



# Obesity and chronic kidney disease: what should pediatric nephrologists know?

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## Key message

- Obesity is not only a comorbidity of hypertension, it may be a risk factor for chronic kidney disease.
- Renal impairment associated with obesity is believed to start early in childhood and continue into adulthood, implying a higher risk of adverse cardiovascular events.
- The identification of kidney injury, implementation of preventive strategies, and prompt treatment are essential to improving clinical outcomes in obese children with early kidney disease.

Obesity, the epidemic of the 21st century, carries a markedly increased risk of comorbid complications, such as type 2 diabetes, cancer, hypertension, dyslipidemia, cardiovascular (CV) disease, and renal failure, which greatly affects CV mortality in adults.<sup>1)</sup> Some degree of obesity-associated renal impairment is believed to start early in childhood, long before the appearance of hypertension, diabetes, and other associated comorbidities known to contribute to renal disease. In fact, a previous study of a large sample of European children showed that about half of them already presented adverse CV risk factors before or at the onset of puberty and that the clustering of 2 or more risk factors was present in approximately 11% of them.<sup>2)</sup>

The pathophysiology of obesity-related hypertension is complex and includes activation of the sympathetic nervous system, renin-angiotensin-aldosterone system, insulin resistance, and inflammation.<sup>3)</sup> These same mechanisms likely contribute to the development of increased blood pressure in children.

Insulin resistance may lead to a proinflammatory state in obese children. Plasma concentrations of some inflammatory mediators such as tumor necrosis factor, C-reactive protein, and interleukin-6 are increased in patients with metabolic syndrome.<sup>4)</sup> These results suggest that inflammation is a key risk factor for obesity and strongly associated with metabolic syndrome. Recent reports have shown that other mechanisms may be involved in the pathogenesis of hypertension in obese children, such as proinflammatory cytokines and oxidative stress pathways. These signaling pathways likely contribute to increased arterial stiffness and endothelial dysfunction.<sup>5)</sup>

Uric acid may also be involved in obesity-induced hyperten-

sion. A high-fructose diet can lead to hyperuricemia due to increased uric acid production by adipose tissue in obese individuals.<sup>6)</sup> Several studies have demonstrated a strong relationship between uric acid and hypertension in children and adolescents. The Moscow Children's hypertension study showed hyperuricemia (>8.0 mg/dL) in only 9.5% of children with normal blood pressure but as many as 49% in children with borderline hypertension and up to 73% of children with moderate or severe hypertension.<sup>7)</sup>

In a recent issue of *Clinical and Experimental Pediatrics*, Yim and Yoo<sup>8)</sup> reviewed the epidemiology of childhood obesity, the mechanism of obesity in kidney disease, and the management of obesity leading to chronic kidney disease (CKD). The authors emphasized the correlation between maternal obesity and offspring CKD, the effects and mechanisms of obesity on renal dysfunction, and prevention methods.

Based on animal experiments and clinical observations, Brenner et al.<sup>9)</sup> postulated that a low number of nephrons (nephron underdosing) predisposes an individual to the development of hypertension later in life. Increased blood pressure is a major factor in the rate of renal disease progression, but a relationship between low nephron numbers and higher blood pressure values presumably develops much earlier in the pathophysiological cascade.

At this point, it is important to underline that obesity affects the kidney, similar to the above-mentioned early life determinants of hypertension. For example, children with reduced nephron mass, those who are born small for gestational age or preterm, in addition to being at increased risk of obesity due to prenatal programming, are also more prone to faster renal deterioration since excessive weight gain will increase the metabolic and hemodynamic load on each individual nephron, the total number of which was fixed at birth.<sup>10)</sup>

Pediatric nephrologists must learn how to assess fat mass distribution, identify metabolically benign obesity in the uremic milieu, and manage and treat obese CKD patients. Specifically, a more precise estimation of regional fat distribution and muscle mass should be introduced into regular clinical practice to complement more commonly used practical markers such

as body mass index. The treatment of obesity requires a multifaceted approach, including weight reduction and physical exercise programs. Pediatric nephrologists should aim to provide interventions that increase muscle mass and decrease visceral fat mass. In this regard, a multidisciplinary approach with other healthcare providers such as dietitians, exercise physiologists, and psychologists is of paramount importance.

In conclusion, the recognition of obesity as a major detrimental determinant of renal function in young children should make pediatric nephrologists aware of the importance of implementing early strategies to prevent and fight childhood obesity.

## Footnotes

Conflicts of interest: There is no potential conflict of interest.

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