

Chronic Renal Failure

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Chronic Renal Failure (outline)

- Definition of Chronic Renal Failure (CRF)
- Pathophysiology
- Epidemiology
- Causes of CRF
- Cases
- Diagnostic approach in patient with renal failure
- Laboratory features of CRF
- Management of CRF

Definition

- Definition of Chronic renal failure
 - Persistent irreversible reduction in overall kidney function
 - Renal functional impairment: reduced GFR
 - Mild GFR: 60-89 ml/min
 - Moderate GFR: 30-59 ml/min
 - Advanced GFR: 15-29 ml/min
 - End Stage GFR: <15 ml/min

Pathophysiology

- Response to reduction of nephrons
 - Glomerular hyperfiltration and glomerular hypertrophy
 - Tubular over-functioning and hypertrophy
- Factor of progression of renal failure
 - Increase glomerular pressure
 - Hypertension
 - Progressive glomerular lesions: mesangial hyperplasia, glomerular hyalinosis and sclerosis
 - Other factors: hyperlipidemia, growth hormone, phospho-calcium disturbances.

Epidemiology of CRF

- ~100-200 patients reach ESRD per million population per year
- In RSA ~4900-9800 ESRD patients per year
- In KZN province ~1000-2000 ESRD patients/year
- Dialysis R100.000/ year per patient
- Incremental need for dialysis R100-200 millions per year

Causes of CRF

- Glomerulonephritis
- Hypertension
- Diabetic nephropathy
- Chronic pyelonephritis
- Adult Polycystic Kidney Disease

Case 1

- 31 y male patient referred to Addington Hosp. for severe renal failure
- Past medical history unremarkable.
- On admission
 - Drowsy but arousable, disorientated with anasarca, pallor
 - S. creatinine 3000Umol/l, S urea 60mmol/l, K⁼ 7.8meq/l, Hb 5g/dl

Case 1(continued)

- No significant past medical history
- No history of hypertension or diabetes
- Does not recall ever having Blood pressure checked
- Immediate management:
 - Potassium shift (glucose insulin IV, Na Bicarbonate)
 - Calcium gluconate
 - Peritoneal dialysis using stick catheter (90 cycles starting with 4.25% dextrose Dianeal solution 1l, dwell-in time 2 h.

Case 1 (continued)

- 3 days later : patient conscious, well oriented
- Further investigation reveals patient is HIV positive CD4: 115, Hepatitis B negative,
- Ultrasound of kidney: bilateral kidneys smooth outline measuring 9cm on the left and 9.5 cm on right side.

- Patient underwent further evaluation
 - Kidney biopsy shows: 70% glomerula sclerosed the remaining features of HIVAN
 - Medical: ECG, Echocardiography (EF 51%),
 - Social
 - Psychological
 - Psychiatric.
- Hemodialysis catheter inserted and hemodialysis started.
- Patient discharged after 1 week to continue HD as out patient pending decision on admission to State Chronic renal programme..

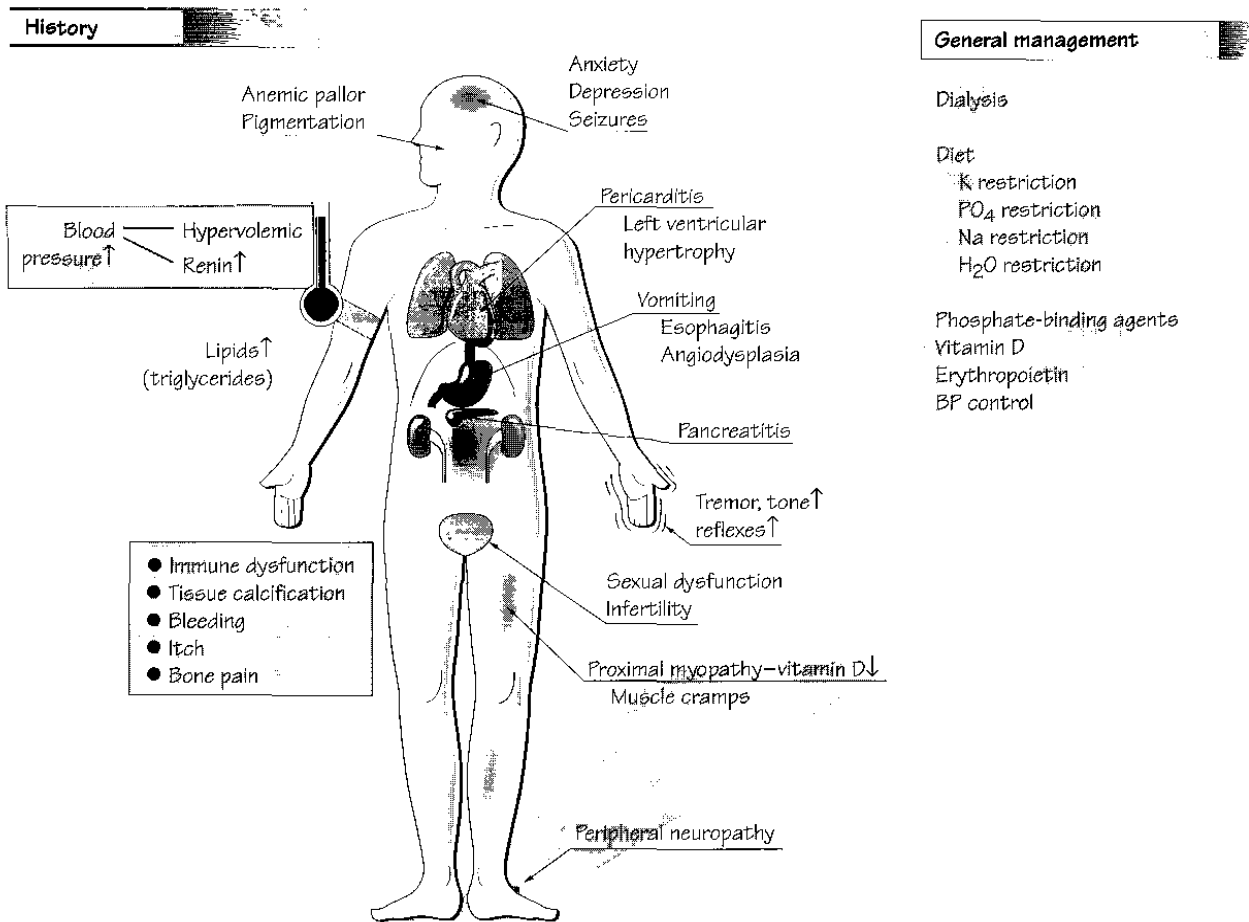
Case 2

- 43 y female patient
- Type 2 diabetic, hypertensive diagnosed 3 years earlier
- Complicated with:
 - Proteinuria 1.5gm/24h
 - Creatininemia 280 μ mol/l
 - Hypercholesterolemia 6mmol/l
 - Hemoglobin 8.5g/dl.

Case 2(continued)

- Treated by:
 - Diabetic diet, low protein and low cholesterol diet
 - ACE inhibitors, Angiotensin 2 antagonist, Statin
 - Iron supplementation, Erythropoietin
- 3 months later,
 - Patient stable feeling well
 - BP well controlled
 - Diabetes well controlled (HBA1c 7%)
 - Hb normal (12gm/dl)
 - Proteinuria 0.6gm/24h
 - Creatininemia 275 μ mol/l

42 Chronic renal failure: clinical complications and their management



From The Kidney at glance (C. O'Callaghan & B.M. Brenner)

Diagnostic approach of a patient with renal failure

- Questions to be answered
 - What is the cause?
 - Is it treatable?
 - Is it acute or chronic?
 - Are there reversible pre renal or post renal factors?
 - How severe is the failure?
 - Are there complications?

Distinguishing features of acute vs chronic renal failure

	Kidney size	Hb
● Acute	normal	normal or slightly reduced
● Chronic	reduced	reduced and well tolerated
●		

Laboratory features of CRF

- Raised plasma creatinine once GFR is less than 60 ml/min and rises exponentially with falling GFR.
- ESRD when creatininemia
~1000micromol/ml
- Creatinine depends on muscular mass
- Urea less reliable, varies with protein diet at end stage

National Kidney Foundation Management Guidelines of Chronic Kidney Disease

Stage	Description	GFR (ml/min)	Action Recommended
0	With risk factors	>90	Screening, risk reduction
I	Kidney damage with normal or decreased GFR	>90	Diagnosis and treatment to slow progression, cardiac risk reduction
II	Mild	60-89	Monitor to evaluate progression
III	Moderate	30-59	Evaluate and treat complications
IV	Severe (advanced)	15-29	Prepare for renal replacement therapy
V	End stage	<15	Renal replacement therapy

Current Guidelines for inclusion into State Chronic renal programme (From DOH-RSA)

- **Medical exclusion criteria**

- Active, uncontrollable malignancy or with short life expectancy
- Advanced, irreversible progressive disease of vital organs such as:
 - cardiac, cerebrovascular or vascular disease
 - advanced cirrhosis and liver disease
 - medically or surgically irreversible coronary artery disease
 - lung disease
 - unresponsive infections e.g HPV, Hepatitis B and C

- **HIV and AIDS are not a medical exclusion criteria** provided the patient has access to a comprehensive AIDS treatment plan
 - including antiretroviral treatment and
 - stable for at least six months and the above exclusion factors are absent.
- **Age (provided above exclusion factors are absent)** is not a contra-indication for chronic renal dialysis. In the UK the median age of starting renal replacement therapy is 63 years and the median age of the population is 54 years.

– Psychological Exclusion Criteria

- Any form of mental illness that has resulted in diminished capacity for patients to take responsibility to their actions.
- Active substance abuse or dependency including tobacco use.
- Obesity

– **Compliance**

- Patients with proven habitual non-compliance with dialysis treatment and lifestyle modification will be excluded or removed from chronic renal dialysis programme.

DIALYSIS IN PATIENTS WITH HIV INFECTION

- HIV infection is common in South Africa and presents our society with numerous challenges. HIV can cause chronic kidney disease (CKD) and can contribute significantly to the burden of patients requiring renal replacement therapy (RRT).
- **HIV associated nephropathy (HIVAN) was the third commonest cause of end stage renal failure (ESRF) in black patients in the USA after hypertension and diabetes, and since the availability of antiretroviral therapy (ART) is now in 7th place (USRDS, 2006)**

- **Furthermore HIV infection may co-exist with end stage renal failure of any other cause and we have even experienced instances of seroconversion to HIV positive of patients already on dialysis.**

- **In South Africa RRT is not freely available.**
 - Patients who can afford it or who have medical insurance may be able to receive these expensive therapies in the private sector.
 - For the majority, however this service is not freely available and is provided to a select few in some state hospitals.
- **Patients are selected for dialysis based on state criteria for acceptance to a transplant programme**

- Even if patients with ESRF fulfil the state criteria most centres are limited by the availability of ‘slots’ for dialysis . These are defined by the institution based on availability of funds, staff and equipment.
- Because the optimal form of RRT is renal transplantation, dialysis is seen as a bridge to transplant and the state ‘criteria’ are underpinned by the ‘transplantability’ of the patient.
- Any guideline on dialysis would have to keep this approach in mind and the availability dialysis for HIV positive patients will be contingent on our ability to transplant them.

2 Dialysis in HIV positive patients.

- In the pre-HAART era the survival of most patients with advanced HIV infection was dismal. Similarly for patients with HIV infection on dialysis the outcome was poor even in the developed world.
- This led some to recommend withholding dialysis from these patients.
- After the advent of anti-retrovirals however several retrospective studies in Europe and the USA have confirmed survival rates in the short term which are similar to the non-infected non-diabetic population.

However predictors of poor outcome include

- Low CD4 counts
- High viral loads
- HIVAN as the cause of ESRF
- Absence of HAART
- Opportunistic infections.

- Given the finding that survival of HIV positive patients receiving HAART is similar to non-infected dialysis patients it has been recommended by guidelines in both the USA and Britain that dialysis not be withheld from these patients on the basis of their HIV serostatus.
- However the survival of HIV positive patients on HAART on dialysis is still worse than that of the general HIV positive population

- Studies have shown a more rapid progression of HIV infection in patients with kidney failure and the presence of kidney disease either in the form of proteinuria or a raised creatinine portends a poorer outcome for the patient
- This has led to the initiation of transplantation in stable HIV positive patients with encouraging early results.

- Both haemodialysis (HD) and peritoneal dialysis (PD) have been employed in these patients.
- Literature review shows that both maintenance HD and PD are effective modes of RRT in HIV patients with ESRD, although there are some points of concern with both modalities

2.1 Haemodialysis

- Haemodialysis exposes the dialysis staff to blood products and contaminated needles.
- The risk of HIV seroconversion after a needle stick injury from an infected patient is estimated to be about 0.3%.
- In addition, the larger the blood inoculum and the later the stage of HIV infection, the greater the risk of seroconversion .
- The use of universal precautions is the best form of prevention of nosocomial infection.

- Dialysis access in the form of an AV-fistula is the best option for these patients and similar patency rates to the non-infected population have been shown.
- Some concern has been raised because of higher rates of PTFE graft infection in HIV positive patients especially those with AIDS.
- This has led some to avoid permanent access if an AVF cannot be successfully created.

- However the use of temporary catheters and permcaths for long term use often lead to inadequate dialysis, not to mention the risks of infection, vascular occlusion and bleeding.
- HIV transmission in a dialysis unit has been documented via inadequate sterilization of re-used needles Other infections have been caused by breaks in universal precautions and infection control procedures.
- Guidelines for infection control and machine disinfection set by the Association for the Advancement of Medical Instrumentation and CDC should be adhered to at all times.

2.2 Peritoneal dialysis (CAPD)

- Theoretically there is less exposure of staff to HIV with PD than with HD because peritoneal fluid is much less infectious than blood, there is less likelihood of needle stick, and the nature of staff to-patient contact is different.
- HIV was shown to survive in PD effluents at room temperature for up to seven days and in PD exchange tubings for up to 48 hours.
- Both sodium hypochloride 50% (Amukin), and household bleach 10% solutions, in dilutions of 1:512, are effective in killing HIV in dialysate

- Patients need to be educated on the need to properly dispose of these fluids Peritoneal dialysis patients should be instructed to pour dialysate into the home toilet and to dispose of dialysate bags and lines by tying them in plastic bags and disposing of the plastic bags in conventional home garbage.

- CAPD may aggravate the malnutrition and hypoalbuminemia in HIV patients with severe wasting syndrome.
- The rate of peritonitis has also been higher in patients with low CD4 counts in the pre-HAART era.
- Both gram positive infections and Pseudomonas infection as well as fungal infections have been reported as being more common.

- Overall, given the fact that outcome does not seem to depend on modality of dialysis the choice of RRT in HIV-infected patients should be based on an individual patient's lifestyle, preferences and availability of family and other support, and not on HIV seropositivity.
- In South Africa the dialysis modality offered will be further restricted by availability.

- The substantial population prevalence of HIV infection (estimated at 6 million), even at a best case scenario of prevalence of HIVAN at 1% of the infected population would mean that 60 000 individuals would face this condition that rapidly progresses to ESRF without appropriate care.

- That comes to almost 1200 patients per nephrologist!
- If only (conservatively again) 10% progressed to ESRF this would mean an additional 6000 individuals requiring dialysis
- -this is more than the current dialysis population in South Africa.

Challenges and Recommendations

- Early detection of CKD and prevention of progression to ESRF is of prime importance.
- The importance of routine screening for kidney disease and appropriate early referral cannot be stressed enough.
- Evidence indicates that treatment with HAART, ACE-inhibitors and possibly steroids may slow or arrest the progression to ESRF[6].

- Early detection also allows for counselling and preparation of patients for RRT.
- This includes early initiation of HAART, exploring options for RRT, allowing patients to acquire a medical aid, pre-emptive transplantation and access creation.

- Co-infection of these patients with Hepatitis B and C may contribute to the burden of renal disease and also complicates therapy. Adequate diagnosis will allow for treatment
- Drug rollout issues-To allow adequate access to dialysis the availability of ARVs to patients with ESRF must be prioritized.
- Opportunistic infection's and malignancies in patients with extremely low CD4 may preclude transplantation.

- This is especially so with certain infections like cryptococcosis or disseminated Kaposi's sarcoma.
- Based on current data we cannot justify excluding patients with HIV infection from receiving dialysis.

- Patients who are stable on HAART at the time of ESRF should not be treated any differently to other patients whatever the cause of the ESRF.
- Similarly, patients in whom HIV infection is coincidental should be started on HAART as soon as possible and dialysis should not be withheld.

- Patients with advanced HIV disease who present acutely ill will need to be assessed on an individual basis to determine if dialysis will be offered.
- This will depend on the following considerations
- Does the patient have acute reversible renal failure ?

- What is the short term prognosis of the patient?
- What is the availability of treatment at the centre?
- Would the patient be able to re-constitute his immune system? This may depend on several things including CD4 count, previous HAART, compliance and disease complications.
- Does the patient have a contraindication to renal transplantation eg lymphoma

Management of CRF mild moderate and advanced stages

- **Management of renal failure**
 - should start early in order to slow progression toward end stage renal failure
 - minimize the risk of complications as much as possible.
 - should include the following components:

- a. Determine and treat the cause
- b. Rule out any acute renal failure on CRF and treat.
- c. All possible causes' acute renal failure on chronic renal failure have to be investigated and treated accordingly.

- Prerenal causes (i.e. hypovolemia, cardiac failure, renovascular disease);
- post-renal or obstructive causes (i.e. prostate, urethral valves, neurogenic bladder)
- intrinsic causes (i.e. glomerulonephritis, interstitial nephritis, tubulonephritis) require a renal biopsy for confirmation,
 - manage to reverse the acute component of renal failure.

– **ii. The nephropathy causing CRF**

- to be determined and treated if possible to delay the progression of CRF.
- Even if a specific treatment is not available, knowing the nephropathy is useful for:
 - For prognostic of progression to renal failure
 - For preparation for transplantation and
 - To know the risk of disease recurrence on the transplant.

Correcting hydration

- It is essential to maintain water balance to avoid complications including pulmonary edema.
- Appropriate rehydration measures should be maintained.
- Beware of hypo and hypernatremia when monitoring and correcting the patient hydration state.

Control of blood pressure

- **Blood pressure control is an essential factor for delaying progression of renal failure secondary to any nephropathy.**
- **An uncontrolled hypertension will precipitate the decline of kidney function.**

Diet

- **Provide adequate diet**
 - **Low protein of 0.8gm protein/kg daily with normal carbohydrate is protective for the kidney**
 - **Low potassium (especially avoid bananas and dry fruits, fruit juices), low phosphorus (soak vegetables 24h prior to cooking).**

Control electrolyte balance

- **Hyperkalemia**

- **Normal K⁺:**

- **Low potassium diet**

- **K⁺ 5.5-6mmol/l :**

- **Ion exchangers (kayexalate to exchange potassium with Na or Sorbisterat to exchange K⁺ for Ca⁺⁺)**

– K⁺ 6.5 mmol/L and above:

- **Potassium shift with insulin 5-10 units IV, 20 ml of 50% glucose IV, Na Bicarbonate (25-100ml of 8.4% NaHCO₃ IV)**
- **Stabilize cardiac rhythm: Calcium gluconate 5ml of 10% Ca gluconate**
- **K⁺ removal : Dialysis (preferably hemodialysis).**

● Acidosis

- Usually asymptomatic unless HCO_3^- below 15 mmol/l.
- Correction should only be done in life threatening conditions:
- increment of 25 -50 mmol of Na bicarbonate. Rapid repair of acidosis may cause convulsions due to hypocalcemia produced by the rebinding to protein of calcium previously displaced by H^+ .

Other Complications

- **Prevention and treatment of renal bone disease**
 - Reduce phosphatemia through phosphate binders,
 - provide calcium and 1α vitamin D3 treatment if hypocalcemia.
- **Detect and treat infection**
 - - especially lung infection and urinary tract infection

- **Detect and treat anaemia:**

- use erythropoietin and iron as soon as CRF is established.
- help maintain or improve cardiac function

- **Adapt drug therapy**

- **Reduce drug dose**

- generally by half (if end stage renal failure) or
- increase administration interval of renally excreted drugs.

Prepare for dialysis and transplantation

- **creation of AV fistula for hemodialysis**
- **Tenckhoff catheter insertion for peritoneal dialysis.**
- **A psychologist and a social consult to assess the suitability and counselling on types of treatment.**

Management of ESRD

- **At the end stage of renal failure:**
 - **Conservative treatment is no longer sufficient.**
 - **Renal replacement is required:**
 - **Hemodialysis,**
 - **peritoneal dialysis**
 - **Transplantation**

Treatment modalities for ESRD

Treatment modality	Advantages	Disadvantages
Peritoneal dialysis	No anticoagulation required, continuous dialysis technically simple, minimal cardiovascular stress	Slow removal of fluid and toxins, needs intact peritoneum, peritonitis, diaphragmatic splinting
Haemodialysis	Great efficiency in removal of toxins and fluid	intermittent, unphysiological, anticoagulation staff and equipment intensive
Transplantation	Physiological, The least expensive	Immunosuppressive treatment, high risk of infection



Screening of kidney transplant

- Educate patient regarding cadaveric and live donation
- Take family and social history and screen for potential donors
- Review ABO compatibility of potential donors
- Tissue type and crossmatch ABO compatible potential donors
- Choose potential donor with patient and family
- Educate donor regarding process of evaluation and donation

Evaluation of donor evaluation

- Complete history and physical examination
- Comprehensive lab screening to include
 - complete blood count
 - urea-electrolyte,
 - Serology (HIV, Hepatitis B, Hepatitis C,CMV)

- GTT, urinalysis, urine culture, pregnancy test
- 24h urine collection for protein,
- Creatinine clearance
- Chest X-ray, ECG, stress ECG
- Kidney ultrasound
- Renal angiogram
- Repeat cross match before transplantation

Exclusion criteria for live-related donors

- Age <18yr or >65-70yr
- Hypertension (>140/90mm Hg, on medication)
- Diabetes
- Proteinuria(>250mg/24)
- History of recurrent kidney stones
- GFR<80ml/min

- Microscopic haematuria,
- urologic abnormalities
- Significant medical illness
- Obesity (30% above ideal weight)
- History of thrombosis or thromboembolism
- Psychiatric contraindications
- Strong family history of renal disease, diabetes, and hypertension