

Obesity and Kidney Disease

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Abstract

Obesity is one of those issues which has become a worldwide epidemic. It is estimated that it might project up to 40% in the coming years. This increased prevalence has heightened the risk of various diseases like diabetes, CVD and chronic kidney disease also known as CKD. One of the strongest risk factors that contribute to chronic kidney disease is the increased body mass index. When the person becomes obese, extra pressure for hyperfiltration is placed upon the kidneys to fulfil the body's heightened metabolic demands. This increased pressure on the glomerulus functioning can damage the kidneys and the risk of CKD development increases to a higher extent in the long run. Obesity is also found linked with nephrolithiasis, and a number of other malignancies like kidney cancer. Obesity has very harmful consequences, many of these are directly linked with kidney diseases, so healthy lifestyle, healthy policy measures and positive behavioral changes are mandatory to cope this issue, and this review paper encompasses all these aspects.

Keywords: Obesity, Adults, Children, kidney cancer.

Introduction

In 2014, a study was conducted which revealed that over 600 million adults, 18 years of age and older, were obese

all around the globe. For kidney disease development, obesity is a potent factor, and when there is kidney disease, risks of diabetes and hypertension automatically increases. End stage renal disease is also associated with obesity. The compensatory mechanism of hyperfiltration occurs in obese persons to cope up with their rising metabolic demands due to increased body weight. The increase in intraglomerulus pressure can cause kidney damage and abruptly affects its structure, thus it ultimately raises the risk of CKD development in the long term.

At present, obesity and diseases related to it are largely preventable. Education and awareness can reduce the risks of obesity, which lead to a healthy lifestyle, proper nutrition and exercise. All these positive factors can dramatically reduce the risks of kidney related diseases. This review paper throws light upon the association of obesity with the kidney disease.

Epidemiology of Obesity in Adults and Children

Over the last decades, the prevalence of obesity issues (BMI ≥ 25 kg/m²) in the adults substantially increased all around the globe. In the US, the obesity prevalence issue among men was observed as 35% and 41% in women in the survey of 2014 to 2015.^{1, 2} This obesity problem also affected the children with age between 2 to 19 years. The rise of obesity prevalence isn't just a problem linked with

any specific region, rather the whole world is concerned about it as it is expected to grow to up to 40% in the coming decade.^{3,4}

The basal metabolic index or BMI gives the most obvious definition of obesity i.e, weight in kg divided by the square of his or her height in meters. The BMI between 18.5 to 25 kg/m² is considered healthy and normal weight of a person by the World Health Organization (WHO), and a BMI between 25 to 30 kg/m² is considered as overweight and a BMI above 30 kg/m² is considered as obese. No doubt BMI is very easy to calculate, but issue arises when a poor estimate of the fat mass distribution and muscular mass is overlapped. Muscular people might have BMI same as of those individuals that are obese, as muscle weight is more than fat weight. People with more intraabdominal fat layer are more prone to CVD and other metabolic issues. However, there are other alternative parameters that measure this visceral fat in more accurate manner including waist circumference (WC) and waist hip ratio (WHR).^{5,6}

Association of Obesity with CKD and Renal Complications

Multiple studies encompassing population of various regions have showed with evidence that obesity plays crucial role in the development and progression of chronic kidney disease. High basal metabolic index is linked with the development and presence of proteinuria in individuals who donot have kidney disease.^{7,8} Moreover, studies have also shown that higher BM is also linked with the development and presence of GFR or low estimated glomerular filtration rate, with rapid loss of GFR with the passage of time and with the occurrence of ESRD.^{9, 10} Increased levels of BMI falls in the category 2 of obesity and becomes the reason of rapid progression of CKD in patients.

In men, studies shown that when higher visceral adipose tissue is measured via computed tomography then a link with higher prevalence of albuminuria was also found. The linkage between abdominal obesity and poor renal outcomes independent of BMI is described in terms of mortality in patients with ESRD and kidney transplant. Under such circumstances visceral adiposity plays a direct role. In other words, it is found that even if obesity is adjusted with possible mediators and the patient is free from the risk of issues regarding high blood pressure and diabetes mellitus, then the obesity still can affect kidney functioning through various mechanisms independent of other underlying causes.

The disastrous impacts of obesity on kidneys not only stays there, rather it also lead to other complications such as kidney malignancies and nephrolithiasis. The higher the BMI the greater the chances of nephrolithiasis. Moreover, obesity is the root cause of various kind of malignancies, specifically cancers of kidneys. In a population based research in the UK, among 5.24 million people, people with 5 kg/m² higher BMI were at 25% higher risk of kidney cancers, and 10% of these cancers were linked with increased weight. In another study of population, it was observed that almost 18 to 28% of all kinds of kidney cancers in men and women, respectively, were due to obesity (over weight). In this meta-analysis, among the cancer examination, kidney cancers had the 3rd highest risk linked with obesity (relative risk per 5 kg/m² higher BMI: 1.24, 95% CI 1.20-1.28, $P < .0001$).^{11,12}

Mechanism of Action of Obesity upon the Renal Functioning

Obesity may trigger the abnormal actions on renal functions, may develop them or if they are already existing, it can exacerbate the situation to an undue level. Distinction of 25% in “metabolically healthy” but obese individuals shows that obesity alone is not sufficient to

trigger the kidney damaging process. Some of the deleterious renal consequences linked with obesity might also be supported by many other underlying issues like diabetes mellitus or hypertension. But many effects are also left directly by the adiposity on the kidneys. These effects are triggered by the production of endocrine activities of adiponectin, resistin and leptin present on adipose tissues. These effects lead to the development of inflammation, abnormal lipid metabolism, oxidative stress, activation of rennin-angiotensin-aldosterone system and higher production of insulin and insulin resistance.^{13, 14}

These negative effects lead to multiple pathological changes in the kidneys that could increase the risk of CKD. These include increased deposition of renal sinus fat, ectopic lipid accumulation, increased glomerular permeability caused by hyper GF barrier injury, development of glomerular hypertension and ultimately focal or segmental glomerulosclerosis and glomerulomegaly. The incidence of obesity related glomerulopathy has been increased 10 fold since 1986 to 2000.¹⁵

Increased body weight is associated with lower pH of urine, increased urinary oxalate ions, uric acid, sodium and phosphate excretion. Protein and sodium rich diets may lead to more acidic urine and decreased urinary citrate, which also contribute to the production of kidney stone. As obesity also increases insulin resistance in the body, so it can also predispose nephrolithiasis because it leaves negative impacts upon tubular Na-H exchanger, ammoniogenesis and promotes acidic milieu. The complicating point is, in various therapies, weight loss instead of improving the situation, began to worsen it and results in kidney stone formation; for instance, gastric surgery can cause a substantial rise in internal absorption of oxalate and increased risk of nephrolithiasis.

Consequent chronic hyperinsulinemia and insulin resistance, hyper insulin like growth factor 1 production and numerous other complex secondary humoral impacts may cause stimulating effects on the growth of various cancer cells and lead to kidney cancers. Moreover, endocrine functioning of adipose tissues, their effect on the immunity and generation of inflammatory milieu also leaves complex effects on cancers.¹⁶

Management of Obesity: Potential Interventions

Diabetes and hypertension along with obesity makes the situation highly complicated falls among the strongest risk factors of CKD by various mechanisms through the deranged synthesis of multiple adipose tissue cytokines with nephrotoxic potential. As the survival chances of an obese person were more, but with the prevalence of end-stage renal disease the mortality rate is rising now. Various strategies have been presented to control and manage obesity in a way that it won't trigger the negative impacts on the kidneys. Countering these issues is the most tantalizing task for health specialists, doctors, diet planners and nephrologists these days.^{17, 18}

- **Countering CKD at Larger Level**

It is imperative to acknowledge people with the intervention of health officials in the community. To treat and prevent CKD at an early stage is far better than treating it at the end stage when mortality rate is quite high. At present, the immediate goals of the health community, all around the globe, is to gather evidence that current interventions for CKD reduction in obese people are helpful or not on the basis of which the management process can be further proceeded. Appropriate documentation of current knowledge of the public, perks of primary and secondary prevention interventions in obese people and latest trials to fill the knowledge gap is imperative.

A successful surveillance system for the CKD is already implemented in various developed countries and is under process in developing countries of the world. The utmost focus of general physicians is the early detection of CKD and better control of hypertension, and increased use of angiotensin receptor blockers and angiotensin converting enzyme. This system, as far as it is observed, better serve as a platform in improving the prevention of obesity related CKD. However, obesity related goals can only be attained when general public fully cooperate and try to modify their lifestyles for their own good.¹⁹

- **Prevention of CKD Progression in Obese People with CKD**

Studies of obese patients who were metabolically healthy, revealed that renal dysfunctioning and kidney damage can even occur without diabetes and hypertension. In obese or over weight diabetic patients, lifestyle modification including caloric restriction and increased physical activities play a positive role and reduce the risk of CKD by 30%. This positive effect was partially owing to the body weight reduction, systolic blood pressure and HbA1c. In this situation, no adverse impacts of weight loss were observed.

However, a recent meta-analysis experimental studies in obese CKD patients showed that, focus on reduction in body weight lead to lower blood pressure, proteinuria and glomerular hyperfiltration. A holistic renal study showed that in proteinuric CKD patients, the nephron protective effect of ACE inhibition was maximal in obese patients, but minimal in CKD patients with low or normal BMI. However, surgical interventions are suggested for some CKD and ESRD patients along with dialysis who are waitlisted for kidney transplantation.²⁰

Globally, three findings so far are proving to be helpful in the favor of weight reduction technique and ACE inhibition interventions for the treatment of CKD in obese

patients. Lifestyle modifications are found to be very helpful to reduce body weight in obese patients prone to CKD, particularly those with diabetes and hypertension issues as well. But, the recommendations on weight loss in non-hypertensive obese and metabolically healthy patients remain unwarranted and doubtful. These considerations suggest that comorbid conditions have to be carefully pursued with proper checkup and therapeutic approach.

Conclusion

The population of the Earth is affected in many ways with the epidemic of obesity. Diseases of the kidneys, arteries, kidney cancers, and nephrolithiasis are among the most insidious effects of obesity. These have huge range of dangerous consequences leading to excess morbidity and mortality rates and costs the entire society. Population wide interventions to control obesity and protect the society from its negative impacts is the utmost priority of the health officials at present. It is also important for the community to play its role and devise long term strategies toward improving their lifestyle and understanding the links between obesity and kidney diseases to better fight it.

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