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The Obesity Epidemic and Kidney Disease: A Literature Review

Veeraish Chauhan, Megha Vaid, Nishtha Chauhan and Akhil Parashar
Drexel University College of Medicine, Hahnemann University Hospital, Philadelphia, PA USA

1. Introduction

It is a fact we are all too well aware of. The world, as we know it, continues to grow fat. The popular press has done an excellent job of educating the lay person about the link between obesity and heart disease, hypertension, etc. However, despite scientific evidence to the contrary, the effect of obesity on the kidneys' function is less well-known. Kidney disease from obesity can progress to End Stage Renal Disease (ESRD), which mandates the use of dialysis to keep the patient alive. It is hence a huge risk factor for morbidity and mortality. Last, but not the least, it puts a tremendous economic and social strain on the healthcare resources of nations around the world.

2. The alarming statistics

The World Health Organization (WHO) considers obesity an international epidemic, stating in 1997 that "obesity's impact is so diverse and extreme that it should now be regarded as one of the greatest neglected public health problems of our time with an impact on health which may well prove to be as great as that of smoking." A quick look at the WHO's statistics paints a scary picture of what we are up against. It is hard to imagine that in 2008 almost one-quarter of humanity, or 1.5 billion people, were reported to be overweight (a body mass index greater than or equal to 25). Of these, over 200 million men and 300 million women were obese (body mass index greater than or equal to 30). Obesity, in combination with diabetes, is the largest epidemic the world has ever faced. It is also the fifth leading cause of deaths worldwide, killing 2.8 million people every year. The prevalence of obesity currently ranges from less than 5% in rural China, Japan and some African countries, to levels as high as 75% of the adult population in urban Samoa. 68% of U.S. adults are either overweight or obese. With this enormous health burden worldwide, the deleterious effects of obesity on kidney function are being increasingly recognized.

2.1 Obesity and kidney disease: The weight of the evidence

There now is a well established risk between obesity and the development of kidney disease. The Framingham Offspring data reported obesity as a major risk factor for the development of kidney disease. This was a large study that followed 1223 men and 1362 women (who were initially free of preexisting kidney disease) for a mean period of 18.5 years. At the end of this follow up period, 244 participants (9.4 percent) had developed

kidney disease (defined as estimated glomerular filtration rate (GFR) of less than 64 and 59 mL/min per 1.73 m2 for men and women, respectively). The researchers also reported a 23% increase in the odds of development of kidney disease for each standard deviation increase in the Body Mass Index (BMI). This risk was present even after adjustment for age, sex, smoking, diabetes, and baseline glomerular filtration rate (GFR). Another study by Hsu et al showed that there is a greater relative risk of development of end-stage renal disease (ESRD) necessitating dialysis, with each gradient increase in BMI. Higher BMI was a risk factor for ESRD in multivariable models that adjusted for age, sex, race, education level, smoking status, history of myocardial infarction, serum cholesterol level, urinalysis proteinuria, urinalysis hematuria, and serum creatinine level. Compared with persons who had normal weight (BMI, 18.5 to 24.9 kg/m2), the adjusted relative risk for ESRD was 1.87 (95% CI, 1.64 to 2.14) for those who were overweight (BMI, 25.0 to 29.9 kg/m2), 3.57 (CI, 3.05 to 4.18) for those with class I obesity (BMI, 30.0 to 34.9 kg/m2), 6.12 (CI, 4.97 to 7.54) for those with class II obesity (BMI, 35.0 to 39.9 kg/m2), and 7.07 (CI, 5.37 to 9.31) for those with extreme obesity (BMI > or = 40 kg/m2). Higher baseline BMI remained an independent predictor for ESRD after additional adjustments for baseline blood pressure level and presence or absence of diabetes mellitus.
Similarly, a recent large cohort study of 177570 individuals found obesity to be one of the most potent risk factors for the development of ESRD.

3. How obesity causes kidney disease

Obesity is associated with multiple other conditions that are known to cause compromised renal function, including hypertension, diabetes, hyperuricemia, and the metabolic syndrome that can independently have a detrimental effect on renal function. However, as we can gauge from the evidence quoted in the above section, obesity has been found to cause kidney disease and ESRD even after adjustment for these factors. Hence, the pathogenesis of obesity related kidney disease can be sub-classified in to direct and indirect effects.

3.1 Direct effects of obesity on kidney function

Data from the Framingham Offspring study, the Hypertension Detection and Follow-Up Program, and the Multiphasic Health Testing Services Program suggest that obesity may be independently associated with the risk of developing chronic kidney disease. Obesity seems to cause a change in the renal hemodynamics that promotes progressive kidney disease. These changes begin early in the course of obesity, even before overt renal manifestations of obesity are clinically apparent. This was shown in a landmark study from a center conducting kidney biopsies on obese patients who presented for weight loss/bariatric surgery in Spain. The investigators studied the glomerular architecture in renal biopsies of 95 patients undergoing bariatric surgery for extreme obesity but whose renal function was clinically normal. These subjects had no known prior history of any kidney disease. These patients were then compared with a control group of 40 patients undergoing nephrectomy or donating a kidney, and having protocol biopsies. This second control group had patients who had normal weight and renal function, and were non-diabetic and non-hypertensive. Logistic regression models were then applied to determine associations between the clinical and biochemical variables and glomerular lesions. Focal and segmental glomerulosclerosis (FSGS) was present in only five extremely obese patients but absent in controls. Increased mesangial matrix, podocyte

hypertrophy, mesangial cell proliferation, and glomerulomegaly were more frequent in the obese cohort than in the control group. Body mass index was found to be a significant independent risk factor associated with glomerular lesions in all 135 patients and in the 95 extremely obese patients. This was hence an elegant demonstration of the fact that even in patients with no overt clinical renal symptoms, there were a variety of glomerular abnormalities that correlated with body mass, even after adjustment for other factors like high blood pressure, diabetes, metabolic syndrome, and sleep apnea.

3.1.1 The role of adipokines

One of the keys to unravel obesity's effect on the kidneys is understanding the concept of body-fat as an independent endocrine organ, rather than simply a passive storage depot for triglycerides. The overarching factor in this is the dysregulated production of bioactive substances called "adipokines" by adipose cells that cause systemic effects, and directly influence insulin sensitivity and vascular injury.

Adipokines, and other neuro-humoral factors, have already been well studied in the pathogenesis of obesity. Serum levels of adipokines like leptin correlate with the total body fat content. Hence, the levels tend to be higher in the obese. In normal-weight subjects, food intake is reduced by systemic leptin administration, but the response to leptin decreases as the subjects become obese. This leads to a vicious circle of hyperphagia and obesity. Another interesting hormone that plays a role in the pathogenesis of obesity is ghrelin, a peptide produced by the stomach and duodenum. This peptide stimulates growth hormone secretion, and increases food intake in rodents and humans. Serum concentrations are suppressed by food ingestion in normal-weight subjects. However, this suppression is impaired in the obese, leading to increased food intake.

Not surprisingly, dysregulated adipokine production also leads to hemodynamic and structural changes in the kidney, and has been shown to play an important pathophysiologic role in obesity related kidney disease. These adipokines include cytokines like leptin, adiponectin, interleukin-6, tumor necrosis factor-alpha, resistin, and angiotensinogen. Whereas some of these adipokines act in an autocrine or paracrine manner, others act as signaling molecules in remote tissues like liver, skeletal muscle, and endothelium. These cytokines then induce a pro-inflammatory state causing glomerular capillary hypertension, and fibrosis in the renal parenchyma. Of these adipokines, one of the best understood roles is that of angiotensinogen. Angiotensinogen is an α-2-globulin that is produced constitutively, mainly by the liver. However, plasma levels of angiotensin are also positively correlated with body fat mass, indicating increased production of this molecule from adipocytes. In fact, all other components of the renin-angiotensin system (RAS), including renin, angiotensin converting enzyme, angiotensin II, and AT-1 and AT-2 receptors, are expressed as well as secreted from adipocytes. Increased angiotensinogen kick-starts the RAS, and in turn increases the downstream effects of this system, namely, fluid retention and increased vascular tone. Elevated levels of angiotensinogen and angiotensin II then lead to efferent arteriolar constriction in the glomerulus. This increases the intraglomerular pressure, leading to a rise in the GFR. From an evolutionary standpoint, acutely this adaptation served to preserve GFR and prevent low blood pressure in the face of volume depletion. However, over the long term, this effect becomes maladaptive. Raised intraglomerular pressure causes injury to the glomerulus and subsequent hyperfiltration. Eventually, the kidneys start to spill protein in to the urine and begin to undergo permanent irreversible fibrosis.

The relation between RAS and body fat is actually a two-way street. In 1998, Karlsson et al demonstrated that angiotensin-II stimulated preadipocyte differentiation, and hence stimulates adipogenesis. Thus, the RAS itself may also be involved in regulation of body weight and development of obesity. RAS has also been postulated to play an important role in the development of the cardiomyopathy commonly occurring in obesity. The discovery of these mechanisms has had immense clinical implications. Drugs that block the RAS now form the mainstay of treatment to decrease glomerular hyperfiltration and proteinuria, and have found clinical applications in the prevention and treatment of endothelial dysfunction, obesity-related glomerulopathy, diabetic nephropathy, cardiomyopathy etc. Clinical trials of strategies to block the RAS after coronary angioplasty have demonstrated significant decreases in inflammatory markers of systemic inflammation, including IL-6, CRP, and TNF-alpha in response to inhibition of the renin-angiotensin axis.

3.1.2 Other hemodynamic and structural effects

The first large renal-biopsy based clinico-pathologic study on obesity-related kidney disease studied the incidence and structural changes seen in obesity-related glomerulopathy (ORG). This study reviewed 6818 kidney biopsies and reported the presence of structural changes like hyperplasia of the juxta-glomerular apparatus, consistent presence of glomerulomegaly and foot process fusion in patients who were diagnosed to have ORG. Another histologic feature noted in some ORG patients was the presence of focal changes in the form of mild focal mesangial sclerosis or mild focal thickening of glomerular/tubular basement membranes. These changes were not very dissimilar to changes that are more often associated with the presence of diabetic nephropathy.

Obese patients have also been shown to have elevations in both renal plasma flow and GFR. A study investigated differential solute clearances to characterize glomerular function in 12 nondiabetic subjects with severe obesity (body mass index >38). Glomerular filtration rate (GFR) and renal plasma flow (RPF) was found to exceed the control value by 51 and 31%, respectively. Consequently, the filtration fraction was increased as well. The augmented RPF suggests a state of renal vasodilatation involving mainly the afferent arteriole. The analysis suggests that the high GFR in very obese subjects may be the result of an increase in transcapillary hydraulic pressure difference. An abnormal transmission of increased arterial pressure to the glomerular capillaries through a dilated afferent arteriole could account for the augmentation in this transcapillary pressure.

3.2 Indirect effects

Certain co-morbid conditions that come as a "package deal" in patients afflicted with obesity serve as indirect agents of destruction of renal function. The strong association between obesity and the dreaded metabolic syndrome, hypertension, diabetes, hyperuricemia, dyslipidemia, and sleep apnea indirectly has deleterious effects on kidney function.

3.2.1 Effect of hypertension on kidney function

Long standing hypertension causes changes in the kidneys' glomeruli, vasculature, and the tubulointerstitium. These changes are broadly referred to as hypertensive nephrosclerosis.

Intimal thickening and luminal narrowing of the renal arteries and glomerular arterioles is seen. This is thought to be a consequence of a hypertrophic response to chronic hypertension causing medial hypertrophy, followed by deposition of plasma protein constituents such as inactive C3b in to the damaged vessel wall. Abnormal metabolism of nitric oxide is thought to play a major role in this process. This can eventually lead to an ischemic state within the kidney.

The glomeruli may undergo focal global/segmental sclerosis as a consequence of the ensuing ischemic injury. This ischemia also causes alterations in antigen expression on the surface of the tubular cells, inciting an inflammatory response that leads to chronic interstitial nephritis. These alterations cause a decrease in GFR.

3.2.2 Effect of diabetes on kidney function

Glomerular hyperfiltration and hypertension is a well studied phenomenon that develops early in the course of diabetes. However, elevated glucose levels are known to stimulate mesangial cell matrix production. Non-enzymatic glycation of tissue proteins also may contribute to the development of diabetic nephropathy. In this process, excess glucose combines with free amino acids on circulating or tissue proteins eventually leading to the formation of advanced glycation end products (AGEs). These AGEs then crosslink with collagen and cause vascular complications. Glomerular permeability is also thought to increase via activation of protein kinase C that happens in diabetes.

Other molecules that have been postulated to have a role in the development of nephropathy in diabetes include prorenin (which activates protein kinases, and hence mitosis), and other cytokines that cause inflammation and fibrosis. These cytokines include vascular endothelial growth factor (VEGF), transforming growth factor-beta (TGF-beta) etc.

3.2.3 Hyperuricemia and kidney function

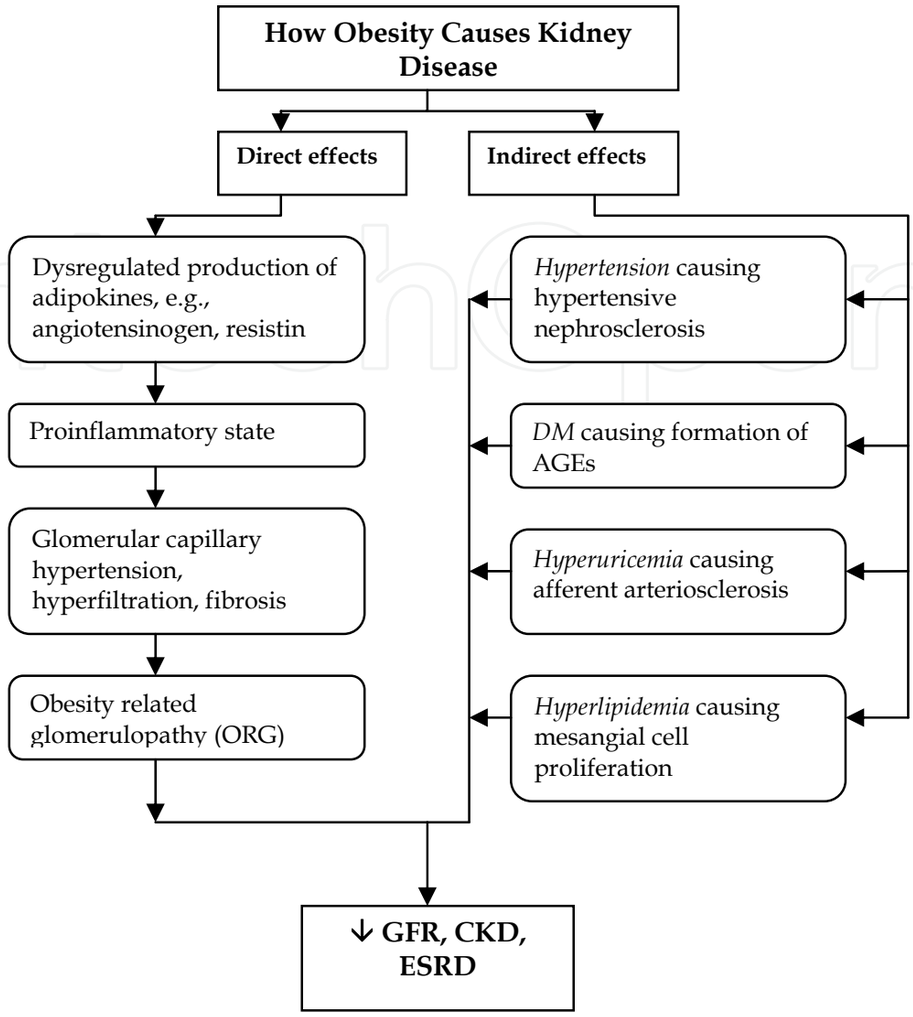
Elevated levels of uric acid, or hyperuricemia, that can progress to gout is more prevalent in the obese population. It has been proposed that hyperuricemia may contribute to worsening of renal function by decreasing renal perfusion. This happens because of arteriolosclerosis of the afferent arterioles. It is believed that uric acid stimulates afferent arteriolar vascular smooth muscle cell proliferation. Long standing hyperuricemia and gout can potentially cause chronic urate nephropathy, and uric acid stones to form in the kidneys or the urinary tract.

3.2.4 Hyperlipidemia and renal function

It has been shown in animal models that hyperlipidemia can cause mesangial cell proliferation by activating LDL receptors present on mesangial cells. This also leads to increased production of inflammatory growth factors and reactive oxygen species.

3.2.5 Metabolic syndrome

Metabolic syndrome is the dreaded constellation of clinical signs that include increased waist circumference, insulin resistance, hypertension, and dyslipidemia. These comorbidities act in concert to cause kidney dysfunction through the pathways outlined above.



4. Obesity and kidney disease: The clinico-pathologic manifestations

Before clinical kidney disease is apparent in obesity, patients might already have very limited renal disease in a few glomeruli, as discussed in section 3.1. Subclinical disease, with sclerotic lesions in a few glomeruli (with no overt proteinuria) was demonstrated in a series of 95 patients who had renal biopsies while undergoing bariatric surgery for extreme obesity. FSGS was observed in approximately 5 percent of extremely obese patients but not in any of the non-obese patients. Mesangial and podocyte hypertrophy also occurred more frequently in obese patients.

Early markers of glomerular disease like microalbuminuria and albuminuria have been reported in as much as 41% and 4% of the extremely obese patients, respectively. Focal segmental glomerulosclerosis (FSGS) and obesity-related glomerulopathy (ORG), characterized by glomerular enlargement and mesangial expansion have been described in patients with severe obesity, and clinically manifest initially with proteinuria, and in severe states can progress to renal failure. Obesity-related glomerulopathy may be reversible with weight loss.

The term "obesity-related glomerulopathy" is sometime used interchangeably with FSGS associated with obesity. However, multiple studies have shown that these might be different processes pathologically. It is entirely possible that these entities represent a spectrum of kidney disease. In 1985, Wesson et al were one of the first ones to report nephrotic range heavy proteinuria in patients who had no glomerulosclerosis and no epithelial cell injury or foot process fusion on renal biopsy. Later studies reported some of such patients to only have mesangial expansion and glomerular capillary loop enlargement leading to glomerulomegaly. Classically, ORG is considered to be distinct from idiopathic FSGS, with a lower incidence of nephrotic syndrome and a more indolent course. Glomerulomegaly is typically more consistent in ORG, as is milder foot process fusion.

Obese patients with FSGS tend to have elevated glomerular filtration rates and increased glomerular size. Serum levels of an adipokine, adiponectin may be seen in the obese. FSGS in obese subjects presents with proteinuria that may reach the nephrotic range. Both weight loss and ACE inhibitors have been shown to reduce this protein excretion by up to 85 percent. However, just like the other causes of secondary FSGS, nephrotic syndrome is atypical and the presence of edema is uncommon. Praga et al studied 15 patients with obesity associated FSGS with significant proteinuria (mean of 3.1 g/day), and found that edema and hypoalbuminemia were not observed in any individual.

It has been suggested that the difference between obesity-related glomerulonephropathy or secondary-FSGS from obesity, and idiopathic FSGS is that only some nephrons leak protein in the former, as opposed to global nephron involvement in idiopathic FSGS. This leakage of protein then leads to abnormal renal handling of sodium, which subsequently causes retention of salt and water. Hence ORG and obesity-related secondary FSGS is not associated with edema while the edema in idiopathic FSGS is severe.

Kambham et al reported in their landmark study that the mean age of patients at the time of biopsy diagnosis of ORG was 42.9 years (range 8–71 years). The youngest patients in the study group included an 8-year-old girl [height 4.0 ft (121.9 cm), weight 190 lbs (86.4 kg)]. The patients' weights ranged from 81.8 kg to 186.4 kg. The mean BMI was 41.7 kg/m^2 (range of 30.9 to 62.7); 38 patients had BMI> 40 kg/m^2 and 33 had BMI <40 kg/m^2. Their was a slight male preponderance with a male-to-female ratio of 44:27 (1.6). The majority of patients were Caucasian (75%), followed by African American (21%) and Hispanic (4%). None of these patients had renal biopsy findings of diabetic nephropathy. Forty-four patients had a prior history of hypertension and eight patients carried a diagnosis of obstructive sleep apnea syndrome prior to renal biopsy.

There are other ways in which obesity can affect renal function. Obesity and weight gain during adulthood have been known to increase the risk of kidney stones. In women, obesity is an important risk factor for urinary incontinence.

4.1 Clinical course

As stated above, weight loss, and drugs like ACE inhibitors can stem the progression of kidney disease in obesity and actually reverse the changes (unless most of the glomeruli are already fibrosed). Weight loss may result in remission of proteinuria. This was demonstrated in a study of 63 patients with biopsy-demonstrated ORG. Patients who started the study had a mean protein excretion of 1.48 g/day. These patients were then followed for two years. Protein excretion was reduced from 1.7 to 1 g/24 hours among 29 patients who successfully lowered their BMI but increased among 9 patients whose BMI went up.

In patients in whom this does not happen, the disease can progress relentlessly with a progressive decrease in GFR. Uremic symptoms can ensue below a GFR of 15 ml/min, and eventually, symptoms like failure to thrive, dysgeusia, nausea, vomiting, itching, insomnia, hyperkalemia, fluid overload, or acidosis can mandate the initiation of dialysis.

5. Managing the disease

Obesity associated kidney disease is a ticking time bomb, and the affected patient stands a huge risk of progression to End Stage Renal Disease (ESRD) that mandates dialysis, a treatment that is hugely cumbersome and expensive. It is hence imperative that the disease be diagnosed and managed aggressively from the outset. It goes without saying that weight loss is of utmost importance and can itself cause remission of the disease to a certain extent. However, treatment of associated risk factors like hypertension, diabetes or insulin resistance, sleep apnea, dyslipidemia is also necessary.

Medications that block the renin-angiotensin axis in the kidney like the angiotensin converting enzyme (ACE) inhibitors, or angiotensin receptor blockers (ARBs) have been shown to have a beneficial effect on reducing glomerular hypertension and proteinuria, and preventing disease progression. Praga at al demonstrated this in 17 obese patients with proteinuria>1 g/day. Their age was 34-70 years; 11 were females and 6 males. Renal biopsy was done in five of these patients. This showed focal glomerulosclerosis in 2 cases, minimal changes in 2 and mesangial proliferation in 1. Nine patients (group 1) were then put on hypocaloric diets and followed for one year. There was a significant correlation between body weight loss and decrease in proteinuria. A second group of eight patients were started on captopril, an ACE inhibitor (without any dietary changes). BMI in this group remained stable but proteinuria showed a dramatic decrease, similar to that in group 1. Given the findings of this study, it makes clinical sense to prescribe both body weight loss and ACE inhibitor treatment to patients suspected to have obesity related kidney disease.

6. Conclusion

The World Health Organization considers obesity an international epidemic, stating in 1997 that "obesity's impact is so diverse and extreme that it should now be regarded as one of the greatest neglected public health problems of our time with an impact on health which may well prove to be as great as that of smoking." Despite scientific evidence to the contrary, the effect of obesity on the function of the kidneys is less well-known. There now is a well established risk between obesity and the development of kidney disease. The Framingham Offspring reported obesity as a major risk factor for the development of kidney disease Kidney disease from obesity can progress to End Stage Renal Disease (ESRD), which mandates the use of dialysis to keep the patient alive. It is hence a huge risk factor for morbidity and mortality.

Obesity is associated with multiple other conditions that are known to cause compromised renal function, including hypertension, diabetes, hyperuricemia, and the metabolic syndrome that can independently have a detrimental effect on renal function. However, obesity has been found to cause kidney disease and ESRD even after adjustment for these factors. The pathogenesis of obesity related kidney disease can be sub-classified in to direct and indirect effects.

Obesity seems to cause a change in the renal hemodynamics that promotes progressive kidney disease. These changes begin early in the course of obesity, even before overt renal manifestations of obesity are clinically apparent. One of the keys to unravel obesity's effect on the kidneys is to understand the concept of body fat as an independent endocrine organ rather than simply a passive storage depot for triglycerides. A central factor in this is the dysregulated production by adipose cells of bioactive substances, called "adipokines" that cause systemic effects and directly influence insulin sensitivity and vascular injury. This results in hemodynamic and structural changes in the kidney. These adipokines include cytokines like leptin, adiponectin, interleukin-6, tumor necrosis factor-alpha, resistin, and angiotensinogen. These cytokines then induce a pro-inflammatory state causing glomerular capillary hypertension and fibrosis in the renal parenchyma. Of these adipokines, one of the best understood roles is that of angiotensinogen. Increased angiotensinogen kick-starts the RAS and in turn increases the downstream effects of this system, namely, fluid retention and increased vascular tone. Elevated levels of angiotensinogen and angiotensin II then lead to efferent arteriolar constriction in the glomerulus. This increases the intraglomerular pressure, leading to a rise in the GFR.

Obese patients have been shown to have elevations in both renal plasma flow (RPF) and GFR. The augmented RPF suggests a state of renal vasodilatation involving mainly the afferent arteriole. The analysis suggests that the high GFR in very obese subjects may be the result of an increase in transcapillary hydraulic pressure difference. An abnormal transmission of increased arterial pressure to the glomerular capillaries through a dilated afferent arteriole could account for the augmentation in this transcapillary pressure.

Certain pathognomonic changes are seen in the kidney as a result of long standing obesity. These changes encompass what is referred to as Obesity Related Glomerulopathy (ORG). These include structural changes like hyperplasia of the juxta-glomerular apparatus, consistent presence of glomerulomegaly, and foot process fusion. Another histologic feature noted in some ORG patients is the presence of focal changes in the form of mild focal mesangial sclerosis or mild focal thickening of glomerular/tubular basement membranes. These changes are not very dissimilar to changes that are more often associated with the presence of diabetic nephropathy.

The strong association between obesity and other entities like the dreaded metabolic syndrome, hypertension, diabetes, hyperuricemia, dyslipidemia, and sleep apnea also causes indirect effects on renal structure and function. Long standing hypertension causes changes in the kidneys' glomeruli, vasculature, and the tubulointerstitium. These changes are broadly referred to as hypertensive nephrosclerosis. Intimal thickening and luminal narrowing of the renal arteries and glomerular arterioles is seen. The glomeruli may undergo focal global/segmental sclerosis as a consequence of the ensuing ischemic injury. Glomerular hyperfiltration and hypertension is a well studied phenomenon that develops early in the course of diabetes. Elevated glucose levels are known to stimulate mesangial cell matrix production. Non-enzymatic glycation of tissue proteins also may contribute to the development of diabetic nephropathy. It has been proposed that hyperuricemia may contribute to worsening of renal function by decreasing renal perfusion. This happens because of arteriolosclerosis of the afferent arterioles. It is believed that uric acid stimulates afferent arteriolar vascular smooth muscle cell proliferation. It has been shown in animal models that hyperlipidemia can cause mesangial cell proliferation by activating LDL

receptors present on mesangial cells. This leads to increased production of inflammatory growth factors and reactive oxygen species.

Before overt clinical kidney disease becomes clinically apparent in obesity, patients may start to develop limited renal disease in a few glomeruli. Early markers of glomerular disease like microalbuminuria and albuminuria have been reported in as much as 41% and 4% of the extremely obese patients, respectively. Focal segmental glomerulosclerosis (FSGS) and obesity-related glomerulopathy (ORG), as explained above, have been described in patients with severe obesity, and manifest initially with proteinuria. These can, in severe states, progress to renal failure. However, as is the case with other causes of secondary FSGS, nephrotic syndrome is atypical and the presence of edema is uncommon. It has been suggested that the difference between obesity-related glomerulonephropathy or secondary-FSGS from obesity, and idiopathic FSGS is that only some nephrons leak protein in the former, as opposed to global nephron involvement in idiopathic FSGS.

Weight loss, and drugs like ACE inhibitors (eg captopril, lisinopril) or angiotensin receptor blockers (like losartan, irbesartan) can stem the progression of kidney disease in obesity, and are sometimes able to actually reverse the changes induced by obesity related kidney disease. However, this is less likely to happen if most of the glomeruli are already fibrosed. In such cases, the disease can progress relentlessly with a progressive decrease in GFR. Uremic symptoms can ensue below a GFR of 15 ml/min, and eventually, symptoms like failure to thrive, dysgeusia, nausea, vomiting, itching, insomnia, hyperkalemia, fluid overload, or acidosis can mandate the initiation of dialysis. It thus makes clinical sense to prescribe both weight loss and ACE inhibitor/angiotensin receptor blocker treatment to patients suspected of having obesity related kidney disease.

7. Methods

We searched PubMed for English, German, French, and Spanish language references published as of June 2011, using combinations of the following terms: “obesity”, “kidney disease”, “glomerulopathy”, “FSGS”, “gastric bypass”, “diabetes mellitus”, “dyslipidemia”, “hypertension”, “metabolic syndrome”, “metabolic effects”, “renal effects”, “nutrition”, “epidemiology”. The bibliographies of the articles thus obtained, as well as those of relevant review articles were also reviewed for inclusion of publications.

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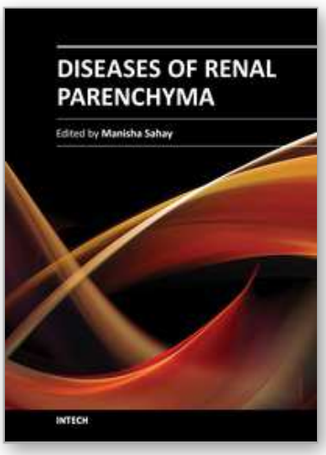

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Clinical nephrology is an evolving speciality in which the amount of information is growing daily. This book gives quick access to some important clinical conditions encountered in nephrology including the diseases of glomeruli, tubules and interstitium. It presents the latest information on pathophysiology, diagnosis and management of important diseases of renal parenchyma. The information is presented in a very user friendly and accessible manner while the treatment algorithms enable the reader to quickly access expert advice on arriving at the most appropriate treatment regimen. The book discusses the renal involvement in various systemic diseases including diabetes and autoimmune diseases. Diabetic nephropathy is fast becoming the commonest cause of end stage renal disease all over the globe and is discussed in this book. The editors believe that this book will be a valuable addition to the reader's library.

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InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

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