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Research Article

Place of Urinary ACR and PCR Ratios in the Investigation of Nephropathies: Epidemiological Profile of a Moroccan Cohort at the Mohammed V Military Teaching Hospital, Rabat

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Abstract

Background: Quantification of proteinuria is central to the management of chronic kidney disease (CKD). The urinary albumin-to-creatinine ratio (ACR) and protein-to-creatinine ratio (PCR), recommended by the KDIGO guidelines, allow their ratio to point towards a glomerular or tubulo-interstitial origin of proteinuria.

Objective: To describe the epidemiological profile of a Moroccan cohort and to evaluate the value of the ACR/PCR ratio in guiding the aetiological work-up.

Methods: Retrospective descriptive and analytical study of 655 adult specimens with simultaneous ACR and PCR determination (June 2023 to June 2026).

Results: Median age was 65 years, with male predominance (sex ratio 1.49). The ACR/PCR ratio discriminated the profiles effectively (ACR area under the curve = 0.87) and increased with CKD severity. Chart review identified glomerular (47.6%), tubulo-interstitial (33.3%) and mixed (19.1%) involvement.

Conclusion: The ACR/PCR ratio is a simple, automatable and non-invasive laboratory tool that helps guide the aetiological work-up of nephropathies.

Keywords: *ACR; PCR; Chronic Kidney Disease; KDIGO; Glomerular Nephropathy; Tubulo-Interstitial Nephropathy*

Highlights

- ACR/PCR ratio discriminates glomerular from tubulo-interstitial proteinuria.
- Largest unselected hospital cohort reported in North Africa (N = 655).
- ACR alone was the best single marker (AUC = 0.87).

- Ratio ≥ 0.40 raised glomerular odds nearly tenfold (OR = 9.86).
- Glomerular profiles increased from 14% (G1) to 55% (G5) of patients.

Introduction

Chronic kidney disease (CKD) is now a major global public health problem, associated with high cardiovascular and all-cause morbidity and mortality and with a considerable socio-economic cost [1]. Worldwide, its prevalence is estimated at approximately 10 to 12% of the adult population, a trend driven by population ageing and the rise of metabolic disorders such as type 2 diabetes and hypertension [2,3]. On the African continent, systematic reviews report equally concerning hospital and community prevalences, particularly in subjects at high metabolic risk [4]. In Morocco, the situation is part of this global context of epidemiological and demographic transition. According to data from the national MAREMAR study (Chronic Kidney Disease in Morocco), the prevalence of CKD is rising critically among hypertensive and diabetic patients [5]; moreover, data from the Moroccan Society of Nephrology and from the Magredial registry (Morocco Transplant Dialysis) confirm that vascular and diabetic nephropathies are the leading causes of end-stage renal disease (ESRD) in the country [6,7].

Within the management strategy, the ACR/PCR ratio on a spot urine sample helps guide the aetiological assessment of the nephropathy: an ACR/PCR ratio ≥ 0.40 indicates a predominance of albumin of glomerular origin, whereas a ratio < 0.40 reflects a substantial proportion of non-albumin proteins, characteristic of tubulo-interstitial involvement (interstitial nephritis, Fanconi syndromes) [8].

Objective of the Study

The main objective of our study was to describe the epidemiological profile of patients followed in nephrology at the Mohammed V Military Teaching Hospital in Rabat, to analyse the laboratory correlation and concordance between the ACR and PCR ratios, and to evaluate the value of this ratio for the rapid aetiological work-up and risk stratification of chronic kidney disease.

Materials and Methods

Study type and population

This was a retrospective descriptive and analytical study of a total of 655 specimens received at the biochemistry laboratory of the Mohammed V Military Teaching Hospital (HMIMV), Rabat.

Data collection and clinical-laboratory correlation

Laboratory data were extracted from the laboratory information system (LIS). To establish the clinical-laboratory correlation, the nephrological diagnosis recorded for each patient was collected through direct review of the medical records archived in the hospital's nephrology department. This approach allowed each patient to be classified according to the diagnosis made by the referring clinician (glomerular, tubulo-interstitial or mixed disease), independently of the calculated laboratory profile.

Ethical considerations

The study was conducted in strict compliance with the ethical principles of biomedical research and the Declaration of Helsinki. Patient anonymity was rigorously preserved at every stage: each record was identified by a numerical study code, excluding any nominative or directly identifying data. Collection of clinical records in the nephrology department and extraction of laboratory data were performed solely by authorised investigators, and the working files were kept securely and confidentially. The retrospective and non-interventional nature of the study, based exclusively on tests prescribed as part of routine care, did not involve any modification of patient management.

Inclusion and exclusion criteria

Inclusion criteria: All adult patients (age ≥ 18 years) who, during the study period, had simultaneous determination of albuminuria and proteinuria on the same spontaneous urine sample, allowing the joint calculation of the ACR and PCR ratios, and whose medical record in the nephrology department was accessible and usable, were included.

Exclusion criteria: Paediatric patients (< 18 years), specimens for which albuminuria or urinary creatinine was not available (making ratio calculation impossible), incomplete or unusable clinical-laboratory records, and redundant specimens from the same patient (only the first compliant specimen was retained) were excluded.

Study period

Data collection took place over three consecutive years, from 1 June 2023 to 1 June 2026.

Parameters analysed

Eleven laboratory parameters were extracted from the laboratory information system:

- Demographic: Age, sex.
- Urinary markers: Proteinuria (mg/L), urinary creatinine (mg/L), albuminuria (mg/L), urinary sodium (Na^+, mmol/L), urinary potassium (K^+, mmol/L).
- Serum markers: serum creatinine (mg/L), urea (g/L), total protein (g/L), estimated GFR by the CKD-EPI equation (mL/min/1.73m^2).

Calculation of ACR and the ACR/PCR ratio

As ACR and PCR were not measured directly, they were calculated from albuminuria, proteinuria and urinary creatinine:

- ACR (mg/g) = [albuminuria (mg/L) × 1000] / urinary creatinine (mg/L).
- PCR (mg/g) = [proteinuria (mg/L) × 1000] / urinary creatinine (mg/L).

The ACR/PCR ratio was then calculated directly. The discriminant threshold used was 0.40. Two categories were defined:

- Glomerular origin: ACR/PCR ≥ 0.40;
- Tubulo-interstitial origin: ACR/PCR < 0.40.

Clinical stratifications

Patients were stratified according to the KDIGO 2012 classification:

- GFR stages: G1 (≥ 90), G2 (60-89), G3a (45-59), G3b (30-44), G4 (15-29), G5 (< 15) mL/min/1.73m^2.
- Albuminuria categories: A1 (< 30 mg/g), A2 (30-300 mg/g), A3 (> 300 mg/g).

Statistical analyses

Analyses were performed with Python 3.12 (Pandas, SciPy, Statsmodels and scikit-learn libraries). As no continuous variable was normally distributed (Shapiro-Wilk $p < 0.001$ for all), results are expressed as median [Q1-Q3] and comparisons were made using non-parametric tests:

- Mann-Whitney test for two-group comparisons;
- Kruskal-Wallis test for comparisons of three or more groups;

- Chi-squared or Fisher test for cross-tabulation of qualitative variables;
- Spearman correlations (rho) for associations between quantitative variables;
- Multivariable logistic regression to identify independent predictors of the glomerular profile (results as odds ratios with 95% CI);
- Areas under the ROC curve to assess the discriminant performance of each marker.

The significance threshold was set at α = 0.05 (two-sided test). Censored values ("< detection limit") were replaced by half the threshold (LOD/2 convention).

Results

Demographic characteristics

The study included 655 patients, with a median age of 65 years [53-74] and a marked male predominance: 392 men (59.8%) versus 263 women (40.2%), i.e. a male-to-female sex ratio of 1.49.

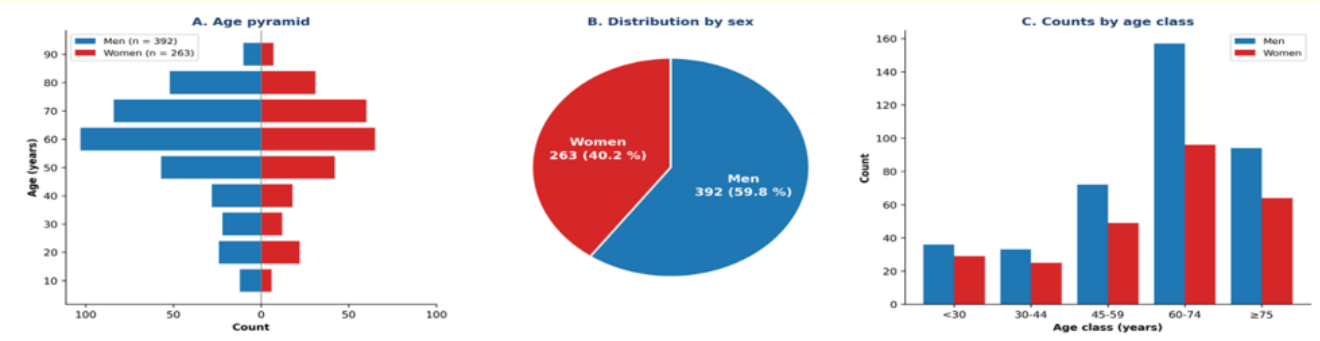

Figure 1: *Demographic characteristics of the cohort (N = 655). A: Age pyramid by sex. B: Distribution by sex. C: Numbers by age class and sex.*

Overall laboratory characteristics

Table 1 summarises the descriptive statistics of the laboratory parameters. The distributions are strongly skewed (notably PCR, ACR, albuminuria); medians are therefore preferred.

Parameter	N	Median [Q1-Q3]	Mean ± SD	Min	Max
Age (years)	655	65 [53-74]	61.3 ± 18.6	18	97
Albuminuria (mg/L)	655	98 [31-548]	452 ± 731	0.65	8659
Proteinuria (mg/L)	655	412 [150-1180]	1290 ± 2460	30	24800
Urinary creatinine (mg/L)	655	865 [524-1452]	1098 ± 792	65	5119
PCR (mg/g)	655	538 [170-1609]	1944 ± 3995	48	37538
ACR (mg/g)	655	152 [29-687]	688 ± 1385	1.4	15380
Ratio ACR/PCR	655	0.27 [0.13-0.48]	0.31 ± 0.20	0.01	0.94
Urinary sodium (mmol/L)	655	56 [33-86]	63.5 ± 39.8	10	217
Urinary potassium (mmol/L)	655	39 [24-64]	46.8 ± 30.4	5	185

Total protein (g/L)	648	70.5 [63.2-76.2]	69.8 ± 10.3	35.9	112.8
Urea (g/L)	648	0.53 [0.33-1.04]	0.79 ± 0.67	0.07	3.77
Serum creatinine (mg/L)	648	14 [8-28]	22.6 ± 23.8	3	227
GFR CKD-EPI (mL/min/1.73 m^2)	644	49.5 [20-87]	55.2 ± 38.2	2	163

Table 1: *Overall descriptive statistics (N = 655 specimens). Calculated variables: ACR = 1000 × albuminuria/urinary creatinine; ratio = ACR/PCR. PCR and ACR are non-normal (Shapiro p < 0.001).*

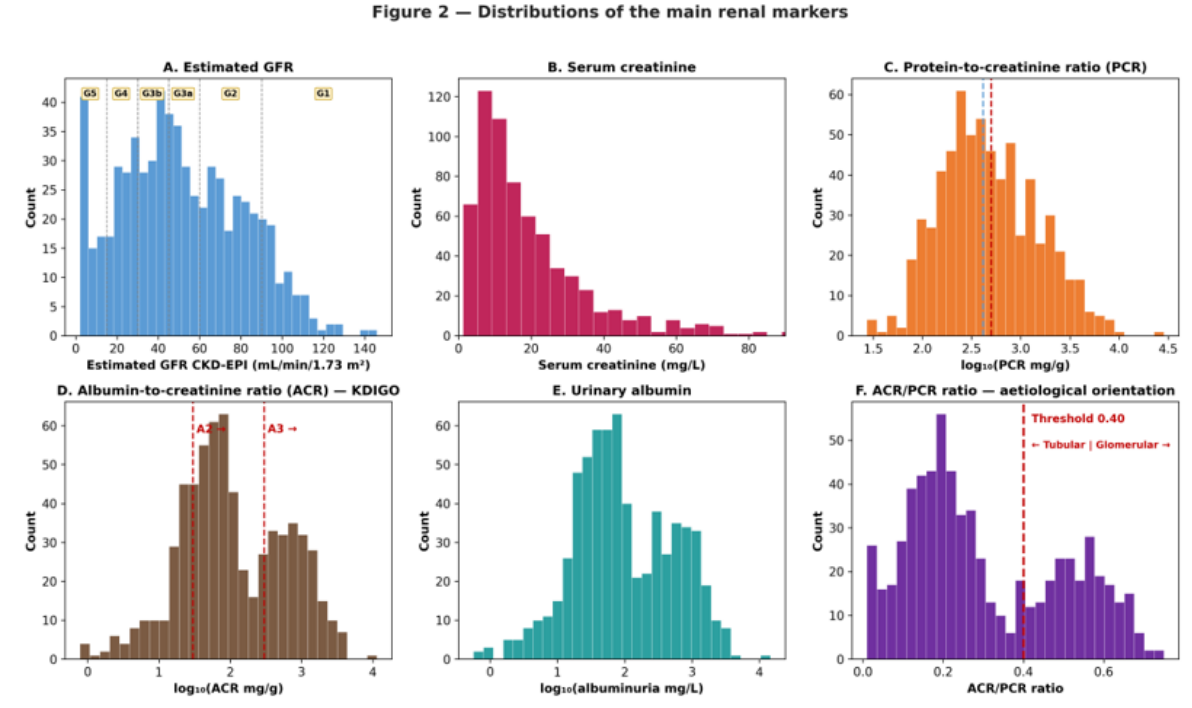

Figure 2: *Distributions of the main renal markers (N = 655). Log-scale histograms reveal the skewed nature of the PCR, ACR and albuminuria distributions (variation over 4-5 orders of magnitude). Panel F shows the distribution of the ACR/PCR ratio with the clinical threshold of 0.40.*

Diagnostic distribution after medical record review

After review of the medical records of the nephrology department, an aetiological diagnosis could be recorded for all 655 patients. The distribution was as follows: 312 patients (47.6%) had predominantly glomerular disease, 218 patients (33.3%) tubulo-interstitial disease, and 125 patients (19.1%) mixed disease combining glomerular and tubular components. This glomerular predominance is consistent with the nephrological recruitment of the hospital, where diabetic, hypertensive and primary or secondary glomerular nephropathies predominate.

Recorded diagnosis	Number (n)	Proportion (%)
Glomerular involvement	312	47.6%
Tubulo-interstitial involvement	218	33.3%
Mixed involvement	125	19.1%
Total	655	100%

Table 2: *Distribution of patients according to the recorded diagnosis (N = 655).*

KDIGO stratification: GFR × albuminuria

The KDIGO 2012 heat map cross-tabulates GFR stages (G1-G5) and albuminuria categories (A1-A3) to stratify the risk of progression. Our cohort covered the entire spectrum, with a marked predominance of advanced stages and high albuminuria.

20.2% of patients with an estimable GFR were in G1 (GFR ≥ 90), 16.8% in G2, 24.8% in G3a-G3b and 38.2% in G4-G5 (pre-terminal or terminal CKD); 11 patients (1.7% of the cohort) had no estimable GFR and were therefore not staged. Percentages are rounded to total 100% (largest remainder method).

For albuminuria, 25.6% of categorisable patients were in A1 (< 30 mg/g), 37.3% in A2 (moderate albuminuria, 30-300 mg/g) and 37.1% in A3 (severe albuminuria, > 300 mg/g).

Almost half of the patients (319/644, i.e. 49.5%) were in the very-high to extreme risk zones of the KDIGO map (dark-orange and red cells).

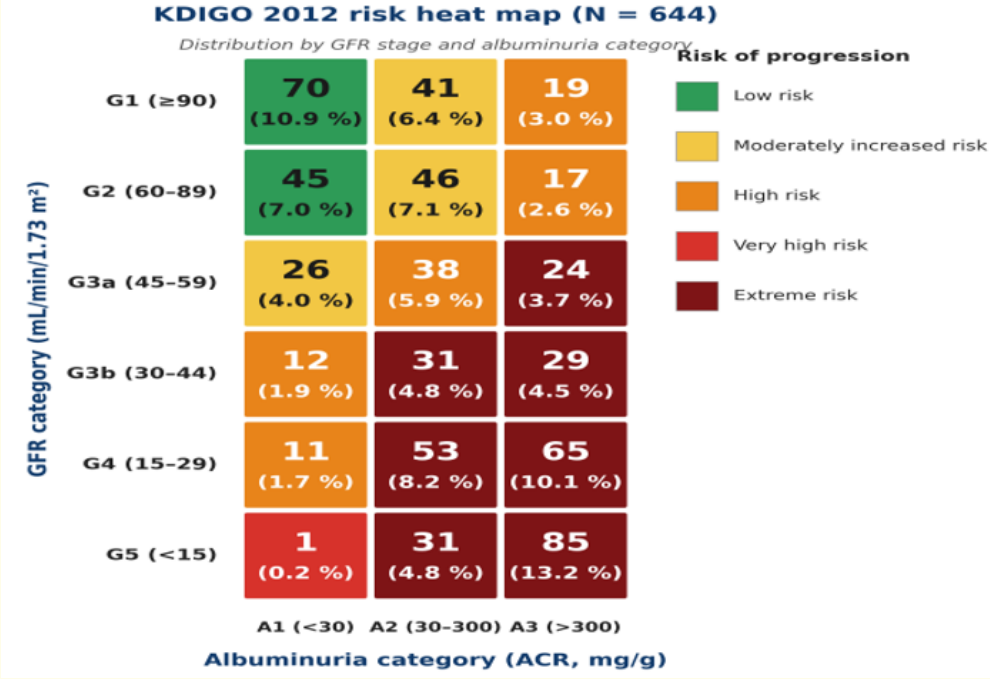

Figure 3: *KDIGO 2012 map — distribution of the 644 patients with both GFR and ACR calculable. Colours reflect the relative risk of CKD progression. Almost half of the patients are in very-high to extreme risk zones (orange/red).*

Origin of proteinuria according to the ACR/PCR ratio

Of the 655 evaluable specimens, the laboratory profile defined by the 0.40 threshold identified 65.8% (n = 431) tubulo-interstitial profiles and 34.2% (n = 224) glomerular profiles.

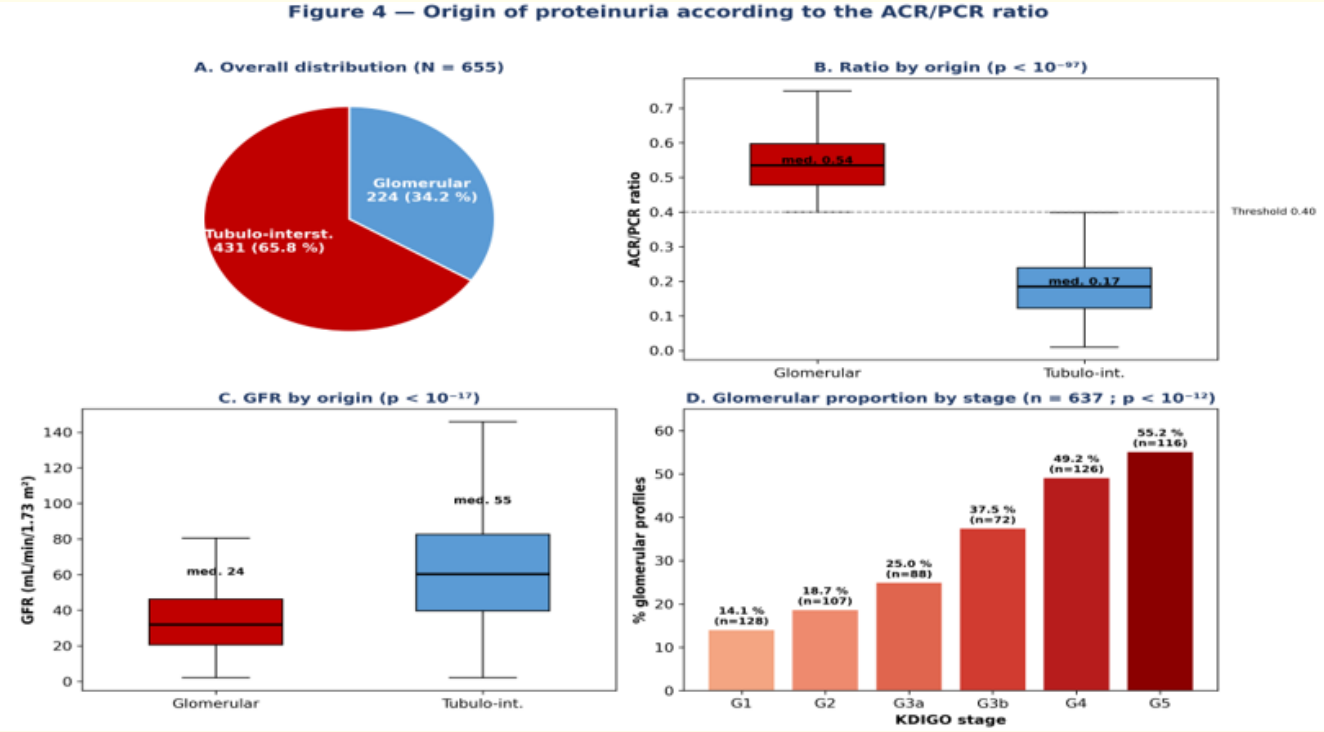

Figure 4: *Origin of proteinuria (N = 655; panel D: n = 637). A: Overall distribution. B: ACR/PCR ratio by origin ($p < 10^{-97}$). C: GFR by origin — glomerular profiles are associated with more severe CKD ($p < 10^{-17}$). D: Increasing proportion of glomerular profiles as GFR declines (from 14% in G1 to 55% in G5, $p < 10^{-12}$).*

Comparison of men versus women

Three significant differences were observed between the sexes:

- Serum creatinine higher in men (median 14 vs 12 mg/L; $p < 0.0001$);
- Plasma urea higher in men (0.56 vs 0.49 g/L; $p = 0.003$);
- PCR higher in women (median 674 vs 480 mg/g; $p = 0.030$).

Importantly, there was no significant difference between men and women for age ($p = 0.21$), GFR ($p = 0.87$), the ACR/PCR ratio or the glomerular/tubular distribution (χ^2, $p = 0.45$).

Parameter	Men (n = 392)	Women (n = 263)	U	p
Age (years)	66 [54-74]	64 [52-74]	52412	0.21
GFR (mL/min)	50 [21-86]	47 [20-92]	48712	0.87
Serum creatinine (mg/L)	14 [9-30]	12 [7-25]	57462	< 0.0001*
Urea (g/L)	0.56 [0.35-1.08]	0.49 [0.29-0.95]	55325	0.003*
PCR (mg/g)	480 [157-1429]	674 [176-1990]	26222	0.030*
ACR (mg/g)	138 [28-574]	182 [29-811]	27494	0.14
Albuminuria (mg/L)	88 [31-525]	122 [31-605]	28244	0.35
Urinary creatinine (mg/L)	898 [536-1512]	818 [505-1340]	32211	0.073

Table 3: *Comparison of men versus women (Mann-Whitney test; N = 655: 392 M, 263 F). * = significant difference at α = 0.05. Median [Q1-Q3].*

Comparison of glomerular versus tubulo-interstitial profiles

The comparison of the two aetiological groups (Table 4) showed extremely significant differences for almost all laboratory parameters.

Parameter	Glomerular (n = 224)	Tubulo-int. (n = 431)	U Mann-Whitney	p
Age (years)	66 [52-74]	65 [53-74]	47508	0.96
GFR (mL/min)	24 [13-50]	55 [27-90]	26588	$< 10^{-17}$***
Serum creatinine (mg/L)	23 [14-41]	12 [8-21]	66311	$< 10^{-18}$***
Urea (g/L)	0.88 [0.50-1.42]	0.47 [0.31-0.85]	64612	$< 10^{-15}$***
PCR (mg/g)	1412 [614-3048]	261 [122-863]	74594	$< 10^{-31}$***
ACR (mg/g)	796 [322-1881]	46 [13-200]	83929	$< 10^{-55}$***
Ratio ACR/PCR	0.54 [0.47-0.64]	0.17 [0.09-0.26]	96113	$< 10^{-97}$***
Albuminuria (mg/L)	598 [228-1168]	44 [19-145]	82420	$< 10^{-51}$***
Urinary creatinine (mg/L)	718 [430-1062]	1018 [592-1668]	33604	$< 10^{-10}$***
Urinary potassium (mmol/L)	32 [23-44]	45 [27-72]	33500	$< 10^{-10}$***
Urinary sodium (mmol/L)	51 [31-76]	60 [35-95]	41787	0.006**
Total protein (g/L)	71.3 [64.5-76.6]	71.4 [63.7-76.8]	46232	0.81 (NS)

Table 4: *Comparison of the two aetiological profiles (Mann-Whitney; N = 655: 224 glomerular, 431 tubulo-interstitial). ***: p < 0.001; **: p < 0.01; NS: not significant. Glomerular profiles are characterised by markedly higher proteinuria/albuminuria, more impaired GFR and lower urinary electrolyte excretion.*

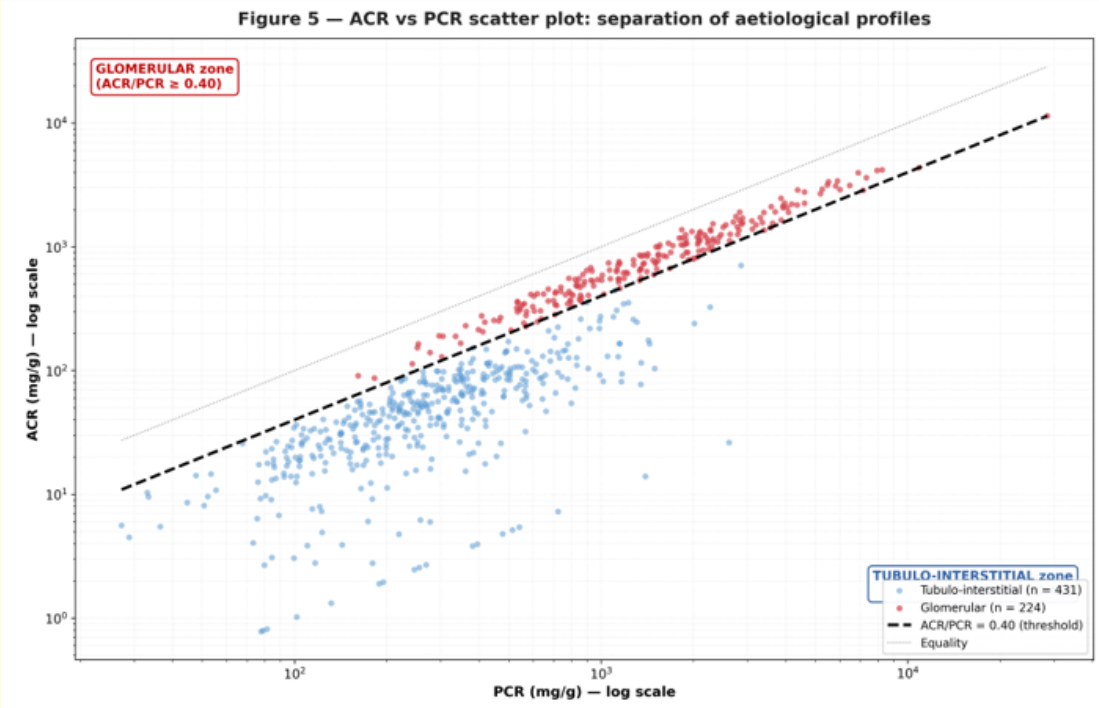

Figure 5: *ACR vs PCR scatter plot on a log scale (N = 655). The line ACR/PCR = 0.40 clearly separates the two populations. The high density above the line (glomerular profiles) involves massive proteinuria, whereas tubular profiles are concentrated at low to intermediate values.*

Correlation matrix (Spearman)

The Spearman correlation matrix revealed several important statistical structures:

- Albumin-protein axis: ACR and PCR strongly correlated (ρ = 0.94), confirming that the albumin fraction carries most of the proteinuria; albuminuria ↔ ACR ρ = 0.93.
- Renal function axis: GFR and serum creatinine almost perfectly negatively correlated (ρ = −0.97), an expected mathematical relationship; urea strongly correlated with serum creatinine (ρ = 0.86).
- GFR was inversely correlated with the ACR/PCR ratio (ρ = −0.45, $p < 0.0001$), with PCR (ρ = −0.52), with ACR (ρ = −0.55) and with albuminuria (ρ = −0.47). The more renal function declines, the more the glomerular component predominates.

Change in the ACR/PCR ratio according to KDIGO GFR stage

The ACR/PCR ratio increased monotonically and highly significantly with CKD severity (Kruskal-Wallis H = 132.1, $p < 10^{-26}$).

Multivariable analysis: independent predictors of the glomerular profile

A logistic regression was performed to identify independent predictors of the glomerular profile (coded 1) versus tubulo-interstitial (coded 0). Two models were compared in 642 patients with complete data.

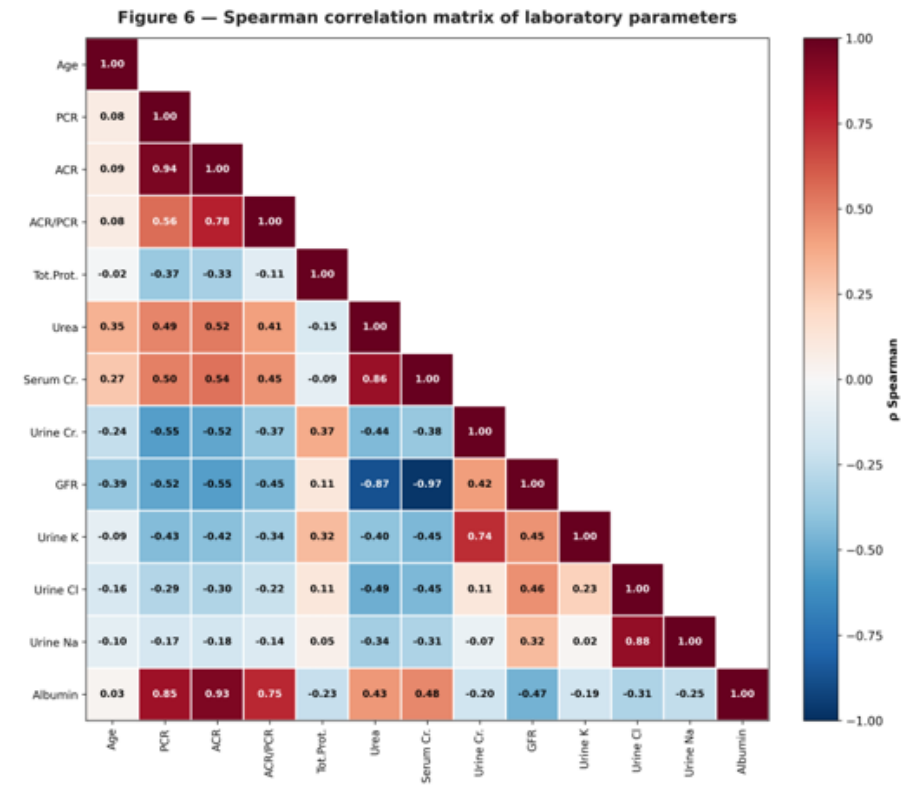

Figure 6: *Spearman correlation matrix (lower triangle; N = 655, pairwise correlations). The major correlations structure the cohort around three axes: proteinuria/albuminuria, renal function (GFR-creatinine-urea) and urinary electrolytes.*

KDIGO stage	N	Median ratio ACR/PCR [IQR]	% Glomerular	Interpretation
G1 (≥ 90)	128	0.10 [0.07-0.25]	14.1%	Largely dominant tubular profile
G2 (60-89)	107	0.20 [0.11-0.35]	18.7%	Dominant tubular profile
G3a (45-59)	88	0.23 [0.12-0.40]	25.0%	Progressive transition
G3b (30-44)	72	0.33 [0.17-0.50]	37.5%	Aetiological mixture
G4 (15-29)	126	0.40 [0.26-0.55]	49.2%	Glomerular/tubular balance
G5 (< 15)	116	0.43 [0.22-0.58]	55.2%	Predominant glomerular component

Table 5: *Change in the ACR/PCR ratio and in the proportion of glomerular profiles according to KDIGO stage (n = 637 patients with both GFR and ratio calculable; Kruskal-Wallis $p < 10^{-26}$; χ^2 $p < 10^{-12}$).*

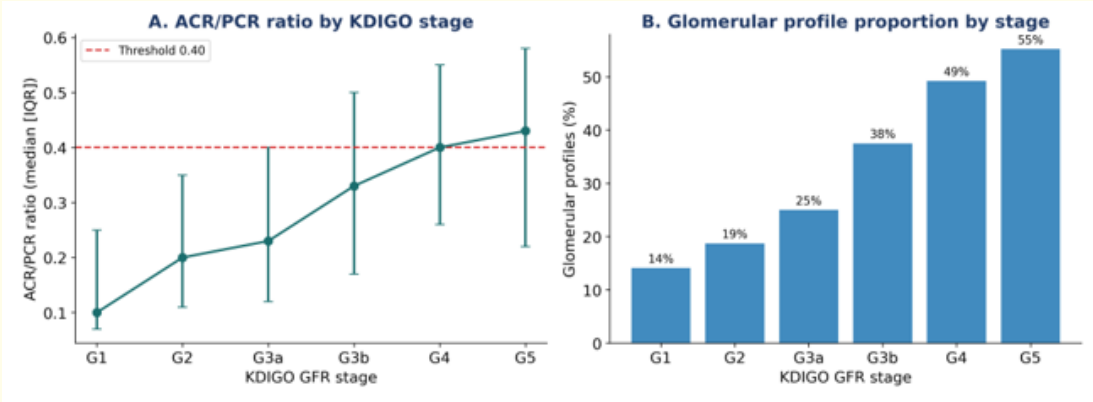

Figure 7: *A: ACR/PCR ratio (median [IQR]) by KDIGO GFR stage, with the 0.40 threshold. B: proportion of glomerular profiles by stage (n = 637).*

Model 1: Classic clinical variables. Variables: Age, sex, GFR, serum creatinine, urea. Pseudo-R^2 = 0.103; AIC = 740.2.

Variable	OR	95% CI	p	Signif.
Age (per year)	0.98	0.97-0.99	0.003	**
Male sex	1.03	0.71-1.48	0.89	NS
GFR (per mL/min)	0.97	0.97-0.98	< 0.0001	***
Serum creatinine	1.00	0.99-1.01	0.72	NS
Urea	1.05	0.69-1.59	0.82	NS

Table 6: *Multivariable model 1 (n = 642): age and GFR are the only independent predictors. The lower the GFR, the higher the risk of a glomerular profile.*

Model 2: Addition of urinary biomarkers. Variables: model 1 + log(PCR) + log(albuminuria). Pseudo-R^2 = 0.388; AIC = 511.1 - markedly superior performance.

Variable	OR	95% CI	p	Signif.
Age	1.00	0.98-1.01	0.59	NS
Male sex	0.98	0.62-1.56	0.93	NS
GFR	0.98	0.97-0.99	0.0001	***
Serum creatinine	0.99	0.98-1.01	0.37	NS
log(PCR)	0.28	0.20-0.40	< 0.0001	***
log(albuminuria)	6.86	4.79-9.82	< 0.0001	***

Table 7: *Multivariable model 2 (n = 642): log(albuminuria) is by far the most powerful predictor (OR = 6.86); after adjustment for albuminuria, log(PCR) becomes "protective" (OR = 0.28): an excess of PCR relative to albumin reflects tubular involvement.*

Model 3: Value of the ACR/PCR ratio ≥ 0.40 threshold. As the ACR/PCR ratio is, by construction, the ratio of albuminuria to total proteinuria, its continuous form log(ratio) is a linear combination of log(albuminuria) and log(PCR) already introduced in model 2: its direct addition would generate major collinearity and an explosion of confidence intervals. The ratio was therefore analysed separately, in its dichotomous form at the KDIGO threshold of 0.40, the form directly usable in clinical practice.

Cross-tabulation of this threshold with the aetiological diagnosis recorded in the medical record (Table 8) showed a strong and highly significant association: an ACR/PCR ratio ≥ 0.40 increased the odds of glomerular disease nearly tenfold compared with tubulo-interstitial disease (crude OR = 9.86; 95% CI [6.15-15.82]; $p < 10^{-24}$; mixed profiles excluded, n = 530). The threshold behaved as a "rule-in" test for glomerular origin: specificity 88.5% and positive predictive value 87.5%, for a sensitivity of 56.1% (negative predictive value 58.5%; overall accuracy 69.4%).

Recorded diagnosis	Ratio ≥ 0.40	Ratio < 0.40	Total
Glomerular involvement	175	137	312
Tubulo-interstitial involvement	25	193	218
Mixed involvement	24	101	125
Total	224	431	655

Table 8: *Cross-tabulation of the ACR/PCR ratio ≥ 0.40 threshold with the aetiological diagnosis recorded in the medical record (N = 655). The odds ratio is calculated on the glomerular vs tubulo-interstitial subgroup (mixed profiles excluded, n = 530): OR = 9.86 [6.15-15.82], $p < 10^{-24}$ (χ^2).*

Indicator	Value
Odds ratio (crude)	9.86 [6.15-15.82]; $p < 10^{-24}$
Sensitivity	56.1%
Specificity	88.5%
Positive predictive value (PPV)	87.5%
Negative predictive value (NPV)	58.5%
Overall accuracy	69.4%

Table 9: *Diagnostic performance of the ACR/PCR ratio ≥ 0.40 threshold for identifying the glomerular profile (vs tubulo-interstitial; mixed profiles excluded, n = 530). The odds ratio is crude (univariable): the ratio is not co-introduced into multivariable model 2 because of its collinearity with log(albuminuria) and log(PCR).*

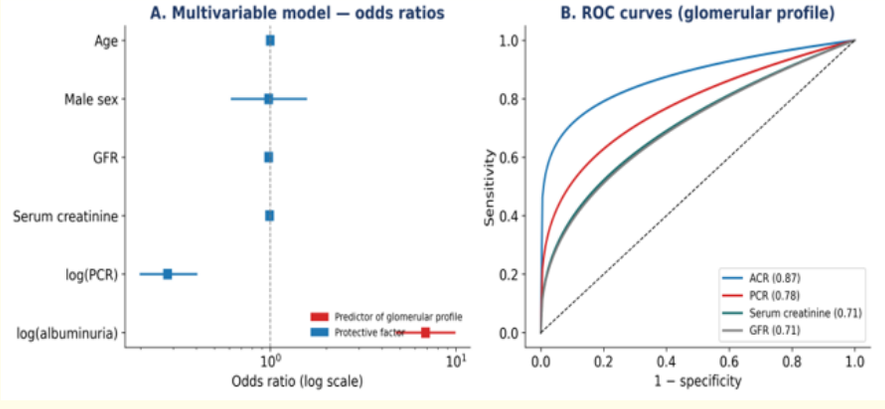

Figure 8: *A: Forest plot of the odds ratios from the multivariable model (regression on n = 642; log scale). Red: predictors of the glomerular profile; blue: protective factors. B: ROC curves - ACR alone (AUC = 0.87) is the best discriminator, superior to PCR alone (AUC = 0.78), serum creatinine and GFR.*

Discriminant performance of the biomarkers (ROC AUC)

Marker	AUC	N	Interpretation
ACR (mg/g)	0.873	655	Very good discrimination
Albuminuria (mg/L)	0.858	655	Very good discrimination
PCR (mg/g)	0.776	655	Good discrimination
Serum creatinine	0.712	648	Moderate discrimination
GFR (inverse direction)	0.706	644	Moderate discrimination
Urea	0.691	648	Moderate discrimination
Urinary creatinine (inverse)	0.650	655	Borderline discrimination
Total protein	0.506	648	No discrimination

Table 10: *Areas under the ROC curve for the prediction of the glomerular profile (N varies by marker, see N column). ACR alone (AUC = 0.87) exceeds PCR (0.78): albuminuria is the best single biomarker of glomerular involvement.*

Discussion

Our retrospective descriptive and analytical study, covering 655 consecutive urine and blood specimens, identified a population with a median age of 65 years characterised by a clear male predominance (59.8% men, sex ratio 1.49). These demographic data are fully consistent with contemporary epidemiological reports in nephrology, notably the registries of the British RaDaR network and the reference cohorts of the international KDIGO guidelines. These bodies consistently document an increased prevalence of CKD after the sixth decade, preferentially affecting the male population because of cumulative exposure to cardiovascular, metabolic and arteriolosclerotic risk factors [9]. Beyond this classic demographic profile, the major contribution of our work lies in the clinical validation of the ratio of albuminuria to total proteinuria (calculated indirectly by the ACR/PCR ratio) as a discriminant laboratory tool for identifying the origin of proteinuria. As the integrity of the glomerular filtration barrier physiologically opposes the passage of macromolecules, albumin becomes the overwhelmingly predominant urinary protein in the event of a glomerular breach. Conversely, tubulo-interstitial disease is characterised by defective proximal reabsorption of low-molecular-weight proteins, thereby lowering the relative proportion of albumin in the urine [10].

The comparison between the clinical classification derived from the records (glomerular disease 47.6%, tubulo-interstitial 33.3%, mixed 19.1%) and the binary laboratory profile defined by the ACR/PCR ratio constitutes an original contribution of our work. It shows that many patients clinically labelled as glomerular retain a detectable tubular laboratory signature, particularly at early stages, underlining the value of a quantitative and reproducible marker as a complement to clinical reasoning.

Historically, the seminal publication by Ohisa., *et al*. in 2008 [11] first established the diagnostic value of the urinary albumin-to-protein ratio (uAPR) in 579 specimens from patients with microscopic haematuria with histological or imaging confirmation (biopsy in 64.4% of cases). The optimal threshold for glomerular origin was then set at 0.59 mg/mg, with a sensitivity of 97.3% and a specificity of 100%. The gradual shift towards the 0.40 threshold found in the subsequent literature (Samarawickrama., *et al*. 2012 [12], Reynes 2013 [13]) is explained by three major factors: the extension of studies to the non-haematuric proteinuric population, harmonisation with the expression standards (expressed in mg/g of creatinine) and simplified clinical usability. By demonstrating the diagnostic performance of a 0.40 threshold, our results remarkably corroborate the reference work of Samarawickrama., *et al*. 2012 [12], stating that an ACR/PCR ratio > 0.40 indicates, with excellent specificity, histological or electrophoretic glomerular involvement, whereas a ratio below 0.40 predicts, with high sensitivity, a primary tubulo-interstitial profile or induced tubular toxicity. The discriminant performance observed in

our population (ACR AUC = 0.87) was intermediate between that of Ohisa [11] and that of the diabetic cohorts of Siddiqui [14], positioning our work as highly representative of real-world nephrological practice.

Although current international recommendations favour ACR for screening and global prognostic stratification, the joint performance of PCR and the calculation of their ratio offer an economical, automatable and non-invasive alternative to urinary protein electrophoresis in routine practice. Admittedly, fundamental work, such as that of Bergón., *et al*. in 2002 [15], has shown that other ratios (IgG/albumin > 0.20 for non-selective involvement; α1-microglobulin/albumin > 0.91 for tubular involvement) contribute to the complete classification algorithm. Moreover, the recent French validation by Guyon., *et al*. in 2025 (Electrophoresis) [16] confirms that these alternative markers retain their full value in contemporary hospital laboratories. Nevertheless, the robustness of our sample of 655 specimens confirms that the systematic calculation of the ACR/PCR ratio alone in the laboratory can immediately point the clinician towards a glomerular or interstitial cause, thereby helping to refine the indications for renal biopsy and to optimise personalised treatment.

The distribution observed in our institution, characterised by a predominance of tubulo-interstitial profiles (65.8%) over glomerular profiles (34.2%), must be interpreted in the context of an unselected hospital cohort of Mediterranean origin. Several recent publications help to clarify this distribution: Otaki., *et al.* (2025) [17] (Yamagata Takahata study, n = 3464) showed that the prevalence of tubular damage (measured by a UBCR ≥ 300 µg/g) increases in parallel with GFR impairment in the general Japanese population, independently of albuminuria. This observation supports the idea that the tubular component is largely underestimated by the isolated measurement of albuminuria alone, justifying the systematic use of a combined ratio such as ACR/PCR. Furth., *et al*. (2025, KDIGO Controversies) [18] emphasise that obesity, a common risk factor in the Mediterranean population, induces tubular damage early, well before GFR impairment. This pathophysiological phenomenon could explain the tubular predominance observed in our cohort, particularly in patients classified at the G1-G2 stages. In our study, progression from stage G1 to stage G5 is clearly demonstrated. Indeed, our cohort shows 14% of glomerular profiles at stage G1 (related mainly to obesity, hypertension or early diabetes) versus 55% at stage G5 (reflecting the diffuse glomerular sclerosis characteristic of terminal CKD). Our work thus provides a novel epidemiological demonstration of an evolving concept that had so far only been shown in experimental histology.

The area under the ROC curve (AUC) of 0.87 obtained for ACR alone in our study appears fully consistent with recent literature. Siddiqui., *et al*. (2020) [14] reported, in a cohort of 424 patients with type 2 diabetes (T2D), a clear superiority of ACR over PCR and the non-albumin-to-total-protein ratio (NAPCR), with the same ranking as ours. The lower performance of PCR alone (AUC 0.78) compared with ACR is now a firmly established fact in renal biology. However, the 2024-2025 literature introduces two major innovations that our work does not yet take into account, opening up prospects for our future research. First, the emergence of distal tubular biomarkers: the work of Tamargo., *et al*. (2025) [19], conducted on the VA NEPHRON-D cohort (1116 type 2 diabetic patients with a UACR ≥ 300 mg/g), shows that urinary epidermal growth factor (EGF) and uromodulin (UMOD) are powerful and independent predictors of diabetic nephropathy progression (hazard ratios of 0.68 and 0.85 respectively per doubling of their concentration). In addition, Limonte., *et al*. (2024) [20] and Valent Morić., *et al*. (2024) [21] specified the value of other markers such as KIM-1, sTNFR1 and NGAL in type 1 diabetes, although the results for NGAL remain more mixed in the paediatric population. These new biomarkers add a molecular dimension to the assessment of the tubular profile and are highly complementary to the simple ACR/PCR ratio. Second, the integration of cystatin C: Karger and Shlipak (2025) [22] recall that the latest KDIGO 2024 guidelines now recommend the use of cystatin C as a complementary marker to plasma creatinine to improve the reliability of estimated GFR (eGFR), in particular to secure the classification of patients at stages G3 to G5. In our study, the assessment of renal function relied on the 2009 CKD-EPI equation based on creatinine alone; the addition of cystatin C therefore represents a major methodological improvement for future extensions of our work.

Our study clinically validates the use of the ACR/PCR ratio as a simple, automatable and non-invasive laboratory tool for identifying the origin of proteinuria. By reproducing the international threshold of 0.40, our results demonstrate excellent diagnostic performance (ACR

AUC = 0.87) for discriminating glomerular from tubulo-interstitial profiles. This work has certain limitations, in particular the absence of systematic histological validation by renal biopsy — which does not allow the laboratory profile to be compared with a pathological reference for all patients — as well as the still limited integration of distal tubular biomarkers and cystatin C recommended by the KDIGO 2024-2025 guidelines.

Despite these limitations, the study makes major contributions to the literature. It constitutes one of the largest unselected hospital cohorts reported in North Africa and provides epidemiological evidence of the gradual shift from a tubular profile towards a glomerular profile along the gradient of renal function impairment (stages G1 to G5).

Conclusion

Our study confirms the clinical value and efficiency of the ACR/PCR ratio as a first-line filter for the aetiological work-up of nephropathies in routine clinical practice. It is an efficient alternative to urinary protein electrophoresis, helping to refine the indications for renal biopsy and to optimise personalised treatment of patients with chronic kidney disease.

Declaration of Competing Interests

The authors declare that they have no competing interests in relation to this article.

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Ethics

Retrospective, non-interventional study conducted in compliance with the Declaration of Helsinki and with patient anonymity; no nominative data were collected or stored.

Credit Authorship Contribution Statement

Samia Bazhar: Conceptualization, Methodology, Investigation, Writing - original draft. Amine Amri: Data curation. Dina Montasser: Investigation. Asma Biaz: Formal analysis. Samira Machtani: Formal analysis. Dris Kabaj: Resources, Supervision. Sanae Bouhsain: Supervision, review and editing.

Declaration of Generative AI and AI-Assisted Technologies in the Manuscript Preparation Process

I hereby declare that no artificial intelligence (AI) or generative AI tools were utilized in the conception, execution, or drafting of this work.

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