Guidelines for the Detection and Management of Chronic Kidney Disease (CKD)

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PREFACE

Chronic Kidney Disease (CKD) has become a global epidemic with attendant high morbidity and mortality which is particularly worse in developing countries including Nigeria. Data on the magnitude and burden are often times unavailable while those available are very limited in scope hence have limited interpretation and applicability or generalizability.

Majority of CKD patients present late and are unable to sustain renal replacement therapy for mainly economic reasons. Early detection of cases would allow institution of measures to retard CKD progression as well as reduce cardiovascular, haematologic, metabolic and social complications.

The introductory pages of this document espoused the magnitude and epidemiology of CKD in Nigeria while its detection and management are subdivided into five sections. Section I highlighted the definition and detection of CKD while Section II discussed the management of CKD under different sub headings. Sections III, IV and V focused on guidelines for haemodialysis, peritoneal dialysis and kidney transplantation respectively.

It is hoped that this document would improve awareness of CKD by all practicing medical doctors and not only internal medicine specialists (physicians). It would allow early detection and management of affected individuals and further standardize the

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practice of nephrology. It would also highlight areas needing further research that may encourage development of new proposals particularly from nephrologists or nephrology trainees.

These CKD detection and management guidelines would benefit practicing doctors in all specialties, specialist physicians and physicians in training.

Guidelines development process

A Committee of Nephrologists was selected during the Annual General Meeting in Zaria, February, 2010. Communications were mainly electronic, after the initial discussions, members were assigned topics to discuss available data or practice in Nigeria and compare with global best practices.

The committee had a retreat from 19th – 21st May, 2010 during which major areas to be covered were highlighted. Areas covered included definition and detection of CKD, conservative management of CKD, Haemodialysis, Peritoneal Dialysis and Kidney Transplantation.

Members presented available data on different topics and this was followed by group discussions that further highlighted deficiencies that needed to be covered. A sketch of important subsections under the different topics was drawn up.

A second meeting was held between 29th and 31st October, 2010, during which the draft guidelines were designed. Subsequent revisions were done electronically.

The first draft practice guidelines were sent to leading Nephrologists in Nigeria and abroad for their appraisal, criticisms and suggestions.

A final version was thereafter produced with the proviso that it should be revised every 5 years when it is hoped that some research areas/questions highlighted would have been answered.

INTRODUCTION

The global burden of Chronic Kidney Disease (CKD) is enormous. The World Health Report 2002 and Global Burden of Disease project reports show that diseases of the kidney and urinary tract caused one million deaths in 2002, ranking twelfth in the list of world's major causes of death [1,2]. The global incidence and prevalence of CKD have increased exponentially in the last decade and now assume epidemic proportions in both developed and developing countries [3].

In Nigeria, like in many other developing countries, accurate data on the prevalence of CKD is lacking principally due to unavailability of a national renal registry. Small scale community studies in Nigeria found that the prevalence of CKD in adults ranges between 19% and 30% while in paediatric population it was estimated to be 15 per million population [4,5,6]. Hospital prevalence studies reported that End Stage Renal Disease (Advanced CKD) represents 6-12% of medical admissions [7,8,9]. A major peculiarity in the epidemiology of CKD in Nigeria is the fact that it affects young individuals aged between 25-40 years, which are the most economically productive years [5,8].

It is established that CKD is largely unrecognized and inadequately diagnosed. Patients with end stage renal disease (ESRD) are thought to represent the tip of the iceberg of the entire burden of CKD.

Apart from the direct implications of CKD on renal function, it is a major risk factor for the development of accelerated atherosclerosis, ischaemic vascular disease, and cardiovascular death. Individuals with even the earliest signs of CKD are at increased risk of cardiovascular disease and may die long before they reach end-stage renal disease[10].

The burden of CKD is therefore not limited to its impact on demand for Renal Replacement Therapy (RRT); it is paralleled by the high cost of healthcare services for these patients, which is unsustainable by governments even in developed countries [11]. This cost includes direct costs such as dialysis and transplant cost as well as indirect costs such as lost man hours from work.

The rising prevalence of CKD can be stemmed and the progression retarded. Preventive measures, early detection and proper management are imperative in achieving regression of CKD (incidence & prevalence) and retardation of its progression to ESRD.

Rationale for management guidelines:

- To improve the awareness and diagnosis of CKD and institute preventive measures, early detection and management among healthcare workers

- To standardize management and decision making in the approach to CKD at various levels of healthcare expertise.
- To adapt the global best practices to management of CKD to patients in Nigeria considering our peculiarities.
- To highlight areas for further research in the epidemiology and management of CKD and its complications in Nigeria.

Research areas identified

1. Well designed community studies that would be sufficiently powered to represent National figures.
2. Studies to define Rural / Urban differences in the incidence and prevalence of CKD
3. Studies to define aetiology of CKD in Nigeria

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EPIDEMIOLOGY OF CHRONIC KIDNEY DISEASE IN NIGERIA

CKD in Nigeria principally affects young individuals in their economically productive years thereby constituting a drain on the economy. Peak age range involved varies between 25 and 45 years [1,2]. The principal causes of CKD in adult Nigerians include Chronic Glomerulonephritis, Hypertension (Essential or malignant), Diabetes Mellitus, Obstructive uropathies and Tubulointerstitial Nephritis [3,4,5]. Other documented but rare causes include Cystic Renal Diseases, Pre-eclampsia / Eclampsia, Chronic Pyelonephritis, Connective Tissue Disease and Analgesic Nephropathy [3,4,5].

In paediatric populations however, acquired disorders were the major causes of CKD. Glomerulopathies (Chronic glomerulonephritis and Nephrotic syndrome) were the commonest causes while congenital disorders, of which only posterior urethral valve was second. No child with hereditary renal disorders as a cause of CRF was identified in a report [6].

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SECTION I

Chronic Kidney Disease (CKD)

Definition

Glomerular filtration rate (GFR) less than 60ml/min or presence of markers of kidney disease for 3 months or more [1].

The GFR should be determined from serum creatinine using Cockcroft-Gault or MDRD equations for adults and Schwartz equation in children [2,3,4].

Formulae for calculating the GFR

Cockcroft-Gault Equation [2]- which has been validated in Nigerians [5].

If using µmol/l as a measure of serum creatinine, use the following formula:

$$GFR = \frac{1.23 \times (140 - Age) \times weight\ (kg)}{serum\ creatinine\ (\mu mol/l)} \quad (\times 0.85 \text{ if female})$$

If using mg/dl for serum creatinine, use the following formula:

$$GFR = \frac{(140 - age) \times weight\ in\ kg}{72 \times serum\ creatinine\ (mg/dl)} \quad (\times 0.85 \text{ if female})$$

To convert µmol/l to mg/dl, multiply by 0.0113
To convert mg/dl to µmol/l, multiply by 88.4

MDRD Formula [3]

The MDRD formula was derived from the Modification of Diet in Renal Disease Trial and has been validated in Nigerians [6,7]

$$GFR = 186.3 \times Serum\ Cr\ (\mu mol/L)^{[-1.154]} * age^{[0.203]} * 1.212 \text{ (if patient is black)} * 0.742 \text{ (if female)}$$

Original Schwartz Equation [4]
GFR (mL/min/1.73 m^2) = k (Height) / Serum creatinine

1. k = Constant
   (i.) k = 0.33 in preemie infants
   (ii.) k = 0.45 in term infants to 1 year of age 3. k = 0.55 in children to 13 years of age 4. k = 0.70 in adolescent males (not females because of the presumed increase in male muscle mass, the constant remains .55 for females)
2. Height in cm
3. Serum creatinine in mg/dL

Markers of kidney disease include:
- Persistent proteinuria
- Dipstick positive proteinuria
- Haematuria - by dipstick and/or urine microscopy
- Abnormal renal imaging - by various techniques such as ultrasonography, Computerised Tomography Scan, intravenous urography or plain radiograph, renal scintigraphy.

Screening for CKD
General Population
Who to screen?
- All adults, on first contact with a Medical Practitioner .
- In children, at birth for those at high risk of CKD (Low birth weight babies, asphyxiated, HIV infection, antenatal diagnosis of congenital anomalies) and at first contact after the age of 3 years.

What to Screen for first contact
- Blood pressure
- Urinalysis
- Serum creatinine and calculate eGFR
- Blood sugar

What to Screen for - Annually
- Blood pressure
- Urinalysis
- Serum creatinine and eGFR for > 25 years (Local data suggest higher prevalence of CKD at earlier age [8,9,10]
- Blood sugar for > 40 years

What to Screen for at 2-5 year intervals for those less than 25 years
- Blood sugar
- Serum creatinine and eGFR
- Children:

Stages of CKD
Table 1: Definition of the five stages of Chronic Kidney Disease

Stage	Description	GFR (ml/min/1.73m^2)	Action
1	At increased risk- Kidney damage with normal or increased GFR	= 90 (with CKD risk factors) = 90	Screening, CKD risk reductionDiagnosis and treatment, treatment of co-morbid conditions, slowing progression, CVD risk reduction.
2	Kidney damage with mild decrease in GFR	60 - 89	Estimating progression
3	Moderate decrease in GFR	30 - 59	Evaluating and treating complications
4	Severe decrease in GFR	15 - 29	Preparation for kidney replacement therapy
5	Kidney failure	<15 (or dialysis)	Replacement (if uraemia present)

(Adapted from the US National Kidney Foundation [1])

High Risk Group

These include the elderly (>60 years) and people with hypertension, diabetes, family history of kidney disease, HIV infection, sickle cell anaemia, obesity and those who regularly use herbal medicines, analgesics and bleaching creams.

- To be screened on first contact with physician and thereafter every six months.
- For diabetics, screen for microalbuminuria at least annually.

What to do when CKD is detected:

0 Stage the disease

0 Take appropriate measures depending on the stage:

(1) *Stage 1 – 2* : where the cause of CKD is known, treat underlying cause and institute measures to retard progression

(2) *Stage 1-2* : where cause is unknown, refer to Nephrologist.

(3) *Stage 3-5*: refer to Nephrologist.

(4) Special conditions irrespective of stage such as – Nephrotic range proteinuria (3+ and above, 24 hour urine protein > 3.5g/ 1.73m^2 BSA/ Day); polycystic kidney disease, ectopic kidneys, children, pregnancy, bone disease and anaemia (Hb <11g/ dl); haematuria where a urological or other cause is not evident – refer to Nephrologist.

Research areas identified:

1. Well designed community studies to define the epidemiology (prevalence, pattern and aetiology) of CKD in Nigeria that would be sufficiently powered to represent National figures.

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SECTION II
MANAGEMENT OF CKD

(A) Patient Counselling and Psychosocial Issues

- Educate patient about the aetiology and natural history of the disease
- Intervention strategies to prevent progression as in (B) below
- Preparation for eventual RRT

(B) Conservative Management of CKD

- Identify and treat underlying cause and intercurrent illness
- Weight management in all patients
- Optimize nutrition in undernourished patients to achieve ideal BMI
- Cessation of smoking
- Avoidance of nephrotoxic agents such as NSAIDs, COXIBs, aminoglycosides, radiocontrast agents and herbal preparations.
- Adjust doses of all medications as appropriate for patients' GFR.
- Dynamic exercise such as brisk walking / treadmill, jogging, swimming, cycling for 30 – 45 minutes at least 3 times a week.
- Low salt diet (2 grams daily)
- Low protein diet (0.6-0.8 g/Kg body weight per day)
- Control of hypertension.
- Control of blood sugar in diabetics.
- Lipid control.

(C) Identification an treatment of primary disease and underlying cause of ckd

The recognition, identification and treatment of the primary or underlying cause of CKD is of paramount importance in its management.

Glomerulonephritides

Minimal Change GN: In adults with Minimal Change GN commence prednisolone 1mg/kg/day up to maximum of 80mg/day for 1 week then taper to half for 8 weeks and if there's remission taper to stop within 4-6 weeks. If there is relapse repeat full dose for 5 days then reduce to half for 1 week and thereafter taper to stop in 4 weeks. If there are 2-3 relapses in 6-9 months then commence second line drugs. Either cyclophosphamide 2mg/kg for 12 weeks or cyclosporine 150mg/m^2 or 3-6mg/kg/day and titrate to achieve target trough plasma level of 50-125ng/ml for 12 months, thereafter taper over 3-6 months. If multiple relapses then commence third line drugs either MMF or anti CD 20 monoclonal antibody - Rituzimab [1, 2].

For children with Minimal change GN steroids are the initial treatment of choice prednisolone 60mg/m^2/day up to maximum of 80mg/day given in 3 divided doses for 2-4 weeks thereafter reduced to 40mg/m^2/day for 4-6 weeks. Non responders or relapsers should be commenced on cyclophosphamide or cyclosporine [3,4].

Membranous GN: If there is mild or non-nephrotic proteinuria, ACEIs and ARBs should be used and patient monitored. If there is nephrotic range proteinuria then use of steroids in combination with cyclophosphamide or cyclosporine. If there's worsening proteinuria and reduced renal function then use calcineurin inhibitor (cyclosporine) or cyclophosphamide and steroids [5, 6]. Rituximab and ACTH could be used if both fails [7]. However steroids alone are not recommended [8].

Focal Segmental Glomerulosclerosis (FSGS): If there is mild non-nephrotic proteinuria, ACEIs and ARBs should be used and patient monitored. If there is nephrotic range proteinuria or worsening proteinuria and reduced renal function commence steroids (prednisolone 1-2mg /kg/day for 6-8 weeks with subsequent tapering but maintained for 6 months. If patient becomes steroid resistant, then commence cyclosporine (3-6mg/kg/day for 4-6months) or cyclophosphamide (2mg/kg/day for 2-4 months) or Mycophenolate mofetil 1-1.5g twice daily for 2-4 months [9,10].

Immunoglobin A Nephropathy (IgA Nephropathy): Though IgA Nephropathy is rare in renal histological biopsy reports from Nigeria, the occasional patients must be managed according to internationally recognised guidelines [11]. Patients with hypertension or non nephrotic proteinuria should be placed on ACEIs or ARBs. Children with nephrotic range proteinuria should be commenced on steroids (0.5-1mg/kg/day up to maximum of 60mg/m^2/day) for 8 weeks and then taper. Those with

crescentic transformation should be commenced on same doses of steroids in combination with cyclophosphamide (2mg/kg/day) for 8 weeks during the induction phase and tapered steroid dose with Azathioprine 2.5mg/kg/day during maintenance phase [11].

Secondary Glomerulonephritis: In secondary glomerulonephropathies, the secondary cause (s) must be treated along with general conservative treatment modalities.

Hypertensive Nephrosclerosis: In hypertension, strict blood pressure control would also assist in retarding progression of nephropathy. Recommended drugs as well as targets for control are outlined in section 2, subsection D.

Diabetic Nephropathy: Once a patient manifests early (incipient) diabetic nephropathy either complicating type I or II DM, intensive glycaemic control using insulin therapy has been shown to retard progression hence this should be encouraged[12,13].

Research areas identified:

1 Defining the histopathology of primary glomerulonephritis in Nigerians.

2 Defining diagnostic criteria for hypertensive nephrosclerosis in Nigeria.

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(D) MANAGEMENT OF HYPERTENSION IN CKD

Hypertension is in itself a cause and a complication of CKD [1]. It is also a cardiovascular disease risk factor which is the single most important cause of death in CKD. Meticulous control of blood pressure to target is perhaps the most important single measure in retarding the progression of CKD [2].

Blood Pressure Targets [3]

Proteinuria < 1g/24hrs 130/80mmHg
Proteinuria >1g/24hrs 120/75mmHg
CKD with diabetes 120/75mmHg
In children ..... Less than 90th percentile for the age, sex and height.

**Paramount factor is the control of blood pressure irrespective of agent used. Most patients would require a diuretic for blood pressure control and correction of fluid overload. However, thiazides are ineffective at low levels of GFR (<25mls/min) and in this situation, loop diuretics are preferred [4]. The use of ACE inhibitors, ARBs or renin inhibitors in diabetics and those with proteinuria is recommended and dihydropyridine Ca antagonists should be avoided in proteinuric states[5]. Ultimately, most patients will require more than one agent to achieve control [3,5].*

Research areas identified:

1. Management of hypertension in CKD patients in Nigeria.
2. Essential hypertension and CKD – hypertensive nephrosclerosis phenotyping.
3. Control of hypertension and proteinuria in glomerulonephritides
4. Genetics of hypertensive CKD

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(E) ANAEMIA AND ITS MANAGEMENT IN CKD

Anaemia is the commonest hematological complication of CKD and worsens with deterioration of renal function [1,2]. In spite of this, it is inadequately recognised and managed.

All CKD patients should be screened for anaemia at time of diagnosis and thereafter, at least every 3 months.

Characteristics of anaemia of CKD

(1) Most patients have normocytic, normochromic anemia
(2) Some patients could have microcytic, hypochromic anemia

Investigations

- FBC with red cell indices
- Reticulocyte count
- Blood film appearance
- Iron studies - Serum iron, ferritin, TIBC and transferrin saturation.

- Hb electrophoresis
- Fecal occult blood
- Serum Vitamin B12 and Folic Acid

Targets for anaemia treatment [3]

(1) Predialysis: Hb - 11 – 12g/dl, serum ferritin 100-500ng/ml, TSAT≥ 20%

(2) Dialysis: Hb - 11 – 12g/dl, serum ferritin 200 – 500ng/ml, TSAT ≥ 20%

(3) In all patients, avoid Hb level > 13g/dl because of risk of haemoconcentration and its effect on morbidity and increased cardiovascular mortality [4].

Treatment of anaemia

(1) Identify and treat non renal causes of anaemia such as bleeding, nutritional deficiencies, hypothyroidism, iron deficiency and haemolysis.

(2a) In predialysis patients and patients receiving peritoneal dialysis or home haemodialysis, optimize iron balance before Epoetin therapy using oral iron. If poor response (TSAT is < 20% and serum ferritin < 100ng/ml for 4 weeks), switch to parenteral iron.

Dose of oral iron: Ferrous sulphate 200mg or Ferrous gluconate 600mg three times daily (approx. 65mg elemental iron) or 2-6 mg /kg /day of elemental iron for paediatric patients

Dose of parenteral iron: Iron sucrose intravenously 200mg weekly for 5 weeks (total of 1000mg) or Iron dextran intravenously 250mg weekly for 4 weeks. For patients in whom adherence may be difficult, total dose infusion should be considered as its been found to be effective and safe [5,6].

(2b) For patients on in-center haemodialysis, start with parenteral iron at 100mg in the last 30-60 minutes of the dialysis session to a total of 1000mg.In cases of poor or inadequate dialysis , higher doses may be given to ensure achieving 1000mg within 4 weeks.

- *Test dose of iron dextran should be administered before the full dose.*
- *For patients that have received blood transfusions, check iron stores (serum ferritin) before giving supplemental iron because of risk of iron overload.*

(3) Erythropoiesis Stimulating Agents (ESAs) [7]
These should be administered preferably after iron deficiency has been corrected and BP controlled.

Choice of ESAs:

For predialysis patients, patients receiving peritoneal dialysis or home haemodialysis and transplant patients, intermediate and long acting ESAs are preferred for practical reasons.

For patients receiving in- centre haemodialysis, the short acting ESAs are preferred.

In situations where the cold chain cannot be guaranteed, the more heat stable ESAs are preferred.

Owing to the frequent reports of pure red cell aplasia (PRCA) associated with the use of epoetin alpha when administered s.c, the i.v route is recommended for the administration [6].

(3a) For predialysis patients and patients receiving peritoneal dialysis, the ESAs may be administered subcutaneously for patient convenience, need to preserve veins and also because lower doses may be required. For doses and frequency of administration, see table 3a.

(3b) For patients receiving haemodialysis, the ESAs could be given either intravenously or subcutaneously at the end of the dialysis session. For doses and frequency of administration, see table 3b.

(3c) For transplant patients, ESAs should be given when indicated in the same doses and routes as in predialysis patients.

Table 3a: Types of ESAs and their characteristics [7]

ESA	Class	Half - Life	Storage Conditions	Risk of PRCA
Erythropoietin alpha	Short acting	6.8 hours	2-8°C strictly	Several cases reported when administered subcutaneously
beta	Short acting	8.8 hours	2-8°C normally, but can be kept at 25°C for 3-5 days	minimal
Darbepoietin alpha	Intermediate acting	48 hours	2-8°C strictly	minimal
Continuous Erythropoiesis Receptor Activator (CERA)	Long acting	134 hours	2-8°C normally, but can be kept at 25°C for up to 28 days.	None

- *Short acting ESAs – Epoetin alfa and Epoetin beta.*
- *Intermediate acting ESAs – Darbepoetin alfa-*
- *Long acting ESAs – CERA*

Table 3b: Doses, routes and frequency of administration of ESAs [3,7]

Product	Route of Administration	Correction Dose	Maintenance Dose
Erythropoietin alpha i.v s.c (not recommended for haemodialysis patients)	50 – 100i.u/kg/ week, in 2-3 divided doses.	Increase dose monthly by 25%. up to a maximum 300 iu/kg/week or 20,000 iu/ week if Hb increase is less than 1g/mont.	Reduce correction dose by 25 % if Hb level approaches 12g/dl Reduce dose by 25 % if Hb increase is more than 2g/ month.
Erythropoietin beta i.vs.c	Subcutaneous administration Initially 3 x 20 IU/kg body weight/week.	Dosage may be increased every 4 weeks by 3 x 20 IU/kg /week if the increase in PCV is<0.5%/ week. Intravenous administration: Initially 3 x 40IU/kg/week. Dosage may be increased after 4 weeks to 3x80 IU/kg/ week and if further increments are needed by 3 x 20 IU/kg/ week at monthly intervals.	For both routes of administration the maximum dose should not exceed 720 IU/kg/week. Reduce dose by 25 % if Hb increase is more than 2g/month. Reduce correction dose by 50% of last correction dose when Hb approaches 12g/dl
Darbepoietinalpha i.v/s.c	0.45mcg/kg once weekly	Adjust to 25% of last correction dose once weekly if Hbapproaches 12g/dl.	It may also be administered once every two weeks using dose equal to twice the previous once weekly dose.
CERA i.v/s.c	0.6mcg/kg once every two weeks	Adjust to 25% of last correction dose and administeronce every	It may be administered once every month using dose equal to twice the previous two-weekly dose. two weeks if Hb approaches 12g/dl.

In case of poor response to ESAs, assess the following:

- Iron deficiency due to nutritional deficiency, GI blood loss etc
- Infections/inflammation
- Haemoglobinopathies
- B12 or folate deficiency
- Inadequate dialysis
- Inadequate dosing
- Poor ESA adherence
- Haemolysis
- Severe uncontrolled hyperparathyroidism
- PRCA
- Occult malignancies
- ACEI or ARB therapy.
- Poor storage (poor maintenance of cold chain)

Treatment monitoring

- During correction phase, blood pressure should be monitored closely.
- Hb levels should be monitored every 2-4 weeks during the correction phase and monthly during the maintenance phase.
- Patients with intercurrent diseases that might influence the Hb concentration will require more frequent monitoring

Androgen Therapy [8]

Androgen therapy may be used in patients aged over 50 years who cannot afford ESA.. Intramuscular nandrolone decanoate 200mg once weekly may alleviate symptoms of anaemia and has associated beneficial effects on nutritional status. Recognized side effects include virilisation, hepatic adenoma, hirsutism and acne in women.

Blood Transfusion

Blood transfusion should be considered in the following situations:

(1) In symptomatic anemia such as heart failure, coronary artery disease.

(2) HD patients with Hb < 7g/dl, if immediate treatment with ESAs is not possible.

(3) Acute worsening anemia due to blood loss.

(4) Severe resistance to ESA therapy.

Research areas identified:

1 Optimal haemoglobin target that would provide good quality of life at lower cost.

2 Optimal doses of ESAs in Nigerians with CKD.

3 Role of parenteral iron and other adjuvants in the management of renal anaemia.

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F. MANAGEMENT OF CKD MINERAL AND BONE DISORDER

Chronic kidney disease (CKD) is inevitably associated with alterations of bone and mineral metabolism as residual kidney function declines [1]. These alterations have been found to be associated with cardiovascular diseases as well as increase in morbidity and mortality in CKD patients[2].

Definition

A systemic disorder of bone and mineral metabolism due to CKD manifested by either one or a combination of the following [3]:

- Abnormalities of calcium, phosphorus, parathyroid hormone (PTH), or vitamin D metabolism
- Abnormalities in bone turnover, mineralization, volume, linear growth, or strength (renalosteodystrophy).
- Vascular or other soft tissue calcification

Diagnosis and follow-up

Diagnosis of CKD-MBD should be done by assessing serum levels of calcium, phosphorus, PTH, and alkaline phosphatase beginning in CKD stage 3. Serum levels of calcium, phosphorus, alkaline phosphatase and serum PTH should be monitored every 3 months while serum PTH should be monitored every 6 months.

In CKD patients with persistent bone pain, unexplained fractures, unexplained hypercalcemia, unexplained hypophosphatemia, bone biopsy may be required to diagnose bone disorders.

Presence of vascular calcification should be ruled out by a lateral abdominal radiograph or other appropriate methods, echocardiogram should be used to detect the presence or absence of valvular calcification.

Goals of treatment

Serum phosphorus should be maintained in the normal range for the laboratory. Serum calcium (adjusted for albumin concentration) should be maintained within the normal reference range for the laboratory [4].

Individual values of serum calcium and phosphorus should be used to guide patients' management rather than the calcium–phosphorus product (Ca X P) [4]. Target value for serum PTH levels is 2-9 times upper reference limit for the assay [4].

Management

Dietary phosphate intake should be limited in patients with hyperphosphatemia. The use of phosphate-binding agents are required in the treatment of hyperphosphatemia.

For choice of phosphate binder, it is reasonable to take into account serum calcium, CKD stage, presence of other components of CKD-MBD, concomitant therapies and side-effect profile of the drug. The dose of calcium- based phosphate binders should be restricted in the presence of arterial calcification and/or adynamic bone disease. In such instances the use of non-calcium based phosphate binders (eg Sevelamer HCl, lanthanum carbonate etc) could be used.

Hypocalcaemia, is treated with calcium salts and active vitamin D analogues. Calcium intake should however, be restricted in patients with hypercalcemia, soft tissue calcification, low PTH and in patients with adynamic bone disease.

The dose of calcitriol or vitamin D analogue should be restricted in the presence of persistent or recurrent hypercalcemia [3].

Calcitriol or vitamin D analogs, or calcimimetics, or a combination of calcimimetics and calcitriol or vitamin D analogs may be used to lower PTH to two to nine times the upper normal limit for the assay in treated patients. Parathyroidectomy is indicated when medical therapy fails.

In children, screening for CKD-MBD should start in CKD stage 2. Treatment is recommended with Human growth hormone when additional growth is required after first addressing malnutrition and biochemical abnormalities of CKD-MBD [3].

Research areas identified:

1. A multicentre study on pattern of CKD-MBD, parathyroid function in CKD and bone histomorphometry.
2. Analysis of various phosphate lowering drugs in Nigerians
3. Dietary modification in CKD aimed at lowering hyperphosphataemia
4. Assessment of phosphate content of our common meals.

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G . CKD AND DYSLIPIDAEMIA

Chronic Kidney Disease causes profound dysregulation of lipoprotein metabolism, resulting in major pro-atherogenic lipid abnormalities. Although lipid profile in CKD patients is complex, the most common abnormalities are hypertrigliceridaemia and low HDL-C (high density lipoprotein-C) [1,2].

Dyslipidaemia in CKD patients should be investigated and treated in view of the fact that cardiovascular disease is extremely common in this population.

Diagnosis

Diagnosis of dyslipidaemia should be made by obtaining a fasting lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides)

It is recommended that evaluation of dyslipidaemia should be made at presentation, or after a change in CKD/nutritional status, or at least annually.

Assessment for secondary causes of dyslipidaemia such as medications and co-morbid illnesses should be carefully undertaken and treated appropriately.

Management

Most of the lipid lowering drugs have excellent safety and efficacy profiles. In addition, available evidence suggests that statin therapy may reduce inflammation and slow the decline in glomerular filtration rate in patients during the earlier stages of CKD [3].

In patients with high total cholesterol who are unresponsive to dietary therapy and LDL-C > 100mg/dl, statin therapy should be initiated. Drug dosage should be titrated as required, depending on the severity of dyslipidaemia.

Pre-dialysis patients with fasting triglycerides $\geq$ 500 mg/dl at any stage of CKD should be treated with recommendation of lifestyle changes and adding gemfibrozil or niacin. Drug dosage should be titrated as required [3,4,5].

Medication safety and adverse effects

Serial monitoring of creatine kinase and alanine aminotransferase should be done in patients treated with moderate to high doses of statins every 3 months.

Co-administration of statins and fibrates should be avoided in patients with CKD due to the risk of rhabdomyolysis [6].

Gemfibrozil is safe to use in patients with CKD. Other fibrate preparations however, should be avoided or the dose significantly reduced in view of an increased risk of toxicity.

In post pubertal paediatric patients adult recommendations as above can be followed. In younger children NCEP-C (ATP III) guidelines should be adopted [3].

Research areas identified:

1. Long term study of the implications of dyslipidaemia and hyperlipidaemia in Nigerians (Adults and paediatric patients).
2. Assessment of common cardiovascular risk factors.
3. Dietary management of hyperlipidaemia in low resource settings.

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H. NUTRITION

Malnutrition is very common in patients with CKD. It occurs in more than 50% of CKD patients starting dialysis [1]. Malnutrition is often associated with chronic inflammation and it is a predictor of mortality in CKD patients on dialysis[2,3,4,5]. Dietary modification is considered one of the cornerstones in the treatment of CKD. The overall aim is to prevent malnutrition, alleviate uraemic symptoms and metabolic derangements such as hyperkalaemia and hyperphosphataemia.

Pre-dialysis CKD patients should be screened for malnutrition at presentation or after a change in CKD status and at least every 3-4 months throughout the follow-up period [6,7]. All patients with CKD stage 3-5 should be referred to a dietician (experienced in the management of nutrition in CKD patients) for assessment and dietary management.

Diagnosis

It is recommended that a panel of tests be utilized in the assessment of nutritional status of patients with CKD rather than relying on a single evaluation [2,6,7].

Clinically relevant assessment of nutritional status should be obtained through

1. Dietary interviews and/or diaries
2. Anthropometric measurements
   a. Actual body weight (dry weight)
   b. Percent standard body weight
   c. Body Mass Index (BMI)
   d. Skin fold thickness
   e. Estimated percent body fat
   f. Mid-arm muscle area, circumference, or diameter.
3. Subjective Global Nutritional Assessment (SGA)

Laboratory assessment should include:

1. Serum Albumin: Patients with serum albumin levels lower than 3.0g/dl should be evaluated for malnutrition.
2. Serum Cholesterol: Patients with total LDL-cholesterol levels less than 30mg/dl should be evaluated for malnutrition.

Serum Albumin level is influenced by a variety of factors (e.g inflammation) apart from nutrition. Therefore, screening for co-morbid illnesses should be done in CKD patients with low albumin level. Low or declining serum cholesterol concentrations are predictive of increased mortality risk in CKD patients.

Goals of treatment

Dietary treatment in CKD patient should aim at achieving desirable weight and adequate nutritional status.

In addition, it should include dietary management of co-morbidities such as good glycaemic control in diabetics, fluid and sodium control in hypertensives and oedematous patients, lipid control in patients with dyslipidaemia, phosphate control in hyperparathyroidism, and weight management in obese patients.

Recommended dietary intake

Energy

Ideal energy intake should be determined based on age, gender, BMI and level of physical activity of the patient. Recommended caloric intake is 30-40 kcal/ Kg ideal body weight (IBW)/day [2,6,7,8,9].

Protein

Moderate protein restriction should be commenced in patients in stage 4 CKD. Protein intake should however not be less than 0.8 g/kg IBW/day. At least 50% should be of high biological value

Fat / Carbohydrate.

Aim of dietary treatment is to prevent protein-energy malnutrition. Fat content of diet should be reduced to less than 30% of daily energy intake, with saturated fat limited to less than 10% of energy requirements. Carbohydrate should be utilized to make up the balance of required energy intake.

Sodium

Sodium intake should be less than 100 mmol / day (<6g of NaCl/day) if the patient is hypertensive or oedematous.

Potassium

Potassium intake should be reduced (50-70 mmol/ day) in hyperkalaemic subjects or patients on medications that may predispose to increased serum potassium levels.

Phosphate

Phosphate intake restricted to 800-1000 mg/day and/ or use of phosphate binders is recommended if serum phosphate is high (>1.49mmol/l).

Vitamins

Vitamin supplements are recommended in accordance with the recommended daily allowances. However caution should be exercised in the use of Vitamin C supplements in view of the risk of Oxalosis.

Fluid

Fluid intake needs to be adjusted in oedematous patients. Dehydrated patients should be hydrated appropriately in accordance with the estimated degree of dehydration. Fluid intake in anuric patients should be restricted to insensible losses.

Nutrition in children

Dietary management is of paramount importance in children with CKD. The challenge for the paediatrician is to optimize the growth and development of these children and make the diet interesting and palatable in order to ensure compliance. Recommended allowance for protein is 1.1-1.2 g/kg IBW/day.

Research areas identified

1. Prevalence and pattern of malnutrition in Nigerian CKD adult and paediatric patients
2. Caloric value of major food products in Nigeria.
3. Dietary management of CKD in low resource settings.

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I. PREPARATION FOR RENAL REPLACE MENT THERAPY

It is important to ensure a smooth transition to RRT in CKD patients requiring renal replacement therapy [1,2].

Counselling and patient education

Patients in stage 4 CKD or stage 5 CKD not on renal replacement therapy (RRT) and their families should be counselled on all available Renal Replacement Therapies.

An informed decision on the best RRT modality for the patient should be made based on availability, affordability by patient or his/her financial support plan, and other relevant issues.

A multidisciplinary, multifaceted, educational approach tailored to the needs of the patient, should be employed to inform him/her of the management of his/her renal condition. This includes individual conversations, interactive group discussion and counseling, written educational materials, videos and DVD/CDs [1,2].

Dialysis access

Timely placement of vascular access or PD catheter should be done in patients with CKD stage 4 in whom a firm decision on dialysis therapy as the most appropriate RRT has been made [1,2,3]. Appropriate counselling and training of patient on access care should also be undertaken.

Insertion of catheters in peripheral veins in the non dominant arm should be avoided as much as possible once GFR < 30ml/min.

J. END OF LIFE CARE

Care in the last days of life is essential in patients who continue to deteriorate on dialysis, or are moribund in view of coexisting co-morbidities, or cannot afford dialysis for financial and other reasons. This should be undertaken with utmost care and empathy for the patient and his/her family [1,2,3,4]. Therapy should aim at achieving good symptomatic relief. In addition, psychological, spiritual and culturally sensitive care for the dying patient and their family should be provided by the managing unit [3,4].

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SECTION III

HAEMODIALYSIS THERAPY

Haemodialysis (HD) is the most common form of renal replacement therapy (RRT) worldwide, 90% of patients starting dialysis start on HD. In Nigeria, most dialysis centres are located in the major cities therefore HD therapy is not readily accessible to those in the rural communities [1].

Choice of dialysis modality

Haemodialysis
Peritoneal dialysis

Choosing an initial mode of renal replacement therapy (RRT)

Choice of treatment is influenced by a range of factors which include financial, medical, psychosocial and availability of RRT modality.

Haemodialysis

When to start haemodialysis (HD)

No universal agreement on optimal time for starting dialysis. Dialysis should be instituted whenever GFR is < 10mls/min^2. However dialysis should be commenced in patients with higher GFR if there is one or more of the symptoms or signs of uraemia, inability to control BP or fluid overload or a progressive deterioration in nutritional status.

Quality assurance

Personnel

It is very important that the quality of dialysis treatment delivered be closely monitored by a regulatory body given the proliferation of dialysis units in the country. To this end, all dialysis units must be run by qualified personnel who comprise of:

a. qualified Nephrologist.
b. Nephrology/dialysis nurses
c. Dialysis technicians
d. Counsellors and social workers
e. Renal dieticians

Water treatment

Water for HD must be treated and must meet a minimum standard as recommended by the AAMI [3,4]. The feedwater therefore requires to be treated by a combination of methods including the use of particulate filters, activated charcoal, water softeners, de-ionizers, use of reverse osmosis, ultraviolet rays and bacterial. **Culled from AAMI website :** . http://www.aami.org/

Achieving this standard of purity requires that feed water should be processed by the following methods:

- Softening: this process removes most of the calcium and magnesium
- Carbon filtration: removes organics and other impurities such as chloramines and chlorine.
- Reverse osmosis: Removes aluminium, bacteria, endotoxin, etc
- Effective disinfection programme for pipework between the treatment plant and dialysis machines

Clinical evaluation and preparation for HD

Vascular access

Reliable vascular access is the cornerstone of HD therapy and timely planning for vascular access is an essential and important part of pre-dialysis management.

Types of vascular access:

- Arterio-venous fistula (AVF).
- Polytetrafluoroethylene (PTFE) graft
- Tunnelled and cuffed dialysis catheter (permcath)
- Temporary dialysis catheter in internal jugular or femoral catheter for immediate use; ideally should be left in place for≤ 2 weeks (femoral < 5 days) [4].

An arteriovenous fistula (AVF) is the optimal form of vascular access and should be created well before the predicted time that dialysis will start and to give enough time for it to mature. Maturation time 4 – 8 weeks minimum. PTFE graft is the second best. Useful if veins are inadequate to create AVF [5,6].

Viral screening and immunisation

All patients for HD therapy should be screened for HIV, HBsAg and HCV infection

Those who are HBsAg negative should be immunized with hepatitis B vaccine. To maximize efficacy, the dose should be doubled in dialysis patients

(40ìg HBsAg), four doses administered to the deltoid region at intervals 0, 1, 2, 6 months [6]. Measure antibody levels; if still not adequate (if <20iu/) give booster doses. This vaccination programme should ideally be instituted pre-dialysis.

Blood pressure

The recommended target immediate predialysis BP should be 140/90mmHg and 130/80mmHg postdialysis. Management of hypertension in HD patients should include normalisation of extracellular fluid (ECF) and dry weight as well as optimisation of dialysis prescription.

Dry weight evaluation

The dry weight is the post dialysis weight at which all or most excess fluid has been removed or clinically defined as the lowest weight a patient can tolerate without intra-dialytic symptoms and hypotension. There is no gold standard for dry weight assessment. In practice the dry weight is determined on a trial-and –error basis. The dry weight changes periodically and should be re-evaluated monthly.

Anaemia

Guidelines for the management of anaemia in CKD should follow the recommendations on Section 2 subsection C. The requirement in HD patients include a target serum ferritin greater than 200ìg/L (200 – 500ìg/L).

Nutrition

Refer to Section 2 subsection H.

Requirement for nutritional management in HD patients include recommended daily vitamin supplement of

- Vitamin C 100mg daily
- Folic acid 5mg daily
- Vitamin B6, 10mg daily
- Thiamine 1.1 – 1.2mg daily
- Riboflavin 1.1 – 1.3mg daily
- Cobalamin 2.4ìg daily
- Niacin 14 – 16mg daily
- Biotin 30ìg daily
- Pantothenic acid 5mg daily
- Alpha – Tocopherol (vitamin E) a daily supplement of 400 – 800IU is recommended for secondary prevention of cardiovascular events

Protein intake 1.2g/kg ideal body weight per day is recommended for patients on HD.

Normalised protein catabolic rate (nPCR).

nPCR is a measure of urea generation rate which is a reflection of nutritional status. It can only be used in patients who are stable. A nPCR > 1.0g/kg/day is required.

Bone disease

Refer Section 2 subsection F.

Haemodialysis prescription

HD prescription should be individualised to achieve adequate dialysis. Variables in the dialysis prescription should include:

Number of sessions per week: ideally 3 four-hour sessions per week and a total duration of 12 hours. (*Unless there is significant residual renal function)*

An increase in frequency and time should be considered for the following category of patients:

- Patients with haemodynamic instability
- Patients with cardiovascular instability
- Patients with uncontrolled hypertension despite maximum possible fluid removal
- Patients with impaired phosphate control

Blood flow rate: a higher blood flow rate is desirable; 300 to 500ml/min through AVF or graft. A blood flow rate of < 250ml/min is suboptimal.

Dialyzer size and type: The larger the surface area of the dialyzer the greater the delivered dose of dialysis per unit time. High flux dialyzers are able to deliver better middle molecule clearance. Dialyzers with biocompatible membranes are preferred (modified cellulose and synthetic membranes).

- Dialysate: Bicarbonate is the preferred buffer
- Anticoagulation: Heparin is usually used given as a bolus injection followed by a constant hourly infusion or a bolus followed by repeated bolus doses as necessary. The heparin infusion is stopped 1 hour before the end of dialysis.

Low molecular weight heparin can also be used for anticoagulation during dialysis.

- For actively bleeding patients, acute stroke, uraemic pericarditis and Heparin Induced Thrombocytopaenia heparin-free dialysis is recommended.
- Shorter duration of HD session of 2-3 hours, is preferred for the first session to prevent disequilibrium syndrome [9].

Prevention and management of complications during HD

The most common complications during HD are: hypotension, cramps, nausea and vomiting, headache, chest pain, back pain, itching, and fever & chills. Other less common complications are seizures, haemolysis, severe disequilibrium syndrome, first use syndromes, air embolism.

1. Intradialytic hypotension

Intradialytic hypotension (IDH) is the most frequent complication observed during haemodialysis and occurs in 15 – 50% of dialysis sessions[10,11]. The causes are numerous ranging from patient specific factors to treatment specific factors.

Management and prevention of IDH include:

Stratified approach to prevent IDH

- Counsel patient to limit salt intake (Sodium restriction)
- Refrain from food intake during dialysis
- Clinical reassessment of dry weight
- Use of bicarbonate dialysis buffer
- Use of a dialysate temperature of 36.5^{o} C
- Check dosing and timing of antihypertensive agents (**give drugs after dialysis**)
- Perform cardiac evaluation
- Prescribe a dialysate calcium concentration of 1.50mmol/L
- Limit weight gains between sessions, limit to 1kg/day.
- Increase haemoglobin, ensure that haematocrit is > 33%
- Keep dialysate sodium level at or above plasma sodium
- Use HD machines with ultrafiltration controller
- Consider use of á –adrenergic agonists midodrine prior to dialysis
- Blood volume monitoring

Treatment of IDH

- Place patient in the Trendelenburg position (head-down) if respiratory status allows this.
- Ultrafiltration should be stopped or reduced to near zero during an episode of IDH
- 100ml of isotonic saline should be infused via the venous line in patients unresponsive to stopping ultrafiltration and Trendelenburg's position
- Infusion of colloid solutions and inotropes should be considered in patients who remain unresponsive to saline. Use of hypertonic solutions appears to offer no benefit over normal saline.
- Intra nasal oxygen may also be of benefit
- If blood pressure does not respond to above measures, exclude other problems like cardiac causes, GI bleeding and sepsis

Other preventive measures

Slower, longer dialysis hours enable slower fluid removal.

Sodium profiling also minimizes hypotensive episodes

Sequential UF and dialysis helps some patients achieve dry weight without hypotension

2. Muscle cramps

Pathogenesis is unclear. The 3 most important predisposing factors are hypotension, patient below dry weight, use of low sodium dialysis solution. Other causes are carnithine deficiency.

Management

- Prevent intra dialysis hypotension
- Use higher sodium dialysate or sodium profiling
- When hypotension occurs with muscle cramps give normal or hypertonic saline and 50% dextrose.
- Carnithine supplementation and quinine sulphate have been used though recently shown to be of little benefit [12].
- Vitamiin E 400IU nocte has been shown to be as effective as quinine
- Other drugs include oxazepam 5 – 10mg given 2 hrs prior to dialysis
- Massage and stretching exercises

Table 1: Maximum recommended concentration of chemical and microbial contamination in water for dialysis for which routine testing is mandatory [3,4]

Contaminant	Maximum recommended	Standards on which	
Initial test frequency	concentration mg/L	limit is based	3-monthly
Aluminium	0.01	EP, AAMI, ISO	3-monthly
Calcium	2 (0.05mmol/L)	EP, AAMI, ISO	
Not less than monthly			
Total chlorine	0.1	EP	3-monthly
Copper	0.1	AAMI, ISO	3-monthly
Fluoride	0.2	EP, AAMI, ISO	3-monthly
Magnesium	2 (0.08mmo/L)	EP	3-monthly
Nitrate	2 (9mg/L)	AAMI, ISO	3-monthly
Potassium	2 (0.05mmol/L)	EP	3-monthly
Sodium	50 (2.2mmol/L)	EP	3-monthly
Chloramines	0.1mg/L	AAMI	3-monthly
Bacteria (total viable count)	100cfu/mL	EP, ISO	Not less than monthly
Endotoxin	0.25IU/mL	EP	Not less than monthly

3. Nausea, vomiting and headache

Common and usually associated with hypotension, hypertension, infection and may be a minor manifestation of disequilibrium syndrome.

Management includes identification and treatment of the cause.

4. Chest pain and back pain

Cause unknown. No specific management or prevention strategy. Angina must be considered in the differential diagnosis of chest pain

Assessment of haemodialysis adequacy

What constitutes optimal HD remains controversial. Urea kinetic modelling is a useful tool to determine adequacy of dialysis despite its limitations. The single-pool Kt/V assumes that at the end of dialysis the concentration of intracellular and extracellular urea are equal. Kt/V is a measure of urea clearance. K = dialyzer clearance; t is the dialysis time; V is the urea volume distribution. The urea reduction ratio (URR) is a simpler measurement of urea clearance which does not take into account the amount of fluid removed by ultrafiltration. URR = 100 x $(1-C_t/C_o)$. Co is the predialysis urea; C_t is the post dialysis urea [1,3].

Assessment of the adequacy of dialysis is based on delivered dose of dialysis rather than prescribed HD treatment. Both clinical and biochemical assessment is recommended [1, 3, 8].

1. The clinical assessment of patients should include:
   General wellbeing
   Nutritional status
   Quality of life
   Blood pressure
   Fluid status.
2. Monitoring of biochemical and haematological parameters
3. Measurement of clearance of solutes

The minimum dose of dialysis should be a urea reduction ratio (URR) of 65% or Kt/V of 1.2. To ensure adequate dialysis, a target URR $\geq$ 70% or Kt/V $\geq$1.4 (determined by single pool urea kinetic modelling) is required if this dose is to be achieved consistently [1,3].

An adequately dialysed patient is a healthy patient, in good frame of mind, without admissions for intercurrent illnesses [8].

Frequency of monitoring should be once a month for all adult and paediatric dialysis patients on regular thrice weekly dialysis [1,8]. The frequency of measurement of delivered dose should be increased when patients are non-compliant with their haemodialysis prescriptions (missed treatments, early sign - off) frequent problems noted in delivery of the prescribed dose e.g. variably poor blood flows, or treatment interruptions or when the haemodialysis prescription is modified.

In this environment where patients dialyse infrequently, weekly Kt/V should be determined (Opinion) [11,13]**.**

If Kt/V fails to meet target, options are:

- Improve vascular access if flow is poor
- Increase blood flow rate
- Increase dialysate flow rate
- Increase dialyser size
- Increase dialysis time and frequency [1].

Care of vascular access

In haemodialysis patients, poor personal hygiene is a risk factor for vascular access site infections. Therefore patients with poor personal hygiene should be taught how to improve and maintain personal hygiene. Education of dialysis staff is also crucial to minimise infection risks. All dialysis staff should be trained in infection control procedures. Handwashing, skin preparation techniques for permanent access and catheter care. Cleanse skin with 70% alcohol or 10% povidone iodine using a circular rubbing motion.

- The catheter exit site should be examined at each haemodialysis session for signs of infection
- Catheter exit site dressing should be changed at each haemodialysis treatment.
- Use of dry gauze dressing combined with skin disinfection, using either chlorhexidine or povidone iodine solution followed by povidone iodine ointment or mupirocin ointment (bactroban) at the catheter exit site are recommended after catheter placement and at the end of dialsysis session.
- ***Catheters should be locked with heparin 1ml = 1000IU and antibiotic solution (opinion)***.
- During catheter connect and disconnect procedures, nurses and patients should wear a surgical mask.

Cost containment measures

Dialysers can be reused to save cost except in HBV, HCV, HIV patients. When haemodialyzers are reused, they should be processed following the Association for the Advancement of Medical Instrumentation (AAMI) Standards and recommended practices for reuse of haemodialyzers during reprocessing it is important to check the total cell volume. Dialyzers having a total cell volume < 80% of the original measured value should not be reused. Where this would not add to cost of treatment, re-use is recommended [14,15].

Infection control

Infection control is of paramount importance within the dialysis unit. Nursing staff must take adequate precautions to prevent the spread of infection within the dialysis unit. This is achieved through the use of universal precautions and isolation of patients and machines, if required. Each dialysis unit must have infection control policies.

HBsAg positive patients require treatment in isolation and with designated machines. This is also desirable for patients that are HCV or HIV positive.

All staff working in the dialysis should be vaccinated against hepatitis B and should be screened annually

Dialysis in the elderly:

There are specific problems in dialysing the elderly. Vascular access problems cause increase use of central catheters with the attendant increased risk of sepsis and hypotension. Some elderly patients are frail with multiple medical and social problems. Pre-existing morbidity affects quality of life and outcomes. Consider conservative management for ESRD and this should be discussed with the patient and relatives. For those who agree to dialysis, PD might be a better option in view of vascular access problems.

Dialysis in pregnancy:

Intensive daily dialysis in the pregnant HD patient has been associated with better outcome although no RCTs have been conducted in this subset of patients. A target Kt/V of 2.5 has been suggested.

Target for HD patients

- Kt/V ≥ 1.2 or URR > 65%
- Hb 10 – 12g/dL
- Serum albumin > 3.5g/dL
- Phosphate < 1.80mmol/L
- Calcium within normal range for local laboratory and adjusted for serum albumin
- Bicarbonate 20 -26mmol/L
- Pre dialysis Potassium < 6.5mmol/L
- Pre-dialysis BP < 140/90mmHg
- Dietary protein of at least 1g/kg ideal body weight
- PTH target between 2-9 times normal

Routine laboratory tests

Forthnightly

- Haemoglobin

Monthly

- Standard kt/v
- Serum albumin
- Calcium, phosphate
- Nutritional assessment

Every 3 months

- Iron studies
- Serum PTH
- Viral screening

Peculiarity of haemodialysis in children [3]:

Outlined treatment targets for adults apply to children older than 5 or more than 15 kg. Haemodialysis is not generally preferred for younger children. Renal transplantation remains the most preferred modality of treatment for paediatric patients with ESRD.

Research areas identified:

1. Maintenance HD dosing that would provide good QOL in Nigerians with advanced CKD.
2. Maintenance HD dosing that would provide good QOL in Nigerian Children with advanced CKD.
3. Management of complications in maintenance HD.
4. Quality of water used in dialysis centres in Nigeria: recommendation based on patients electrolyte needs.

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SECTION IV

PERITONEAL DIALYSIS

INTRODUCTION

Peritoneal dialysis (PD) is an established, effective mode of renal replacement therapy that is particularly relevant in Nigeria and other developing countries because of its rural adaptability.

It has been used in the management of acute kidney injury in adults and children for more than 4 decades but major constraints have limited its continuous use in the management of end stage renal disease (ESRD), hence local experience in this area is limited [1-6].

PD should be provided as part of integrated renal replacement therapy care such that patients would have access to other modalities of care should the need arise [7-9].

Unfortunately, major limiting factors for sustainability of acute or chronic PD treatment in Nigeria have been unavailability of necessary consumables and exhorbitant cost when available. Others include the very high infection (peritonitis) rate and lack of and progressive attrition of well trained and skilled nursing personnel [10].

Contraindications to use of PD [9]: is unsuitable for some patient populations. These include severe obesity, hernias, those with recentabdominal surgery, active or past history of peritonitis, abdominal aortic aneurysm, absent anterior abdominal wall, inflammatory bowel disease, abdominal masses etc.

The use of peritoneal dialysis is also contraindicated in patients with physical or mental incapacitation or those with uncorrectable mechanical defects in the abdomen (eg, Prune Belly syndrome, surgically irreparable hernia, omphalocele, gastroschisis, diaphragmatic hernia, and bladder extrophy), as well as those with extensive abdominal adhesions.

It is also not encouraged in patients with intolerance to increased intra-abdominal pressures_eg in patients with concomitant obstructive airway disease.

Other limitations to use of PD include presence of abdominal infections like tuberculosis, inflammatory or ischemic bowel disease, abdominal wall or skin infection and severe malnutrition.

Choice of PD modality

The various modalities in practice are:

- *Continuous Ambulatory Peritoneal Dialysis*

(CAPD) Continuous Ambulatory peritoneal dialysis (CAPD) is used in the management of patients with established ESRD. It is the commonest modality of peritoneal dialysis in use worldwide. It should be presented to our ESRD patients as a viable choice of renal replacement therapy when the necessaryequipment(s) are available and affordable.

It could serve our rural population that may have to travel long distances to get to renal care centres.

- *Automated Peritoneal Dialysis*

Automated peritoneal dialysis is used in the management of acute exacerbation of chronic kidney disease (CKD) and in established ESRD. Its use in the first scenario is usually hospital based while that for ESRD is home based. It has various subtypes namely continuous cyclic peritoneal dialysis (CCPD) and Nightly intermittent peritoneal dialysis (NIPD). This is the preferred modality for children under 5 years and/or less than 15kg.

- *Acute Peritoneal Dialysis*

It should not be prescribed for patients with established ESRD except during special circumstances such as inability to secure vascular access, cerebrovascular disease, cardiovascular instability / severe arrhythmias and other intercurrent illnesses.

EQUIPMENT AND RESOURCES

The equipment necessary for a successful peritoneal dialysis program includes:

- **Peritoneal Dialysis Catheters:**

There are 2 major types –

- Rigid PVC catheters equipped with trocar and blade for bedside insertion. This is used for acute PD and for very short periods usu ally less than 1 week but may be retained with special precautions for up to 2 weeks.
- Soft silastic rubber catheter which is inserted laparoscopically or through open surgery. It has various modifications ie straight, coiled, cuffed (single or double), non-cuffed etc. It is used for automated PD and CAPD and could be used for prolonged periods particu larly if the procedure is uncomplicated.

- **Connectology**
  Connectology refers to the tubing used to link the PD catheter to the fluid source. There are different systems developed to address particular complications, the commonest being

PD peritonitis

- Y system
- Baxter 2 system
- Fresenius Safe-lock mechanism
- Twin bag system
- Direct connection between PD fluid and catheter using adaptable infusion sets though not encouraged because of propensity for peritonitis, could be lifesaving in rural communities in developing countries. If it is expedient to institute acute PD using such sets, transfusion set could be used but must be discarded after every exchange.
- PD connectology has undergone various modifications hence the latest varieties are now produced with the PD fluids which is not manufactured locally.

- **PD Fluids**

The fluids are manufactured in different concentrations ie hypotonic, isotonic or hypertonic and their use depends largely on the patient's clinical state and needs. The PD fluid could be glucose, glycerol, amino acid or icodextrin based, while the buffer used could be lactate or bicarbonate. The commonly available fluids are glucose based with lactate buffer. The availability of these fluids is the major limiting factor of peritoneal dialysis in Nigeria, hence efforts to develop indigenous production must be encouraged and sustained. This would reduce the cost of PD in Nigeria by 50-75%.

- *Standard Theatre*
  A standard theatre is vital for PD catheter insertion particularly for CAPD.

- *PD training room (s) & Private treatment room (s) :*
  The patient that would utilize CAPD would need to be trained on catheter care, fluid exchange and need for maintenance of sterility of the procedure and personal cleanliness. A private room with its conveniences would serve this purpose.

- *Personnel*
  Specialist PD nurses are vital to a success ful PD program hence units desiring to commence this treatment modality should engage in capacity development of their staff.

Clinical evaluation and preparation for PD

Patients with chronic kidney disease (CKD) who have reached stage 4 (Page 3) should be counseled about ESRD and renal replacement therapy options, including peritoneal dialysis (PD), haemodialysis (HD) and kidney transplantation as well as conservative management.

- **Placement of PD catheter**

There are different insertion methods for different catheter types.

- Laparoscopic insertion
- Open surgery
- Other special bedside techniques eg Y-Tech insertion method by Ash *et al*.
  - In all these instances the catheter must be tunneled.
  - Other insertion methods are used for various modifications of CAPD catheters.
  - Timing of PD catheter insertion should be well before commencement of CAPD procedure. An allowance for 4-6 weeks would allow correction of any early catheter-related problems. Early break in can be allowed when the need arises.
  - The blind method is usually used to insert Rigid PVC catheters equipped with trocar and blade at the bedside. This is used for acute PD and for very short periods.

Viral screening

This is desirable at initiation of therapy so as to ensure total care for the patient and protect the health personnel. Screening for anti HCV, HBsAg and anti HIV antibodies could be performed but all necessary pre and post test counseling must be ensured. It is particularly important as the patient could consider transplant in future.

Immunization

Immunization for Hepatitis B virus is desirable for similar reasons and influenza and pneumococcal vaccination could be offered to CAPD patients as well when available.

Peritoneal dialysis procedure

- Peritoneal dialysis prescription [7-9] Peritoneal dialysis should be prescribed for willing patients after careful evaluation. To optimize middle-molecule clearance in patients who have minimal residual renal function (RRF), the CAPD prescription should preferentially include dwells for the majority of the 24-hour day.

A minimum prescription should be Four 2L PD fluid exchanges during the day with or without night dwells depending on the peculiar needs of the patient. Indwelling time of 3-4 hours should be observed between exchanges. If there is need to augment clearance, the instilled volume per exchange should be progressively increased before increasing the number of exchanges per day.

For patients on automated PD, the exchanges are carried out at nights, 4-5 exchanges with or without a day dwell.

To achieve volume control, the lowest possible dialysate dextrose concentration should be used while dietary sodium and fluid restriction as well as the use of diuretics can be undertaken to control hypertension.

A combined urinary and peritoneal Kt/V[urea] of ≥ 1.7/week or a creatinine clearance of 50L/week/1.73m^2 considered as minimal treatment doses by other guidelines should be adopted. This should however be increased in symptomatic uraemic patients [7-9].

In addition strategies that retard progression of CKD or preserve residual renal function should be encouraged. These include control of anaemia, blood pressure (using ACEI and ARBs), calcium-phosphate homeostasis, dyslipidaemia, avoidance of nephrotoxins (including NSAIDs), hydration and malnutrition.

- Peritoneal equilibration test (PET) Peritoneal membrane function should be monitored at least 6 weeks after commencing CAPD or automated PD and annually thereafter except when clinically indicated. Peritoneal equilibration test should be used.

- Assessment of PD adequacy Both residual endogenous creatinine and peritoneal dialysis clearances are important in CAPD and should should be monitored every 6 months except otherwise clinically indicated. The minimal treatment doses mentioned above should be maintained.

Medical management of PD patient

- *Hypertension :* Hypertension should be managed according to recommendations on Section 2 subsection D. In CAPD patients with residual renal function who is hypertensive, preference should be given to the use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs). While in those without hypertension but still has residual renal function, ACE inhibitors or ARBs should be considered further preserve the residual function.
- *Malnutrition* (Refer to Section 2 subsection H.) Nutritional status of CAPD patients should be assessed at least once in 6 months.

Dietary protein allowance is generally >1.2g/kgbody weight /day to cater for losses through the PD fluid. It should not be lower than 0.8g/kg/day [15]. (Refer Section 2 subsection H.)

- Anaemia (Refer Section 2 subsection E.)
- Bone Disease (Refer Section 2 subsection F.)
- Dyslipidaemia (Refer Section 2 subsection G.)

Achievement of treatment targets

Local experience is very limited on achievability of treatment targets in CAPD. To improve ultrafiltration, clearance and quality of life it may be desirable to increase dwell volume, frequency of exchange, number of night dwells, etc [7-9, 16].

PD Peritonitis and care of PD catheter/exit site

- PD Peritonitis can be diagnosed if the patient presents with two of the following criteria

- Cloudy effluent or abdominal pain

- Elevated WBC count (>100 cells/cu mm)or Neutrophil count (>50 cells/cu mm)

- Positive culture of PD effluent

o Prevention Strategies.

PD units should observe universal precautions on sterility and cleanliness.

Hand washing with antiseptic soap must be ensured before and after performing procedures both by the patients and the hospital personnel.

It is important that units should undertake regular audit of their infection rates, and identify causative organism(s) and treatment outcomes. Local treatment and prevention protocols need to be developed.

Flush-before-fill dialysis delivery systems is encouraged and patients should undergo regular revision of their technique and receive regular intensified training.

Antibiotic prophylaxis is encouraged after initial catheter insertion. Clavulanate potentiated Amoxicillin, quinolones, ceftriazone or ceftazidime have been used in various units in Nigeria with success.

Topical antibiotic administration could be used to reduce the frequency of exit-site infection and peritonitis

o Treatment

Exit site infections usually present with pain, swelling, serous and / or purulent discharge. Swabs should be taken for culture and initial em piric therapy should be commenced with oral antibiotics that will cover *S. aureus, Klebsiela spp, Escheri chia coli and P. aeruginosa.*

Dose adjustments as recommended in ISPD guidelines could be employed [8].

Initial treatment regimens for peritonitis should cover for both Gram positive and Gram negative bacteria pending microbiology results [9].

Intraperitoneal antibiotic treatment is instituted after confirmation of peritonitis. Antibiotic combinations should include quinolones, ceftriazone or ceftazidime clavulanate potentiated Amoxicillin pending the availability of culture results. Catheter should be removed if there is relapsing peritonitis, refractory peritonitis, refractory tunnel infection and fungal peritonitis.

Systemic antibiotic therapy should be given in cases of sepsis but particular attention must be paid to dose adjustments in ESRD patients on CAPD [8].

Research areas identified:

1. Wider multicentre prospective study on applicability and usefulness of CAPD in Nigeria.
2. Peritoneal membrane characteristics and its impact on mortality in Nigerians.
3. Cost containment measures in CAPD management.
4. Pattern of peritonitis and modalities of controlling and reducing it.
5. Health related QOL in CAPD patients in Nigeria.

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SECTION V

KIDNEY TRANSPLANTATION

INTRODUCTION

Kidney transplantation remains the best option for management in established ESRD conferring survival benefits in the short and long-term, significant cost saving benefits and the best possible 'Quality of Life'[1,2,3].

The shorter the time spent on dialysis prior to the transplant, the better the outcome of graft survival [4].

Sources of kidneys:
Cadaveric
Living-related
Living emotionally related

As of now, only Living-related and Living emotionally related transplantations are the available modalities in Nigeria.

Indication: Established ESRD with GFR less than 15mls/min (Stage 5 CKD) for at least 3 months.

Absolute contraindications [5]
These include unresolved malignancy, active chronic infections, life expectancy of recipient less than 10 years and other end stage organ disease. Others include severe cardiovascular disease and insufficient finances for post transplant medications.

Relative contraindications [6]
These include a history of non-compliance, obesity/malnutrition, extremes of ages less than10 years or more than 65 years and emotional instability/psychosis. Others include decreased mental capacity/dementia, poorly controlled diabetes, possibility of recurrence of primary disease and substance abuse.

Assessment of recipient for appropriateness for transplantation.

(1) Patients must be confirmed to be in established End Stage kidney failure (ESRD), stage 5 CKD. These should include (but not limited to)
   (a) eGFR by MDRD
   (b) 24hr Creatinine Clearance
   (c) USS examination of the Kidneys
   (d) Exclusion of potentially reversible causes of renal dysfunction.

(2) Exclusion of any contraindications to renal transplantation above.

Suitable live donors should include [7**];**

- Aged between 18yrs and 65yrs
- Genetically related individuals
  - Parents
  - Siblings
  - Offsprings
  - Cousins (up to 3rd Cousins).
- Emotionally related individuals (including but not limited to)
  - Spouses
  - Friends

Altruism in these cases would need to determined by both a legal affidavit and the opinion of a separate ethics committee (consisting of at the least a legal practitioner, a physician unrelated to the program, a religious leader) meeting the donor and recipient together and separately and must give a written attestation of the altruism involved. Every effort must be made to discourage organ trafficking and transplant commercialism as enshrined in the Declaration of Instanbul [8].

(d) Must have two physiologically and anatomically normal kidneys with no medically discernable risk of shortened life span as a consequence of kidney donation.

(e) Must have no chronic infection or malignant condition that may be transferred to the recipient during the process of the transplant.

(f) Must be in a position to give a fully informed and signed consent and must be under no Psychological, Emotional, Physical or Commercial compulsion of any sort.

(g) Must be assured of long term follow-up geared towards identifying any potential complications of kidney donation.

(h) Should be assured of an accelerated consideration in any deceased donor renal transplant Program in the event that he/she in the future develops renal failure and the need for a kidney transplant.

(i) Should share compatible blood group and have good HLA match.

Recipient Pre- Transplant Investigations

- Blood Group
- Genotype
- HIV, HBsAg, HCV, VDRL, EBV, CMV Screening
- Chest X-Ray (CXR)
- Electrocardiography (ECG)
- Echocardiogram.
- Coronary angiography if evidence of coronary artery disease or in diabetics older than 50 years.
- Venous/ Arterial Doppler studies of femoral vessels if long term femoral cannulations or evident bruits.
- Electrolytes, Urea, Creatinine, Calcium, PO4, serum protein (total and albumin)
- LFTS and lipids screen
- FBC + ESR.
- Urinalysis + MSU M/C/S
- Renal USS + Abd USS.
- PsA definitive if male and > 40yrs.
- FBS + OGTT if necessary HbA1C
- Full Breast Examination if female
- + (plus)Mammogram if older than 40 years.
- Pap smear in Females.
- Dental Examination
- HLA typing and Cross Match.
- + PRA'S, DSA'S

Donor Pre-Transplant Investigations

- Blood Group
- Genotype
- Weight – Height BMI
- HIV, HBsAg, HCV, CMV, VDRL, EBV Screening.
- E/U/Cr, eGFR (MDRD) or Cockcroft)
- LFTS
- FBC ESR + CRP
- FBS + OGTT if abnormal. HbA1C
- Lipid profile
- 24hr Creatinine Clearance
- Urinalysis + M/C/S
- Renal USS
- CXR.
- ECG.

- Echocardiogram if > 50yrs
- HLA Typing and Cross match
- Renal Angiogram after review of all above and decision taken to go ahead with the transplant.
- Group and X match 2 unit's blood

Other Considerations for immediate preop

- **o** Dialyze patient effectively thrice weekly for at least 2 weeks prior to the date of the transplant.
- **o** Patient must be dialyzed not earlier than 24hr before the intended transplant to obviate the need for dialysis within 48hr post transplant in the event of delayed graft function or accelerated acute rejection.
- **o** Avoid transfusion once the HLA typing and Cross match have been done and crossmatch negative. In case of any transfusion, wait at least 2 weeks and repeat crossmatch before transplantation.
- **o** Insert a central venous catheter prior to the transplant for CVP monitoring post operatively
- **o** Review by Urologist or Transplant surgeon
- **o** Review by anesthetist experienced with peculiarities of anesthesia in transplant recipient
- **o** Adequate control of BP and Blood Glucose (if Diabetes)
- **o** Adequate correction of anemia preferably by EPO and Iron Infusion.
- **o** Exclusion of any ongoing acute and chronic infections.

PROPHYLAXIS IN RECIPIENTS

- Prophylactic antibiotic; I.V. Rocephin 1G stat at induction and repeat daily for 3days.or Vancomycin 1G Stat + Genticin 80mg Stat. (If pt is allergic to penicillin and cephalosporin)

- Prophylactic antifungal; Oral Nystatin 200,000 units as part of premed and repeat 200,000unit 8 hourly till 4 Weeks post transplant or till discharged, whichever is later [9].

- Prophylaxis for Pneumocystis carinii; Co-trimoxazole 1 Tablet daily for six months [10].
- Ulcer Prophylaxis; Omeprazole 20mg daily for 6 month or until prednisolone dosage is 7.5 mg dly or less whichever occurs earlier [11].

- Thrombosis prophylaxis;

- **o** Aspirin 75mg stat with premed and daily thereafter or Heparin 5000units 12hourly post surgery (stop only if frank bleeding, not routinely for biopsy) [12].

- Osteoporosis prophylaxis [13];

- **o** 1 alpha calcidol O.25mcg daily

- Protection From Ischemia [14]

- **o** Nifedipine SR 10mg or Amlodipine 10mg

- Tuberculosis prophylaxis [15];

- **o** Isoniazid 150mg daily + Pyridoxine 50mg daily.

- CMV prophylaxis for high risk groups;

- **o** Acyclovir 200mg thrice daily or ValGancyclovir 450mg daily till six months with dose adjusted to renal function [16].

- Malaria Prophylaxis

- **o** Proguanil 100mg daily

- Till six months post transplant. Start only after serum creatinine is less than 2 mg/dl [17]

IMMUNOSUPPRESIVE DRUGS, INDUCTION AND MAINTENANCE

(A) Induction therapy[18]

This is a major cost and has been demonstrated to reduce acute rejection rates without major impact on long term graft survival. Another major consideration is the risk of opportunistic infections due to the greater degree of immunosuppression.

Induction should thus be considered only in high risk patients

(j) Previous transplant
(ii) Previous multiple Blood transfusions
(iii) Previous multiple Pregnancies
(iv) Children
(v) Haplotype Mismatches
(vi) Presence of HLA antibodies or Donor specific antibodies
(vii) Deceased donor kidney transplantation.

Options include

a. Thymoglobulin (ATG) 5mg/kg daily x [2/7] then 3.5mg/kg daily x [5/7]
b. Basiliximab (Simulect) 20mg days O and 4 use 10mg if <35kg

Standard Triple regimen induction for low risk patients:

(i) Cyclosporine (Neoral) 5mg/kg bd started 24hrs preop.
In children do "priming induction" and start 72 – 96 hrs preop.
Give with a little water on the morning of the transplant.
(ii) a. I.V. Azathioprine 3mg /kg as part of premed on Morning of the transplant.
(iii) (a.) I.V. Methylprednisolone 500mg as part of premed (slowly) on the morning of the transplant.
(b.) I.V. Methylprednisolone. 500mg stat at release of clamps.

(B) Maintenance immunosuppressive

Even though the use of the anti proliferative agent Azathioprine has declined in developed countries with the introduction of Mycophenolate, the Myss study convincingly demonstrated that long term efficacy of Azathioprine and MMF are comparable even though MMF costs 15 times more [19].

The Calcineurin inhibitors are however indispensable and there is an increased risk of graft loss and increased incidence of acute rejection if avoided or withdrawn.

Cyclosporine and Tacrolimus are both accepted although Tacrolimus has lower acute rejection rates and Nephrotoxicity but higher incidence of post transplant diabetes.

Combination of Cyclosporine (CsA) with ketoconazole 100mg daily reduces the dose requirements of CsA by 50- 70% whilst Diltiazem reduces the dose of CsA by 30-50%.

Combination with Rifamipicin however increases the dose requirements by 100%.

Standard Triple Regimen;

(1) Corticosteroids
Methylpred O.5g I.V. with Pre med
Methylpred O.5g I.V. with release of clamps
Oral prednisolone 20mgfrom day 1 after 2 weeks reduce 2.5mg every fortnight to 7.5mg daily till 1yr Reduce to 5mg daily after 1yr.

(2) Azathioprine
3mg / kg I.V. with Premed
2mg / kg I.V. when clamps released
1mg / kg orally daily from day 1 stop if WBC $<3.5x10^9$/L.
Reintroduce when WBC > 5.0×10^9/L

(3) Cyclosporine (Neoral)
Start at 5mg/ kg twice daily orally
Give first dose with premed.
Avoid I.V. Cyclosporine but if necessary give as [1/3] dose of oral.

Adjust dose depending on C^o or C^2 levels.
If dose of CsA is changed do not measure blood levels till 36hrs after.Aim for 3mg /kg bd by 6 months post transplant.

Co Levels for CyA [20]
1-3 months 250 – 350 ng/ ml
4-6 months 150 – 250ng/ ml
6 -12 months 100 – 200ng/ml
> 12 months 100 – 200ng/ml

C_2 Levels for CyA [21]
1st Month 1,700ng /ml
2nd Month 1,500ng/ml
3rd Month 1,300ng/ml
4 – 6 month 1,100ng/ml
6 – 12 month 900ng/ml > 12 month 800ng/ml

(4) Mycophenolate may also be given if the patient is high risk or there are any episodes of acute rejection.

The EARLY Postoperative Period

1. Observations
   a. Half hourly BP, Pulse and respiration
   b. Hourly CVP
   c. Hourly urine output
   d. Hourly temperature
   e. Hourly Glucometer Checks
   f. Daily weight
2. Routine investigations
   a. FBC 12hourly
   b. E/U/Cr 12hourly
   c. Urinalysis daily
   d. Check WBC before each dose of Azathioprine and omit if WBC < 3.5 x 10^9/L
3. I.V. Fluids;
   Titrate fluid administration to keep CVP >10cm
   Alternate Ringers Lactate with Normal Saline with 5% Dextrose
4. Urinary Catheter usually left for 3 – 5 days but check with surgeon.
5. Drains;
   Wound drains usually removed after 48 -72 hrs Check urea and electrolytes if any suspicion that it contains urine.
6. Doppler USS assessment by 72 hrs or earlier if any suspicion of vascular complications.
7. Diet;
   Normal diet when bowel sounds heard and food is tolerated.
8. Mobilize patient early
   Give LMW Heparin if bed bound for > 48 hours
9. Indicate boldly on notes if ureteric JJ stent in place.
   Remove at 6 weeks.
10. Avoid dialysis for 24- 48 hrs post op if possible.

SPECIAL SITUATIONS

Acute Rejection

(a.) Hyperacute Rejection occurs only with preformed antibodies. Remove the graft.

(b.) Accelerated acute rejection occurs within 24 hrs – 4 days. Due to sensitization from previous transplant, transfusions and pregnancies.

(c.) Acute Rejection
Occurs days to weeks post op. Systemic disorder with multiple cyctokine (TNF)induced constitutional symptoms. Multiple acute episodes, late episode >1yr, more severe episodes all increase risk of chronic rejection. Severe acute rejections include vascular rejection and those resistant to steroids.

Treatment

1. Pulse Methylpred 125 mg – 1 kg (3-5mg /kg) daily for 3 – 5 days. (Successful reversal in 75% of cases).
2. ATG 3mg/kg daily for 8- 10/7.
3. OKT3 5mg bolus dly for 7 – 14/7
   Reserve 2 & 3 only for severe acute rejection or biopsy proven antibody-mediated rejection . If on Azathioprine, switch to Mycophenolate formulations [22]

Follow-up;

Discharge recipient usually by 10 days to 2weeks.
Outpatient follow-up, twice weekly for first month.
Weekly, second month.
Two weekly third month
Monthly thereafter

Cyclosporin / Tacrolimus Assay

Day 3 post op by which time you should expect to achieve therapeutic levels.

Weekly for 1st 4 weeks or 36hours after any dose changes.

Repeat if any unexpected rise in Urea or Creatinine

Renal Graft Biopsy

Graft biopsy should be done if clinically indicated.

Indications include:

a. Delayed Graft Function
b. Acute Rejection
c. Rising Urea or Creatinine Values.

Pregnancy and Contraception Post-Transplant
Approximately 1 in 50 women of child bearing age with a functional transplant becomes pregnant. Although the incidence of spontaneous abortions may be higher than normal, there is no increase in the incidence of congenital abnormalities in pregnancies carried to term. There is a definite risk of rejection in pregnancy (about 9%) and permanent impairment of graft function in 15% [23] .

. Pregnancy is best achieved 2-5 years post transplant when graft function is relatively normal and stable. A successful outcome is more likely if creatinine less than 1.5mg/dl.

Contraception
This should be addressed prior to discharge after transplantation.

The risks to the graft of pregnancy and the need to wait till at least 2 years post-transplant must be clearly explained to the patient. Oral contraceptive pills have a potential for drug interaction with cyclosporine and if used would necessitate frequent drug level monitoring, The intrauterine contraceptive devices may increase the risk of infection but this risk is worse close to the time of insertion and as such use the longer acting alternatives and cover with prophylactic antibiotics at the time of insertion. Barrier methods are safest, show least risk of side effects and offer the added advantage of reduction in risk of transmission of STD's.

Kidney transplant in HIV seropositive patients
HIV infection is not a contraindication to a successful kidney transplant. Life expectancy of at least five years is considered appropriate to go ahead with a renal transplant [24].

Criteria

- CD4 > 200cells/microlitre for at least 6 months.
- Undetectable HIV viraemia (<50 copies/ml) for 6 months.
- Adherence to HAART for >6 months.
- Absence of AIDS defining illnesses following immune reconstitution after HAART.
- Available HAART options in the future.
- Absence of chronic infections that may reactivate with immunosuppression.
- Absence of any malignancies e.g. Kaposi Sarcoma.

Immunosuppression is as with other patients but drug/drug interactions between antiretrovirals is a consideration that would necessitate more frequent assessment of drug levels.

Paediatric patients: renal transplantation is the preferred modality of treatment of terminal CKD and pre-emptive transplantation is encouraged. The need for potent immunosuppression is greater in children. Rapid steroid tapering is advised because of stunting of growth. Human growth hormone may be added if increased growth is desired [25].

Major action point: Providing legal framework for transplantation in Nigeria

Research areas identified:

1. Assessing cost effectiveness and survival post renal transplantation in Nigeria.
2. Determining the appropriate immunosuppressive dosing regime in renal transplant recipients in Nigeria.
3. Assessment of infectious complications of renal transplantation.
4. Assessment of malignancies complicating renal transplantation in Nigeria.
5. Assessment of morbidity and adequate follow-up of kidney donors.

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