

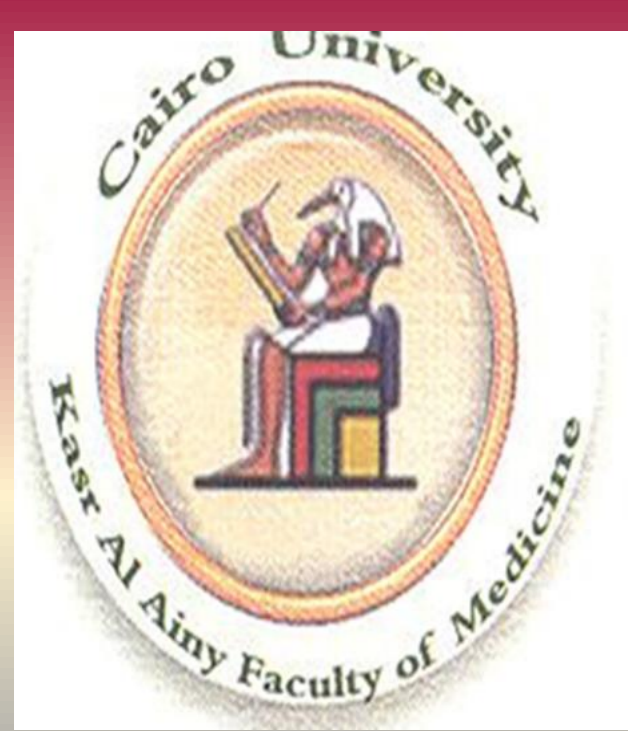
Assessment of Urinary Podocalyxin as a marker of Glomerular Injury in Obesity Related Kidney Disease in Obese children and adolescents compared to Urinary Albumin Creatinine Ratio

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Introduction: Obesity is associated with high risk of renal injury in children¹. Although proteinuria cannot distinguish ongoing glomerular disease activity from persistent glomerular injury, urinary podocyte is a biomarker for glomerular disease activity². A recent study showed that obese subjects with normal albumin excretion and GFR showed evidence of renal alteration through the detection of a higher number of podocalyxin (PCX) cells being a transmembrane protein expressed in kidney podocytes³.

Objective: To assess urinary PCX in obese children and adolescents as a marker of obesity related kidney disease (ORKD) compared to urinary albumin creatinine (A/C) ratio as the standard marker for glomerular injury.

Methodology: This case-control study included 64 obese children (BMI > 95th percentile for age and sex) between 8 and 12 years old with long standing obesity (≥ 5 years duration) in addition to 34 healthy age and sex matched controls. Cases with diabetes mellitus, chronic illness, glomerulonephritis or other renal diseases as well as patients with endocrinal or genetic causes of obesity were excluded from the study. Study population were subjected to **full history taking** including age, sex, obesity onset and duration, feeding habits, dietary history, exercise, family history of obesity, type 2 diabetes mellitus, hypertension or renal diseases as well as **thorough physical examination** including anthropometry (weight, height, waist circumference, hip circumference, body composition), blood pressure assessment, pubertal staging, signs of insulin resistance as acanthosis nigricans. Urine samples for A/C ratio and podocalyxin were collected from study population as well as blood samples for assessment of serum creatinine and fasting lipid profile.

Results: The current study included 30 males and 34 females with mean age of 10.66 (± 1.69) years, mean birth weight of 3.15 (± 0.57) kg and mean duration of obesity of 7.9 (± 2.5) years. Family history was positive for obesity in 75%, T2D in 48.4%, hypertension in 42.2% and renal disorders in 10.9% within the study group. Most of the cases had normal renal function tests (95.3%). However, many patients had hypercholesteremia (85%), hypertriglyceridemia (92.2%).

Table 1: Clinical, anthropometric and biochemical data of the study group

Study parameters	Mean (SD)	Median (IQR)
Clinical data		
Age (yrs)	10.66 (1.69)	10.5 (9 – 12)
Birth Weight (kg)	3.15 (0.28-5.7)	3 (3 -3.5)
Duration of obesity (yrs)	7.9 (2.5)	8 (6 -12)
Anthropometric data		
Height SDS	0.99 (1.2)	1.1 (0.4 -1.18)
Weight SDS	5.5 (2.5)	5.5 (3.6 -6.8)
BMI SDS	3.2 (0.5)	3.3 (2.9 -3.52)
Waist/hip ratio	0.95 (0.069)	0.945 (0.90 -0.99)
Waist Circumference (cm)	99.4 (14.8)	98 (75 – 129)
Fat %	45 (2.8)	47 (41-52)
Biochemical tests		
Creatinine (mg/dl)	0.558 (0.12)	0.6 (0.5 -0.605)
GFR (ml/min/1.7m)	110.49 (24.37)	106.9 (92.3 -126.8)
Triglycerides (mg/dl)	90.56 (39.06)	81 (65 – 107.75)
Cholesterol (mg/dl)	162.11 (34.21)	154 (140 -179.75)
HDL (mg/dl)	38.75 (5.63)	40 (34 -43)
LDL (mg/dl)	101.97 (25.11)	96 (87 -108)
HbA1c (%)	5.1 (0.4)	5.0 (4.7-5.4)
Urinary A/C (ug/mg)	44.99 (103.19)	11.49 (3.78 -30.16)
Urinary podocalyxin (mg/dl)	3.006 (0.407)	3 (2.8 – 3.3)

SDS: standard deviation score, GFR: glomerular filtration rate, A/C: albumin creatinine ratio, HDL: high density lipoprotein, LDL: low density lipoprotein

Table 2: Sex distribution, pubertal staging, dietetic and family history, biochemical status of the study group

Study parameters	No. (%)
Gender	
Male	30 (46.9)
Female	34 (53.1)
Pubertal stage	
Tanner 1	29 (45.3)
Tanner 2	19 (29.7)
Tanner 3	11 (17.2)
Tanner 4	5 (7.8)
Tanner 5	0 (0)
Dietetic History	
Sweetened Beverages (Daily)	
Yes	56 (87.5)
No	8 (12.5)
Fast Food (Daily)	
Yes	57 (89.1)
No	7 (10.9)
Faulty food practice	
Yes	61 (95.3)
No	3 (4.7)
Family History	
Obesity	
Yes	48 (75.0)
No	16 (25.0)
Hypertension	
Yes	27 (42.2)
No	37 (57.8)
Type 2 diabetes	
Yes	31 (48.4)
No	33 (51.6)
Renal disorders	
Yes	7 (10.9)
No	57 (89.1)

Table 3: Correlation between urinary A/C and podocalyxin with other study parameters

Study parameters	Urinary A/C		Urinary Podocalyxin	
	Correlation Coefficient (r)	p value	Correlation Coefficient (r)	p value
clinical characteristics				
Age (yrs)	0.116	0.78	0.122	0.81
Birth Weight (kg)	0.017	0.89	0.125	0.86
SBP (mmHg)	-0.181	0.153	-0.080	0.53
DBP (mmHg)	-0.064	0.62	-0.042	0.74
Stage of Puberty	-0.056	0.66	-0.095	0.45
anthropometric measures				
Weight SDS	0.376	0.003	0.107	0.41
Height SDS	0.222	0.08	0.079	0.54
BMI SDS	0.288	0.023	0.007	0.96
Waist circumference (cm)	0.223	0.046	0.081	0.57
Waist/hip	-0.056	0.66	-0.016	0.89
Fat percentage (%)	0.077	0.55	0.113	0.37
laboratory parameters				
Urinary PCX (mg/dl)	0.197	0.12		
Urinary A/C (mg/g)			0.197	0.12
Serum creatinine (mg/dl)	0.139	0.37	0.009	0.94
GFR (mL/min/1.73 m ²)	0.334	0.007	0.019	0.88
Triglyceride (mg/dl)	0.335	0.007	-0.052	0.68
HDL (mg/dl)	-0.038	0.76	0.154	0.23
LDL (mg/dl)	-0.125	0.32	0.068	0.59
Cholesterol (mg/dl)	0.066	0.6	-0.002	0.99

SBP: systolic blood pressure, DBP: diastolic blood pressure, SDS: standard deviation score, GFR: glomerular filtration rate, A/C: albumin creatinine ratio, HDL: high density lipoprotein, LDL: low density lipoprotein, PCX: podocalyxin

Table 4: Comparison between microalbuminuric and normoalbuminuric patients within study

Variable	Microalbuminuria (n=16)	Normal A/C (n=48)	p value
Age	11.39 (1.27)	10.57 (1.69)	0.09
Birth weight	3.32 (0.81)	3.12 (0.52)	0.52
Weight SDS	6.18 (3.24)	5.089 (1.96)	0.37
BMI SDS	3.373 (0.49)	3.16 (0.504)	0.43
Waist circumference	118.7 (12.4)	99.6 (10.2)	0.042
Waist-hip ratio	0.98 (0.049)	0.95 (0.073)	0.034
Fat %	47 (0.88)	39 (0.74)	0.05
SBP (mmHg)	114.64 (8.76)	110.63 (13.51)	0.31
DBP (mmHg)	76.09 (4.16)	73 (10.01)	0.39
Creatinine (mg/dl)	0.55 (0.08)	0.52 (0.07)	0.35
GFR (mL/min/1.73m ²)	102.44 (11.72)	109.44 (23.02)	0.46
Triglycerides (mg/dl)	137.6 (33.84)	88.5 (38.33)	0.018
Cholesterol (mg/dl)	169 (36.59)	159.79 (33.72)	0.43
HDL (mg/dl)	41.8 (3.03)	38.19 (5.96)	0.06
LDL (mg/dl)	111.5 (22.89)	101.04 (25.65)	0.99
Urinary PCX (mg/dl)	3.091 (0.38)	2.96 (0.42)	0.33

SBP: systolic blood pressure, DBP: diastolic blood pressure, SDS: standard deviation score, GFR: glomerular filtration rate, A/C: albumin creatinine ratio, HDL: high density lipoprotein, LDL: low density lipoprotein, PCX: podocalyxin

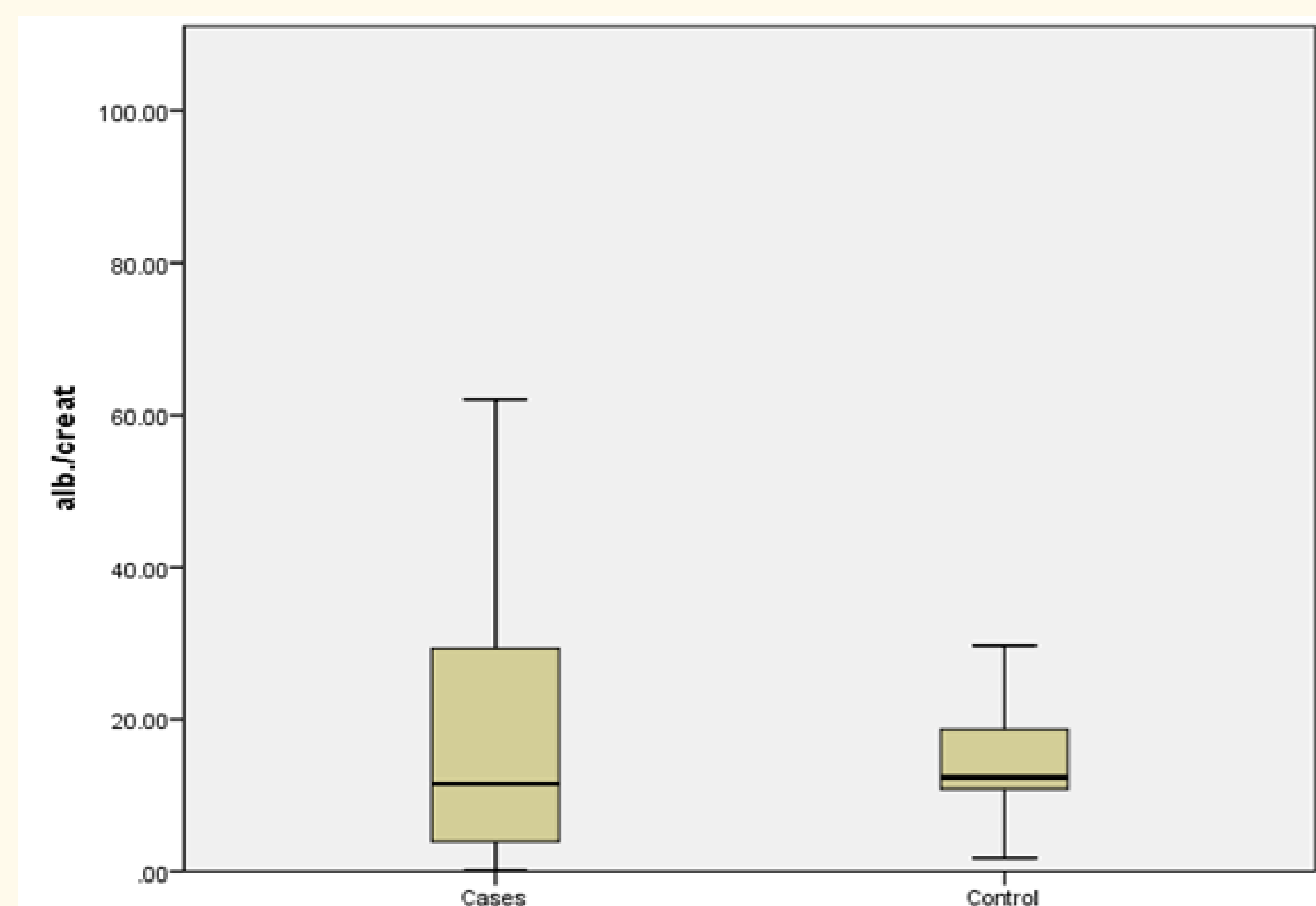


Figure 1: Urinary albumin creatinine ratio in cases and controls (p=0.021)

No statistically significant difference was found between cases and controls regarding urinary podocalyxin (p =0.115). However, urinary A/C showed a statistically significant difference between both groups (p =0.021). No significant correlation was detected between urinary A/C and different study parameters. However, there was a statistically significant positive correlation between urinary A/C and weight SDS, BMI SDS, GFR as well as TGs. Obese children with microalbuminuria had a significantly higher waist-hip ratio and higher TG level compared to those with normal A/C ratio (p =0.034 & 0.018 respectively).

Conclusion: Urinary A/C ratio was increased in obese children and correlated significantly with BMI, GFR and TGs. On the other hand, urinary podocalyxin was not a sensitive marker of ORKD in children.

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