Analysis of the Relationship among Kidney Volume, Obesity, and Blood Pressure in Mexican-American Children

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Abstract

Background and Aim: Obesity causes a decrease kidney function and an increase in kidney volume. The aim of this study was to understand the relationship among kidney volume, obesity and blood pressure in Mexican-American children in South Texas.

Methods: To study those effects, data was collected from 454 ultrasound done on 289 girls and 762 ultrasound done on 382 boys visiting a pediatric clinic in South Texas from 2003 to 2018. The relationship between kidney volume and obesity was analyzed. IBM SPSS is used for data analysis.

Results: Children with fatty livers have a higher kidney volume when compared to children with non-fatty livers. When comparing children classified as BMI percentile (0, 50%), BMI percentile [50%, 85%), BMI percentile [85%, 95%), and BMI percentile above 95%, the kidney volume is increasing as BMI percentile increases. We also found that there is a positive relationship between the kidney volume and systolic blood pressure. Children with high systolic blood pressure (above 119 mmHg) have a larger volume when compared to children with low blood pressure (above 110 but less than or equal 119 mmHg), 110 and below mmHg.

Conclusion: Obesity causes inflammation, and lipid accumulation. These effects can cause an increase in kidney volume. Kidney volume increases can be caused by hypertension. This is even severe for Mexican-American children in south Texas.

Keywords: Obesity; Kidney volume; Hypertension; Child.

Introduction

Obesity causes a decrease kidney function and an increase in kidney volume. The metabolic and inflammatory changes may cause glomerular and tubular damages and elevation of blood pressure, which results in enhancement of hypertension and hyperfiltration, preceding the gradual loss of kidney function (1, 2). Kidney volume increase can be caused by lipid accumulation and microvascular proliferation in glomerular.

Leptin levels are known to be elevated in individuals with higher body mass index (BMI), including children with obesity (3). Leptin stimulates cellular proliferation and type IV collagen production in glomerular endothelial cells, promoting renal fibrosis.

Leptin infusion in normal rats causes glomerulosclerosis and proteinuria. Obese children have higher lipid and lipoprotein compared with their normal-weight peers (4). Obesity-related glomerulopathy segmental glomerulosclerosis (FSGS) occurring in obese patients with BMI>30 kg/m^2 (5) . The glomerular volume was significantly greater in obese children than in control non obese FSGS children (6). Stemmer and colleagues demonstrated that high body adiposity induces an inflammatory and proliferative microenvironment in rat kidneys that promotes the development of pre-neoplastic lesions. Nephropathies in diet-induced obesity rats were characterized by glomerular damage, which was accompanied by "scarring" of some glomeruli, as well as by tubular regeneration, including dilatation of glomerular blood vessels, exfoliation and shedding of proximal tubular cells into the tubular lumen, proteinaceous cast formation, thickened basement membrane, and interstitial inflammation (7).

Obesity affects the blood pressure, which contributes to the increased size in kidney and decrease of kidney function. Obese children have larger kidneys than their normal weight counterparts and correspondingly increased renal blood flow (8). Obesity is associated with glomerular hyperperfusion and hyperfiltration, likely due to afferent arteriolar dilatation (9). Hypertension is probably a major cause of renal dysfunction in obese patients but is likely not the sole hemodynamic cause (10). Hall's mentioned that Glomerular filtration rate (GFR) and filtered sodium load increased markedly, as did renal vasodilation and renal plasma flow, during the development of obesity (11). Sodium retention was caused by increased tubular reabsorption, because total sodium reabsorption and fractional sodium reabsorption both increased markedly during a high-fat diet. Hall's experiments also showed that systolic pressure increased from 128 ± 6 to 149 ± 8 mmHg, and diastolic pressure increased from 66 ± 4 to 80 ± 3 mmHg after 35 days of a high-fat diet (11). Compression of blood vessels, lymph vessels, and ureters in the renal sinus (12) may obstruct the renal outflow tract and increase intrarenal hydrostatic pressure providing a stimulus to increase renal size and activates the renin angiotensin aldosterone system (RAAS), which promotes hypertension and other adverse physiological effects related to obesity. As a result, kidney size may increase (13). Chughtai's study showed that the amount of renal sinus fat was higher in those with stage I and II hypertension (14), and renal sinus fat remained associated with renal size (spearman's correlation 0.42, p < 0.001), serum creatinine (spearman's correlation 0.28, p < 0.001), and the number of prescribed antihypertensive medications (spearman's correlation 0.18, p=0.01). Hyperfiltration was significantly higher in overweight and obesity groups than in normal weight group. Subjects with kidney alteration had higher BMI, body fat markers, lower high-density lipoproteins (HDL) cholesterol, and a non-significant trend to higher systolic blood pressure (BP) than those without abnormalities. Hyperfiltration has also been associated to kidney adiposity and microvascular proliferation in the presence of metabolic syndrome (15).

Fat deposition in the glomerulus may alter renal production of vasoactive and inflammatory mediators related to glomerular damages (1, 16, 17). Lipotoxicity, or cellular lipid overload, contributes to atherosclerosis and organ dysfunction, including renal disease. It involves cellular accumulation of non-esterified free fatty acids (18). There is some evidence that lipids may cause renal mesangial and epithelial cell injury and promote renal-disease progression (19). Alternative animal models of obesity reported lipid accumulation within the renal parenchyma, supporting proposed mechanisms of obesity leading to kidney damage and hypertension through lipotoxicity, oxidative stress, inflammation, and fibrosis (20, 21). The study by Kume and colleagues (22) has demonstrated that with subsequent accumulation of lipid in the kidney, glomerulosclerosis and interstitial fibrosis. In diet-induced obesity (DIO) rats, kidney demonstrated massive and sustained regenerative renal cell proliferation, resulting in simple tubular hyperplasia, indicated by a broad increase of cell number and multilayered tubules. Stemmer et al. evaluated that a potential contribution of circulating free fatty acids and renal triglyceride accumulation to the observed renal pathology in DIO rats (7).

No research has been done related to increase kidney volume in obese children in South Texas.

The objective of this study was to understand the relationship among kidney volume, obesity and blood pressure in Mexican-American children in South Texas.

Methods

To study the effect of obesity and blood pressure in kidney volume, blood pressure, BMI, and liver enzymes where measured. Ultrasonography was requested for patients whenever the patient was gaining excessive weight and the readings for alkaline phosphatase levels were 2 times the standard deviation (2SD) above the normal population or when liver enzymes were elevated, SGOT above 50/46, SGPT above 47/41, and GGT above 32/28 for both boys and girls respectively. BMI percentiles were calculated using the CDC (23) (Centers for Disease Control and Prevention) BMI-for-age growth charts. Since overweight occurs in kids in south Texas often, the amount of children, who have BMI percentile less than 5% is very few. Thus, we set the BMI percentile into four categories: BMI (0, 50%), BMI (50%, 85%), BMI (85%, 95%) and BMI above 95%. By the liver size, fatty liver was recorded as 1 (fatty liver) and 0 (non-fatty liver). Similarly, hepatomegaly was recorded as 1 (hepatomegaly) and 0 (non-hepatomegaly). The variable systolic blood pressure has three categories: 110 mmHg below, 110-119, and 119 mmHg and above. The image readings were made at three different facilities assigned to two groups of radiologists. Ultrasound included three measurements of the right kidney. This allowed the calculation of kidney volume: length×width×depth×0.5236. We obtained 454 ultrasounds for 289 girls and 762 ultrasounds for 382 boys visiting a pediatric clinic in South Texas from 2003 to 2018. A summary of the data can be found in Table 1. Data analysis was done with IBM SPSS. Analysis of variance was used to study the relationship between the variables. The analysis of the data was done under TAMIU IRB approval # 2012-01-13.

Results

There are no differences for kidney volume between children with fatty liver and non-fatty liver, when comparing children with BMI percentile less than 50%, 50 to 82 percent, and 85 to 95%. However, for BMI percentile above 95%, children with fatty liver have larger kidney volume when compared with children with non-fatty liver, [Figure 1 (df1 = 1, df2 = 1206, F = 97.95, p < 0.01)].
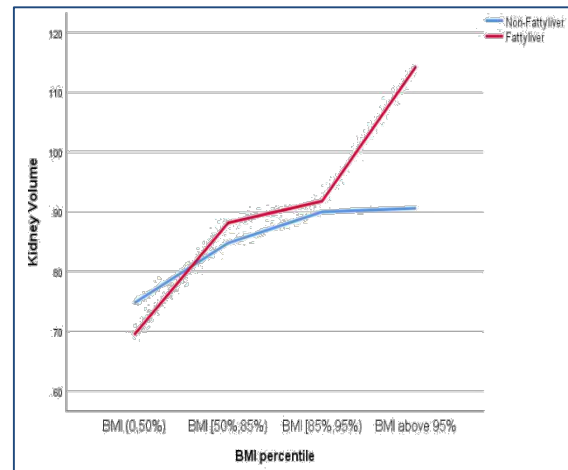
Figure 1. Relationship between BMI percentile and kidney volume for fatty liver and non-fatty liver.

When comparing children with BMI percentile less than 50%, BMI percentile 50% to 85%, BMI percentile 85% to 95% and BMI percentile above 95%, the kidney volume increases as BMI increases (df1 = 3, df2 = 1212, F = 11.21, p < 0.01), (Figure 2). There is a statistically significant difference in kidney volume between BMI percentiles 50%, BMI percentile 50% to 85%, and BMI percentile 85% to 95% when compared with BMI above 95 (p < 0.000, p = 0.001 and p = 0.002, respectively) (Figure 2).
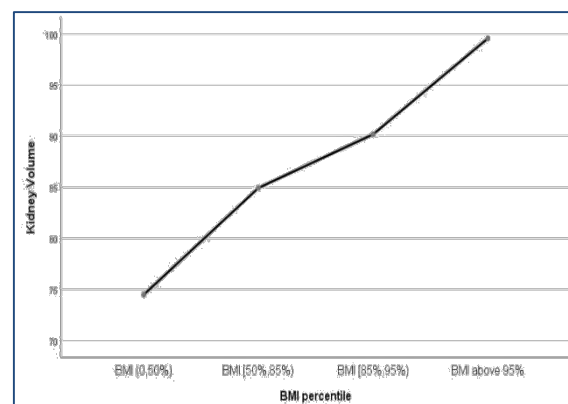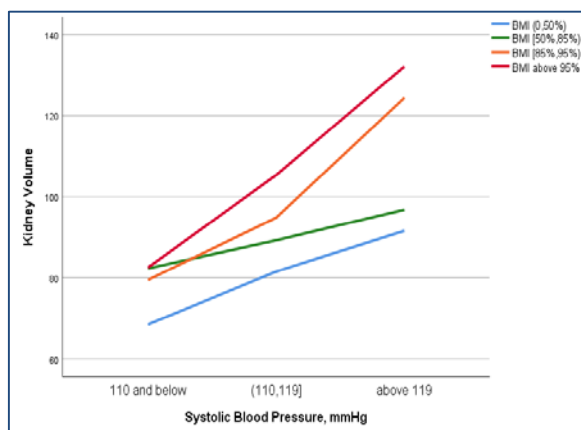

Figure 2. Relationship between BMI Percentile and kidney volume.

We also found that there is a positive relationship between kidney volume and systolic blood pressure. Children with high systolic blood

pressure, above 119 mmHg have a larger kidney volume when compared to children with low blood pressure, above 110 mmHg but less or equal to 119 mmHg, and 110 mmHg and below; 129.28 mL, 101.88 mL, and 81.27 mL (df1=2, df2=1189, F=143.2, p < 0.01), (Figure 3). Children with systolic blood pressure less than 110 mmHg have less kidney volume when compared with children with blood pressure from 110 to 119 mmHg and children with systolic blood pressure above 119 mmHg. Mean difference 29.60 mL and 48.01 mL, respectively (p < 0.00). Children with systolic blood pressure from 110 to 119 mmHg have less kidney volume than children with systolic blood pressure above 119 mmHg. Mean difference 27.41 mL (p< 0.00). Kidney volume increases for every BMI percentile classification as blood pressure increases, (Figure 4).
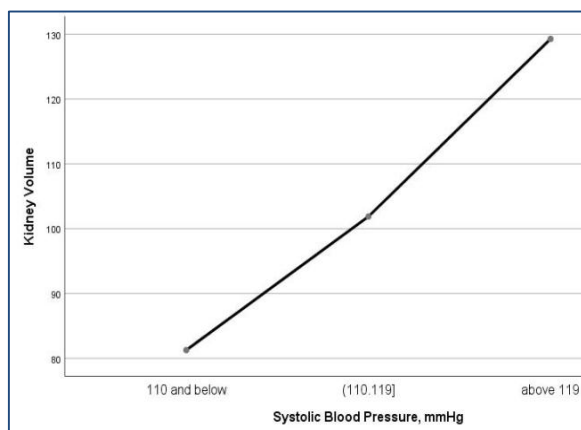
Figure 3. Relationship between systolic blood pressure and kidney volume.

Figure 4. Relationship between systolic blood pressure and kidney volume by BMI levels.

Discussion

We can conclude from the results of this study that there is a statistically significant difference in kidney volume between BMI percentiles above 95% and any other three categories of BMI percentile. The differences in kidney volume between BMI percentile (0, 50%) and [50%, 85%) are not statistically significant. These make sense since based on CDC (23) BMI percentile (5%, 85%) is defined in the category healthy weight and BMI percentile [85%, 95%) is defined as category overweight while BMI percentile 95% and above is defined as category obese.

Foster MC. and colleagues (24) showed that individuals with fatty kidney had higher systolic blood pressure and diastolic blood pressure compared to those without fatty kidney (both p < 0.0001). The results suggest renal sinus fat may be associated with blood pressure regulation and chronic kidney disease in humans and provides additional insight into the pathophysiologic role of adiposity in renal dysfunction. We can also see that in our study the three categories of systolic blood pressure are statistically significantly different for kidney volume. The higher systolic blood pressure, the larger kidney volume. Tu et al. showed that for BMI > 85th percentile, there was a fourfold increase in the prevalence of high blood pressure across all age groups (25). Sorof et al. showed that the prevalence of hypertension increased progressively in school children as the BMI percentile increased from <5th to >95th percentile (26).

Martin-Del-Campo and colleagues (27) have shown that kidney alteration is more frequent in children and adolescents with overweight/obesity than in those with normal BMI. Gunta et al. concluded that the epidemiological and scientific evidence is convincing and indicates that reduction in obesity might help decrease the burden of chronic kidney disease in the population (28). Nehus E. and Mistsnefes, M. summarized the mechanisms of kidney disease in obesity (29). They described three main mechanisms. Hemodynamic factors that include sodium retention and the activation of the renin-angiotensin-aldosterone system which explain the relationship between blood pressure and kidney volume.

Table 1. Children BMI percentile, kidney volume, systolic blood pressure, and fatty liver

BMI percentile	N	Kidney Volume*(mL)	Systolic BP*(mmHg)	Fatty liver %
(0,50%]	44	74.49 ± 25.74	108.93 ± 11.04	5 %
[50%, 85%)	91	84.94 ± 28.24	108.72 ± 8.43	6 %
[85%, 95%)	189	90.19 ± 32.78	110.06 ± 13.45	13 %
Above 95%	892	99.57 ± 40.66	112.72 ± 10.57	38 %

* Mean± Standard error

Adipokines, obesity increases the secretion of leptin and reduces the secretion of adiponectin, adiponecin is an anti-inflammatory factor and leptin is an inflammatory factor. The changes in adipokines concentrations explain why the kidneys increase in volume as BMI increases, and Dysregulated lipid metabolism, lipotoxicity which explain the accumulation of lipids in the kidney cells, increase of kidney volume, and kidney disease.

When we compare the results of our previous kidney's function study (30) that showed that eGFR decreases as BMI increases, and the mechanisms of kidney disease in obesity described above (29), we can conclude that the increase in kidney volume caused by obesity and the increase in blood pressure results from a change in the metabolism, histology of the kidneys, and accumulation of lipids in the kidneys cells. These changes include inflammation, glomerular filtration rate, adipose tissue accumulation, and fibrous tissue formation. All of them cause an increment of total kidney volume and decreasing function.

Our previous study (30) showed that liver size increases for boys and girls as the child becomes overweight and obese and this relationship is maintained as the child ages. It also showed that BMI percentile increases as the probability of fatty liver and hepatomegaly increases. It comes as no surprise, as we can see that children with fatty liver have a higher kidney volume when compared to children with no fatty liver, Figure 1. Kidney volume was higher for children with fatty liver for BMI percentile 95% as can be seen in Figure 2. Earlier reports have associated renal lipid accumulation with the pathogenesis of chronic kidney disease in animal models of DIO (31, 32, 22) and (33, 17) diabetes. Dwyer's study has observed this conclusion, in which obese rabbits exhibited larger kidneys with larger fat deposits within the renal sinus (34).

Wan et al. (35) compared diets with different levels of fat and their relationship with cardiometabolic risk factors.

Higher-fat diets showed an increase in C-reactive protein, hs-CRP, leukotriene, LTB, thromboxane B2, TXB2, and prostaglandin E2, PGE2 all involved in inflammation and tissue damage. These findings support the relationship between higher lipid levels and inflammation.

Millar et al. (36) found a positive association between frequency of consumption of sugar sweetened beverages and BMI z-scores and between frequency of consumption of high fat food and BMI z-scores, where higher consumption was associated with a greater proportion of BMI z-scores.

Ma and colleagues (37) concluded that daily dietary glycemic index was positively associated with BMI, with a five-unit increase in glycemic index being significantly associated with an increase of 0.75 units in BMI.

Conclusion
The children visiting our pediatric clinic showed an increase of kidney volume when they were overweight, obese, and when they had high blood pressure.

Conflict of Interest
The authors declared no conflict of interest.

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