggestive of left ventricular hypertrophy from long standing hypertension.
- Bibasal lung crepitations
- Raised jugular venous pressure (distended neck vein)
- High pulse rate (tachycardia)
- High respiratory rate (tachypnoea)

### **Gastrointestinal/abdominal examination**

- Palpable enlarged kidneys may suggest polycystic kidney disease.
- Abdominal bruit may suggest renal artery stenosis.
- Ascites from fluid retention

### **Neurologic examination**

- Confusion
- Reduced level of consciousness
- Flapping tremors
- Seizures

## **Screening for CKD**

### **Rationale for Screening<sup>3,4</sup>**

- Early CKD is asymptomatic.
- Early diagnosis of CKD offers the opportunity to institute appropriate management that may slow the rate of decline of kidney function and reduce cardiovascular disease risk.
- There are accurate low-cost testing and effective treatment interventions for early CKD.
- Screening populations at risk of CKD will improve outcomes for these patients and reduce healthcare economic burden on the patient, relatives, and nation.

### **Who to Screen**

- People at risk of CKD should be screened.
- Patients with the following conditions are at high risk of CKD and should be targeted for screening.
  - Hypertension
  - Diabetes mellitus
  - Cardiovascular disease



- In addition, CKD screening should be implemented in other high-risk groups, such as those with:
  - Other medical conditions that impact kidney function (e.g. systemic lupus erythematosus (SLE), HIV, Hepatitis B, Hepatitis C, obesity)
  - Genetic risk factors
  - High-risk occupations and environmental exposures (e.g. illegal small-scale mining {galamsey})
  - Pre-eclampsia
  - Nephrotoxins (e.g. abuse of NSAIDs and unlicensed herbal medications)
  - Poor access to healthcare or low socioeconomic status
  - Age 40 years and above
  - Family history of kidney disease
  - History of acute kidney injury

#### **Recommended screening for patients with diabetes mellitus**

- In type 2 DM: at diagnosis and yearly thereafter
- In type 1 DM: five years after diagnosis and yearly thereafter

#### **Recommended screening for patients with hypertension**

- Patients with hypertension should be screened at least yearly for CKD

#### **How to Screen**

The initial screening tests for CKD should include:

- Urine dipstick for proteinuria
- Urine albumin creatinine ratio (UACR) to detect albuminuria
- Serum creatinine and Cystatin C (if available) to estimate glomerular filtration rate (eGFR)
- Blood pressure measurement
- Blood glucose estimation
- Weight and height measurement for BMI calculation
- Urine albumin creatinine ratio (UACR) is preferred for the assessment of the degree of albuminuria. However, if this is unavailable in low resource settings, urine dipstick for proteinuria may be used.
- Screening tests should be conducted any time a high-risk individual has contact with the healthcare system.



See suggested screening test for CKD according to the level of healthcare facility in table 8 below.

Level of facility	Screening test	Remarks
CHPS/ Health Centre	Urine dipstick for proteinuria	If dipstick protein of $\geq 1+$ , repeat dipstick testing within two weeks. If still positive, refer to a health centre with a doctor or district hospital for further evaluation.
Health centre with a doctor/physician assistant or district hospital	Urine dipstick UACR (if available) Serum Creatinine and eGFR	If dipstick protein of $\geq 1+$ , repeat dipstick testing within two weeks. If still positive, refer to a specialist. For persistent UACR $> 30\text{mg/g}$ , refer to a specialist
Tertiary facility (Specialist available)	Urine dipstick UACR and other markers of kidney damage Serum Creatinine /Cystatin C (if available) and eGFR	Evaluate further to stage patient and refer to a nephrologist based on the risk of progression (Refer to fig heatmap)

**Table 8: Suggested screening test for CKD according to the level of healthcare facility.**

Rescreening of population at risk of CKD who have normal screening tests should be based on the individual's risk of developing CKD.

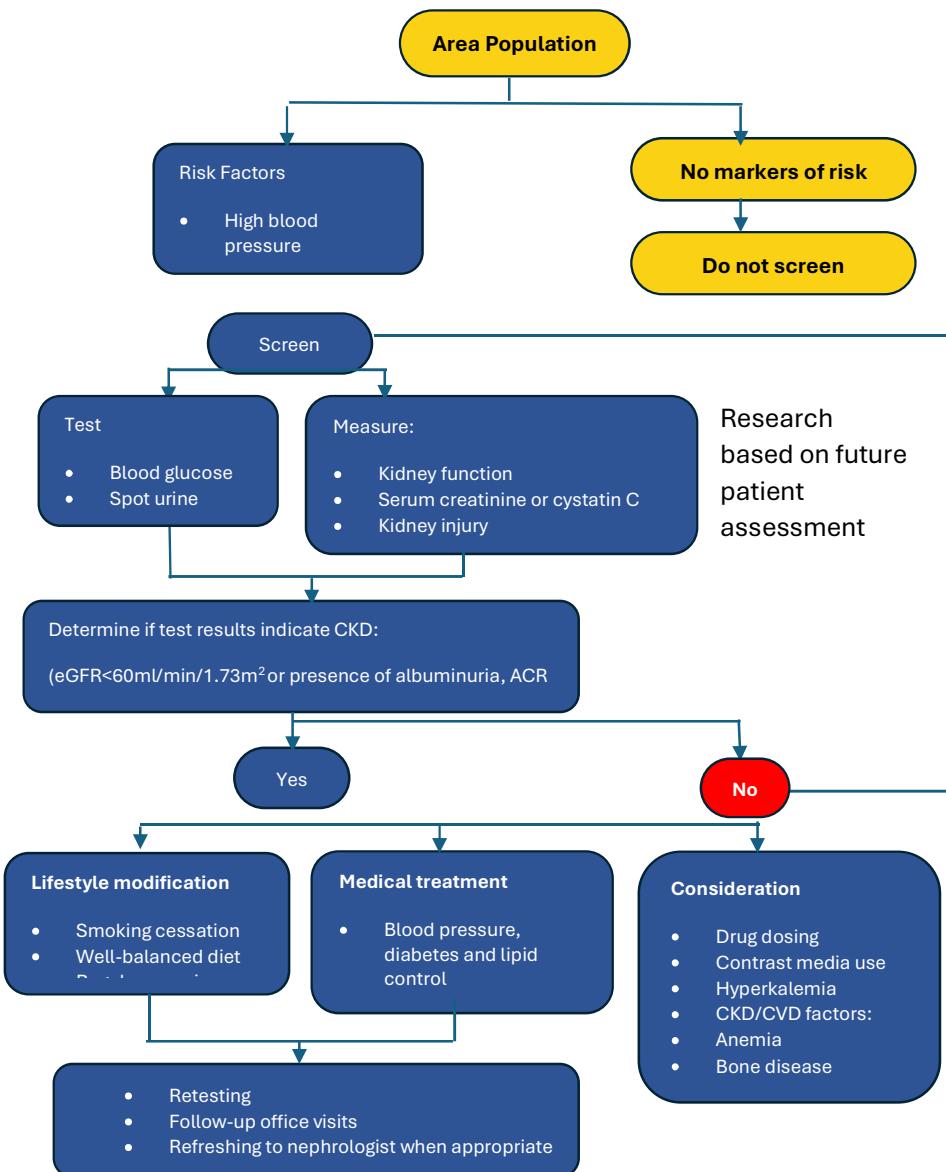
## Diagnosis of CKD

A diagnosis of CKD is made<sup>3</sup> if any of the following is present for 3 months or more:

- eGFR  $<60\text{ml/min}/1.73\text{ m}^2$
- Markers of kidney damage
  - Proteinuria (urine ACR  $>30\text{mg/g}$  (3mg/mmol), dipstick proteinuria  $\geq 1+$ )
  - Haematuria (microscopic or macroscopic)
  - Abnormal ultrasound findings (shrunken kidney, cystic kidney)



Figure 4 below suggests an approach to screening and diagnostic testing for CKD.



**Figure 4: Algorithm showing the approach to screening and diagnostic testing for CKD.**

- Individuals diagnosed with CKD should be risk stratified using the degree of UACR and the eGFR (refer to module 2).
- The eGFR and degree of UACR determine the risk of progression of CKD and cardiovascular disease, frequency of monitoring of patients and timing of referral to a nephrologist.
- Referral to a nephrologist is appropriate for patients with potentially treatable underlying disease and those who are likely to progress to ESRD.



## **Investigating CKD**

Investigations conducted in individuals diagnosed with CKD include urine tests, blood tests, imaging, and kidney biopsy.

The main aims of investigating patients with CKD are to<sup>4</sup>:

- Identify the underlying cause of CKD where possible, since this may influence the treatment
- Screen for complications of CKD, such as anemia and renal osteodystrophy
- Screen for cardiovascular risk factors.
- Identify reversible factors that may worsen kidney function, such as hypertension or urinary tract obstruction
- Exclude acute kidney injury

The recommended investigations in patients with CKD are summarized below:

### **CHPS, Health Center, clinics (without a doctor)**

- Blood Pressure measurement
  - Blood glucose testing - Fasting or Random blood sugar
  - Measurement of weight and height for BMI estimation
  - Urinalysis (urine dipstick) - may show proteinuria or hematuria.
  - Full blood count - may show anemia.
- If not available or results are abnormal, refer to a facility with a doctor.

### **Clinics/Polyclinics and Hospitals (with a doctor)**

All investigations above **PLUS**:

- Blood urea, electrolytes, and creatinine (including eGFR)
- Urine Albumin Creatinine ratio (UACR) to quantify the degree of albuminuria.
- Lipid profile
- Glycated hemoglobin (HbA1C)
- Full blood count – may show normocytic normochromic anemia.
- Serum Albumin
- Serum calcium, phosphate, alkaline phosphatase, parathyroid hormone
- Serum uric acid
- Iron studies - Transferrin saturation and serum ferritin.
- Test for Blood borne viruses - Hepatitis B, Hepatitis C and HIV
- Chest X-ray
- 12-lead Electrocardiogram (ECG)
- Abdominal ultrasound - to assess kidney size and rule out urinary tract obstruction.



### District hospitals, Regional and tertiary hospitals (Health facility with a Specialist)

All investigations above PLUS

- Serum Cystatin C for estimating GFR (if available)
- Echocardiogram for those with symptoms and signs of heart disease
- Doppler ultrasound of the renal arteries if renal artery stenosis is suspected.

Table 9 below shows specific tests related to the suspected etiology based on other clinical assessments.

Suspected Etiology	Tests
Multiple myeloma	Serum and urine protein electrophoresis, serum and urine free light chains
Systemic lupus erythematosus (SLE)	Antinuclear antibodies (ANA), double-stranded DNA antibody levels
Glomerulonephritis	Serum complement levels
ANCA - associated vasculitis	Cytoplasmic and perinuclear pattern antineutrophil cytoplasmic antibody (C-ANCA and P-ANCA)
Anti-glomerular basement membrane disease (Good pasture syndrome)	Anti-glomerular basement membrane (anti-GBM) antibodies
Kidney stones and other possible causes of urinary tract obstruction	MRI/ CT scan of abdomen
Unknown etiology or definite cause	Kidney biopsy

*Table 9: Specific tests related to suspected etiology based on other clinical assessments*

## Monitoring patients with CKD

- Once CKD diagnosis has been confirmed, arrangements should be made for regular monitoring of kidney function (eGFR) and albuminuria. Monitoring should preferably take place in a district hospital or a health centre with a doctor.
- In patients with low risk of eGFR decline, this can be done annually.
- Patients with high risk of eGFR decline should be monitored more frequently.
- More frequent monitoring may also be indicated in people with changing clinical status, intercurrent events, and after therapeutic interventions to assess response, adherence, and safety (e.g. monitoring of eGFR changes and hyperkalemia after initiating ACE inhibitors or ARBs)<sup>4</sup>.



Table 10 below shows suggested frequency of monitoring for CKD progression based on stage.

Stage of CKD	Frequency of Monitoring of eGFR/Albuminuria
G1-G2	Annually
G3	Every 3 - 6 months
G4	Every 1- 3 months
G5	Every 2- 4 weeks

**Table 10: Suggested frequency of monitoring for CKD progression based on stage**

When monitoring patients with CKD, small fluctuations in eGFR are common and may not be due to progression. Decline of eGFR of more than 20% should prompt evaluation for potential reversible causes (e.g. intravascular volume depletion, exposure to nephrotoxic medications, intercurrent infections, etc.).

Refer to a nephrologist if there is a sustained decrease in eGFR of more than 25ml/min in 12 months per year as this is considered as accelerated decline in eGFR.

A significant drop in eGFR (>30%) while initiating antihypertensive agents, renin angiotensin system inhibitors (RASI) or SGLT2i should prompt a review into other causes (e.g. dehydration, nephrotoxic drugs, infections) and warrants close monitoring. Withholding these kidney protective medications should be rarely done as these dips are potentially reversible<sup>3</sup>.

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# MODULE 5: CKD PREVENTION AND MANAGEMENT

## Objectives:

1. To outline the goals of management of chronic kidney disease (CKD)
2. To describe the appropriate management for each level of care
3. To emphasize strategies for prevention and delaying progression of CKD
4. To discuss the management of common complications of CKD and kidney failure

## Goals of Management

The goals of management include:

- Preventing and delaying the progression of CKD
- Management of the complications of CKD
- Management of underlying cause
- Identification and management of acute kidney injury (AKI) in patients with CKD

## Management of CKD according to levels of care

Chronic kidney disease is managed depending on the underlying cause and availability of expertise<sup>1</sup>. Management often includes reducing complications, managing symptoms, and slowing the disease course. If the kidneys are severely damaged, the patient will require management for kidney failure<sup>1,2</sup>. This section will provide treatment strategies suitable for each level of care.

### Health facility without a doctor (CHPS, Health Center, clinics without a doctor)

#### 1. Prevention of CKD

1. Screen for risk factors of CKD and manage appropriately
2. Educate on:
  - adequate hydration
  - Balanced and healthy diet (low salt diet, adequate fruits and vegetables etc.)
  - regular exercise and weight reduction
  - Avoidance or reduction of alcohol intake
  - Avoidance or cessation of tobacco use including smoking cigarettes, shisha, chewing tobacco etc.
  - Avoidance of unlicensed herbal medication
  - Indiscriminate or prolonged use of analgesics especially NSAIDS, and illicit drug use e.g. heroin, cocaine, etc
3. Counsel patients on adherence to medication.



## 2. Delaying progression of CKD

### Non-pharmacologic approach

- Advise on moderate intensity physical activity suitable with cardiovascular health, tolerance, and frailty level; attain the ideal body mass index (BMI).
  - Healthcare professionals should offer guidance on exercise types and intensities (light, moderate, or vigorous) for individuals who are more likely to fall. (aerobic vs. resistance, or both)
  - A total of 150 min per week of exercise
- Advise on cessation of tobacco use including smoking cigarettes, shisha, chewing tobacco etc.
- Advise on healthy and balanced diet that includes more plant-based foods than animal-based foods and less highly processed foods. Advice of a dietician (where available) should be sought to ensure that the appropriate interventions are implemented in all cases. Such dietary interventions may include:
  - For persons with CKD G3–G5, daily protein consumption should be 0.8 g/kg.
  - Protein consumption should not be restricted in adults suffering from severe muscle loss, wasting, or other disorders that cause malnutrition.
  - High protein consumption (>1.3 g/kg/day) should be avoided in persons with CKD
  - Restrict salt intake: less than 5 g of sodium chloride (salt) per day (less than half a teaspoon of salt per day; no added salt at table). Reduce intake of salted foods including momoni, koobi, kako etc.
  - Increase intake of fruits, vegetables, and reduce intake of carbohydrates
- Encourage weight loss for patients with obesity and CKD
- Advise against the use of unlicensed herbal medication
- Advise against indiscriminate or prolonged use of analgesics especially NSAIDS and illicit drugs.
- Advise on adequate hydration especially during warm weather.

### Pharmacologic approach

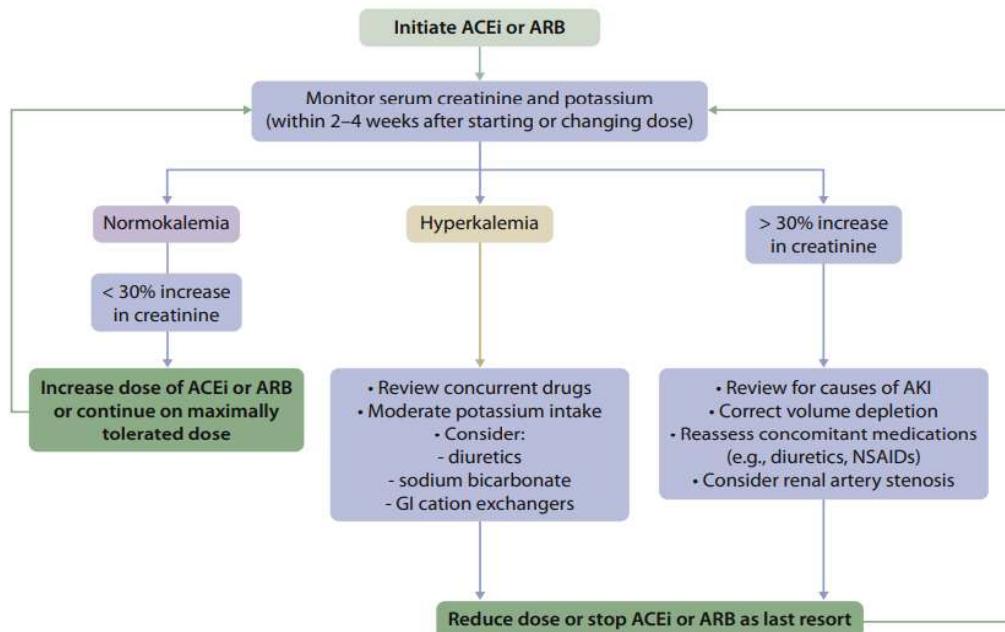
Treat underlying causes of CKD to target:

- **Hypertension**
  - Target BP < 130/80mmHg
  - Patients with proteinuria ( $\geq 1+$ ), use ACE-I or ARB to slow the progression of disease (table 1)



- Changes in blood pressure, serum creatinine, and serum potassium should be monitored within 2-4 weeks of starting or increasing the dose of ACEi or ARBs, depending on the current GFR and serum potassium (table 1)
- Hyperkalemia caused by ACEi can generally be addressed by lowering serum potassium levels instead of decreasing the dose or discontinuing ACEi using diet or drugs (figure 5)
- Refer patients with severe or difficult to control hypertension, progressive CKD, worsening proteinuria, symptomatic hypotension, and uncontrolled hyperkalemia despite pharmacological treatment

Figure 5 shows an algorithm for monitoring of serum creatinine and potassium during ACEi or ARB treatment.



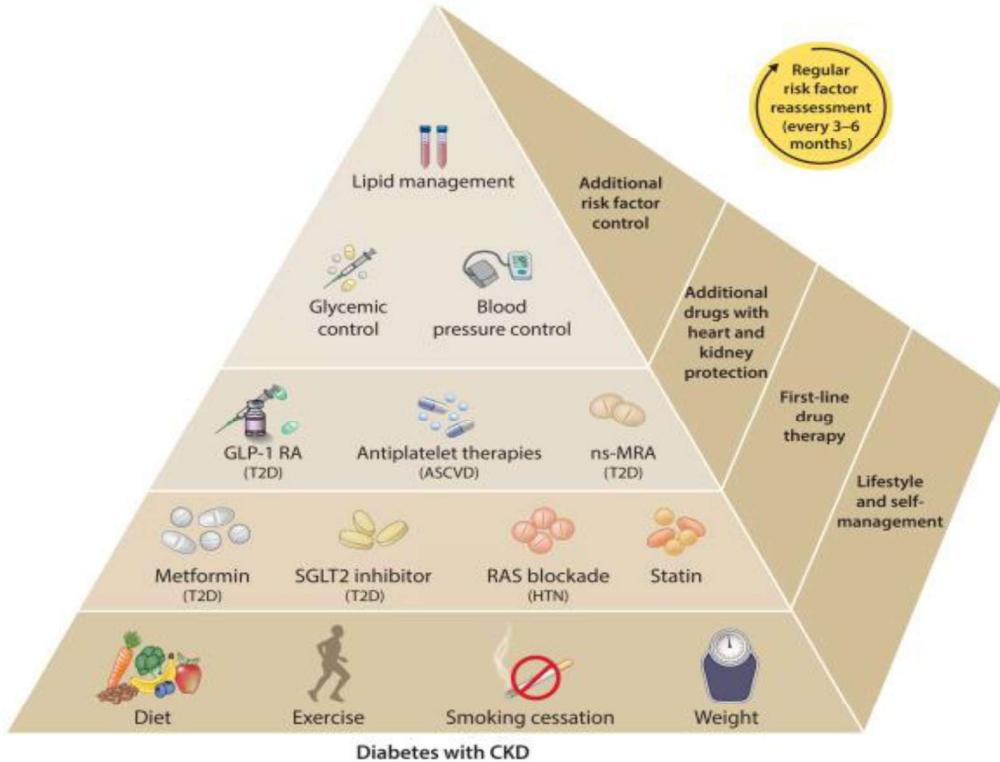
**Figure 5: Monitoring of serum creatinine and potassium during ACEi or ARB treatment—dose adjustment and monitoring of side effects: Adapted from KDIGO 2020 guideline on diabetic nephropathy**

- **Diabetes mellitus**

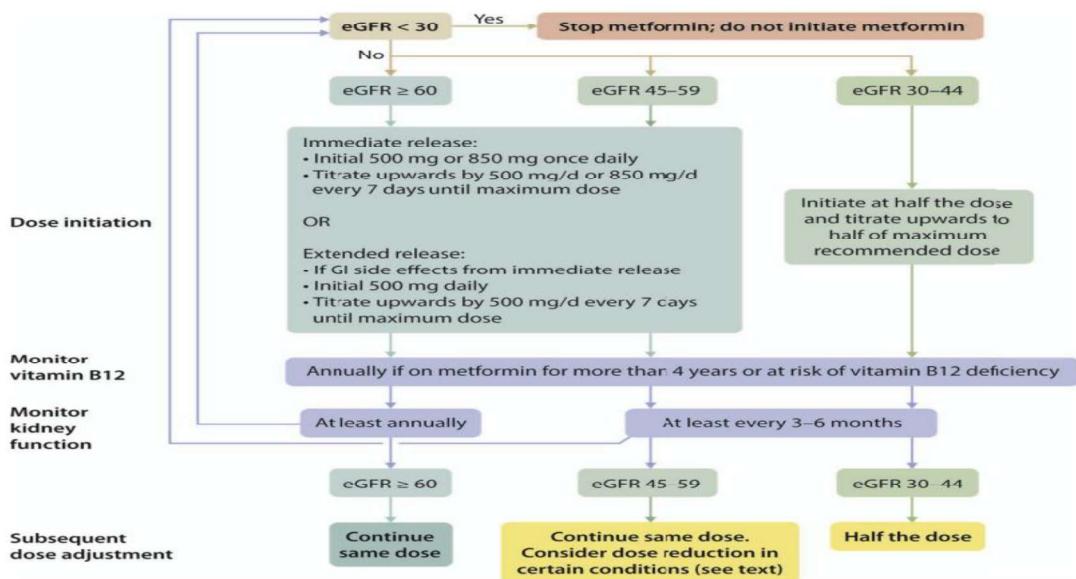
- Keep FBS between 4 - 7 mmol/L. For very ill, frail and elderly patients, the FBS should be kept between 6 – 8 mmol/L to avoid hypoglycaemia.
- Target glycated haemoglobin (HbA1C) < 7.0%; for early CKD target HbA1C < 6.5%. Advice caution with aggressive targets in elderly patients who are at a higher risk of hypoglycaemia (Figure 6)
- Manage high blood pressure as discussed above
- Refer patients with CKD, uncontrolled hypertension or uncontrolled DM, worsening proteinuria, and GFR.



See figure 6 and 7 for algorithm on managing CKD in patients with Diabetes.



**Figure 6: Management of diabetic kidney disease: KDIGO 2022 Clinical Practice Guideline for Diabetes**



**Figure 7: Monitoring and reviewing dose of Metformin patients with diabetes: Adapted from KDIGO 2020 guideline on diabetic nephropathy.**



## **Health facility with a doctor (Clinics/Polyclinics and Hospitals)**

All preventive measures, non-pharmacologic and pharmacologic measures stated above  
**PLUS:**

### **Pharmacologic approach**

- Assess patients for risk of cardiovascular disease.
- Assess patients for risk of CKD progression, urine routine examination or urine albumin: creatinine ratio (UACR), and eGFR
- For CKD patients with proteinuria and at risk of CKD progression with or without diabetes, consider SGLT2 inhibitors to delay progression of kidney disease
- For CKD patients with cardiovascular disease, consider using ACEI or ARBs, sodium glucose transporter-2 (SGLT2) inhibitors, and mineralocorticoid receptor antagonist (figure 5)
- In patients with CKD who are already on RAAS inhibition, continue ACEi or ARB even if the eGFR drops below 30 ml/min per 1.73 m<sup>2</sup>.
  - It is strongly recommended to use an SGLT2i in patients with type 2 diabetes (T2D), CKD, and an eGFR of 20 ml/min per 1.73 m<sup>2</sup> with or without heart failure (figure 5)
  - If an SGLT2i is initiated (recommend with eGFR of ≥20mL/min), continue even if the eGFR drops below 20 ml/min per 1.73 m<sup>2</sup>, unless it's not tolerated or KRT is started
  - It is appropriate to withhold SGLT2i during prolonged fasting, surgery, or urgent medical sickness (when persons are more likely to develop ketosis) (figure 5)
- Glucagon-like peptide-1 (GLP-1) receptor agonist in persons with T2D and CKD who have not met individualised glycaemic targets after metformin and SGLT2 inhibitor treatment, or who are unable to use those drugs. Examples include Semaglutide, Exenatide and Dulaglutide.
- Steroidal MRAs be used in heart failure management, hyperaldosteronism, or refractory hypertension. Use of steroidal MRAs may cause hyperkalemia.
- Non-steroidal MRAs (if available) can be used for the benefit of slowing CKD progression, and reduction of proteinuria
- Refer patients with uncontrolled hypertension, diabetes, worsening proteinuria, and GFR and high risk of cardiovascular disease.

Table 11 below shows dosage recommendations for ACEi/ARBs



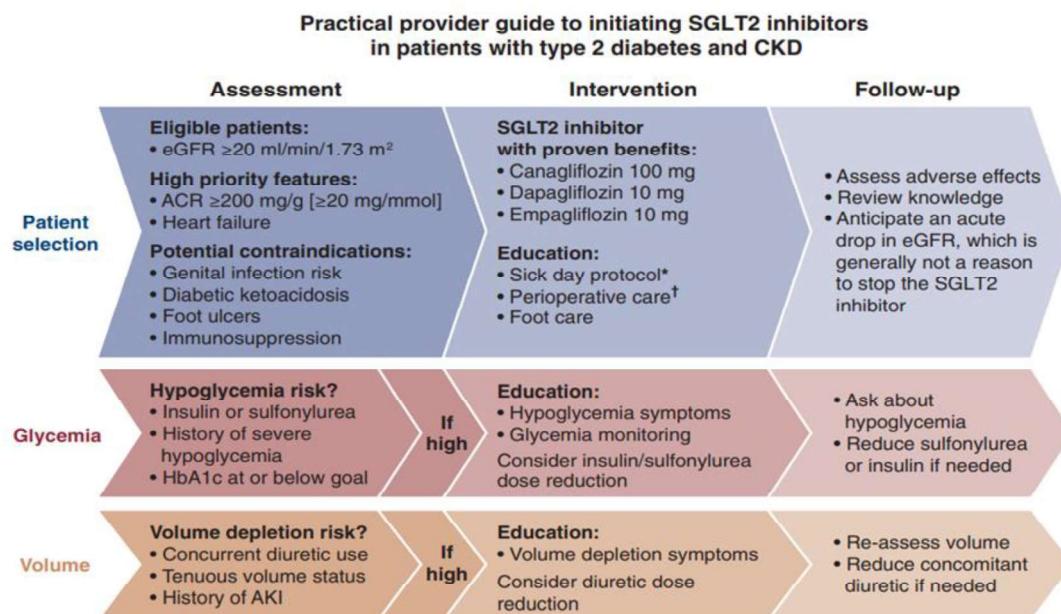
### Dosage recommendations ACEi/ARBs

ACEI/ARBs	Starting dose	Maximum daily dose	Kidney impairment
Enalapril	5 mg once daily	40mg	eGFR ≤30 ml/min: reduce initial dose to 2.5 mg PO once daily. 2.5 mg PO after haemodialysis on dialysis days; dosage on non-dialysis days should be adjusted based on clinical response
Lisinopril	10 mg once daily	40mg	eGFR 10–30 ml/min: Reduce initial recommended dose by 50% for adults. Max: 40 mg/day eGFR <10 ml/min: Reduce initial dosage to 2.5 mg PO once daily. Max: 40 mg/day
*Perindopril	2mg once a day	8mg	Use is not recommended when eGFR <30 ml/min. Perindopril and its metabolites are removed by haemodialysis
Ramipril	2.5mg once a day	20mg	Administer 25% of normal dose when eGFR < 30ml/min. Minimally removed by haemodialysis
Candesartan	16mg once a day	32mg	Not removed by haemodialysis
*Irbesartan	150mg once a day	300mg	No dosage adjustment necessary. Not removed by haemodialysis
Losartan	50mg once a day	100mg	No dosage adjustment necessary. Not removed by haemodialysis
*Olmesartan	20mg once a day	40mg	No initial dosage adjustment is recommended for patients with moderate to marked kidney impairment (eGFR < 30ml/min)
*Telmisartan	40mg once a day	80mg	No dosage adjustment necessary. Not removed by haemodialysis
Valsartan	80mg once a day	320mg	Dosage adjustment for eGFR < 30ml/min- use with caution. Not significantly removed by haemodialysis

\*Drugs not on Ghana's Essential Medicines list



**Table 11: Dosage recommendations for ACEi/ARBs**



**Figure 8: Adapted from KDIGO guideline 2022: [KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease](#).**

### Health facility with physician specialist (District, Regional and Teaching hospitals)

All measures above PLUS:

- Offer counselling on dialysis access and pre-emptive transplant if eGFR < 20ml/min and refer to the nephrologist
- Offer comprehensive conservative management for those with eGFR < 15ml/min who opt out of kidney replacement therapy (refer to section on conservative management in this module).
- Treatment of any identifiable causes of the CKD.

Some underlying causes of CKD stated below should be referred to, or managed in consultation with the nephrologist

- Diabetic kidney disease
- Obesity
- Glomerular disease (proteinuria, haematuria, dysmorphic, casts- pathological)
- Autosomal dominant polycystic kidney disease
- Viral Infections (chronic kidney disease associated with hepatitis B, hepatitis C, HIV etc)
- Autoimmune disorder
- Haematological disorders
- Hepatic or cardiac disorders



## Management of complications associated with CKD

Management of these patients should be in consultation with a nephrologist<sup>3,4</sup>.

- **Treatment and modification of cardiovascular disease risk**
- Use statin or statin/ezetimibe combination therapy in persons aged 50 years and above with eGFR of < 60 ml/min per 1.73 m<sup>2</sup> not on chronic dialysis or kidney transplantation (GFR categories G3a-G5)
- Use statin in persons over the age of 50 years with CKD and an eGFR of ≥ 60 ml/min per 1.73 m<sup>2</sup> (GFR categories G1-G2)
- Use statin medication in persons aged 18-49 years with CKD who are not receiving chronic dialysis or kidney transplantation and have one or more of the following:
  - a history of coronary artery disease (myocardial infarction or coronary revascularization)
  - diabetes
  - previous ischemic stroke
  - a 10-year estimated incidence of coronary mortality or nonfatal myocardial infarction of more than 10%.
- Use oral low-dose aspirin for prevention of recurrent ischemic cardiovascular disease events (i.e., secondary prevention) in people with CKD and established ischemic cardiovascular disease.

### Metabolic acidosis

Definition: Serum bicarbonate < 22 mmol/L

Common Symptoms/Signs: Nausea, vomiting, fast breathing, and lethargy

- Consider using nutritional and/or pharmacological treatment in persons with CKD to prevent severe acidosis.
- Reduce intake of animal protein
- Increase intake of plant protein, fruits and vegetables
- Initiate treatment with bicarbonate if serum bicarbonate < 22mmol/L
- Target bicarbonate level should be ≥24mmol/L
  - Start with oral sodium bicarbonate 500mg twice a day.
  - Increase dose appropriately to maximum of 1g thrice a day if serum bicarbonate level remains < 22mmol/L
  - Treat other causes of metabolic acidosis such lactic acidosis or ketoacidosis if present



- Sodium bicarbonate can alter volume status by virtue of its sodium content. Use bicarbonate with caution. Monitor patient's volume status and blood pressure regularly.

## Hyperkalaemia in CKD

Definition: Serum potassium levels > 5.5mmol/L

Common Symptoms/Signs: palpitations, muscle weakness, numbness, chest pain, arrhythmia, nausea and vomiting

- Dietary interventions e.g. reduce intake of potassium sources of food (fruits, vegetables, avocado etc)
- Resin exchangers: eg. Kayexelate or calcium resonium, sodium zirconium cyclosilicate
  - Sodium polystyrene sulfonate (Kayexelate)
  - Calcium polystyrene sulfonate 2.5g to 15g daily up to 5 days, then check serum potassium levels
  - Patiromer 15mg to 30mg (if available)
  - Sodium zirconium cyclosilicate 1.25g to 15g up to 4 weeks (if available)
  - Add a laxative to the above to prevent constipation
- Loop diuretics (if patient still passing urine)
- Consider reviewing dose of ACEi/ARB, beta-blockers, potassium-sparing diuretics, nonsteroidal anti-inflammatory drugs (NSAIDs)
- Refer for haemodialysis if hyperkalaemia is refractory
- ***Emergency management if serum potassium > 6.5mmol/L:***
  - *Look for ECG changes of hyperkalaemia*
  - *10mls of 10% Calcium Gluconate: stabilizes myocardium over 1-3 mins. May be repeated multiple times*
  - *5 units of Insulin in 50-100mls of 50% Dextrose infusion works over 10-20 mins*
  - *Nebulization with β-2 agonists (eg. 10-20mg Salbutamol). May be repeated multiple times*
  - *Haemodialysis if refractory (refer to a centre where dialysis is available)*



## Anemia

Definition: Haemoglobin level < 12g/dl for females and < 13g/dl for males

Common Symptoms/Signs: Easy fatigability, dizziness, shortness of breath on exertion, pallor, rapid breathing and heart rate

- CKD with eGFR <30ml/min/1.73m<sup>2</sup> is associated with normocytic normochromic anemia caused by reduction in erythropoietin and shortened red cell survival
- Initiate iron therapy when Transferrin Saturation (TSAT) ≤ 30% and ferritin ≤ 500ng/ml (IV iron for dialysis and oral for non-dialysis patients)
- Oral trial of iron for 1-3 months in CKDND (not on dialysis) switch to IV if response not satisfactory
- FBC: look for red cell indices; low MCV, MCH, and MCHC suggest iron deficiency
- Dietary; encourage intake of green leafy vegetables, turkey berries ('Kwahu nsuasua')
- When iron replacement is adequate, initiate erythropoiesis stimulating agent therapy for patients with HB <10g/dl with target HB of 9.5g/dl to 11.5g/dl
- Monitoring of HB levels in non-anaemic CKD patients: yearly for CKD stage 3
- Monitoring of HB levels in CKD stage 4-5: 6 monthly and 3 monthly for dialysis patients
- CKD patients with anemia on iron replacement should have HB monitored 3 monthly and monthly if on dialysis
- Investigate for other causes of anemia in patients with CKD and treat appropriately

## Calcium and phosphate abnormalities in CKD

- CKD tends to cause a reduction in the excretion of filtered phosphate load which leads to phosphate retention and hyperphosphatemia
- This causes secondary hyperparathyroidism (high phosphate and parathyroid (PTH), and low calcium).
- In patients with an eGFR >30ml/min/1.73m<sup>2</sup> elevation of PTH tends to maintain calcium and phosphate balance but can cause bone weakness
- Common Symptoms/signs: growth delays, bow legs, bone pain, bone fractures
- Management options for hyperphosphatemia include:
  - Dietary phosphate restriction
  - Oral phosphate binders are recommended.
    - Calcium carbonate 500mg to 1g thrice a day with meals



- Sevelamer 800mg twice a day with meals
- Treat with Vitamin D3 when indicated to achieve normal serum levels
- Target PTH levels should be 2-9x of the upper limit of normal. If PTH levels are elevated or rapidly rising, treat with vitamin D analogues, calcitriol, calcimimetic agents, to suppress PTH – consult a nephrologist

### **Nausea and vomiting**

A significant proportion of patients with G5 CKD experience nausea and vomiting. Uraemia and metabolic acidosis may be an underlying factor, but it is also important to note that in patients with diabetes gastroparesis may also contribute.

- Agents such as metoclopramide may help reduce symptoms.
- Proton Pump Inhibitors such as omeprazole could be used in cases of uraemic gastritis
- Haloperidol may also be used to manage nausea and vomiting associated with CKD.
- Refractory nausea and vomiting when due to uraemia is an indication of haemodialysis

### **Oedema**

Advanced kidney disease is usually associated with volume overload and fluid retention.

- Salt and fluids restriction are necessary to reduce this complication.
- Loop diuretics, often in high doses, may be necessary.
- Thiazide-like diuretics ( eg metolazone) may also need to be co-administered.

### **Pruritus**

Pruritus is one of the commonest dermatological manifestations of CKD, and it can be very debilitating. It is believed to be associated with the accumulation of uremic toxins, systemic inflammation, disorders of calcium, phosphate and parathyroid hormone metabolism and dry skin.

- Therapeutic options include water-based skin softening creams
- Antihistamines such as cetirizine (dose adjusted) could be used
- Treatment of the underlying calcium and phosphate abnormality
- Refer to nephrologist for dialysis when due to uraemic symptoms



## **Uraemic complications**

Uraemic complications of kidney failure include:

- Pericarditis
- Gastritis
- Encephalopathy

These require dialysis and eventually kidney transplant where available and affordable

## **Kidney replacement therapy**

When CKD progresses to kidney failure, patients will require kidney replacement therapy in the form of dialysis or kidney transplantation (KT) for survival and to improve quality of life.

Kidney replacement therapies (KRT) form an integral part in the management of patients with kidney failure.

**Modalities used include:**

- Haemodialysis
- Peritoneal dialysis
- Kidney transplantation

**Choice of KRT modality is dependent on multiple factors including:**

- Availability of KRT modality
- Patient presentation
- Patient preference
- Cost involved
- Underlying cause of kidney disease
- Predicted life expectancy
- Predicted quality of life
- Among other sociocultural and economic factors

It is important that adequate preparations are made toward KRT. In an ideal situation, a patient will be known to his/her clinician and will have had ample time for extensive discussions and adequate preparation to be had prior to initiation.



In our setting, a significant proportion of CKD patients requiring KRT present as emergencies to healthcare facilities requiring urgent intervention hence missing on the preparatory phase. This is associated with poorer prognosis.

The preparatory phase includes:

- Counselling/education on ESKD
- Treatment modalities
- Dialysis access
- Pre-emptive transplant

### **Dialysis Access**

A good access is required for dialysis initiation. An arteriovenous (AV) fistula is recommended as the ideal vascular access for haemodialysis. It should be done by an experienced vascular surgeon about three months in advance before dialysis initiation. In patients who present late, the following are options are commonly instituted:

- Femoral temporary catheter
- Internal jugular vein temporary catheter
- Internal jugular vein tunneled catheter
- Peritoneal dialysis catheter for peritoneal dialysis (currently available for paediatric patients)

The choice of the access depends on factors such as:

- Availability of a particular catheter type
- Patient clinical condition
- Bleeding risk
- Patient preference

### **Haemodialysis (HD)**

This involves blood being pumped through a dialysis machine and being filtered by a dialyzer. Should be carried out by experienced personnel.

### **Peritoneal dialysis (PD)**

In PD, the peritoneal lining of the abdomen acts as a semi-permeable membrane after a specialized solution is instilled into the peritoneal cavity for a certain amount of time, after which the solution is emptied from the peritoneum.



### **Timing of commencement of dialysis**

Initiate dialysis based on an overall evaluation of:

- Patient's symptoms
- Quality of life
- Patient preferences
- GFR level
- Laboratory findings

Initiate dialysis if the following complications are present where medical management has failed or not available;

- Refractory pulmonary oedema
- Refractory metabolic acidosis
- Refractory hyperkalaemia
- Uraemic syndrome; pericarditis, encephalopathy, gastritis

Overall, the decision of initiation of dialysis should be taken by the nephrologist.

Practical guide for referrals.

**Table 12: Referral Algorithm**

## **Patient Referral**

### **Indications for referral to/consult with the nephrologist (table 12)**

- GFR <30ml/min/1.73m<sup>2</sup>
- Patients with uraemic complications (refer section on uraemic complications)
- Persistent albuminuria UACR >300mg/g
- Hypertensive patient with persistent proteinuria on urine dipstick ≥ 1.
- Acute kidney injury or abrupt sustained fall in GFR
- Atypical progression of CKD
- Refractory Hypertension (4 or more antihypertensive agents)
- Urinary red cell cast, RBC more than 20 per HPF sustained and not readily explained
- Persistent abnormalities of serum electrolytes e.g. serum potassium or sodium
- Hereditary kidney disease
- Recurrent or extensive nephrolithiasis



				ACR categories (mg/mmol) Description and range		
				A1	A2	A3
GFR categories (ml/min/1.73m <sup>2</sup> ) Description and range	Normal to mild increased			Moderately increased		Severely increased
	No CKD in the absence of markers of kidney damage	Manage in primary care according to recommendations (see algorithm (C))			Refer for specialist assessment if the person has:	
		G1	Normal and High	≥90	<ul style="list-style-type: none"> <li>- a sustained decrease in GFR of 25% or more and a change in GFR category or sustained decrease in GFR of 15 ml/min/1.73 m<sup>2</sup> or more within 12 months</li> <li>- hypertension that remains poorly controlled despite the use of at least 4 antihypertensive drugs at therapeutic doses</li> <li>- known or suspected rare or genetic causes of CKD</li> <li>- suspected renal artery stenosis</li> <li>- genetic causes of CKD</li> <li>- Suspected renal artery stenosis</li> </ul>	
		G2	Mild reduction related to normal range for a young adult	60-80	<ul style="list-style-type: none"> <li>- a sustained decrease in GFR of 25% or more and a change in GFR category or sustained decrease in GFR of 15 ml/min/1.73 m<sup>2</sup> or more within 12 months</li> <li>- hypertension that remains poorly controlled despite the use of at least 4 antihypertensive drugs at therapeutic doses</li> <li>- known or suspected rare or genetic causes of CKD</li> <li>- suspected renal artery stenosis</li> <li>- genetic causes of CKD</li> <li>- Suspected renal artery stenosis</li> </ul>	
		G3a	Mild-moderate reduction	45-59	<ul style="list-style-type: none"> <li>- a sustained decrease in GFR of 25% or more and a change in GFR category or sustained decrease in GFR of 15 ml/min/1.73 m<sup>2</sup> or more within 12 months</li> <li>- hypertension that remains poorly controlled despite the use of at least 4 antihypertensive drugs at therapeutic doses</li> <li>- known or suspected rare or genetic causes of CKD</li> <li>- suspected renal artery stenosis</li> <li>- genetic causes of CKD</li> <li>- Suspected renal artery stenosis</li> </ul>	
		G3b	Moderate-severe reduction	30-44	<ul style="list-style-type: none"> <li>- a sustained decrease in GFR of 25% or more and a change in GFR category or sustained decrease in GFR of 15 ml/min/1.73 m<sup>2</sup> or more within 12 months</li> <li>- hypertension that remains poorly controlled despite the use of at least 4 antihypertensive drugs at therapeutic doses</li> <li>- known or suspected rare or genetic causes of CKD</li> <li>- suspected renal artery stenosis</li> <li>- genetic causes of CKD</li> <li>- Suspected renal artery stenosis</li> </ul>	
		G4	Severe reduction	15-29	Refer for Nephrologist assessment	
		G5	Kidney failure	<15	Refer for Nephrologist assessment	

## Kidney transplantation

The preferred mode of kidney replacement therapy (KRT) is kidney transplantation which involves receiving a functioning kidney from a suitably matched donor.

- It requires extensive and adequate preparation. The transplantation process involves surgery which is performed by an experienced team of surgeon with support from the nephrologist.
- Post-transplant care requires admission, regular scheduled visits and adequate immunosuppression to prevent rejection and prolonged survival of the graft.
- Offer pre-emptive kidney transplantation and/or dialysis access in persons with GFR less than 20 ml/min per 1.73 m<sup>2</sup>



## **Conservative management of CKD (where KRT is not accessible)**

A significant proportion of patients in Ghana requiring KRT opt out of dialysis or transplantation. This may be due to factors such as financial, socio-cultural, geographical constraints.

**CCC involves management of the complications of kidney failure (refer to section on complication management) and palliative care.**

Comprehensive conservative care (CCC) is a holistic patient-centred care for patients with G5 CKD. It involves many facets, including shared decision-making, symptom management, psychosocial support, and palliative care among others.

## **Myths and misconceptions around CKD, dialysis, and transplantation**

There are many myths about CKD, kidney failure, dialysis and transplantation which are detrimental to effective management of kidney disease. Common myths that are encountered in everyday practice are discussed here.

### **Demystifying myths in CKD**

#### **Myth 1: “CKD is a death sentence”**

CKD is not a death sentence. There are different stages of CKD and the approach to treatment varies depending on the stage. At each stage of management, there are viable and readily available treatment options. The earlier it is diagnosed, the better the outcome, and it is more likely to slow down the progression to kidney failure.

#### **Myth 2: “Antihypertensive medications cause CKD”**

There are many varying causes of CKD. In Ghana, hypertension is one of the leading causes of CKD. Uncontrolled hypertension causes damage to the kidneys, and antihypertensive medication, combined with lifestyle modification is important to reduce the effects of elevated blood pressure on the kidneys. As CKD progresses, however, modifications to some anti hypertensives may be required to prevent adverse effects that are more likely to occur at a late stage of CKD. Infact antihypertensive prevent CKD and its progression to kidney failure.

#### **Myth 3: “Antidiabetic medications cause CKD”**

One of the key strategies for slowing down the progression of CKD is to manage the underlying causes such as diabetes or hypertension. To achieve this, we use medications such as antidiabetic medication to control blood sugar. Antidiabetic medication do not cause kidney



disease. Discontinuation of the medication may be required in late stages of kidney disease as sugar level may reduce significantly causing hypoglycaemia.

**Myth 4: “CKD is curable”**

CKD, in contrast with AKI, is largely not curable. CKD is associated with irreversible kidney damage. There are no medications that can replace the damaged kidney. When CKD is detected early, however these destructive changes can be stopped or slowed down with aggressive risk factor control and drug therapies targeting the changes.

**Myth 5: “Once I am passing urine, my kidneys are fine”**

Many people equate passing good amounts of urine to having healthy kidneys. This is not always the case. In CKD, the concentrating ability of the kidney is affected and patients may thus pass dilute urine which could be of large volumes in certain instances. Also, people who have uncontrolled diabetes mellitus may pass large volumes of urine while having poor renal function.

**Myth 6: “Herbal medications are natural and safe, and won’t harm you like orthodox medication”**

The exact contents of some herbal preparations sold on the open market are unknown. There is a risk of consuming potentially nephrotoxic agents that may be in some of these unlicensed herbal products. Natural does not mean safe and its sale in some pharmacy shops does not guarantee safety. When in doubt, consult your physician.

**Myth 7: “If you have kidney disease you will know”**

This is not true. Early kidney disease is mostly without symptoms. Symptoms appear as kidney disease progresses. It is therefore imperative to know about kidney disease, have a risk assessment and be screened especially if you have risk factors like diabetes and hypertension.

## **Demystifying myths in haemodialysis:**

**Myth 1: “Dialysis is a death sentence”**

Dialysis is not a death sentence. Dialysis improves patient’s general wellbeing and serves as a bridge to kidney transplant. Early diagnosis of kidney failure with timely intervention is essential to improve survival and quality of life.

**Myth 2: “Dialysis patients do not have the time or energy to work”**



When patients have regular (three-times-a-week) sessions, with regular follow ups and are compliant on their medications, they are able to live normal lives.

### **Demystifying myths in kidney transplant:**

#### **Myth 1: “Donating a kidney is a dangerous procedure”**

Most donors spend only a couple of nights (3-4 nights) on admission after donation and return to full work in 2-3 weeks. Risk of complication to the donor is very low.

#### **Myth 2: “The donor needs to be a family member”**

Donors can be related biologically or unrelated to the patient. They must be willing to donate and compatible with the recipient.

#### **Myth 3: “The surgery will affect the donor/recipient’s ability to have children”**

Kidney transplant does not affect the donor or recipient’s ability to have children. The surgical procedure does not affect any reproductive organ in males and females.

#### **Myth 4: “Donating a kidney reduces the donor’s life expectancy”**

There is no evidence to suggest that donating a kidney reduces life expectancy or increase your risk of kidney failure.

#### **Myth 5: “Kidney transplant recipient does not need any follow up”**

Kidney transplant recipients need to be followed up by a nephrologist and need to be compliant on their medications and follow up to avoid losing the transplanted kidney.

#### **Myth 6: “Members of transplant team will force someone to be a donor”**

Members of transplant team do not coerce anyone, and a donor can change his/her mind any time.

#### **Myth 7: “I can make money by selling my kidney”**

Kidney donation is voluntary without any expected financial gains. It is illegal to sell your kidneys, and you can be arrested and prosecuted.



## **References:**

1. Johnson R. J, Floege J, Tonelli Marcello (2022). Comprehensive Clinical Nephrology. 7th Edn (Canada: Elsevier) pg 927-959
2. Michael G. Shlipak, SriLekha TummalaPalli, et al. The case for early identification and intervention of chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney International* (2021) 99, 34–47
3. KDIGO Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease, public review draft, July 2023
4. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl.* 2013;3:1–150.



# MODULE 6: ACUTE KIDNEY INJURY (AKI) IN A PATIENT WITH CKD

## Objectives:

1. To understand that an isolated rise in creatinine is not enough to diagnose CKD
2. To highlight that patients with CKD are at increased risk of AKI
3. To identify AKI as a risk factor for CKD progression

## Acute kidney injury

Acute kidney injury is defined<sup>1</sup> as:

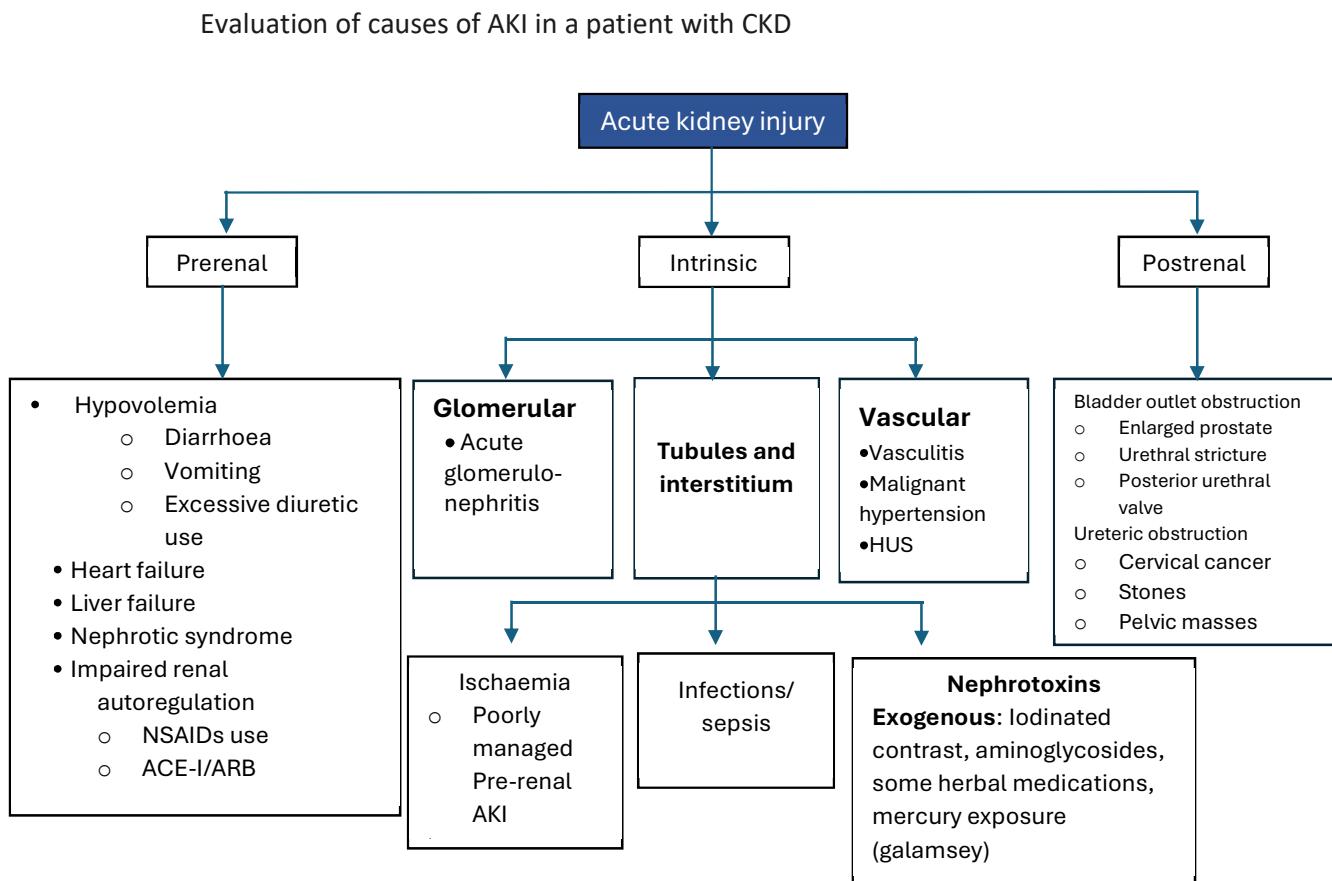
- An increase in serum creatinine by 26.5umol/L within 48 hours or
- An increase in serum creatinine to by 50% of the baseline in 7 days or
- A sudden reduction in urine volume of less than 0.5ml/kg per hour for 6 hours

## Introduction

- Acute kidney injury (AKI) and chronic kidney disease (CKD) are closely linked and likely to promote one another.
- CKD is a risk factor for AKI, as both decreased glomerular filtration rate (GFR) and proteinuria are associated with AKI.
- Acute kidney injury particularly in those requiring dialysis accelerates the progression of CKD.
- The association between AKI and subsequent kidney function decline is influenced by:
  - Pre-existing stage of CKD
  - Severity of the AKI
  - Cumulative number of AKI episodes
- An isolated rise in serum creatinine requires further investigations or a duration of more than three months for CKD to be diagnosed (discussed in module 1)
- Risk factors for AKI in CKD patients are the same as expected for the general population, however the prevalence and severity of AKI among CKD patients are generally much higher.
- Due to multiple comorbidities, CKD patients are more prone to acute medical illnesses requiring hospitalizations and procedures that increases their risk of exposure to nephrotoxic insults.
- Evaluation of acute kidney injury is by:
  - History of urine output or potential causes of AKI
  - Examination for signs of possible causes of AKI and its complications
  - Investigate with urinalysis, serial serum creatinine and ultrasound to rule out obstruction. Its important to investigate for causes and complications of AKI.



- The evaluation for possible causes of AKI should be categorized as pre-renal, intrinsic and post renal AKI. Figure 9 shows evaluation of possible cause of AKI in a patient with CKD<sup>2,3</sup>.



**Figure 9: Evaluation for possible cause of AKI**

## Management of AKI in patients with CKD

- When AKI is appropriately managed, patients can recover their kidney functions to get back to their baseline stage of CKD<sup>3</sup>
- Prevent AKI in your patient with CKD including<sup>4</sup>:
  - Educate your patient with CKD to avoid nephrotoxins
  - Patients with CKD should be advised to attend reviews regularly
  - Advise your patient to hydrate appropriately based on their urine output and stage of CKD as advised by the nephrologist
  - Hydrate appropriately in patients with hypovolaemia
  - Ensure blood pressure is well controlled in patients with hypertension
  - Ensure blood sugar is controlled in patients with diabetes



- **In a facility without a doctor: (CHPS, Health center, Clinics without doctors)**
  - Advise on preventive measures
  - Refer to facility with a doctor immediately AKI is suspected or diagnosed
- **In a facility with a doctor: (Clinics/Polyclinics and Hospitals)**
  - Monitor urine output and consider referral/consult a nephrologist if urine output is still less than 0.5ml/kg per hour after initial management and monitoring for 6 hours
  - Examine and investigate for complications of acute kidney injury such as pulmonary oedema, hyperkalaemia and metabolic acidosis and manage acutely in a facility with a specialist (as discussed in module 6)
  - Acute kidney injury can be managed conservatively in most cases without dialysis when diagnosed early promptly managed
  - Identify indications for dialysis and refer immediately to a nephrologist
  - Common indications for dialysis in acute kidney injury are:
    - Refractory pulmonary oedema
    - Refractory metabolic acidosis
    - Refractory hyperkalaemia
    - Uraemic encephalopathy
    - Uraemic pericarditis

## **References:**

1. Johnson R. J, Floege J, Tonelli Marcello (2022). Comprehensive Clinical Nephrology. 7th Edn (Canada: Elsevier) pg 927-959
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# MODULE 7.1: DIABETES MELLITUS AND CKD

## Objectives:

1. To recognize diabetes mellitus as a cause of CKD
2. To screen patients with diabetes for CKD
3. To ensure optimal control of Diabetes in patients with and without CKD
4. To identify and manage the cardiovascular complications of DM in patients with CKD

## CKD and Diabetes mellitus

- About 40% of people with diabetes develop CKD during their lifetime.
- The prevalence of DM directly reflects on the burden of CKD globally and in Ghana.<sup>1</sup>
- The prevalence of DM in Ghana is 6.5% according to a recent systematic review and meta-analysis.<sup>2,3</sup>
- Poor glycaemic control results in chronic complications which are macro-vascular (coronary heart disease, ischaemic stroke, peripheral vascular disease) and micro-vascular (retinopathy, neuropathy, and nephropathy).
- Diabetic nephropathy (DN) or diabetic kidney disease (DKD) is said to occur when the pathophysiology of kidney injury is primarily due to diabetes<sup>4,5,6</sup>.
- Generally, kidney biopsy is not needed unless another cause is suspected for the CKD.
- CKD occurring in patients with diabetes is the leading cause of kidney failure requiring kidney transplantation or dialysis worldwide<sup>1</sup> thus culminating in increased cost of care, morbidity, and implications on quality of life.

## Screening

- Patients with DM have a high-risk for developing CKD as well as for CKD progression so should be included in a routine screening program.
- Timely screening allows for early identification of CKD before advanced disease.
- Screening is recommended to be done yearly starting at diagnosis for T2 DM and 5 years after diagnosis for T1 DM (refer to module 4).

## Diagnosis

- Appropriately stage and risk stratify to guide further monitoring, treatment, or referral.
- Chronic kidney disease (CKD) occurring in a patient with DM is usually attributed to diabetes, unless there is evidence of other causes<sup>4,5</sup>.
- A cause of CKD other than diabetes should be considered in any of the following:
  - Persistent haematuria (micro or macroscopic) or active urinary sediments
  - Rapidly declining eGFR
  - Low eGFR with little or no proteinuria
  - Absence of other complications of diabetes



- Known duration of diabetes < 10 years (if Type 1 DM)
  - Family history of non-diabetic kidney disease (e.g. polycystic kidney disease)
  - Symptoms and signs suggestive of other systemic diseases.
- Signs and symptoms of CKD in patients with DM are no different from the general population.
- Screening is recommended for early detection for timely intervention to prevent disease progression, manage, prevent complications, improve quality of life and survival.

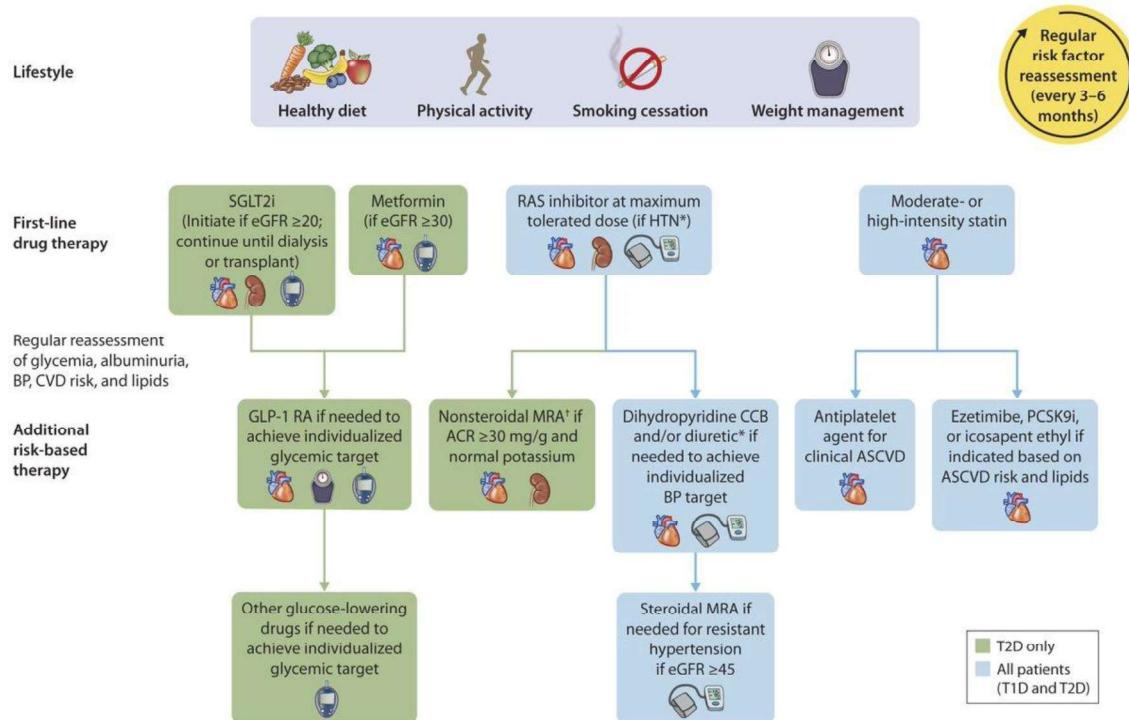
## Management of CKD in diabetes

### Comprehensive care

- Multi-disciplinary care, patient empowerment through structured education and lifestyle modifications is strongly advised.
- A comprehensive approach to DM patients in CKD including Medical Nutrition Therapy, increase physical activity/exercise, cessation of tobacco use, and weight control, together with evidence-based pharmacologic therapies to achieve glycaemic, lipid and blood pressure control to prevent complications is the goal<sup>7</sup>.
- Patients with diabetes and CKD usually have multiple co-morbidities and are by virtue of DM and CKD independently at high risk of cardiovascular events and mortality.
- Management should thus be timely, including early appropriate referral, comprehensive and well-coordinated.

Figure 10 below shows a holistic approach for improving outcomes in patients with diabetes and chronic kidney disease<sup>5,6</sup>.





\*Angiotensin-converting enzyme inhibitor (ACEi) or angiotensin II receptor blocker (ARB) should be first-line therapy for hypertension (HTN) when albuminuria is present, otherwise dihydropyridine calcium channel blocker (CCB) or diuretic can also be considered; all 3 classes are often needed to attain blood pressure (BP) targets. † Finerenone is currently the only non-steroidal mineralocorticoid receptor antagonist (MRA) with proven clinical kidney and cardiovascular benefits. Icons presented indicate the following benefits: blood pressure cuff  $\checkmark$  blood pressure-lowering; glucometer  $\checkmark$  glucose-lowering; heart  $\checkmark$  heart protection; kidney  $\checkmark$  kidney protection; scale, weight management; ACR, albumin-creatinine ratio; ASCVD, atherosclerotic cardiovascular disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide1 receptor agonist; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; RAS, renin-angiotensin system; SGLT2i, sodium-glucose cotransporter-2 inhibitor; T1D, type 1 diabetes; T2D, type 2 diabetes.

**Figure 10: Holistic approach for improving outcomes in patients with diabetes and chronic kidney disease. Adapted from KDIGO guideline 2022.**

## Lifestyle and self-management

- Non-pharmacological management of patients with DM include medical nutrition therapy, increased physical activity, self-monitoring of blood glucose (SMBG) and patient education.
- Patient education should be targeted at empowering patients to achieve good self-care and lifestyle modifications.
- Refer to Ghana Diabetes Guidelines 2023, Chapter 4 for details of non-pharmacological management of patients with diabetes.<sup>4</sup>
- Among patients with DM and CKD the non-pharmacological management of DM remains a backbone with particular attention to the individualized requirements posed by the CKD.



## **Medical Nutrition Therapy/ Diet**

- A Registered Dietician (RD) should provide individualized MNT and information for people with CKD about dietary adaptations regarding sodium, phosphorus, potassium, and protein intake, tailored to their individual needs, and severity of CKD.
- For persons with CKD G3–G5, daily protein consumption should be 0.8 g/kg/day but in adults with CKD G3–G5 and on maintenance dialysis who are often catabolic or malnourished protein consumption should be 1.0–1.2 g/kg/day
- Protein consumption should not be restricted in adults suffering from severe muscle loss, wasting, or other disorders that cause malnutrition.
- High protein consumption (>1.3 g/kg/day) should be avoided in persons with CKD who are at risk of progression.
- Restrict salt intake: less than 5 g of sodium chloride (salt) per day (less than half a teaspoon of salt per day; no added salt at table). Reduce intake of salted foods including momoni, koobi, kako etc.
- Increase intake of more fruits, vegetables, and reduced intake of carbohydrates
- Advise on adequate hydration especially during warm weather.
- Cessation of smoking and avoiding tobacco use is recommended.

## **Physical activity and weight**

- Moderate-intensity physical activity for at least 150 minutes per week to a level compatible with their cardiovascular and physical tolerance considering age, ethnic background and access to resources.
- People with CKD should be advised to avoid sedentary lifestyles.
- Obese patients with CKD, particularly eGFR  $\geq 30$  ml/min per 1.73 m<sup>2</sup> should be advised to lose and maintain healthy weight through diet, physical activity, and behavioural therapy.

## **Glycaemic control**

### **Glycaemic monitoring**

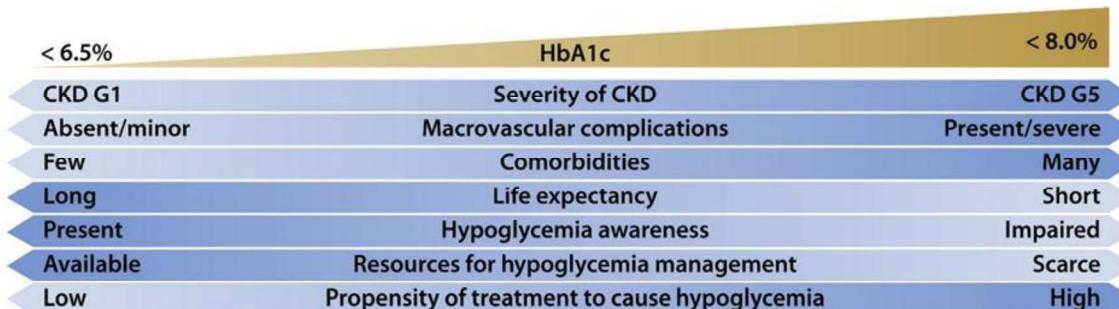
- Assessment of glycaemic control using glycated haemoglobin (HbA1c) among stable patients who are meeting treatment goals should be done 6-monthly, and 3-monthly among those who are intensively managed, whose therapy has changed, or whose treatment goals are not met.
- Although HbA1c is recommended in assessing long term glycaemic control but accuracy and precision declines in advanced CKD (G4 and G5) and among patients on dialysis.
- Anemia from reduced red blood cell life span and haemolysis, can all falsely lower the HbA1c



- Falsely increased HbA1c can result from iron deficiency anemia, carbamylation of haemoglobin and the presence of acidosis.
- HbA1c cannot adequately capture glycaemic variability and hypoglycaemic events.
- Monitoring of blood glucose by Self-monitoring blood glucose (SMBG) or Continuous glucose monitoring (CGM) where available should be emphasized among DM patients with CKD to validate glycaemic control and also guide medication adjustment especially in those at higher risk of hypoglycaemia.
- Refer to Ghana Diabetes Guidelines 2023, Chapter 4.4 for details of CMG and SMBG among patients with diabetes.<sup>4</sup>

#### **Glycaemic targets**

- Glycaemic targets must be individualized, in patients with diabetic kidney disease not on dialysis, glycaemic targets ranging from <6.5% to <8.0% is recommended and is associated with improvements in survival, cardiovascular and micro-vascular outcomes, as well as lower risk of CKD progression.
- Factors guiding individualized glycaemic targets<sup>5</sup> are illustrated in Figure 11 below.



**Figure 11: Factors guiding decisions on individual HbA1c targets.** Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; G1, eGFR  $\geq 90$  mL/min/1.73 m<sup>2</sup>; G5, eGFR <15 mL/min/1.73 m<sup>2</sup>; HbA1c, glycated haemoglobin. **Adapted from KDIGO guideline 2022.**

- Keep FBS between 4 - 7 mmol/L. For very ill, frail and elderly patients, the FBS should be kept between 6 – 8 mmol/L
- Target glycated haemoglobin (HbA1c) < 7.0% for early CKD target HbA1c < 6.5%.
- For patients with CKD, hypertension or uncontrolled DM, refer to the next level of care.



### **Glucose lowering therapies**

- All patients with DM need to start lifestyle therapy
- Type 1 DM patients are insulin dependent and will require insulin.
- In Type 2 DM patients, first-line treatment with both metformin and a sodium-glucose cotransporter-2 inhibitor (SGLT2i), and additional drug therapy as needed for glycaemic control is recommended.

### ***Metformin***

- It is recommended for treating patients with T2DM, CKD and an eGFR  $\geq 30$  ml/min per  $1.73\text{ m}^2$ .
- For an eGFR of  $45\text{--}59$  ml/min per  $1.73\text{ m}^2$ , dose reduction may be considered in the presence of conditions that predispose patients to hypoperfusion and hypoxemia.
- The maximum dose should be halved when the eGFR declines to  $30\text{--}45$  ml/min per  $1.73\text{ m}^2$ . Treatment should be discontinued when the eGFR declines to  $<30$  mL/min/ $1.73\text{ m}^2$  or when the patient is initiated on dialysis, whichever is earlier.

### ***Sodium-glucose cotransporter-2 inhibitors (SGLT2i)***

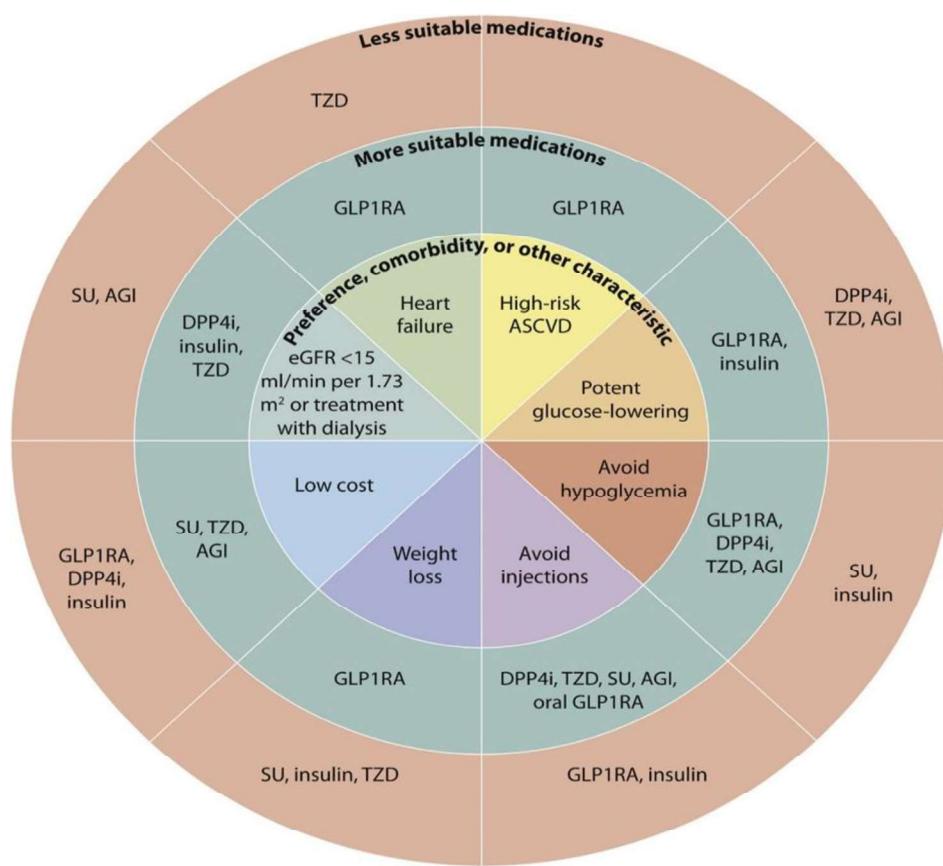
- It is recommended for treating patients with diabetic kidney disease and an eGFR  $\geq 20$  ml/min per  $1.73\text{ m}^2$ .
- Once an SGLT2i is initiated, it is reasonable to continue an SGLT2i even if the eGFR falls below  $20$  ml/min per  $1.73\text{ m}^2$ , unless it is not tolerated or renal replacement is initiated.
- It is reasonable to withhold SGLT2i during times of prolonged fasting, surgery, or critical medical illness (when people may be at greater risk for ketosis).
- SGLT2i have been proven to reduce risks of CKD progression and major CVD events, especially heart failure even independent of glycaemia.

### ***Glucagon-like peptide-1 receptor agonists (GLP-1 RA)***

- Are recommended in patients with Type 2 DM and CKD who have not achieved individualized glycemic targets despite use of metformin and SGLT2i treatment, or who are unable to use those medications.
- GLP-1 RA are safe and effective glucose-lowering agents with eGFR as low as  $15$  ml/min per  $1.73\text{ m}^2$ . They demonstrate cardiovascular benefits, particularly among patients with established atherosclerotic cardiovascular disease (ASCVD) even with eGFR  $<60$  ml/min per  $1.73\text{ m}^2$ , as well as kidney benefits by reducing albuminuria and slowing the rate of eGFR decline.



- Other classes of glucose-lowering agents may also be used, considering the patient factors – age, comorbidities, current medications, cost, side effect profile, patient preferences, literacy, and convenience for the patient (Figure 12) and dosed according to eGFR<sup>6,8</sup>.
- For example, sulfonylureas that are long-acting or cleared by the kidney should be avoided at low eGFRs.
- Dipeptidyl peptidase-4 inhibitor (DPP-4 inhibitors) lower blood glucose with low risk of hypoglycemia but have not been shown to improve kidney or cardiovascular outcomes and should not be used in combination with GLP-1 RA.
- All insulin preparations can be used in CKD, but modifications of insulin type and dose may be necessary to reduce the risk of hypoglycemia, as reduction in GFR results in prolongation of the insulin half-life.
- Refer to Ghana Diabetes Guidelines 2023, Chapter 5 for pharmacological therapy in DM.<sup>4</sup>



**Figure 12: Patient factors influencing the selection of glucose-lowering drugs other than sodium-glucose cotransporter-2 inhibitor (SGLT2i) and metformin in type 2 diabetes (T2D) and chronic kidney disease (CKD). Adapted from KDIGO guideline 2022.**

AGI, alpha-glucosidase inhibitor; ASCVD, atherosclerotic cardiovascular disease; DPP4i, dipeptidyl peptidase-4 inhibitor; eGFR, estimated glomerular filtration rate; GLP1RA, glucagon-like peptide-1 receptor agonist; SU, sulfonylurea; TZD, thiazolidinedione.



## Lipid management

- A statin is recommended for all patients with Type 1 DM or Type 2 DM and CKD, moderate intensity for primary prevention of ASCVD or high intensity for patients with known ASCVD and some patients with multiple ASCVD risk factors.
- For some patients, intensification of statin therapy; addition of ezetimibe, or addition of a PCSK-9 inhibitors such as evolocumab or alirocumab is recommend based on ASCVD risk and attained LDL cholesterol concentrations.
- Refer to Ghana Diabetes Guidelines 2023, Chapter 8 Cardiovascular risk assessment and management of dyslipidaemia in DM.<sup>3</sup>

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# MODULE 7.2 CHRONIC KIDNEY DISEASE AND HYPERTENSION

## Objectives

- To recognize hypertension as a cause and complication of CKD
- To encourage screening of patients with hypertension for CKD
- To ensure optimal control of hypertension in patients with and without CKD
- To prevent the cardiovascular complications of hypertension in patients with CKD

## CKD and Hypertension

- Hypertension and chronic kidney disease (CKD) often occur together, and the interrelation between these two pathophysiological states is bidirectional.<sup>1,2</sup>
- Persistent elevated blood pressure can increase the progression of CKD
- Progression of CKD makes it more difficult to control blood pressure.<sup>1</sup>

### Definition

- Hypertension is defined as systolic blood pressure (SBP) values  $\geq 140$  mm Hg and/or diastolic blood pressure (DBP) values  $\geq 90$  mmHg in individuals  $\geq 18$  years.<sup>3,4</sup>
- Most CKD patients have hypertension which is more severe than non-CKD patients.
- Control of hypertension and albuminuria are important interventions in delaying progression of kidney disease

### Causes of hypertension

The causes of hypertension are classified into two main groups: primary and secondary hypertension. In patients  $\leq 40$  years, it is important to screen for secondary causes of hypertension (refer to the National CVD guidelines)

**Prevention:** Lifestyle changes are essential in preventing hypertension (See Module 5).

### Diagnosis

- Proper measurement of blood pressure is very vital to accurately diagnose hypertension.
- The recommended device for blood pressure measurement is a calibrated electronic sphygmomanometer for use both in hospitals and at home (refer to the CVD guidelines for details of accurate blood pressure measurements).



## Screening for CKD in patients with hypertension

- Patients with hypertension should be screened at least yearly for chronic kidney disease (CKD).
  - The screening tests should include Urine dipstick, Urine ACR (if available), Blood urea, electrolytes and creatinine (including eGFR)
  - Refer any abnormalities detected to the next level if the facility does not have a doctor.
  - In a facility with a doctor, refer to module 4 and 5 for diagnosis and management.
- Figure 13 below is an algorithm for managing CKD in patients with hypertension<sup>5</sup>.

### Algorithm for management of hypertension in people with CKD

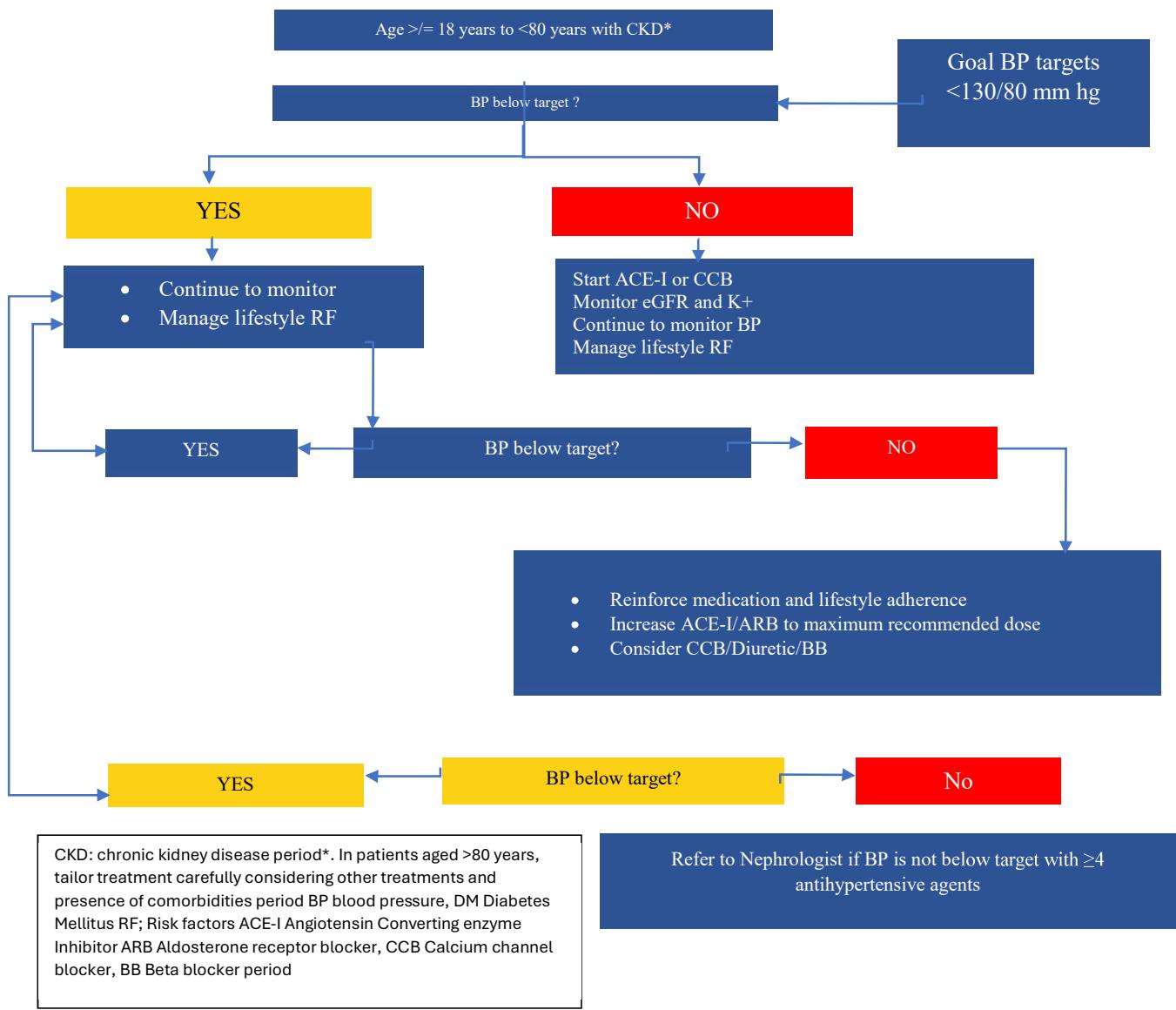


Figure 13: Algorithm for management of hypertension in people with CKD



### Clinic Blood Pressure Targets<sup>6</sup>

In person under age 80 years with:	Blood Pressure Target
Chronic kidney disease plus albumin to creatinine ratio less than 70 mg/mmol.	Below 140/90 mmHg
Chronic kidney disease plus albumin to creatinine ratio of 70 mg/mmol or more.	Below 130/80 mmHg
<b>In person over age 80 years with:</b>	
Hypertension	Below 150/90mmHg
Chronic kidney disease plus albumin to creatinine ratio less than 70 mg/mmol	Below 140/90 mmHg
Chronic kidney disease plus albumin to creatinine ratio of 70 mg/mmol or more	Below 130/90 mmHg

*Table 13: Clinic blood pressure targets (Adapted guidelines from NICE's guideline on chronic kidney disease- 2021)<sup>6</sup>*

### Indications for specialist referral

- Urgent (in-patient) treatment needed:
  - Particularly severe hypertension (>220/120mmHg).
  - Accelerated hypertension (severe BP, with retinal bleeds ± papilledema)
  - Hypertensive emergency (e.g. encephalopathy, eclampsia, aortic dissection).
- Possible secondary hypertension.
- Resistance to treatment ( $\geq 3$  drugs).
- Multiple drug intolerances.
- Multiple drug contraindications.
- Persistent non-adherence or non-compliance.
- Unusual blood pressure variability.
- Possible white coat hypertension.
- Hypertension in pregnancy.

### Referral to a nephrologist is recommended.

- when eGFR < 30 mL/min per 1.73m<sup>2</sup> and/or
- Proteinuria (urine dipstick of  $\geq 1+$  or urine albumin creatinine ratio > 300 mg/g.



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# MODULE 7.3 CHRONIC KIDNEY DISEASE IN CHILDREN

## Objectives

- To define CKD in children
- To outline causes of CKD in children
- To classify CKD in children
- To outline the clinical manifestation of CKD in children
- To highlight investigations required in children with CKD.
- To outline treatment of CKD in children

## CKD Definition in children

- Paediatric CKD is defined based on at least one of the following clinical criteria<sup>1,2</sup>:
  - GFR of **less than 60 mL/min per 1.73 m<sup>2</sup>** for greater than three months with implications for health regardless of whether other CKD markers are present
  - GFR **greater than 60 mL/min per 1.73 m<sup>2</sup>** that is accompanied by evidence of structural damage or other markers of functional kidney abnormalities including proteinuria, albuminuria, renal tubular disorders, or pathologic abnormalities detected by histology or inferred by imaging. This category also includes patients with functioning kidney transplants.

In general, the definition of CKD in adults applies to children (birth-18 years) with some allowances or exceptions as follows:

- The criteria for duration >3 months, does not apply to newborns or infants ≤3 months of age.
- The criteria of a GFR <60 ml/min/1.73 m<sup>2</sup> does not apply to children <2 years of age in whom an age- appropriate standard deviation is a better comparative.
- A urine protein or albumin excretion rate above the normal value for age may be substituted for albuminuria ≥30 mg/24 hours.
- Electrolyte abnormalities are to be defined with age reference values.



### **Estimation of GFR in children:**

In children, the estimation of GFR is done using the Schwartz equation given as: eGFR in ml/min/1.73m<sup>2</sup> (eGFR) = K x height (cm)

Serum Cr

K is a constant and currently stands as:

- 0.4313 for sCr in mg/dl
- 36.52 for sCr in µmol/l

### **Causes of CKD in children**

In children, structural abnormalities in the form of Congenital Anomalies of the Kidneys and Urinary Tracts (CAKUT) accounts for about 60% of the causes of chronic kidney disease followed by, unknown pathologies and glomerular diseases<sup>1,2</sup>. (See Table 14)

*Causes of CKD in children*

CAUSE	CHARACTERISTICS	PREVALENCE
CAKUT	Commoner in younger children e.g. Aplasia, hypoplasia, dysplasia, obstructive uropathies (PUV), polycystic kidney disease	60%
Glomerular	<ul style="list-style-type: none"><li>• Commoner in older children- accounts for ~45% of CKD in children &gt;12yrs (USA) e.g. FSGS, haemolytic uraemic syndrome (HUS)</li><li>• Secondary glomerular disease – SLE</li></ul>	10-20%
Others	<ul style="list-style-type: none"><li>• Unidentified or unknown primary underlying cause.</li><li>• Genetic diseases e.g. hereditary nephritis, cystinosis, oxalosis</li><li>• Interstitial nephritis</li></ul>	20-30%

*Table 14. Causes of CKD in children*

### **Classification of CKD in children**

- The classification of CKD in children is based mainly on estimated GFR (eGFR).
- Estimated GFR is typically low at birth and gradually reaches adult levels by age 2yrs.
- Due to this, use of eGFR for classifying CKD in children less than 2yrs has limitations and hence eGFR standard deviation are used in this group instead.
- Below is the classification for children above age 2yrs (Table 15)



**Stages of chronic kidney disease for children based on the KDIGO 2012 clinical practice guideline**

GFR category	GFR (mL/min/1.73 m <sup>2</sup> )	Terms
G1	≥90	Normal or high
G2	60 to 89	Mildly decreased*
G3a	45 to 59	Mildly to moderately decreased
G3b	30 to 44	Moderately to severely decreased
G4	15 to 29	Severely decreased
G5	<15	Kidney failure

In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD.

KDIGO: Kidney Disease: Improving Global Outcomes; GFR: glomerular filtration rate; CKD: chronic kidney disease.

\* Relative to young adult level.

**Table 15: GFR criteria for CKD classification in children (same as adult classification)<sup>1</sup>**

*Albuminuria/Proteinuria criteria for CKD classification in children*

Category	AER (mg/24hours)	ACR (approx. equivalent)		Terms
		mg/mmol	mg/g	
A1	<30	<3	<300	Normal to mildly increased
A2	30-300	3-30	30-300	Moderately increased
A3	>300	>30	>300	Severely increased

**AER- Albumin Excretion Rate, ACR – albumin Creatinine Ratio 9Table 17)**

**Table 16: Albuminuria/Proteinuria criteria for CKD classification in children<sup>1,2,3</sup>**

Classification of CKD by NFK-K/DOQI (National Kidney Foundation Disease Outcome Quality Initiative)<sup>4</sup>

STAGE	GFR ML/MIN/1.73M <sup>2</sup>	DESCRIPTION	ACTION PLAN
I	≥90	Kidney damage with normal or ↑ GFR	Diagnose and treat comorbid conditions, slow CKD progression
II	60-89	Kidney damage with mild ↓GFR	Slow CKD progression Evaluate rate of decline in GFR
III	30-59	Moderate ↓ GFR	Evaluate & treat complications Slow CKD progression
IV	15-29	Severe ↓ GFR	Prepare for Renal replacement therapy
V	<15	Kidney failure	Start Renal replacement therapy

**Table 17: Classification of CKD by NFK-K/DOQI (National Kidney Foundation Disease Outcome Quality Initiative)**



## Clinical features of CKD in children

- Asymptomatic in early stages
- Growth failure/stunting/failure to thrive.
- Bodily swelling
- Anorexia; nausea; vomiting
- Hypertension
- Anaemia due to chronic disease and erythropoietin deficiency
- Decreased urine output
- Straining at micturition or dribbling of urine
- Foamy or frothy urine
- Passage of bloody urine
- Polydipsia; Nocturia; enuresis (bedwetting)
- Flank mass or palpable kidneys
- Loss of concentration
- lethargy; seizures; coma
- Metabolic acidosis, metabolic flap,
- Muscle cramps
- GIT bleeding, pruritus
- Electrolyte derangements: Hyperkalaemia, hyponatraemia, hyperphosphatemia, hypocalcaemia, hypomagnesemia
- CKD - Mineral and Bone disorder (MBD). Manifests as bowed legs and hands (rickets)
- Dermopathy – uraemic frost; dermatitis, hyperpigmentation or excoriation
- Cardiac- left ventricular hypertrophy; pericarditis

## INVESTIGATIONS

### Diagnostic

- Serum urea and serum creatinine (calculate the eGFR using the Schwartz formular)
- Serum Calcium, magnesium & Phosphate (CMP)
- Parathyroid hormone (PTH)
- Urine albumin-to-creatinine ratio or urine protein-to-creatinine ratio
- Urinalysis (proteinuria, haematuria, pyuria, specific gravity, casts especially broad waxy cast)
- Plasma cystatin C
- Kidney, Ureter and Bladder (KUB) ultrasound scan ± doppler
- Intravenous urogram
- CT and MRI scans of the kidneys
- Micturition cystourethrogram
- Radionuclide scan of the kidneys
- Kidney biopsy in those with unexplained CKD



### **Supportive**

- Full Blood Count
- Arterial blood gases (ABGs)
- Blood glucose,
- Hb electrophoresis
- Skeletal survey
- Echocardiogram
- Liver function tests
- Serum lipids & albumin

## **Management of CKD in children**

### **Who is to manage CKD in children?**

- CKD in children should be managed preferably by a paediatric nephrologist but can be managed by a pediatrician in consultation with a paediatric nephrologist, even if remotely.
- CKD management follows the action plan in the NKF/DOQI classification of CKD and are outlined below:

### **Maintenance of general health and treatment of CKD complications:**

#### **Nutrition**

- The aim of nutritional management in children with CKD is to provide adequate nutrients that will aid optimal growth while attempting to avoid excessive catabolism, acidosis and to manage metabolic abnormalities.
- The following are suggested modifications to diet which should be done in conjunction with a dietician.

#### **Total Energy requirements:**

According to the KDOQI - 2008 guidelines<sup>4</sup>, the total energy needs of a child with chronic kidney disease are expected to be the same as that of a healthy child of the same age. Estimated needs can be adjusted based on growth velocity and weight trends as shown in table 18 below.

Age group	Energy (kcal/kg/day)
Preterm	110-135
0-2 months	96-120
3-12 months	82-96
1-3 years	78-82
4-10 years	64-78
11-18 years	48-64



**Table 18: Recommended Energy Requirements in children with CKD**

**Protein requirement:**

- Strict protein restriction is not recommended in children with CKD as it adversely affects kidney function in children and lead to impaired growth.
- Generally, 2g/kg/day of protein is recommended to allow for growth.
- When urea is persistently > 20 mmol/l, a gradual reduction of daily protein intake to not less than 1g/kg/day is advised.
- See KDOQI recommended guidelines (2008) for protein needs in children with CKD<sup>4</sup> (table 19)

Age group	Protein (g/kg/day)	
<i>Conservative management</i>	<i>CKD stage 3</i>	<i>CKD stage 4-5</i>
Preterm	2.5-3.0	2.5-3.0
0-2 months	1.5-2.1	1.5-1.8
3-12 months	1.2-1.7	1.2-1.5
1-3 years	1.05-1.5	1.05-1.25
4-10 years	0.95-1.35	0.95-1.15
11-18 years	0.85-1.2	0.85-1.05

**Table 19: Recommended Protein requirements in children with chronic kidney disease<sup>4</sup>**

**Practical application of protein estimation:** 7g of protein will be obtained from the following food types:

- 2 dessert spoon of fresh whole milk
- 1 dessert spoon of powdered whole milk
- 1 soup ladle of beans
- 1 dessert spoon of groundnut paste
- 10-12 pieces of roasted groundnuts
- 1 match box-size of meat/chicken
- 1 whole egg or 2 of egg white (albumin)
- Salt should be restricted, and no added salt diet is recommended especially in those with hypertension.
- Processed foods with added salt such as crisps, sausages, cheese, should be avoided. Similarly, salted food like koobi, momoni and monosodium glutamate (MSG)-based spices should be restricted.

**NB:** Children with salt wasting renal diseases e.g. obstructive uropathy and renal dysplasia are exempted from salt restriction. Sodium requirement here may be up to 4-6 mmol/kg/day.

- Low **potassium** diet is recommended for most cases of CKD. Some foods to avoid include coconut water, bananas, chocolate and chocolate drinks, avocados and tomatoes.
  - NB: children with Bartter syndrome, cystinosis and CKD with polyuria may have hypokalaemia which should be treated accordingly.



- **Phosphate** restriction may be necessary – phosphorus is naturally occurring in protein rich foods. Restriction should start once there is biochemical evidence of hyperphosphatemia. In addition, chelation should be done using phosphate binders such as calcium carbonate or calcium citrate. Some phosphate rich food to avoid include: dairy products, egg yolk, peanut butter, meat and poultry.
- **Calcium and vitamin D** supplementation is recommended.
- **Anemia:** Iron supplementation 2-4mg of elemental iron/kg/day and SC erythropoietin to aim at Hb of 9-12g/dl.
- Supplement **micronutrients** such as folic acid, vitamins, C, E and B complex.
- Fluid restriction when oedematous and when GFR< 15ml/min/1.73m<sup>2</sup> to insensible loss (400mls/m<sup>2</sup>) plus previous day's urine output may be necessary.
- Treatment of metabolic acidosis with sodium bicarbonate.
- Control of Potassium with Na-K exchange resins (e.g. Kayexalate).

**Immunization:** Routine immunization schedules should be followed except for patient with stages 4 and 5 CKD where live attenuated vaccines such as hepatitis B, pneumococcal and varicella vaccines are given only with careful consideration for immune status of the child.

## Delaying progression of kidney disease

- **Treat treatable causes of CKD:**

In some cases, identifying and treating primary kidney disease (eg CAKUT) will slow down the progression of CKD e.g.: corrective surgeries for obstructive uropathies immunosuppressive therapy for autoimmune conditions such as SLE, etc.

- **Avoid further insults to the kidney:**

- Acute episodes of kidney injury will often cause a sharp decline in already existing CKD so steps should be taken to ensure such episodes are prevented.
- Reduced kidney perfusion or the administration of nephrotoxic agents are two instances that may result in decline in kidney function in children with CKD.
- Actions to take include avoidance of NSAIDS and unlicensed herbal medications, prevention of dehydration and shock, severe sepsis, malaria prevention and avoidance or caution in nephrotoxic drug administration.

- **Strict BP control:**

The target BPs are: Systolic and diastolic BPs <90<sup>th</sup> percentile for age, sex, and height for children <13yrs and BP ≤120/80 mmHg for children ≥ 13yrs. Table 20 shows selected first line antihypertensive drugs and their dosage.



Drug Class	Specific Medicines	Dose
Calcium channel blockers	Amlodipine	0.05-0.2mg/kg orally once daily
	Nifedipine	0.25 – 0.5mg/kg per day once or in 2 divided doses
Beta blockers	Atenolol	0.5-1mg/kg/dose orally 12-24hourly daily. Maximum 25-50mg
	Labetalol	1-2mg/kg/dose 12 hourly. Maximum 50-100mg/dose
Alpha blockers	Doxazosin	0.02-0.1mg/kg orally once daily
Vasodilators	Hydralazine	0.4-1.5mg/kg/dose orally 6-8 hourly. Maximum 50mg/dose
ACEI/ARB (especially if proteinuric CKD)	Lisinopril	0.2-1mg/kg orally once daily
	Losartan	0.5-2mg/kg orally once daily
Centrally-Acting	Methyl dopa	3-15mg/kg/dose orally 8 hourly

**Table 20: Selected first line antihypertensives.**

- **Control proteinuria:**

Proteinuria is ultimately detrimental to the kidneys and their function and therefore needs to be controlled. This can be aided supportively with ACEi or ARBs even in the absence of hypertension.

#### **Note on blood transfusion in CKD**

Where there is the potential for kidney transplantation in a child with CKD, then as much as possible, blood transfusion should be avoided especially where WBC- poor or filtered blood cannot be offered.

#### **Kidney replacement therapy:**

- As the disease approaches stage 4 (eGFR <30mL/min per 1.73m<sup>2</sup>), preparations need to start for kidney replacement therapy (KRT).
- Kidney replacement will generally be needed when the glomerular filtration rate (GFR) falls below 15 mL/min per 1.73 m<sup>2</sup> (CKD stage 5).
- Preparation will involve providing family and caregivers information relating to the timing and choice of KRT (pre-emptive kidney transplantation, peritoneal dialysis, and haemodialysis).
- By this stage, the child will be under the care of a nephrologist in conjunction with transplant team as part of a multi-disciplinary team in a tertiary facility, to help in the conversation and transition.



### **Follow up:**

- For all children, growth monitoring involving the measurement of height and weight is crucial. The height over a period may be used to determine growth velocity, an important measure that helps determine the effect of a chronic disease and/or its intervention on rate of growth. For children <3 years, also monitor head circumference.
- Nutritional assessment in the form of three-day diet record or three 24-hour dietary recalls and food frequency questionnaires will provide insight into growth faltering as a result of stringent food restrictions rather than just the disease process.
- Most children with CKD due to CAKUT especially obstructive uropathies will require follow up after surgical interventions e.g. valve ablation for PUV, pyeloplasty for PUJ, ureterostomies or vesicostomies for severe hydronephrosis. These follow up visits should be done with the paediatric nephrologist in conjunction with paediatric urologist or paediatric surgeon as much as possible.
- Counselling and reinforcing of counselling sessions should also be done at follow up visit to help address challenges that arise in between visits.
- The clinical psychologist should be a member of the multi-disciplinary team at follow up visits.

### **When to refer a child with CKD to the paediatric nephrologist:**

- Preferably, all cases of CKD
- Where caregivers would not be compliant with the referral, consider case management in consultation with a nephrologist
- If recommended management regimen is not available e.g. KRT
- When surgical intervention is the required treatment, especially CAKUT
- When kidney transplantation is a feasible treatment option

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4. KDOQI clinical practice guidelines for nutrition in children with CKD – 2008 update



# MODULE 7.4 CHRONIC KIDNEY DISEASE IN PREGNANCY

## Objectives

1. To identify pregnancy as a risk factor for acute kidney injury and CKD
2. To understand pregnancy as a risk factor for progression of CKD
3. To identify CKD as a risk factor for poor pregnancy outcomes

## Introduction

Women with CKD have higher risk of complications during pregnancy which may affect them as well as the foetus.

These risks are more pronounced with increasing severity of CKD.

Adverse maternal outcomes include:<sup>1,2</sup>

- Gestational hypertension
- Pre-eclampsia
- Eclampsia
- Maternal death.

Adverse foetal outcomes include:

- Premature birth
- Intra-uterine growth retardation
- Small-for-gestational age
- Low birth weight
- Still birth and neonatal mortality.<sup>1</sup>

Predictors of adverse maternal-foetal outcomes are:<sup>2</sup>

- Baseline stage of chronic kidney disease
- Baseline proteinuria (>1 g/day or dipstick ≥1+)
- Presence of systemic disease (e.g. diabetes, hypertension, sickle cell disease, systemic lupus erythematosus)

## Physiological changes in pregnancy

- Due to physiological changes in pregnancy, there is an increase in kidney filtration (increase in eGFR) and reduced serum creatinine.
- Currently, there are no standardized equations for estimating GFR in pregnancy.
- In pregnancy, a serum creatinine >80umol/l is abnormal and should be investigated.



## Risk of AKI in pregnant women

- During pregnancy women are at increased risk of acute kidney injury (AKI) especially when they develop some pregnancy related complications.
- AKI in pregnancy is a risk factor for development of CKD and progression of CKD.

Some of these risk factors for pregnancy-related AKI are:

- Septic abortion
- Hyperemesis gravidarum
- Antepartum and postpartum hemorrhage
- Hypertensive disorders in pregnancy including preeclampsia.
- Haemolysis, Elevated Liver enzymes and Low Platelets (HELLP) syndrome
- Thrombotic microangiopathies (thrombotic thrombocytopenic purpura (TTP)/atypical hemolytic uremic syndrome (aHUS)
- Acute Fatty Liver of Pregnancy
- Intake of nephrotoxic agents such as NSAIDs and some herbal medications

## When to avoid or delay pregnancy in patients with CKD

Women with CKD should receive extensive counselling to consider the use of safe and effective contraceptive methods.<sup>4,5</sup>

A CKD patient who becomes pregnant should be referred for management by a multidisciplinary team of specialists.

Pregnancy should be delayed or avoided in women with CKD with the following conditions:

- Moderate to severe chronic kidney disease (stage 3–5 CKD)
- Poorly controlled hypertension
- Heavy proteinuria of >1g/day or dipstick ≥1+ (delay pregnancy until proteinuria is managed and reduced to <1 g/24 h for at least 6 months)
- Women with diabetic kidney disease with moderate or severe kidney disease
- Active systemic disease
- Women currently taking teratogenic medications.
- Women with active glomerulonephritis (e.g. lupus nephritis)
- Women who have had a kidney transplant less than a year

## CKD medications to avoid in pregnancy

- When a woman with CKD wishes to get pregnancy she should be advised to stop some of her medications at conception.
- When she gets pregnant accidentally, her medications should be reviewed immediately to avoid foetal abnormalities.

The medications to avoid in pregnancy include:

- Angiotensin converting enzyme inhibitors
- Angiotensin receptor blockers



- Statins
- Calcimimetics (e.g. Cinacalcet)
- Non-calcium-based phosphate binders (e.g. Sevelamer and Lanthanum)
- Cyclophosphamide
- Mycophenolate Mofetil
- Sodium glucose transporter 2 (SGLT2) inhibitors

#### **Management of medications<sup>5</sup>:**

List of medications to avoid or considered safe in pregnancy

Drug	Conception	Pregnancy			Lactation
		Overall	Maternal considerations	Foetal considerations	
Labetalol	Safe	Safe	License for pregnancy. Avoid if asthmatic.	No association with congenital abnormalities.  Reduced birth weight in unadjusted observational data.  Neonatal bradycardia (2%) and hypoglycaemia (5%).	Safe
Nifedipine	Safe	Safe	None	No association with congenital abnormalities	Safe
Amlodipine	Safe	Limited data	None	Limited data. No adverse effects reported.	Safe
Methyldopa	Safe	Safe	Avoid in depression or if risk of depression.	No association with congenital abnormalities	Avoid in all due to risk of postnatal depression.
Doxazosin	Safe	Limited data	None	No evidence of harm in animal studies	<1% maternal dose detected.
Hydralazine	Safe	Safe	Risk of hypotension, tachycardia	No association with congenital abnormalities	Safe
Beta-blockers	Safe	Limited data on individual drugs	Avoid if asthmatic. Use in pregnancy determined by maternal indication.	No association with congenital abnormalities.  Reduced birth weight, clinical significance unclear.  Neonatal bradycardia (1%)	No adverse effects reported



				and hypoglycaemia (3%).	
Angiotensin converting enzyme inhibitors	No apparent increase in risk with first trimester use when data are corrected for underlying hypertension. Continue until conception if required for nephroprotection	Unsafe	None	Fetotoxic in second and third trimesters leading to fetal and neonatal renal failure, bone and aortic arch malformations, oligohydramnios, and pulmonary hypoplasia.	Safety data available for captopril and enalapril.
Angiotensin receptor antagonists	Insufficient data on exposure in early pregnancy. Discontinue in advance of pregnancy.	Unsafe	None	Fetotoxicity in second and third trimesters comparable to angiotensin converting enzyme inhibitors.	No data
Thiazides	Insufficient data on exposure in early pregnancy. No evidence of harm.	Unsafe	Reduced plasma volume expansion in pregnancy	No evidence of thrombocytopenia, jaundice, hypokalaemia or hyponatraemia in meta-analysis but advised to avoid.	Potential suppression of lactation. Avoid.



Corticosteroids	Safe	Safe	Potential risks: diabetes, hypertension, pre-eclampsia, infection, preterm rupture of membranes. Aim for minimum maintenance dose.	Fetus exposed to <10% maternal dose due to placental deactivation. No evidence of increase in congenital abnormalities.	Safe. Small amounts in breast milk. Consider timing feeds to 4 hours post administration if high dose given (e.g. methylprednisolone induction) and monitor neonate.
Hydroxychloroquine	Safe	Safe	Withdrawal may precipitate lupus flare. Indicated throughout pregnancy if patient has a history of lupus nephritis.	Placental transfer. No increase in miscarriage or congenital abnormality. May reduce risk of congenital heart block if maternal anti-SSA and or anti-SSB antibodies.	Safe
Azathioprine	Safe	Safe	Recommend check TPMT status before dosing.	Placental transfer. No association with congenital abnormalities.	Safe. Low concentration in breast milk
Ciclosporin	Safe	Safe	Monitor pre-dose levels more frequently in pregnancy and immediately post partum. May need higher dose in pregnancy. Avoid medications which interfere with calcineurin inhibitor metabolism (e.g. erythromycin, clarithromycin). Increased risk of gestational diabetes	Placental transfer. No association with congenital abnormalities.	Safe



Tacrolimus	Safe	Safe	Monitor pre-dose levels more frequently in pregnancy and immediately post-partum. May need a higher dose in pregnancy. Avoid medications which interfere with calcineurin inhibitor metabolism (e.g. erythromycin, clarithromycin). Increased risk of gestational diabetes	Placental transfer. No association with congenital abnormalities	Safe
Mycophenolate mofetil	Unsafe. Effective contraception during treatment and for 6 weeks after treatment. Ensure disease/transplant stability prior to conception.	Unsafe	None	Placental transfer. Teratogenic causing ear, heart, eye, lip/palate, kidney, and bone abnormalities, tracheoesophageal fistula, congenital diaphragmatic hernia. Increased miscarriage.	Avoid use during lactation due to insufficient data
Cyclophosphamide	Unsafe. Effective contraception during and for 3 months after treatment. Dose- and age-related risk of infertility.	Unsafe	None	Placental transfer. Teratogenic. Congenital abnormalities of the skull, ear, face, limb and visceral organs. Increased risk of miscarriage.	Excreted in breast milk. Discontinue breast-feeding during and for 36 hours after treatment.
Rituximab	Unclear (limited data available). Treatment	Unclear (limited data availabl	If indicated for severe disease, aim to give dose	Active placental transfer in 2nd and 3rd trimester. Potential risk of	Unclear (limited data available).



	decision depends on indication and alternative options.	e)	before, or in early, pregnancy to minimise the risk of neonatal B-cell depletion.	neonatal B-cell depletion. Avoid unless potential benefit to woman outweighs risk. Long term effects unknown.	Possible excretion of trace amounts but neonatal absorption unlikely
Iron	Safe	Safe	Intravenous preparations may offer better bioavailability in CKD	Safety data available in 2nd and 3rd trimesters but limited data on exposure on the first trimester. Expert consensus is not to withhold IV iron if indicated in the first trimester.	Safe
Low-molecular-weight heparin	Safe	Safe	Level of proteinuria which confers a significant risk of VTE in pregnancy is unclear. All pregnant women should be risk assessed for VTE.	No placental transfer	Safe
Erythropoietin	Safe	Safe	Monitor blood pressure	No placental transfer	Safe
Metformin	Safe	Safe	Use contraindicated outside of pregnancy if eGFR <30ml/min/1.73m <sup>2</sup> (approximates to serum creatinine >150µmol/L in pregnancy).	None	Levels in milk are low, infants receive <0.5% of maternal weight-adjusted dosage. No reported adverse effects.

**Table 21: List of medications to avoid or considered safe in pregnancy**

## When to consider termination of pregnancy in a patient with CKD

Termination of pregnancy is recommended if the underlying CKD is worsening leading to progression to kidney failure or will endanger the life of the mother.



Factors that may lead to decision to terminate pregnancy include:

- Severe deterioration of mothers underlying cause of CKD
  - Uncontrolled hypertension
  - Nephrotic syndrome not in remission
  - Pre-eclampsia or HELLP syndrome with severe disease
  - Rapid increase in proteinuria and/or serum creatinine
- 
- The decision should be made in consultation with multidisciplinary team, taking into account the severity of the CKD, the presence of other health conditions, and the potential impact on the mother's long-term health.
  - The multidisciplinary team involves obstetrician gynecologists, rheumatologists, feto-maternal specialists, and nephrologists is often required for decisions on termination to be made.

## Pregnancy and dialysis

- Pregnant women can undergo dialysis if indicated.
- Pregnant women requiring dialysis should be managed in the tertiary centre
- Pregnancy outcomes in women receiving dialysis are poor but can be improved with intensive dialysis.

## Solid organ transplants

- All pregnant women with kidney transplant should be managed at the tertiary unit by a nephrologist.
- Women with kidney transplants should wait until their kidney function is stable before conception, which is usually more than one year after transplantation.

## Referrals

- All pregnant women diagnosed with CKD should be referred to a centre with obstetrician gynaecologists, rheumatologists, and nephrologists for comprehensive multidisciplinary care.

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# MODULE 7.5 CKD IN THE ELDERLY

## Objectives

- To emphasize age as a risk factor for CKD
- To understand that traditional risk factors for CKD are common in the elderly
- To encourage the screening of CKD in the elderly during routine care

## Definition

Generally, elderly is defined as an individual who is 65 years and above<sup>1</sup>.

## Introduction

- The life expectancy in Ghana is increasing and currently at 65.2 years<sup>2,3</sup>.
- Advancing age is a major risk factor for CKD.
- Elderly patients with CKD often have other co-morbidities often accompanied by polypharmacy, frailty, and cognitive impairment.
- From 40 years, the kidneys begin to decrease in size progressively to about 20-30% by the 7th decade<sup>4,5</sup>.
- There is a physiologic decline in GFR of about 8 mL/min per decade from 40 years, but usually does not lead to kidney failure.

## Management of CKD in the elderly

- Institute measures to prevent CKD in any patient aged 65 years and above (refer to module 5)
- Screen and diagnose CKD as in the general population (refer to module 4)
- Serum creatinine is less reliable as an indicator of kidney function in the elderly and should be interpreted with caution when used.<sup>5</sup>
- Identify other risk factors of CKD such as hypertension, diabetes, NSAIDs abuse and malignancies and manage appropriately.
- Common geriatric issues such as frailty, quality of life, life expectancy, end of life issues, must be addressed in the management of CKD in the elderly.<sup>4</sup>
- Look out for acute kidney injury (sudden increase in serum creatinine) and refer to a facility with a doctor or a nephrologist.
- Institute general measures to slow down CKD progression (Refer to Module 5)
- Identify and manage complications (Refer to Module 5)
- Elderly with CKD 3-5 or rapid decline in eGFR should be referred to a facility with a doctor.



Characteristics of CKD compared to normal aging kidneys<sup>4,5</sup>

Characteristics	CKD	Ageing kidney	Comment
<b>GFR</b>	< 60 ml/min/1.73m <sup>2</sup>	< 60 ml/min/1.73m <sup>2</sup>	
<b>albuminuria</b>	Present	Absent	
<b>Urea</b>	Increased	Normal	
<b>Anemia</b>	Present(erythropoietin deficiency)	May be present (usually nutritional)	
<b>Acid base balance</b>	Metabolic acidosis	Normal	
<b>Calcium-Phosphate metabolism</b>	Hypocalcaemia, decreased active vitamin D, increased PTH	Possible hypocalcaemia, normal active vitamin D normal PTH	Normal kidney aging will not be associated with CKD complications

**Table 22: CKD versus normal kidney aging**

#### Approach to shared decision-making in the elderly with advanced chronic kidney disease<sup>5</sup>:

- **Explore goals of care in chronic kidney disease**
  - Identify substitute decision-maker or power of attorney
  - Explore goals, wishes, values of the patient in the management
  - Explore limitations in the management of patient and discuss with family
  - Explore cultural/spiritual context of the patient in decision making
- **Disclose prognostic information to patients who may have limited benefit from dialysis (e,g decreased quality of life or limited survival benefit).**

Incorporate patient goals and values to outline a treatment plan. Options to consider include:

- Kidney transplant
- In-centre hemodialysis
- Home options such as home hemodialysis and peritoneal dialysis
- Conservative kidney management

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