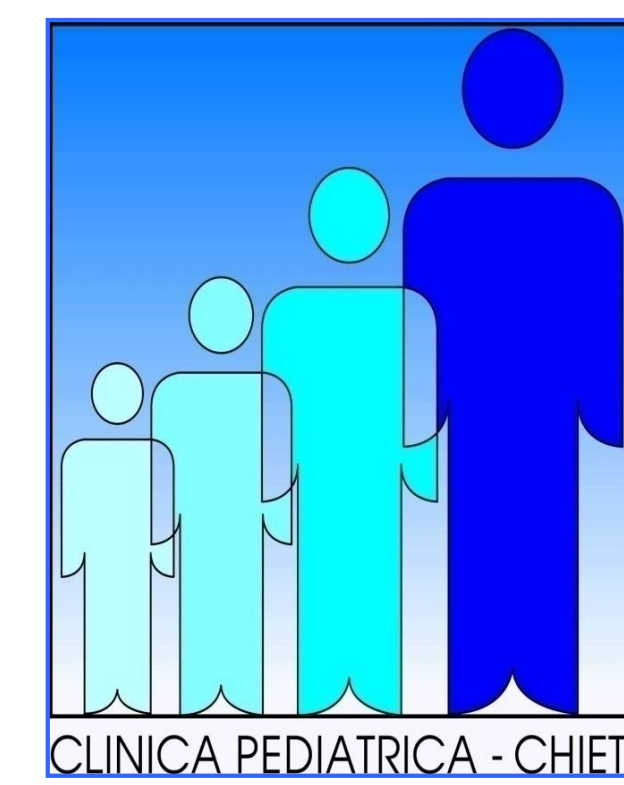# Role of urinary NGAL and KIM-1 as early kidney injury biomarkers in obese prepubertal children

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Background

Childhood obesity is one of the most important causes of end-stage renal disease. The onset of obesity-associated renal disease is insidious and asymptomatic. To date available markers do not perfectly mimic kidney injury and may not characterize kidney changes especially in early stages and of renal tubulointerstitium. Tubular changes (KIM-1 and NGAL) are already apparent before the onset of proteinuria or alterations of GFR and thus might represent biomarker that directly reflects kidney injury and which are easily measured from urine, facilitating a direct monitoring of kidney damage early in the course of the disease.

Aims of the study

❖ we aimed to characterize kidney injury in a group of 40 obese prepubertal children compared to 40 healthy prepubertal matched peers
❖ we aimed to evaluate correlation between these renal injury biomarkers and obesity related alterations including also markers of oxidative stress and renal morphostructural changes detected by kidney ultrasound

Materials and methods

❖ 40 obese prepubertal children (22M/18F) compared to 40 healthy prepubertal age- and gender matched peers (18M/22F)
❖ Anthropometric measurements were determined
❖ Adiposity indices: BMI, SDS-BMI, Waist Circumference, Hip Circumference
❖ Body composition: Body Fat Mass (BFM%), Total Body Water (TBW%), Body Lean Mass (BLM%), Bone mass (B%), Waist-to-height-ratio (WHtR)
❖ Fresh first-morning urine samples : to assess urinary NGAL and KIM-1

❖ Twenty four-hour urine collection: for the evaluation of urinary isoprostanes (PGF-2α)
❖ Venous blood samples: for glucose, insulin, creatinine, cystatin C, transaminases and lipid profile
❖ Insulin resistance was estimated using HOMA-IR
❖ The estimated GFR was calculated using the Schwarz formula
❖ Kidney length was measured as the maximum pole to pole length in the oblique sagittal plane
❖ Renal length for both kidneys was taken in triplicate and the average was used for the analysis

Statistical Analysis

❖ All values were expressed as means and SD
❖ Mann-Whitney U test was used to explore differences between two groups
❖ Fisher's exact test was used to analyzed differences in gender between two groups
❖ Spearman correlation analysis was performed to explore any potential relationship between variables of interest
❖ Statistical significance level was $P<0.05$

Results

Results[1]

	Obese Mean (±SD)	Healthy controls Mean (±SD)	*P*-values
Auxological characteristics			
Age (years)	9.7 (±1.9)	9.6 (±2.2)	0.92
Gender (M/F)	22/18	18/22	0.22
Weight (Kg)	54 (±11)	27 (±4)	<0.01
Height (cm)	144 (±0.1)	122 (±0.09)	<0.01
SDS Height	0.7 (±1.1)	-1.1 (±1.2)	<0.01
Obesity indices			
BMI (Kg/m^2)	26.9 (±3.2)	16.6 (±1.7)	<0.01
SDS BMI	2.06 (±0.3)	-0.5 (±1.08)	<0.01
WC (cm)	82 (±8)	56 (±4)	<0.01
HC (cm)	90 (±8)	66 (±5)	<0.01
WC/HC	0.9 (±0.04)	0.8 (±0.05)	0.03
WHtR	0.5 (±0.04)	0.4 (±0.03)	<0.01
Body composition			
BFM %	27 (±5)	14 (±3)	<0.01
TBW %	55 (±2)	58 (±1.9)	<0.01
Biochemical data			
Total cholesterol (mg/dl)	155 (±30)	158 (±24)	0.47
HDL cholesterol (mg/dl)	49 (±4)	60 (±10)	0.01
LDL cholesterol (mg/dl)	39 (±16)	37 (±19)	0.26
Triglycerides (mg/dl)	91 (±50)	57 (±22)	0.02
Glucose metabolism			
Glucose (mg/dl)	85 (±7)	75 (±9)	<0.01
Insulin (qU/ml)	14 (±9.2)	5.9 (±4.1)	<0.01
HOMA-IR	2.9 (±2.05)	1.1 (±0.9)	<0.01
Kidney function			
SCr (mg/dl)	0.5 (±0.06)	0.4 (±0.08)	0.12
eGFR (ml/min/1.73m^2)	156 (±20.4)	153 (±25.7)	0.35
Kidney damage			
Cystatin C (mg/l)	0.8 (±0.10)	0.7 (±0.10)	<0.01
U- Isop (ng/ml)	17.5 (±5.9)	12 (±4.8)	<0.01
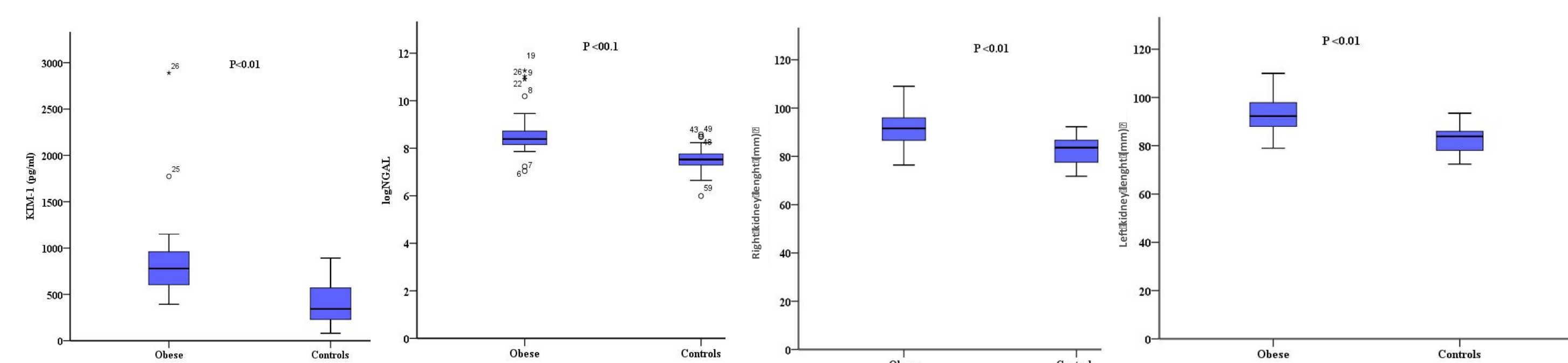
Results[3]

Parameters	Mean NGAL (pg/ml)		Mean KIM-1 (pg/ml)	
	r	*P* values	R	*P* values
Obesity indices				
BMI	0.68	<0.01	0.62	<0.01
SDS BMI	0.72	<0.01	0.63	<0.01
WC (cm)	0.63	<0.01	0.61	0.01
HC (cm)	0.64	<0.01	0.58	<0.01
Biochemical data				
HDL cholesterol (mg/dl)	-0.43	<0.01	-0.36	0.03
Triglycerides (mg/dl)	0.46	<0.01	0.42	<0.01
Insulin (qU/ml)	0.49	<0.01	0.37	0.02
HOMA-IR	0.5	<0.01	0.39	0.01
SCr (mg/dl)	-0.01	0.87	0.05	0.65
eGFR (ml/min/1.73m^2)	0.25	0.03	0.10	0.40
Kidney ultrasound				
Right kidney lenght (mm)	0.56	<0.01	0.37	0.02
Left kidney lenght (mm)	0.56	<0.01	0.44	<0.01

Results[4]

Results[2]
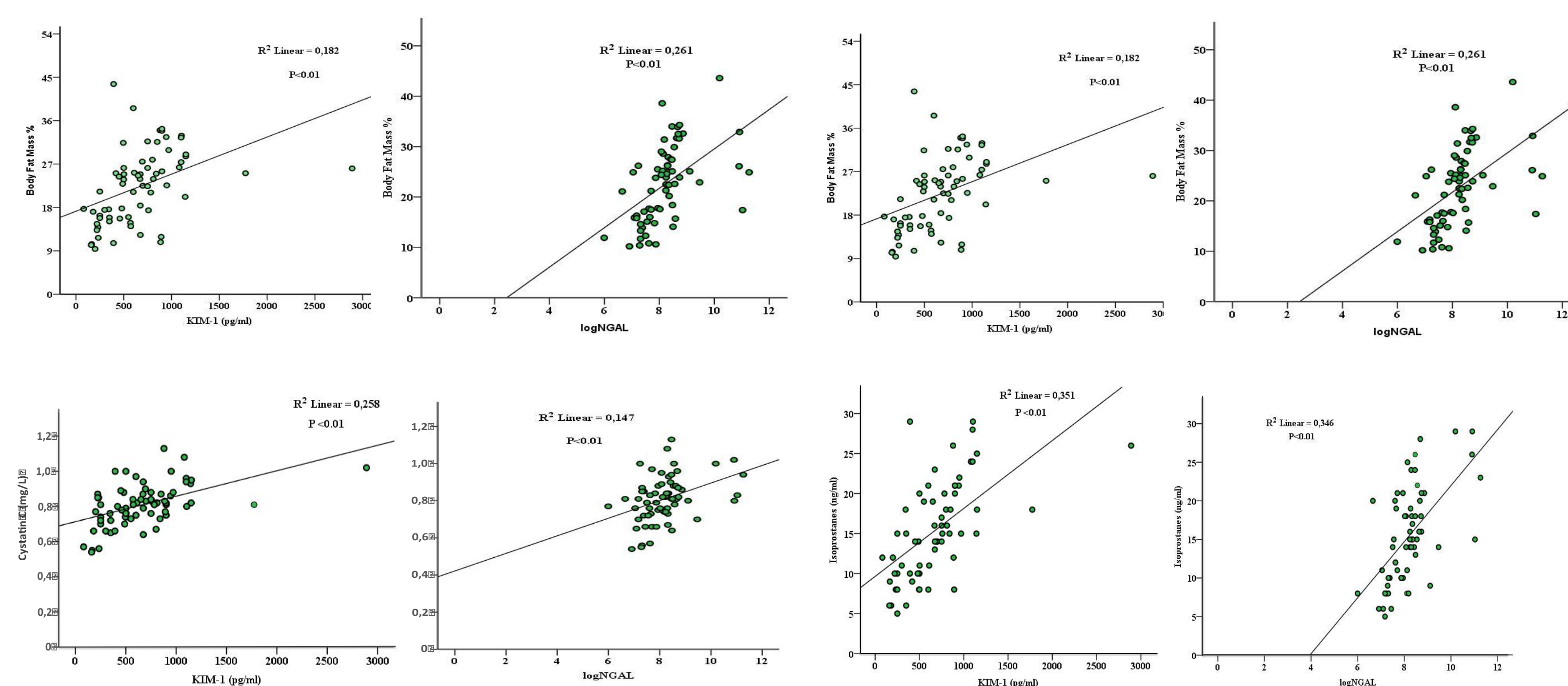
Conclusions

These findings postulate that obese subjects exhibit a certain degree of renal damage before kidney function loss and it seems to confirm the hypothesis that the tubular phase of damage precedes the manifestations of classic glomerular lesions.

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