



The RPSG

The Renal Patient Support Group

Proteinuria

Proteinuria



The presence of variable and persistent amounts of proteins in the urine and a sign of renal damage.



Proteinuria and eGFR are a base of CKD evaluation.



Proteinuria identifies recipients whom are at high risk of progressive renal damage and increased morbidity.



The presence of protein in urine is a strong indicator that a recipient is likely to experience progressive renal function decline.



The association of proteinuria and eGFR improves the capacity of prediction of CV and CKD.



Proteinuria is a marker of renal outcome, independent of other risk factors.

Proteinuria Physiology

The glomerulus produces the primary urine by filtering blood and retains larger proteins including serum albumin.

Proteins with a molecular weight below 60kd pass freely through the glomerular basement membrane and are actively reabsorbed within the tubular system.

The renal tubule reabsorbs proteins and some of albumin that passes freely through the glomerulus.

40-80mg of proteins is excreted per day, 30-40% of them are albumin

Universal value for proteinuria does not exist, other factors such as kind of specimen and the age need to be considered.

Albuminuria

An urinary albumin excretion rate of less than 30mg per day is considered as normal.

Albuminuria is defined as the elimination of urinary albumin excretion above 30mg per 24h.

Urinary albumin excretion in a continuous variable and the lower values the better.

In case of levels higher than 300mg/g or 300mg/d, the term is proteinuria.

Albuminuria is a sensitive marker for the detection of incipient nephropathy.

Proteinuria Classification

Urine protein concentration can be the result of different mechanisms

Type of Proteinuria	Characterisation
Prerenal	<ul style="list-style-type: none">- Caused by overproduction- Observed in haemoglobinuria rhabdomyolysis, myelomonocytic leukaemia, and myeloma
Glomerular	<ul style="list-style-type: none">- Caused by modifications of the electronic glomerular base membrane,- Disturbance of the filtration barrier- Observed in glomerulonephritis, infections, systemic erythematous lupus, diabetes, hypertension, neoplasia, congenital disease
Tubular	<ul style="list-style-type: none">- Decreased reabsorption of the proteins usually filtered by the glomerulus,- Small proteins appear in the urine- Observed in congenital or systemic diseases, and in cases of toxicity caused by drugs and toxins
Postrenal	<ul style="list-style-type: none">- Consequence of inflammatory, infectious, or haemorrhage processes,- epithelial tubular cells add proteins to the tubular fluid and affects lower urinary tract
Orthostatic	<ul style="list-style-type: none">- Caused by supine position and it is caused by hemodynamic glomerular alterations

Proteinuria and Diagnostics

Screening method

Dipstick for the screening of proteins

Dipstick for the screening of albumin

Quantitative methods

Quantitative methods to measure proteins

Quantitative methods to measure albumin

24-hour urine collections

24-HR Collections

- Inconvenient for recipients, but historically are helpful
- Helpful in recipients with tubular proteinuria or follow-up of recipients with glomerular diseases.



Screening Methods

Dipstick for the screening of proteins	Dipstick for screening of albumin
<ul style="list-style-type: none">• It is a cellulose surface with bromotetraphenol at pH 3.0 produces a colour change in contact with proteins. The colour varying depending on the protein concentrations.• It is not possible to detect concentration less than 300mg/L.• False negatives are very frequent.• Positive result should be reconfirmed by a quantitative measurement.	<ul style="list-style-type: none">• A cellulose surface impregnated with tetrabromosulfoftalein is able to detect small concentration of albumin (30-40mg/L).

Quantitative Methods for Detection

Quantitative methods to measure proteins	Quantitative methods to measure albumin
<ul style="list-style-type: none">- The protein detection in urine has variability.- The modalities most used are turbidimetric or benzethonium methods.	<ul style="list-style-type: none">- The most usual methods are immunoturbidimetry and nephelometry.- High liquid chromatography can detect nonimmunoreactive albumin.

PCR and/or ACR



K/DOQI guidelines recommend the urinary ACR for diagnosis and follow-up in adults.



When the ACR is high (>500 mg/g), it increase the removal of other proteins than albumin urine (tubular proteinuria)



PARADE Guidelines recommend the implementation of protein/creatinine ratio in children. The kidney disease are often associated with abnormal urinary tract or tubular defects, which are characterised by elimination of small proteins.



ACR is recommended in diagnosis of diabetes mellitus, hypertension, and glomerular disease



Protein/creatinine ratio is used in tubulointerstitial diseases.

Proteinuria and CKD Progression



The presence of proteinuria is an indicator that the recipient has a high probability of renal disease progression, even with normal GFR.



Disease progression and risk of renal damage correlates with degree of proteinuria.



Proteinuria is a modifiable factor, the more it is reduced, the better protection for recipient from disease progression and ESRD.

Evaluation of PCR and/ or ACR

The presence of proteinuria helps identify population at risk for CKD.

In CKD recipients and suspect risk for CKD, albumin and/or protein excretion in urine may/ can help with disease prediction.

ACR may be obtained, to detect presence of non-glomerular proteinuria.

A value of albumin/ creatinine more than 2.5g/mmol in males, more than 3.5 mg/mmol in female, or protein/ creatinine more than 22.6 mg/mmol are indicative of proteinuria.

First-morning urine is adequate for detection because of the less biologic variability and the good correlation with 24-hour albumin/ protein excretion.

Mechanisms for Proteinuria Progression in CKD

Proteinuria can accelerate kidney disease progression, and this process occurs through multiple pathways, including induction of tubular chemokine expression and complement activation that lead to inflammatory cell infiltration

Glomerular sclerosis is the progressive lesion beginning at glomerular capillary wall, the site of abnormal filtration of plasma proteins.

Albuminuria/ proteinuria results from defects in the glomerular filtration barrier.

Overload proteinuria appears as a consequence of increased glomerular permeability enabling glomerular passage of proteins.

Treatment



The use of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, aldosterone antagonists, and renin inhibitors in recipients with proteinuria and CKD has shown beneficial effects on the progression of CKD.



The reduction in proteinuria with drugs (ACEI or ARB) that blocked the RAAS is associated with long-term renal protection.



Due to risk factors, some recipients present response to these therapeutic agents.



Diuretic therapy is/ can be effective in improving the antiproteinuric action on inhibition of RAAS and reduction of proteinuria.



Aliskiren (renin inhibitor) reduces albuminuria.

Orzechowska, K

Coventry University,
England – United Kingdom

The Renal Patient Support Group (RPSG),
England – United Kingdom

Christine, H

The Renal Patient Support Group (RPSG),
England – United Kingdom

The Kidney Disease and Renal Support
(KDARs) for Kids,
England – United Kingdom