In Focus

Is there an obesity-related epidemic of CKD starting already in childhood?

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The obesity epidemic is spreading all over the world. In this issue of NDT we learn that children between the ages of 5 and 18 years in a developing country like Turkey show high and increasing levels of overweight of 9.3% and obesity of 8.9%. Very importantly, the authors also show that already at a young age, obesity and hypertension have started to influence the kidney function. A sub-normal, GFR <90 mL/min/1.73 m², was found in 4.9% of the obese children compared with between 2.8 and 3.2% in the other groups of children. The mean estimated GFR values were significantly lower in the obese children, 122.7 mL/min/1.73 m², compared with 128.2–133.3 mL/min/1.73 m² in the other two groups of children.

The highest levels of obesity were found in urban areas and in the richer western parts of the country. Previous studies from Turkey have shown that being part of a high-income family is a risk factor for obesity [1]. This is in contrast to studies from some other parts of the world. There seems to be a pattern that in low-income countries obesity is more common in children from wealthier families while the opposite can be seen with more obesity in disadvantaged children and in particular in girls in more developed countries [2, 3].

Among the overweight and obese children, a total of 7.6 and 11.4% were hypertensive and 3.8% of the obese children showed blood pressure levels defined as stage II hypertension (5 mmHg above the 99th percentile). Similar figures on hypertension are found from several parts of the world: 11% in the USA and 20% of obese adolescents in China [4, 5].

The strong relationship between metabolic syndrome, and its different components, and chronic kidney disease (CKD) has become increasingly recognized. Several very good reviews have recently been published on this topic [6, 7]. The first to point out this relationship was Weisinger et al. [8]. They published 40 years ago a paper on four very obese individuals who had developed nephrotic syndrome without any signs of diabetic nephropathy. The proteinuria was significantly reduced when the subjects managed to lose weight. This problem seems to increase rapidly and in year 2000 a 10-fold increase in obese patients with nephrotic-range proteinuria was noted compared with 14 years earlier [9].

Several observational studies, like the Framingham cohort, have found a relationship between BMI and the incidence of CKD also in individuals who are less overweight [10]. This risk seems to start already at a BMI >25–30 kg/m² [11, 12]. The NHANES III data found a relationship between BMI and a raised cystatin C also in individuals with normal GFR and without proteinuria [13]. The OR for a raised cystatin C was 1.46 in the overweight subjects and 2.36 and 2.82 in those with moderate or severe obesity. They thus concluded that a graded relationship existed between higher BMI and increased cystatin C levels. Another recent study showed that CKD was more common in patients between the ages 60 and 64 if they had had a raised BMI from a young age compared with people whose obesity had developed later [14].

Waist circumference seems to be a better measurement of potentially harmful fat deposition than BMI. Thomas et al. [15] did a meta-analysis on 11 studies (30 146 individuals) where waist circumference had been used in all but 3 studies. They found that all of the different components of metabolic syndrome contributed to an estimated GFR <60 mL/min/1.73 m²; the odds ratios for high blood pressure was 1.61, elevated triglycerides 1.27, low HDL cholesterol 1.23, abdominal obesity 1.19 and impaired fasting glucose 1.14.

Overweight and obesity seems to also increase the risk for end-stage kidney disease (ESRD). This has been studied in over 320 000 people from northern California [11]. The relative risk for ESRD was 1.9 for overweight subjects and 3.6 and 7.1, respectively, in class I and class II obesity.

Weight loss was, in a Cochrane review, associated with a reduction in proteinuria [16]. No studies have evaluated the durability of this response and no medical weight loss intervention has been able to show any improvement of GFR. Bariatric surgery did, however, in a study by Chagnac et al. [17]...
improve both albuminuria and GFR when BMI decreased. Similar findings have been confirmed in a 2–5-year follow-up of patients with established kidney disease who had undergone bariatric surgery [18]. Three out of the 45 patients showed some improvement in their kidney function while in the remainder the previous deterioration halted and the GFR became stable. In another study on bariatric surgery in 25 patients with CKD III, mean GFR over a 12-month period improved from 47.9 to 61.6 mL/min/1.73 m² [19].

Glomerulomegaly can be seen on the initial kidney biopsy [20]. In one study, in later stages, a majority, 57 of 71 patients, were shown to have focal and segmental glomerulosclerosis [9]. The podocyte lesion has been further characterized and increased foot process width and reduced density has been found [21].

What can explain the relationship between obesity and proteinuria and reducing GFR? Hypertension and type 2 diabetes play important roles but they are not the only causes [22]. Other potentially pathogenic factors that have been identified are high salt intake [23] and insulin resistance [2]. Many components of the Western style diet such as the high content of sugar, salt, fat and protein from red meat are also associated with CKD [24–26].

It thus seems from the recent literature quite clear that the ongoing obesity epidemic will be followed by an epidemic of CKD and later by increased numbers of patients with ESRD. There will most likely be a several decade long time delay between these events but it is likely to develop. What can we do about it?

Advice on a healthier lifestyle is a cornerstone in the treatment of obesity. This includes dietetic advice and recommendations on increased physical activity are given. It is however unfortunately so that there are major difficulties in long-term reduction of body weight in obese individuals. The only weight-reduction method that has shown long-term beneficial effects on GFR and proteinuria is bariatric surgery [3, 18, 19, 27].

It is however not likely or even desirable that bariatric surgery will influence the development of obesity and the presumed CKD epidemic, rather it will only help in selected individual cases. Very different population-based measures are needed. There are however several obstacles to such approaches. One is the lack of agreement on the major causes of obesity. The common view has for many years been that obesity is the result of a net positive energy balance. We eat more calories than we expend. With this view we must thus reduce the amount of food that we eat and increase our physical activity.

This view is however increasingly challenged by the hypothesis that obesity is a hormonal regulatory disorder [28]. The proponents of this view ask the question ‘Why do we store too much fat?’ and not the question, ‘Why do we eat too much?’ They claim that the increased appetite is a consequence of and not a cause for the increased fat storage. Some authors argue that it is really about how much sugar, and in particular fructose, that we ingest [29]. And consequently they want to primarily limit the sugar intake.

How could all this be achieved? There are in principal two rather different views on how we should go about improving the population’s health, which were recently debated in the BMJ [30, 31]. One view is that the medical and political community should collaborate with the food industry to get them to improve the nutritional quality of their products. The opposite view does not rely on voluntary contributions from companies whose prime goal is to maximize profit for their shareholders but instead they want the state to legislate to be involved in these matters. The proponents for this view point out that the food industry spent 1 billion euros to successfully dissuade the European parliament from legislating proper labelling of food.

Both the Royal College of Physicians and the Academy of Medical Royal Colleges in the UK have launched reports with suggestions on concrete steps on how to respond to the crisis [32]. The Academy of Medical Colleges suggestions include banning the marketing of unhealthy food on television before 9.00 p.m., a 20% tax on sweetened drinks and reducing the proximity of fast food outlets to schools. These kinds of actions are however seen by many as part of a ‘nanny’ state and the British government continues to focus on self-regulation of the food industry.

The mayor of New York City, Michael Bloomberg, has taken a more interventional approach, and his Board of Health issued a ban last year on sugar-sweetened drinks larger than 16 fluid ounces. This is quite interesting as Mr Bloomberg is a multi-millionaire and is said to have the seventh largest fortune in the USA and thus has a deep knowledge on what is driving private business. This ban has, however, on legal grounds, been struck down by the New York State Supreme Court.

In summary, we might be seeing the onset of an epidemic of CKD starting already in childhood. This epidemic can only be tackled with population-based measures aiming at healthier food intake and a less sedentary life style. The debate on how to achieve this will continue.

None declared.


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