

HIV and renal disorders

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Abstract

Despite advances in HIV medicine it is widely acknowledged that people living with HIV (PLWH) are at particular risk of renal problems although the pattern of disease has changed significantly over time. Renal disease, also known as kidney disease or nephropathy, is currently one of the most common non-infectious comorbidities seen among PLWH. It is vital that health care professionals are aware of this risk in order to facilitate early detection, assessment

and monitoring of the condition. A range of interventions are available to minimise further deterioration and to treat end-stage renal disease. There is a clear role for nurses working in the field of HIV alongside multidisciplinary colleagues in the provision of evidence-based screening and care for those affected, in order to improve clinical outcomes and quality of life.

Key words: renal disease, HIV, assessment, monitoring, treatment

Introduction

Renal disease was recognised as a complication of HIV infection soon after the disease itself was identified in the early 1980s. As the natural history of HIV infection evolves, and with the ageing cohort (plus increased exposure to potentially nephrotoxic medications), prevalence of other non-infectious comorbidities, such as diabetes and cardiovascular disease (CVD), renal disease in people living with HIV (PLWH) is also increasing and growing in importance. Renal disorders can occur at all stages of HIV infection. They range from acute kidney injury (AKI) and fluid and electrolyte imbalance to end-stage renal disease (ESRD). HIV-associated nephropathy (HIVAN) is the most common form of kidney disease amongst PLWH [1] and is still prevalent despite the success of contemporary antiretroviral therapy (ART). Given that renal impairment is associated with increased rates of morbidity and mortality, early detection and effective management of associated risk factors may help to limit overall disease burden.

This CPD article summarises normal kidney structure and function, discusses risk factors, causes and symptoms of renal disease, outlines acute renal failure (ARF) and then focuses on chronic kidney disease (CKD) and the pathogenesis and treatment of HIV-related renal disorders.

A. Revalidation

This article has been prepared with continuing professional development (CPD) in mind and can be used to support your revalidation. It is estimated that 4 hours of CPD activity will be required for completion of the reading, 'Time out' activities, the quiz and writing a reflective account in relation to your learning and its applicability to your practice. (You could test your knowledge by completing the self-assessment

quiz before reading the article, returning to it afterwards to see how much you have learned.)

B. Aims and intended learning outcomes

This article aims to increase knowledge and confidence. On completion of reading, undertaking the included activities and self-assessment quiz you should be able to:

- Describe the structure and function of the healthy kidney;
- List a range of investigations used to determine renal function and show an understanding of some of their advantages and limitations;
- Describe a number of risk factors for renal disease;
- List a range of common symptoms of renal dysfunction;
- Describe the staging system for CKD;
- Outline the most common renal disorders found in PLWH and explain some possible underlying HIV-related risk factors;
- Give the rationale for regular monitoring of renal function in PLWH;
- Summarise a variety of treatment options available to those with renal disease and how these apply to PLWH in the era of successful ART.

C. Kidney anatomy and renal function: a summary

The kidneys are located at the rear of the abdominal cavity in the retroperitoneal space. A normal, healthy kidney is bean-shaped and about 10–13 cm long, and 5.0–7.5 cm wide in the average adult with the left kidney being usually slightly larger than the right.

The main body of the kidney is divided into two major structures; the outer renal cortex and the inner medulla. These structures are divided into

cone-shaped segments and contain the renal cortex and surround a portion of the medulla (called the renal pyramid). Between the renal pyramids are projections of cortex called renal columns. Nephrons span both the cortex and medulla. The initial section of a nephron acts as a filter and flows into the renal corpuscle and this is followed by a renal tubule.

The tip of each renal pyramid empties urine into a minor calyx then on to the major calyces and ultimately into the renal pelvis, which in turn becomes the ureter. The left and right renal arteries supply the circulation directly from the abdominal aorta. Despite their relatively small size, the kidneys are very well perfused, receiving approximately 20% of cardiac output.

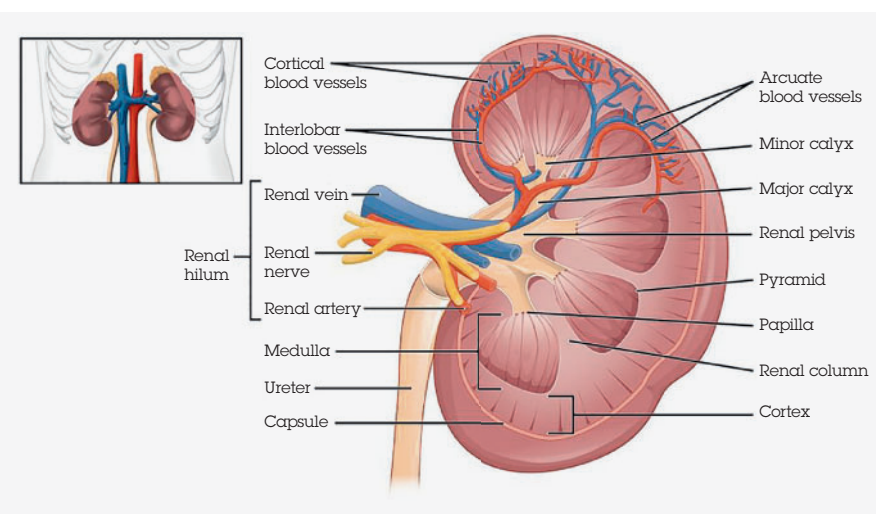


Figure 1: Cross-section showing the structure of a healthy kidney

The glomerulus is a network of capillaries located at the beginning of a nephron. It is surrounded by a sac known as the Bowman's capsule. A glomerulus and its surrounding Bowman's capsule provide the basic filtration unit for plasma. The rate at which blood is filtered through all of these glomeruli is the glomerular filtration rate (GFR) and, therefore, provides a robust marker of overall renal function.

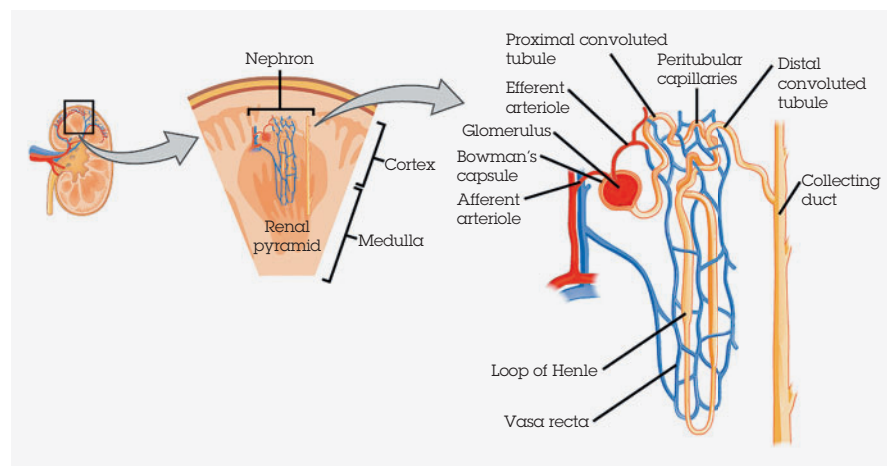


Figure 2: Structure of the glomerulus

Time out activity 1

Before reading on consider how much you can recall about the function of the kidney? Make brief notes on the role of this vital organ then compare them to the summary provided.

The kidneys have several vital functions, which are largely achieved through the mechanisms of filtration, re-absorption, secretion and excretion:

- Excretion of waste products such as urea and uric acid
- The regulation of fluid balance and blood pressure
 - Maintaining osmolarity, i.e. the regulation of water and salts
 - Acid/base homeostasis, i.e. the stabilisation of pH
 - The re-absorption of vital nutrients such as glucose and amino acids
 - The production of enzymes and hormones such as calcitriol, erythropoietin and renin

D. Assessing renal function

Renal function is an indication of the state of the kidney and its efficacy as previously stated. The glomerular filtration rate (GFR) describes the flow rate of filtered fluid through the kidney. Creatinine clearance rate (CrCl) is the volume of blood plasma that is cleared of the waste product creatinine over time and is a measure for estimating the GFR. There is a range of different equations for assessing renal function with most taking into account the individual's age, weight gender and race.

I. Urinalysis

Nurses are familiar with performing these quick and informative tests. Box 1 summarises the key findings in relation to renal function specifically. Note that the urine dipstick analysis primarily detects albumin (rather than all proteins), useful as a marker of glomerular disease but this is inadequate in the detection of renal tubular disease.

Box 1. Dipstick urinalysis: key findings in relation to renal disorders**Visual appearance**

Colourless urine may indicate nephritis.

Haematuria may be visible and can indicate a urinary tract infection, renal trauma, glomerulonephritis, nephrolithiasis or malignancy.

Dark urine often indicates dehydration.

Specific gravity (SG)

Hydrated patients will have an SG <1.010 whereas an SG >1.020 indicates dehydration.

pH

This should range from 5–7, i.e. it is normally acidic, except after a meal.

Glucose

The presence of glucose in urine may indicate a renal tubular disorder.

Proteinuria

The presence of protein in the urine may be caused by a glomerular leak.

NICE guidance [2] highlights the importance of proteinuria as a marker for chronic kidney disease, which may be as significant as glomerular filtration rate (GFR).

Leukocytes

This relies on the reaction of leukocyte esterase produced by neutrophils and a positive result suggests urinary tract infection.

Nitrates

Many Gram-negative and some Gram-positive bacteria are capable of producing this reaction and a positive test suggests their presence in significant numbers.

On microscopy

Acute glomerulonephritis will show cells and casts but chronic glomerulonephritis often shows little sediment.

Source: adapted from Simerville *et al.* [3]

Time out activity 2

Go to the following webpage and read a little about the invention and history of dry reagent urinalysis in the 1950s: www.acs.org/content/acs/en/education/whatischemistry/landmarks/diagnosticteststrips.html

II. Creatinine clearance

Creatinine is produced by the muscles at a relatively constant level and plasma concentration therefore depends on the rate of excretion by the kidneys. This can be used as a measurement of GFR. A blood

sample to measure plasma creatinine is taken alongside a timed urine collection (usually over 24 hours) and both are used to calculate creatinine clearance.

III. Blood urea nitrogen

A blood urea nitrogen (BUN) result is often given alongside the creatinine result and the ratio calculated. These tests are, however, rather limited by their time-consuming nature, problems with accurate urine collection (a single 'missed catch' makes the test inaccurate) and also because they tend to overestimate the filtration rate. In addition levels are affected by age, gender, ethnic group, muscle bulk, ingestion of cooked meat, malnutrition and some drugs, for example, the antibiotic trimethoprim. As a result these only provide a rough guide to renal function.

IV. Estimated GFR

GFR varies as a function of normal physiology as well as in the presence of disease. Its measurement is based on determining the volume of plasma from which a substance is cleared by the glomerulus during its passage through the kidney.

For all serum creatinine requests, laboratories should report an estimated GFR (eGFR) using a prediction equation, in addition to reporting the serum creatinine result. An eGFR is currently the most frequently used test of renal function and is recommended by NICE [2]. Different equations exist to calculate this and accuracy can vary. The most recently advocated formula was developed by the Modification of Diet in Renal Disease (MDRD) Study Group [4] and most laboratories in the UK now use this. The '4-variable MDRD formula', estimates GFR using serum creatinine, age, ethnicity and gender. This makes necessary adjustments for the elderly, for people of African-Caribbean or African ethnic origin and children. Adjustment is also required for those with unusual body mass. Note that it can underestimate the GFR in healthy individuals and that it also assumes that the creatinine levels are stable over several days. It is not a valid test if levels are fluctuating.

Nurses should advise people not to eat any meat in the 12 hours before having a blood test for eGFR creatinine. It is also important to avoid delays in transporting blood samples to the laboratory to ensure that they are processed within 12 hours of venepuncture [4].

V. Cystatin C

Given the potential inaccuracy of creatinine level measurement, more accurate measurements have been sought. Cystatin C is a protein secreted by most cells and filtered at the glomerulus. After filtration, cystatin C is reabsorbed by the tubular cells. As only

small amounts are excreted in the urine, cystatin C levels are measured by blood tests and are used, in addition to other measurements, at initial diagnosis, to confirm or rule out CKD in people with certain comorbidities such as diabetes.

VI. Albumin/creatinine ratio

Most routinely used reagent strips are not capable of specifically measuring albumin at low concentrations and are, therefore, unreliable for identifying proteinuria. NICE [2] recommends that to detect and identify proteinuria, a urine albumin/creatinine ratio (ACR) test should be used. This is also in preference to protein/creatinine ratio (PCR), because it has greater sensitivity for low levels of proteinuria, especially in people with diabetes. The higher the ACR level the increased likelihood of and severity of disease. An early-morning urine sample is required.

VII. Inulin GFR

This is the gold standard for measurement but it is a complex procedure used only when a more accurate result is vital. Isotopic GFR is also sometimes performed using radioactive isotopes.

E. Causes of renal dysfunction

Many nephrologists categorise the causes of kidney injury based upon whether they are 'pre-renal' (primarily due to circulatory volume depletion or reduced blood supply to the kidneys), 'intrinsic renal' (when there is inflammation, damage or death of cells, as with glomerular or tubulo-interstitial damage), or 'post-renal' (largely due to an obstruction of the urinary tract). However, there can be some overlap because renal functions can be interdependent. Box 2 illustrates factors influencing deteriorating renal function and disease.

Box 2. Factors influencing deteriorating renal function and disease

- Older age
- Diabetes
- Hypertension, atherosclerosis and circulatory disease
- Genetic and ethnicity related factors
- Smoking and recreational drug use (e.g. ketamine, heroin, steroids)
- Pharmacological toxicity (e.g. long-term exposure to non-steroidal anti-inflammatory drugs [NSAIDs], lithium and some chemotherapy agents) and some herbal preparations, e.g. yohimbe
- Trauma, renal stones, polycystic kidney disease
- Severe dehydration
- Immune system diseases (e.g. lupus)
- Dietary protein toxicity
- Viral infections and bacterial infections

F. Acute kidney injury

Acute kidney injury (AKI) refers to a decline in kidney function that develops rapidly over a few days, and which, if left untreated, may be life-threatening. Subsequent damage to other organ systems is common. Acute kidney injury may be a result of drug exposure or poisoning causing acute tubular necrosis (ATN); or a severe allergic reaction causing acute interstitial nephritis (AIN). The glomerulus can also become inflamed due to infections or the immune system's response (glomerulonephritis). Viral infections such as cytomegalovirus, Epstein–Barr, influenza, adenovirus and parvovirus are able to trigger or support an acute post-infectious glomerulonephritis [5]. Bacterial infections such as staphylococcus and salmonella are also potential causes. Secondary glomerulonephritis can occur with malignant tumours and in hepatitis (B and C) infection. Half of all cases present with intermittent haematuria. IgA nephropathy (IgAN), also known as Berger's disease, is the most common glomerulonephritis seen worldwide [6].

G. Chronic kidney disease

Chronic kidney disease (CKD) describes abnormal kidney function and/or structure over a period of >3 months with implications for overall health. It is common, often unrecognised and may co-exist alongside other conditions such as CVD and diabetes. Moderate to severe CKD is associated with an increased risk of other significant adverse outcomes such as acute kidney injury, frailty and falls, especially in older people, and mortality. CKD can progress to ESRD in a small but significant percentage of people [2].

As a result of minor or the absence of symptoms in the early stages, the condition is often not diagnosed until late in the progression of the disease. When symptoms do occur they are similar to those in acute kidney disease as listed in Box 4. Timely treatment can prevent or delay the progression of CKD, reduce or prevent the development of complications, and reduce the risk of CVD.

The classification of CKD has changed over time and is described today in five categories as shown in Box 3. The stages of CKD are largely based on eGFR. Kidney function is normal in stage 1, and only minimally reduced in stage 2. The aim at stages 1–3 is to identify individuals at risk of progressive disease through close monitoring, and to reduce any associated risks such as CVD and bone disease.

Box 3. Categorisation of CKD

Disease stage	eGFR level (mL/min/1.73 m ²)	Description	Treatment
1	90+	Normal kidney function but <i>must have</i> either microalbuminuria, proteinuria, haematuria or structural abnormalities of kidneys	Observation, control of blood pressure
2	60–89	Mildly reduced kidney function, but <i>must have</i> either microalbuminuria, proteinuria, haematuria or structural abnormalities of kidneys	Observation/annual monitoring, control of blood pressure and assessment of other risk factors
3A	45–59	Moderately reduced kidney function with or without evidence of kidney damage	Observation (6–12 monthly), control of blood pressure and other risk factors, medication review, consider imaging and immunisations
3B	30–44	Moderately reduced kidney function with or without evidence of kidney damage	Observation (6–12 monthly), control of blood pressure and risk factors as for 3A
4	15–29	Severely reduced kidney function	3-monthly reviews, investigations for sepsis, heart failure etc., management of related anaemia, osteoporosis, acidosis etc., referral to specialist service, planning for end-stage renal failure
5	<15	Very severe, or end-stage kidney failure	Discussion and decision of treatment choice e.g. haemodialysis, peritoneal dialysis, transplant or conservative management

eGFR: estimated glomerular filtration rate.

Source: adapted from the Renal Association [7]

H. Symptoms of renal insufficiency

Symptoms of a slow decline in renal function can be missed initially because they are often non-specific, even asymptomatic or can resemble those of several other underlying disorders. Symptoms that do occur can be varied as shown in Box 4.

Box 4. Symptoms of renal disease

- Fatigue, insomnia and/or drowsiness
- Reduced appetite
- Hypertension
- Nausea and vomiting
- Headache
- Difficulty concentrating
- Pruritis
- Periorbital and/or ankle oedema
- Changes in urination habit especially reduced urine output
- Darkening skin colour
- Muscle cramps and paraesthesia

I. HIV and renal disease

Rates of HIV-induced and specific kidney disease have remained stable in recent years following an initial decrease in the mid-1990s attributed to successful ART, however non-HIV-related kidney disease in patients with HIV has not declined. This is probably due to an ageing HIV-positive population, many of who have diabetes and hypertension [8]. Immunodeficiency, viral replication, immune-reconstitution, HIV-associated neuropathy (HIVAN) and other inflammatory processes associated with the infection itself probably all play a part in enhancing the risk of renal disease in PLWH. Comorbidities such

as hypertension, diabetes, co-infection with hepatitis C (HCV), and other factors such as the ageing process, a family history of renal disease, cigarette smoking, obesity, extensive prior use of nephrotoxic medications such as NSAIDs and cocaine use, which has been linked to hypertensive renal changes in patients with HIV infection [9], also contribute to risk.

Renal manifestations of PLWH are common and also diverse. Some are related directly to HIV infection; others are linked, for example to antiretroviral (ARV) use, or unrelated. The most common glomerular disease in PLWH is HIVAN. This is typically seen in individuals of black African descent, with advanced immunodeficiency and detectable viral load [10], and will be discussed in more detail later. A variety of other glomerular diseases occur less commonly and acute kidney injury (AKI) is also seen, possibly related to drug effects. The incidence of AKI in PLWH is increased compared with people without the virus, although, incidence is decreasing in the era of ART [11].

Time out activity 3

Look for and compare incidence data from Western and developed countries, in particular the UK. Identify at least three reasons for the differing prevalence of renal disease in PLWH across world regions?

Fanconi syndrome can also be an acquired disorder in PLWH. Multiple defects in renal proximal tubular reabsorption occur. Symptoms include osteomalacia and muscle weakness. Diagnosis is made on identification of glucose, phosphates and amino acids in the urine. HIV immune complex disease (HIVICK) is an immune complex attack on the kidney that leads

to a variety of glomerular lesions. Unsuppressed viral activity is necessary for this to occur. Furthermore, HIV disease does not preclude the occurrence of other causes of kidney disease. Diabetic nephropathy and other vascular and metabolic effects on the kidneys for example, have been documented in PLWH [12]. Chronic kidney disease can be caused by diabetes and/or hypertension and also increases risk of CVD.

J. HIV medications and renal toxicity

The association between some ARVs used in the treatment of HIV infection and CKD is a controversial topic. Most HIV medications are well tolerated, even in the presence of renal insufficiency and data suggest that kidney function improves following commencement of ART [13]; however, some studies indicate a potential for drug induced renal toxicity. The British HIV Association (BHIVA) states that most ARVs have the potential to cause renal injury with tenofovir disoproxil fumarate (TDF) most frequently associated and implicated [13]. A recent study [14] investigated the association between duration of exposure to ARVs and the development of CKD in people with initially normal renal function. The annual incidence of CKD increased for up to 6 years of exposure to the following drugs: TDF, ritonavir-boosted atazanavir and ritonavir-boosted lopinavir therapy. The authors concluded that treatment with these particular medications might result in an increasing and cumulative risk of renal disease; however, additional factors such as low BMI and older age also play a part [13].

The aminoglycoside antibiotics, acyclovir, foscarnet, amphotericin, long-term use of NSAIDs, trimethoprim and rifampin, among others, have also been associated with deterioration in renal function [15]. As a result PLWH who are taking these potentially nephrotoxic medications and/or those at high risk of CKD, should be closely monitored [1]. Early detection and discontinuation of TDF, for example, usually leads to improvement of renal abnormalities with a recent study finding that people who switched to tenofovir alafenamide (TAF) from TDF experienced significant improvements in kidney function [16].

As yet there are no conclusive data with which to inform ART decisions in individuals with known CKD; however, BHIVA guidelines [13] recommend avoiding using ARV drugs that are potentially nephrotoxic in individuals with known stages 3–5 CKD, assuming that sufficiently potent alternative ARV agents are available. In addition, BHIVA recommends that dose adjustments of renally cleared ARV drugs are required in individuals with reduced renal function.

K. HIV immune complex kidney disease

There is some debate over how to define HIV immune complex kidney disease (HIVICK) but most agree there must be immune complex deposition in the glomeruli in varying patterns, together with interstitial infiltration [17]. An immune response scenario happens whereby a secondary inflammatory response occurs. Complexes of antibodies and HIV antigens become lodged in the kidneys, potentially leading to permanent injury unless diagnosed early. Even after initiating ART and resolution of viraemia, the lesions can leave 'holes' in the glomeruli. HIVICK is typically associated with concurrent infections such as hepatitis C and genetic variants do not appear to be associated with risk [18].

In those with HIVICK, without signs of HIVAN, there is currently very little evidence-based guidance on management but ART, ACE inhibitors, blood pressure control, statins and occasionally steroids are used.

L. HIV-associated nephropathy

HIV-associated nephropathy (HIVAN) was previously known as 'AIDS-associated nephropathy'. Although the clinical features of HIVAN are well defined, the true prevalence of this disease is not known because, in practice, kidney biopsies are performed relatively infrequently [8]. Without ART, HIVAN leads to rapid progression of renal dysfunction and ESRD; however, with prompt diagnosis and where ART is widely accessible and timely, a decline in incidence has been seen and the trend is towards delayed disease progression. Box 5 provides a summary of typical investigatory findings for a HIVAN diagnosis.

Box 5. HIVAN characteristics

- Significant levels of proteinuria, also micro-haematuria, leukocytes, hyaline casts on urinalysis
- Azotaemia (an abnormal increase in concentration of urea and other nitrogenous substances in the blood plasma)
- Electrolyte abnormalities on serum chemistry, e.g. hyponatraemia and hyperkalaemia
- Enlarged kidneys on ultrasound and described as 'highly echogenic'
- Normal renal blood pressure
- Renal biopsy is essential for ruling out other renal disorders and findings include:
 - Focal segmental glomerulosclerosis (FSGS), (that is a hardening and scarring of the glomeruli), Figure 3
 - Collapsing glomeruli capillaries
 - Degeneration of tubular cells

Source: adapted from Choi and Rodriguez [1]

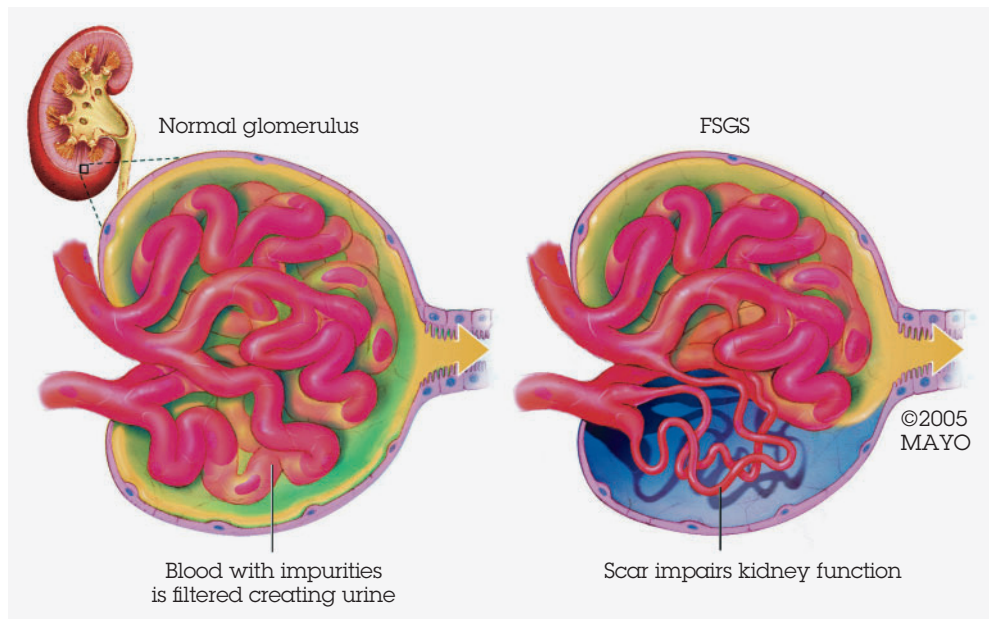


Figure 3: A normal glomerulus alongside glomerulus affected by FSGS that is typical of HIVAN. Used with permission of Mayo Foundation for Medical Education and Research. All rights reserved.

It is widely acknowledged that interaction of genetic factors between the host, in this case the PLWH, and pathogens, influences every aspect of HIV infection from initial acquisition through to the development of ARV drug resistance and the immune response as well as influencing specific organ disease [19]. HIVAN has been found to have the strongest association with black populations but seems to be very rare in the Asian population. HIVAN is still a predominant cause of renal disease in countries with limited resources, for example in sub-Saharan Africa [12]. Numbers of individuals with black African ancestry, often with advanced immunodeficiency and detectable viral loads plus restricted access to ART are all contributing factors. In the US most patients with HIVAN are young black men, and approximately 50% of patients with HIVAN are intravenous drug users. Overall, HIVAN is observed more often in men than in women, with a male-to-female ratio of 10:1 [19].

The severity of any clinical symptoms such as oedema, tiredness, reduced performance, susceptibility to infections, hyperlipidaemia, anaemia, metabolic acidosis, venous thrombosis and hypertension all depend on the duration and intensity of the renal insufficiency. Many of these signs do not occur until the later stages of the disease.

M. Acute interstitial nephritis

Acute interstitial nephritis (AIN) is most frequently caused by one of three categories. It is most commonly

drug induced, alternatively it can be associated with infections such as bacterial pyelonephritis, opportunistic infections (OIs) in PLWH; with neoplastic disease or other immune disorders such as lupus. The list of drugs implicated in causing AIN continues to expand and includes cephalosporins and penicillins, NSAIDs, ranitidine and acyclovir. Development of drug-induced AIN is not dose related and may only become evident ≥ 2 weeks or after starting a new medication [20].

Individuals typically present with non-specific symptoms of acute renal failure as described in Box 4. The clinical presentation can range from asymptomatic (in two-thirds of people) to a high fever, severe rash and flank pain. A relatively rapid decrease in renal function is typical. A raised white cell count (eosinophils in particular) is common and abnormal urinary sediment is often found on urinalysis. It also is important to note that AIN from NSAIDs almost always causes proteinuria, while renal biopsy findings may be inconclusive [21].

N. Assessing and monitoring renal function in HIV

An awareness of the recommended frequency and the rationale for renal function investigations is useful. The list in Box 6 provides a summary of key recommendations and is adapted from the BHIVA guidelines (2016) for the routine investigation and monitoring of adult HIV-1-positive individuals [22].

Box 6. Summary of key recommendations for assessing and monitoring renal function

- Assessment of renal function, (eGFR), and urinalysis (looking specifically for protein, blood and glucose) should be performed *at the point of ART commencement and annually thereafter for those on HAART or for those not on treatment but with CD4 counts >500 cells/mm³.*
- If urine dipstick is 1 positive for protein then a protein/creatinine ratio test should be carried out.
- Renal function in *individuals on TDF* should be monitored more closely by assessing eGFR, serum phosphate and urinalysis *at each clinic visit.*
- For those with *known CKD* NICE guidelines [2] for the general population suggest *6–12 monthly monitoring* of renal function. BHIVA states that this frequency of monitoring is also appropriate for most PLWH with concurrent CKD.
- For those with known CKD annual blood pressure, lipid profile, BMI, smoking status and a review of antiretroviral therapy and other medications is recommended.
- Kidney transplant recipients should be reviewed at 6–12-monthly intervals with monitoring of renal function and CD4 cell count.
- Monitoring and risk-reduction strategies should be conducted in partnership with GPs and renal physicians to avoid replication.
- Blood pressure monitoring. Note that the target blood pressure for patients with known CKD should be <140/90 mmHg (<130/80 mmHg if proteinuria is present).

Source: BHIVA [22]

Time out activity 4

If you don't already know find out if your clinic area uses a clinical pathway or policy for the monitoring of renal function in your caseload? How closely are the BHIVA guidelines followed and has this aspect of care been audited?

O. Treatment options



Figure 4: Summary of key interventions used in the management of renal disease for PLWH.

- I. Timely antiretroviral therapy: there are currently insufficient data to suggest that PLWH with, or deemed at risk of CKD, will benefit specifically from earlier ART initiation however BHIVA do recommend those diagnosed with HIVAN start ART immediately, irrespective of CD4 cell count. Individuals with ESRD who are suitable candidates for renal transplantation should start ART immediately [13].
- II. Lifestyle measures: smoking and recreational drug-use cessation, management of obesity and dyslipidaemia, for example, are modifiable risk factors and advice is as per the general population.
- III. Dietary modifications: may be advised by a specialist dietitian. Low-protein diets, which decrease catabolism, may be beneficial and are adjusted depending on eGFR and nutritional status. A limit on sodium, potassium and phosphorus is often advised but fluid restriction is not warranted unless renal failure occurs [23].
- IV. Medical management: of diabetes, hypertension, hepatitis, bone mineral density etc. is important.
- V. Treatment with angiotensin-converting enzyme inhibitor or angiotensin-receptors (ACE inhibitors): can be valuable. The renin-angiotensin system blockade reduces proteinuria and can slow progression of CKD independent of blood pressure lowering [24].
- VI. Corticosteroids: use can be beneficial [25], particularly in nephropathy caused by immune response/IgA deposition mentioned earlier.
- VII. ARV: regimens should be evaluated and renal dose adjustments made according to renal function [13].
- VIII. Switch ARVs: away from nephrotoxic choices where possible [13].
- IX. Haemodialysis: commonly 3–4 sessions per week are required, via a catheter inserted into a major vein or an arterio-venous fistula or graft. Fluid intake and dietary restrictions i.e. a reduction in foods high in potassium, phosphate and sodium, are usual.
- X. Peritoneal dialysis: the process uses the peritoneum to filter the blood via a catheter inserted through the abdominal wall, exchanging used dialysis solution 4–6 times a day or during the night. 'Continuous ambulatory peritoneal dialysis' does not require a machine, alternatively 'automated peritoneal dialysis' uses a machine called a cycler to perform fluid exchanges during the night, with an additional day-long exchange.

Both dialysis processes are evidently time consuming, restrictive and cumbersome. The potential for a negative impact on lifestyle, work and body image for individuals can be very significant.

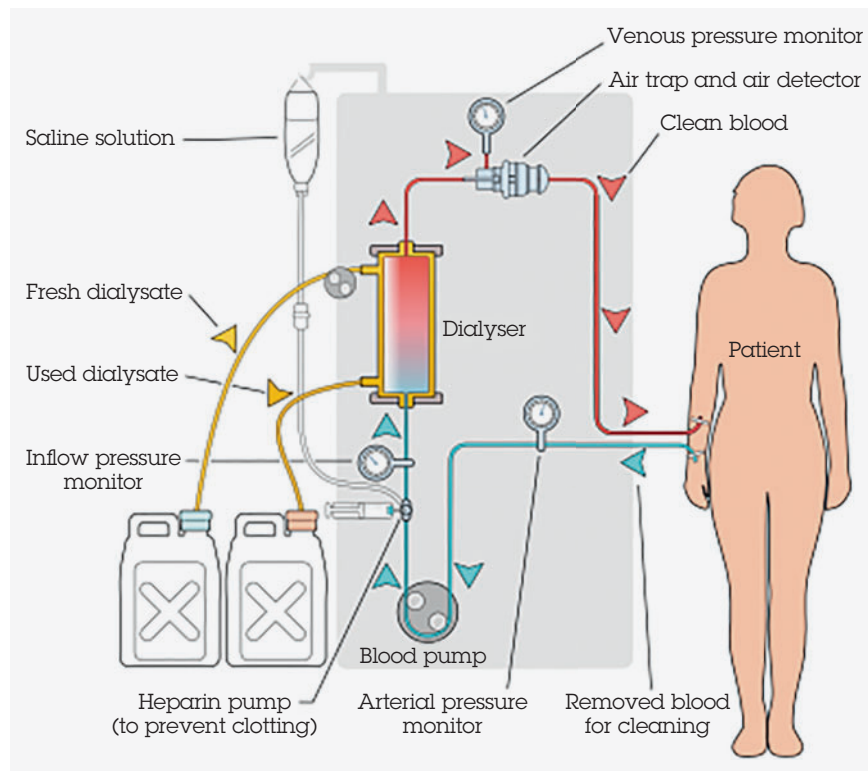


Figure 5: Illustration of the process of haemodialysis

Time out activity 5

Go to the following website and search under 'Health/Kidney Information' topics. Spend 10 minutes reading more about peritoneal and haemodialysis on this informative website.

<https://www.kidneyresearchuk.org/health-information/continuous-ambulatory-peritoneal-dialysis>

P. Kidney transplant

End stage renal disease and dialysis both increase the risk of CVD and death in both the general and HIV-positive populations but for the latter, until recently, HIV infection was seen as an absolute contraindication to solid organ transplantation [26]. The main concern appeared to be that the required anti-rejection therapy could speed up HIV disease progression. Since the end of the 1990s, however, with the success of ART and improved life expectancy, transplantation as an option for PLWH has increased. Excellent outcomes have occurred in those with suppressed viral loads and CD4 cell counts >200 cells/mm³ [13].

During the last decade the results of many studies have shown that transplantation can be safe and effective as long as viraemia is suppressed. One study looked at the risk of graft-loss and death and compared data for those with HIV-positive and -negative patients. Short- and mid-term survival rates, for both the graft and the PLWH as a transplant recipient, were found to be comparable with those of the transplant population as a whole. HIV was not associated with an increased risk of death after kidney

transplant; however, the incidence of acute rejection episodes was higher [27]. Another study from 2010 found that, reassuringly overall, transplant did not complicate HIV disease management. The incidence of rejection was again found to be greater in PLWH but many responded to steroid therapy [28]. It appears that the challenges of achieving therapeutic and non-toxic levels of immunosuppressive drugs alongside ART contributes significantly to higher organ rejection rates [28]. The British Transplantation Society advises that the most appropriate antiretroviral therapy is determined before transplantation, in order to anticipate potential drug interactions and appropriate dosing of medication [29]. There are criteria specific to PLWH in respect of eligibility for kidney transplant. PLWH are only put on the waiting list if:

- They are concordant with treatment, particularly ART;
- They have a CD4 T cell count >100 cells/mm³ (ideally >200 cells/mm³) and stable during the previous 3 months;
- Their HIV RNA has been undetectable during the previous 6 months;
- They have had no opportunistic infections during the previous 6 months; and
- They have no history of progressive multifocal leucoencephalopathy, chronic intestinal cryptosporidiosis, or lymphoma.

Source: British Transplantation Society guide [29]

Furthermore, and very recently, the suitability of organ donation from HIV-positive donors to PLWH has also been explored. An editorial for the *New England Journal of Medicine* discussed recent study findings

and stated that these 'go a long way to allaying fears about the safety of using organs from deceased HIV-positive donors in HIV-positive recipients' [30]. The authors conclude: 'these transplantations now appear to be not only feasible but also, in fact, desirable for many patients'.

Q. The nurse's role

As always high-quality nursing care requires vigilance. Recognition of the risk of renal disease in PLWH and an awareness of the signs and symptoms will enable early diagnosis and early intervention, which can help to prevent progression of the condition. Nurses have the clinical knowledge, the communication skills and a holistic overview of the individuals in their care and are, therefore, well placed to assess clinical risks and deliver a range of interventions.

In addition to ensuring that robust clinical monitoring is carried out as per Box 6 other suggested nursing interventions are outlined below, with some points informed by NICE guidelines [2]:

- The provision of education and information to patients – especially for those with long-term renal disease. This needs to be tailored to the severity and cause, the associated complications and the risk of progression.
- Any education should also take account of the psychological aspects of coping with the condition and offer access to appropriate support, for example, support groups (such as those listed at the end of this article), counselling or referral to a specialist nurse.
- Encourage and facilitate behaviour change to modify lifestyle and so reduce risk of progression, e.g. to take exercise, adjust diet, achieve a healthy body weight and stop smoking.
- With guidance from a dietician, offer dietary advice about potassium, phosphate, protein calorie and salt intake appropriate to the severity of disease.
- Enable shared decision-making, act as a patient advocate where needed and support self-management.
- Provide appropriate medical data and suggestions for documenting this so patients can maintain a record (including their test results, treatments and correspondence) to assist self-management.

Time out activity 6

Go to <https://www.patientview.org/#/> and explore the website for one such self-management record system called 'Renal Patient View'.

Consider if this could be viable to use in your clinical setting for PLWH and renal dysfunction?

R. Conclusion

As this article has demonstrated, despite advances in HIV medicine, nurses among other healthcare professionals need to remain alert to the risk of renal disease in PLWH. Robust processes, embedded in routine clinical practice will result in early detection and timely intervention with reduced risk of deterioration in renal function and subsequent associated risks. Furthermore, educating patients about this particular condition, its causes and symptoms and supporting appropriate modification of relevant lifestyle factors is an important aspect of the nurse's role.

S. Useful resources

NHS Choices: Living with chronic kidney disease. Available at: www.nhs.uk/Conditions/Kidney-disease-chronic/Pages/living-with.aspx

Kidney Care UK: Available at: www.kidneycareuk.org/

Kidney Patient Guide. Available at: www.kidney-patientguide.org.uk/contents.php

Kidney patients UK. Available at: www.kidney.org.uk/

Health talk.org. Available at: www.healthtalk.org/kidney-health

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