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Original Article

Histopathological Association between Vascular Hypertensive Changes and Different Types of Glomerulopathies

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Abstract

Introduction: The term hypertensive nephrosclerosis has traditionally been used to describe a clinical syndrome characterized by long-term essential hypertension, hypertensive retinopathy, left ventricular hypertrophy, minimal proteinuria, and progressive renal insufficiency. In the absence of renal biopsy, the diagnosis of hypertensive nephrosclerosis is one of exclusion.

Methods: We retrospectively studied 735 patients who had renal biopsies at Ain Shams University Hospitals between January 2008 and Dec 2010. The prevalence of vascular hypertensive changes was studied in relation to clinical presentation and the glomerular pathology pattern.

Results: Male to female ratio was 1:1 and the mean age was 27±17 years. No vascular hypertensive changes were found in 44.5% of biopsies while mild, moderate and severe changes were found in 28%, 22% and 4.2% respectively. Malignant hypertensive changes were seen in 1.2% of biopsies. Lupus nephritis was the most common etiology representing 18.9% of all cases, followed by focal segmental glomerulosclerosis (FSGS) (13.5%), membrano-proliferative glomerulonephritis (13.3%) and membranous glomerulonephritis (8.2%). Moderate to severe vascular hypertensive changes were more common in biopsies with FSGS compared to other glomerulopathies. Hypertensive nephrosclerosis as the sole cause of renal failure represented only 1.6% of cases. Significant associations were found between the degree of vascular hypertensive changes and the grade of hypertension. Patients with severe vascular hypertensive changes were significantly older and had significantly higher serum creatinine levels compared to other groups.

Conclusion: History and grade of hypertension significantly influence the degree of vascular hypertensive changes in renal biopsy. Moderate to severe vascular hypertensive changes were more common in biopsies with FSGS compared to other pathologies.

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Editor's note: See editor's note at the end of this study.

Introduction

The link between hypertension and the kidney has been considered a villain-victim relationship. Nephrosclerosis, benign nephrosclerosis, and hypertensive kidney disease are terms that clinicians use when renal damage is thought to be secondary to essential hypertension [1,2]. The term hypertensive nephrosclerosis has traditionally been used to describe a clinical syndrome characterized by long-term essential hypertension, hypertensive retinopathy, left ventricular hypertrophy, minimal proteinuria, and progressive renal insufficiency. Most cases are diagnosed based solely on clinical findings [3]. The syndrome is often mildly symptomatic, but the prognosis is never benign, due to cardiovascular and renal burden. The main differential diagnoses are atherosclerotic ischemic renal disease, poorly symptomatic nephropathies or the sequel of unnoticed malignant hypertensive nephrosclerosis [4].

The syndrome is characterized histologically by vascular, glomerular, and tubulointerstitial involvement [5]. In the future, recognition of the variants on the ApoL1 gene on chromosome 22 is likely to provide a sensitive and specific diagnostic tool [6]. Upon gross pathologic examination, the kidneys are shrunken and scarred. Pathologic abnormalities seen on renal biopsy specimens include obsolescence of glomeruli, interstitial fibrosis, arterial intimal fibroplasia and hyalinization of arterioles and small arteries. Fibro-intimal proliferation of the arcuate arteries, myointimal hypertrophy of the interlobular arteries and hyaline degeneration and sclerosis of afferent arterioles are the most characteristic findings. Interlobular arteries often show reduplication of the internal elastic lamina and medial hypertrophy. The

arterial wall shows hyaline changes. The arteriolar lumen is narrowed [7].

The risk of end-stage renal disease is increased when atherosclerotic lesions in large renal arteries coexist. Older age, systolic hypertension, proteinuria, and concomitant cardiovascular disease are well-known promoters of renal failure. A multi-factorial strategy including antihypertensive and antiproteinuric drugs along with lipid-lowering and anti-platelet agents could improve cardiovascular and renal outcomes in patients with nephrosclerosis [1].

Methods

This study was conducted on 735 patients who underwent renal biopsy in Ain Shams University Hospitals during the period from January 2008 to December 2010. Patient's data were collected retrospectively from their medical records. Hypertension was graded according to the European Societies of Hypertension and Cardiology guidelines [8].

All renal biopsies were stained with H&E, trichrome, Congo red and PAS stains. Examination of the blood vessels and grading of the vascular hypertensive changes, if present, was done according to a classification made by Saltz et al in 1957 [9]: Grade I: minor localized thickening of the vessel wall; Grade II: thickened vessel wall equal to the diameter of the lumen; Grade III: the wall thickening exceeded the diameter of the lumen. Malignant vascular hypertensive changes were reported as a separate entity.

Data was analyzed using SPSS® version 18.0. Fisher's exact test and Yates' corrected chi-square were computed for 2x2 tables. One-way ANOVA test was used to compare quantitative variables. P value<0.05 was considered significant.

Results

A total of 735 reports of renal biopsies done during the past three years were checked. Male to female ratio was 1:1 and the mean age was 27±17 years. One hundred and eighteen patients (16.1%) had past history of hypertension. The most common clinical presentations are shown in Figure-1. Only 65 patients (8.8%) were maintained on steroid therapy at the time of biopsy. Grades of hypertension according to European Societies of Hypertension and Cardiology are shown in Figure-2. The degrees of vascular hypertensive changes are shown in Figure-3.

Figure-1: Clinical presentation of studied patients

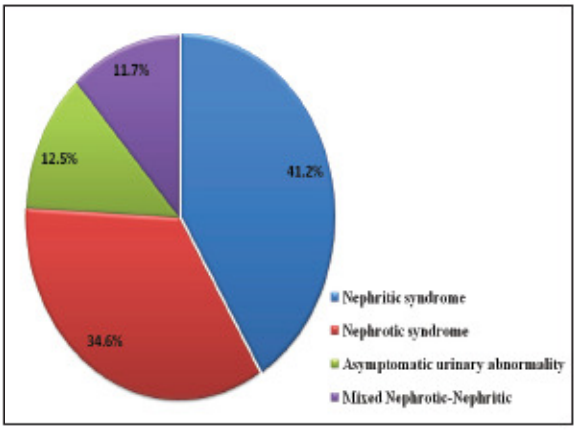


Figure-2: Grades of hypertension in studied patients.

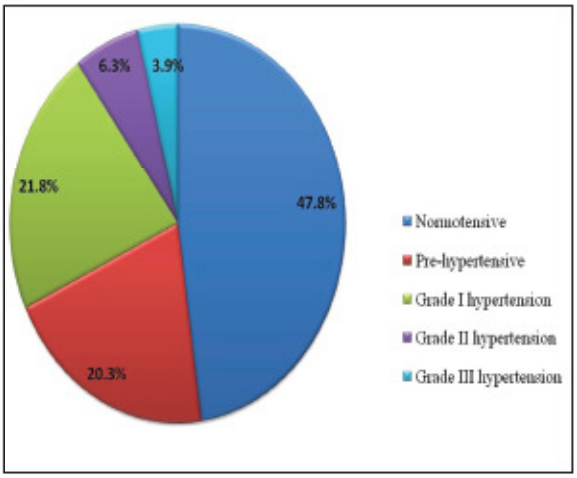
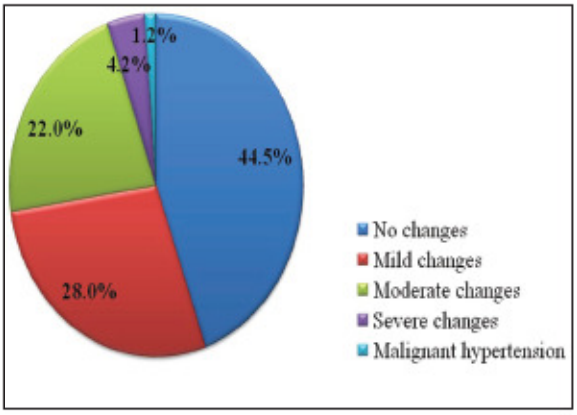


Figure-3: Degree of vascular hypertensive changes in studied biopsies.



Lupus nephritis was the most common etiology representing 18.9% of all cases, followed by focal segmental glomerulosclerosis (FSGS) representing 13.5%, membrano-proliferative glomerulonephritis (MPGN) representing 13.3% and membranous glomerulonephritis (MGN) representing 8.2%. Hypertensive nephrosclerosis as the sole cause of renal impairment was seen in only 1.6% of biopsies.

There was no significant association between maintenance on steroid therapy and the degree of vascular changes. Patients with history of hypertension represented 6.4% of biopsies with no vascular hypertensive changes, 13.6% of biopsies with mild changes, 32.1% of biopsies with moderate changes, 41.9% of biopsies with severe changes, and 44.4% of biopsies with malignant hypertensive changes ($p<0.001$).

Significant associations were found between the degree of vascular hypertensive changes and the grade of hypertension (Table-1), the clinical presentation (Table-2) and the pathological diagnosis (Table-3).

Mean age, mean systolic blood pressure (SBP), mean diastolic blood pressure (DBP) and mean serum creatinie levels were significantly different between different categories of vascular hypertensive changes (Table-4).

Table-1: Association between the degree of vascular hypertensive changes and the grade of hypertension

Grade of hypertension	Vascular hypertensive changes				
	No changes	Mild	Moderate	Severe	Malignant hypertension
Normotensive (n=351)	215 (61.3%)	94 (26.8%)	38 (10.8%)	2 (0.6%)	2 (0.6%)
Pre-hypertension (n=149)	57 (38.3%)	55 (36.9%)	31 (20.8%)	5 (3.4%)	1 (0.7%)
Stage I (n=160)	48 (30.0%)	43 (26.9%)	60 (37.5%)	8 (5.0%)	1 (0.6%)
Stage II (n=46)	2 (4.3%)	9 (19.6%)	25 (54.3%)	8 (17.4%)	2 (4.3%)
Stage III (n=29)	5 (17.2%)	5 (17.2%)	8 (27.6%)	8 (27.6%)	3 (10.3%)

P<0.001

Table-2: Association between the degree of vascular hypertensive changes and the clinical presentation

Clinical presentation	Vascular hypertensive changes				
	No changes	Mild	Moderate	Severe	Malignant hypertension
Nephrotic syndrome (n=254)	137 (53.9%)	76 (29.9%)	39 (15.4%)	2 (0.8%)	-
Nephritic syndrome (n=303)	109 (36.0%)	84 (27.7%)	81 (26.7%)	23 (7.6%)	6 (2.0%)
Mixed (n=86)	22 (25.6%)	19 (22.1%)	36 (41.9%)	6 (7.0%)	3 (3.5%)
Asymptomatic urinary abnormality (n=92)	59 (64.1%)	27 (29.3%)	6 (6.5%)	-	-

P<0.001

Table-3: Association between the degree of vascular hypertensive changes and the pathological diagnosis

Pathological diagnosis	Vascular hypertensive changes				
	No changes	Mild	Moderate	Severe	Malignant hypertension
Lupus nephritis (n=139)	67 (48.2%)	48 (34.5%)	16 (11.5%)	4 (2.8%)	4 (2.9%)
FSGS (n=99)	28 (28.3%)	24 (24.2%)	37 (37.4%)	8 (8.1%)	2 (2.0%)
MPGN (n=98)	38 (38.8%)	33 (33.7%)	25 (25.5%)	2 (2.0%)	0
MGN (n=60)	27 (45%)	19 (31.7%)	14 (23.3%)	0	0
Hypertensive nephropathy (n=12)	0	0	8 (66.66%)	2 (16.7%)	2 (16.7%)

P<0.001

Table-4: Difference between different categories of vascular hypertensive changes with regardto age, SBP, DBP and serum creatinine

Pathological diagnosis	Vascular hypertensive changes					
	No changes	Mild	Moderate	Severe	Malignant hypertension	p
Age (years)	21.9±15.3	25.3±17.0	34.5±17.8	40.2±15.8	33.8±17.6	<0.001
SBP (mmHg)	118.9±17.5	123.4±20.4	137.4±22.7	153.9±24.7	156.7±31.2	<0.001
DBP (mmHg)	73.4±12.1	75.7±11.9	82.9±12.6	90.3±12.2	94.4±17.	<0.001
Serum creatinine (mg/dL)	1.7±2.7	2±2.6	3.3±3.3	6.2±5.3	3.6±2.6	<0.001

P<0.001

Discussion

We found that mild vascular hypertensive changes were the most prevalent finding in studied renal biopsies while both malignant and severe changes were uncommon. This coincides with Saltzet et al who examined renal biopsies from 1251 hypertensive patients over 10 years and graded the abnormalities of the small arterioles based upon the degree of thickening of their walls at the expense of the lumen [9]. They found that severe vascular disease was uncommon (5% of all cases) while moderate or slight arteriolar sclerosis predominated (93% of all cases) in these patients with essential hypertension.

Our study showed significant association between the degree of vascular hypertensive changes and history of hypertension as well as between it and the grade of hypertension.These findings agree with Fogo et al who found that renal biopsies in non-diabetic hypertensive African-Americans with mild to moderate renal insufficiency in the absence of marked proteinuria were over whelmingly likely to show renal vascular lesions consistent with the clinical diagnosis of hypertensive nephrosclerosis [10]. Also our results agree with Ninomiya et al who studied the relationship between the severity of renal arteriosclerosis and BP levels among 652 consecutive population-based autopsy samples. They found that both hypertensive and pre-hypertensive subjects had significantly higher frequencies of renal arteriosclerosis than subjects with normal BP [11].

In this study most of the patients diagnosed as FSGS showed evidence of vascular hypertensive changes (71.7%). This came in agreement with Dumoulin etal who studied 72 patients with idiopathic membranous glomerulonephritis (IMGN) progressing to renal insufficiency. Those patients were divided into two groups: 42 patients had MGN only (group I) and 30 patients had superimposed FSGS (group II). Group II patients were more hypertensive, and all renal lesions were significantly more severe [12]. Conversely, Meyrier et al stated that a number of nephropathies were characterized histologically by severe vascular lesions in the absence of hypertension. Glomerular pathologies with such assumptions included FSGS. FSGS was commonly associated with severe vascular lesions before significant hypertension developed [13].

Our study showed significant relation between the level of systolic and diastolic blood pressures and the degree of vascular hypertensive changes in studied biopsies. This agrees with Burchfiel et al whose study was conducted on 150 renal biopsies. They demonstrated that diastolic blood pressure (DBP) was positively associated with an elevated degree of renal arteriolar hyalinization [14].

Moreover, our study showed significant relation between the degree of vascular hypertensive changes and the level of serum creatinine at presentation. This agrees with Caetano et al whose study was conducted on 81 hypertensive outpatients. They found that in 65% of patients, hypertensive nephrosclerosis was the sole histological abnormality associated with renal dysfunction. They stated that hypertensive nephrosclerosis, in both its benign and malignant forms, could be a definite cause of chronic renal insufficiency and that a substantial fraction of patients with renal insufficiency and clinical diagnosis of HTN may actually have primary nephrosis (PN) [15].

We found that vascular hypertensive changes tend to be more severe with increasing age of patients. This result came in agreement with Rule et al who biopsied 1203 adult living kidney donors to see whether the prevalence of these histological abnormalities in the kidney increases with age in healthy adults. Their results showed that the prevalence of nephrosclerosis increased with increasing age of the patients. Thus, the prevalence increased from 2.7% for patients aged 18 to 29 years, to 73% for patients aged 70 to 77 years [16].

Conclusion

History of hypertension, grade of hypertension, age, clinical presentation, level of serum creatinine at presentation, and pathological diagnosis are important factors that significantly influence the degree of vascular

hypertensive changes seen on renal biopsy. FSGS is the most common glomerulopathy associated with different degrees of vascular hypertensive changes on renal biopsy.

Acknowledgment

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Editor notes

The information given by the analysis in this study can be useful, only when the reader is aware of the nature of problems with this type of studies.

In this descriptive study, the authors used not only the patients' clinical records but also the original pathology records. Accordingly, time- lead bias and interpreter's disagreement are likely major drawbacks that a ppreciably limit the validity of the provided conclusions. It would have been better if one author examined all slides, using agreeable pre-defined criteria while masked for the clinical and laboratory data.

By default, description cannot detach what is secondary from what is primary. This adds heavily to the problem of validity mentioned above.

Professor Assem K El-Sherif

Associate Editor

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