

ORIGINAL ARTICLE

Establishment of a Reference Interval for Urinary Protein Markers for the Healthy Population in East China

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SUMMARY

Background: The importance of the ratio of creatinine to urinary microalbumin, low-molecular weight protein, and urinary enzymes as urinary markers in patients with chronic kidney disease is widely recognized. However, to date, no reference intervals (RIs) have been established for these markers in East China. The present study aimed to investigate and establish RIs for urinary protein markers in East China's healthy population using the laboratory information system database.

Methods: A total of 6,786 healthy individuals were subjected to periodic health examinations in the First Affiliated Hospital of Zhejiang University School of Medicine from January 2022 through December 2023 and were thus included in the study. We used Box-Cox conversion combined with Tukey's method to normalize the data and eliminate outliers. The Mann-Whitney U test was performed to decide on groupings, and a nonparametric method was used to estimate the RI. The upper limit of the RI was set at the 95th percentile of the urinary protein markers.

Results: The urinary protein markers were significantly different between males and females, except for retinol binding protein (RBP). The urinary levels of immunoglobulin G (IgG), α 1-microglobulin (α 1-MG) (female group), transferrin (TRF), N-acetyl- β -D-glucosidase (NAG), RBP/creatinine (Cr), IgG/Cr, mAlb/Cr, TRF/Cr, α 1-MG/Cr, and NAG/Cr increased with age. Significant age-related differences in urinary protein marker levels were observed, except for RBP, mALB, and α 1-MG (male group). For the significant differences in RIs between age and gender groups, we recommend establishing gender- and age specific RIs for urinary markers.

Conclusions: Our study established age- and gender-specific RIs for six urinary protein markers and their ratios to creatinine based on healthy individuals from East China, which was of great significance for kidney disease screening, treatment, and recurrence monitoring.

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Supplementary Data

Table S1. Comparison of urinary protein markers after grouping by age.

Indicators	Gender	Age	M (Q1, Q3)	p
RBP (mg/L)	M and F	< 60	0.35 (0.23, 0.43)	0.147
	M and F	≥ 60	0.34 (0.22, 0.43)	
IgG (mg/L)	M	< 60	3.4 (1.7, 5.2)	0.018
	M	≥ 60	3.7 (2.0, 5.6)	
	F	< 60	3.1 (1.4, 4.7)	0.0007
	F	≥ 60	3.3 (1.7, 5.6)	
α1-MG (mg/L)	M	< 60	11.3 (7.3, 16.5)	0.168
	M	≥ 60	11.7 (7.5, 17.9)	
	F	< 60	6.9 (4.7, 10.3)	< 0.001
	F	≥ 60	7.8 (5.4, 11.2)	
TRF (mg/L)	M	< 60	0.24 (0.14, 0.43)	0.008
	M	≥ 60	0.28 (0.14, 0.51)	
	F	< 60	0.21 (0.12, 0.37)	< 0.001
	F	≥ 60	0.26 (0.15, 0.48)	
mAlb (mg/L)	M	< 60	11 (6, 19)	0.623
	M	≥ 60	12 (6, 22)	
	F	< 60	10 (5, 17)	0.610
	F	≥ 60	10 (5, 22)	
NAG (U/L)	M	< 60	5 (3, 7)	0.004
	M	≥ 60	5 (3, 9)	
	F	< 60	3 (2, 5)	< 0.001
	F	≥ 60	4 (2, 6)	
RBP/Cr (mg/g)	M	< 60	0.19 (0.12, 0.28)	< 0.001
	M	≥ 60	0.22 (0.13, 0.33)	
	F	< 60	0.26 (0.15, 0.42)	< 0.001
	F	≥ 60	0.33 (0.19, 0.51)	
IgG/Cr (mg/g)	M	< 60	1.90 (1.09, 3.05)	< 0.001
	M	≥ 60	2.59 (1.42, 4.17)	
	F	< 60	2.40 (1.33, 3.91)	< 0.001
	F	≥ 60	3.52 (2.02, 5.55)	
mAlb/Cr (mg/g)	M	< 60	5.78 (3.75, 9.42)	< 0.001
	M	≥ 60	7.08 (4.27, 11.03)	
	F	< 60	7.55 (4.64, 12.21)	< 0.001
	F	≥ 60	9.79 (5.34, 15.25)	
TRF/Cr (mg/g)	M	< 60	0.14 (0.09, 0.24)	< 0.001
	M	≥ 60	0.19 (0.11, 0.31)	
	F	< 60	0.17 (0.11, 0.27)	< 0.001
	F	≥ 60	0.25 (0.17, 0.42)	
α1-MG/Cr (mg/g)	M	< 60	6.70 (4.84, 9.19)	< 0.001
	M	≥ 60	8.12 (5.83, 11.26)	
	F	< 60	6.36 (4.28, 8.47)	< 0.001
	F	≥ 60	8.72 (6.53, 12.04)	
NAG/Cr (U/μmol)	M	< 60	2.71 (1.89, 3.91)	< 0.001
	M	≥ 60	3.71 (2.49, 5.23)	
	F	< 60	2.65 (1.76, 3.77)	< 0.001
	F	≥ 60	3.94 (2.65, 5.42)	

Table S2. Gender- and age-specific reference intervals of urinary protein markers.

Markers	Gender	Age (years)	95th percentile (90% CI)	Current RIs
RBP (mg/L)	M and F	18 - 90	0.57 (0.56, 0.57)	0.00 - 0.70
IgG (mg/L)	M	< 60	9.1 (8.8, 9.6)	0.0 - 30.0
	M	≥ 60	10.5 (9.6, 11.6)	
	F	< 60	8.4 (7.8, 8.7)	
	F	≥ 60	11.2 (9.9, 12.4)	
α1-MG (mg/L)	M	18 - 90	28.1 (26.3, 29.3)	0.0 - 12.0
	F	< 60	16.6 (16.2, 17.2)	
	F	≥ 60	19.0 (17.3, 20.7)	
TRF (mg/L)	M	< 60	0.91 (0.87, 0.94)	0.00 - 2.12
	M	≥ 60	1.05 (0.97, 1.10)	
	F	< 60	0.84 (0.79, 0.90)	
	F	≥ 60	0.95 (0.89, 1.08)	
mAlb (mg/L)	M and F	18 - 90	33 (32, 35)	0.0 - 25.0
NAG (U/L)	M	< 60	14 (13, 14)	0.0 - 12.0
	M	≥ 60	16 (15, 18)	
	F	< 60	9 (9, 10)	
	F	≥ 60	10 (10, 11)	
RBP/Cr (mg/g)	M	< 60	0.48 (0.47, 0.50)	
	M	≥ 60	0.55 (0.51, 0.59)	
	F	< 60	0.72 (0.70, 0.74)	
	F	≥ 60	0.82 (0.79, 0.85)	
IgG/Cr (mg/g)	M	< 60	5.29 (5.10, 5.46)	
	M	≥ 60	6.94 (6.48, 7.62)	
	F	< 60	6.89 (6.70, 7.15)	
	F	≥ 60	8.71 (8.41, 9.19)	
mAlb/Cr (mg/g)	M	< 60	17.61 (17.15, 18.21)	
	M	≥ 60	20.86 (18.95, 22.70)	
	F	< 60	21.55 (20.84, 22.74)	
	F	≥ 60	27.66 (25.72, 29.39)	
TRF/Cr (mg/g)	M	< 60	0.51 (0.49, 0.53)	
	M	≥ 60	0.64 (0.58, 0.65)	
	F	< 60	0.55 (0.53, 0.58)	
	F	≥ 60	0.67 (0.63, 0.69)	
α1-MG/Cr (mg/g)	M	< 60	13.86 (13.56, 14.27)	
	M	≥ 60	18.00 (16.26, 18.99)	
	F	< 60	12.56 (12.22, 12.87)	
	F	≥ 60	18.42 (17.51, 19.51)	
NAG/Cr (U/μmol)	M	< 60	6.46 (6.25, 6.70)	
	M	≥ 60	8.30 (7.86, 8.81)	
	F	< 60	6.21 (6.02, 6.39)	
	F	≥ 60	8.21 (7.88, 8.97)	