

# ASSESSMENT OF THE LEVEL OF EXCRETION OF MARKERS OF ANGIOGENESIS IN PATIENTS WITH RENAL NEPHROSCLEROSIS DUE TO CHRONIC PYELONEPHRITIS

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## Abstract:

Currently, based on the results of a large number of population and scientific studies conducted worldwide, special attention is paid to the development of optimal treatment regimens depending on the presence of clinical components of renal nephrosclerosis in chronic pyelonephritis. At the same time, identifying tubulointerstitial fibrosis in the formation of chronic kidney disease in a pathogenetic interrelationship with inflammatory processes is one of the urgent tasks of optimizing differential therapy.

The article fully covers the determination of the prognostic value of markers for predicting the degree of damage to kidney structures during the treatment stages of patients with nephrosclerosis on the basis of chronic pyelonephritis.

**Keywords:** chronic pyelonephritis, kidney nephrosclerosis, angiogenesis regulators, kidney microcirculation network, antiangiogenic factor, endothelial cells.

## Introduction

Today, based on the results of a large number of scientific studies conducted worldwide, special attention is paid to the development of appropriate treatment regimens depending on the presence of clinical components of renal nephrosclerosis in chronic pyelonephritis. At the same time, identification of tubulointerstitial fibrosis in the formation of chronic kidney disease with factors of pathogenetically related inflammatory process management is one of the urgent tasks of coordination of differential therapy.

The concept of chronic kidney disease, which reflects the nature of kidney pathology and the rate of progression, determines the need to search for biomarkers of kidney damage to coordinate the treatment and diagnosis of patients. The problem of kidney nephrosclerosis in patients with chronic pyelonephritis remains one of the main problems of nephrology and internal medicine in general due to the high prevalence of kidney disease among the population. It is known that 30-60% of patients with kidney diseases develop nephrosclerosis, and its pathogenetic mechanisms have been actively

studied in recent years. Early diagnosis of these conditions, effective treatment and creation of principles of prevention is an urgent problem of medicine.

The interdependence of clinical, biochemical and molecular indicators of the development of kidney nephrosclerosis based on chronic pyelonephritis indicates the need for a comprehensive assessment of the initial indicators of the development of nephrosclerosis in patients in the research group. This prognostic model combines the pathophysiological significance of clinical and molecular biomarkers of the development of renal nephrosclerosis in patients with chronic pyelonephritis and confirms the necessity of using nephroprotective therapeutic principles.

In modern conditions, it is very important to identify and improve the functional characteristics of certain biomarkers for the purpose of more objective and early assessment of kidney tissue damage, as well as new signs of kidney tissue damage. Searching for new non-invasive signs of chronic kidney disease and evaluating their interaction with known risk factors on the risk of developing renal nephrosclerosis is a priority task of the internal medicine clinic in the treatment of patients with chronic pyelonephritis.

## **2. Materials and Methods**

In this case, the markers can be directly involved in the processes of renal parenchyma fibrosis and inflammatory processes, intercellular interaction, indirectly involved in the processes of activation of fibrosis. This is related to the polyfactorial process of fibrosis in chronic pyelonephritis. An important pathogenetic link in the development of chronic kidney disease is damage to the cells of the renal tubules, as well as damage to the vascular endothelium in the area of inflammation, growth factors and cytokines that support active inflammation and cause the proliferation of interstitial fibroblasts. leads to production.

The level of angiogenesis-activating factor (VEGF) was determined in large quantities in the urine of the examined patients. At the same time, the production of VEGF in the epithelial cells of kidney balls and tubules was closely related to the level of proteinuria and cholesterol.

A large amount of VEGF activator of angiogenesis was detected in kidney glomeruli (its vascular rings) and tubulointerstitium (vascular endothelial cells and tubulocytes). VEGF protects the endothelium from damage, increases the permeability of blood vessels, causes vasodilation by activating the NO system, and interacts with the blood clotting system.

When assessing the state of the kidney microcirculation network, it was observed that the higher the production of VEGF by the renal glomeruli, the higher the density of atherosclerosis, glomerulosclerosis and peritubular capillary network. Antiangiogenic factor thrombospondin-1 (THSBN-1) and its secretion increased in the presence of decreased kidney function and morphological signs of severe nephrosclerosis.

According to our data, higher values were associated with severe atherosclerosis and decreased peritubular capillary density, which reflected its role as an angiogenesis inhibitor. High urinary excretion of VEGF, THBSN-1 was observed in patients with renal nephrosclerosis, marked proteinuria with chronic pyelonephritis, nephrotic syndrome and associated hyperlipidemia. At the same time, VEGF is a strong stimulator of angiogenesis.

It is known that it protects the endothelium from damage, increases the permeability of blood vessels, causes vasodilation, interacts with the blood clotting system, which is important for patients with nephrosclerosis of the kidneys, who have endothelial dysfunction. and is characterized by a tendency to hypercoagulation.

### 3. Results

Based on the results of the study on the relationship between VEGF, THBSN-1, angiogenesis regulators, and the secretion of polyuria and its symptoms of kidney damage in patients with proteinuric forms of nephrosclerosis accompanied by chronic pyelonephritis, it is shown that the main test, which reflects the damage of the renal glomeruli, is can be considered as an indicator and indicate proteinuric/hypoxic damage to the tubulointervention.

At the same time, it is accompanied by the release of a large number of cytokines, including the production of regulators of angiogenesis, and this, in turn, is an additional stimulus to intensify the process of nephrosclerosis in the kidneys.

According to the results of the study, the level of angiogenesis-activating factor was determined in large quantities in the urine of the examined patients.

VEGF production in glomerular and tubular epithelial cells was associated with proteinuria and cholesterol levels. In addition, it was found that the production of VEGF by tubulocytes in severe chronic kidney disease is inversely related to the morphological indicators of sclerosis activity.

Significant differences were noted in the quantitative parameters of thrombospondin-1 in both groups of patients ( $1585.56 \pm 24.52$  pg/g) and were reliably higher compared to healthy subjects (Table).

**Table Urinary excretion of markers of angiogenesis according to the presence/absence of nephrosclerosis in patients with chronic pyelonephritis**

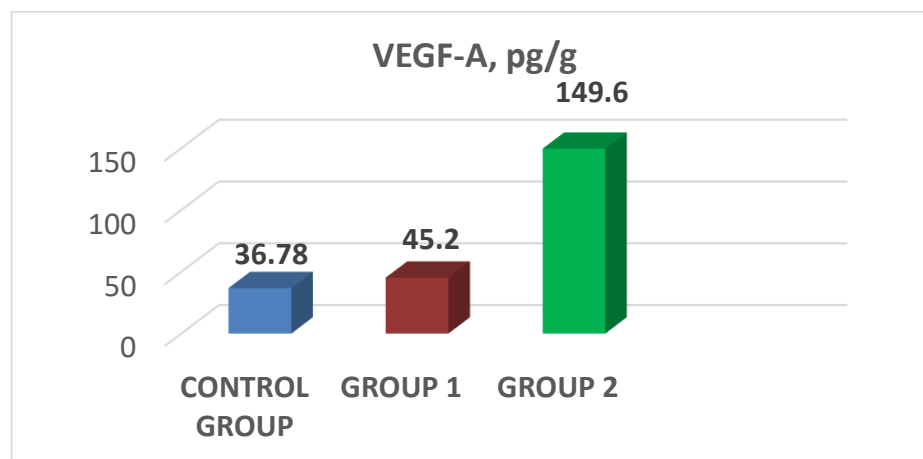
| Indicators    | Control group<br>n= 24 | Group 1<br>n = 40  | Group 2<br>n = 38     |
|---------------|------------------------|--------------------|-----------------------|
| VEGF, pg/g    | $36,78 \pm 3,12$       | $45,24 \pm 3,68$   | $149,56 \pm 8,52^*$   |
| THSBN-1, pg/g | $228,61 \pm 11,79$     | $498,56 \pm 18,74$ | $1585,56 \pm 24,52^*$ |

Note: \*- significant compared to control group,  $P < 0.05$ .

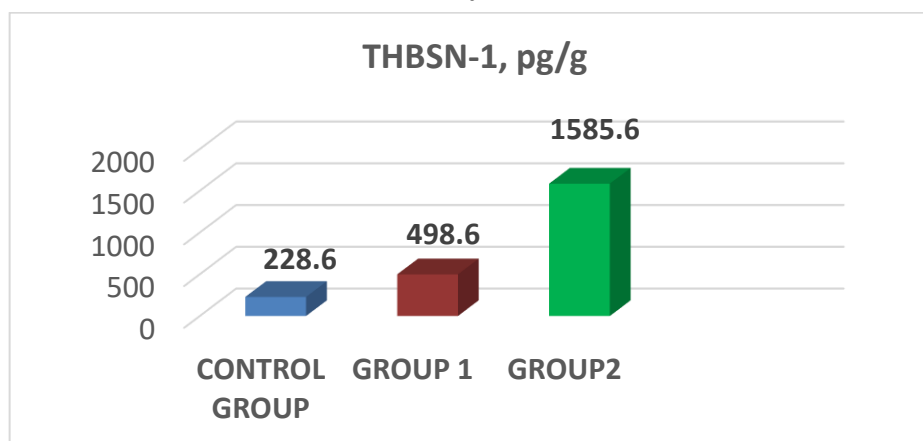
According to the results of the study, the secretion of the antiangiogenic factor thrombospondin-1 was higher in the presence of reduced kidney function and morphological signs of severe nephrosclerosis.

Elevated levels of THBSN-1 are associated with severe atherosclerosis and decreased peritubular capillary density, reflecting its role as an angiogenesis inhibitor. High urinary excretion of VEGF, THBSN-1 was observed in patients with renal nephrosclerosis with chronic pyelonephritis, together with proteinuria, nephrotic syndrome and associated hyperlipidemia.

In this group, VEGF ( $45.24 \pm 3.68$  pg/g and  $149.56 \pm 8.52$  pg/g) and THBSN-1 ( $498.56 \pm 18.74$  and  $1585.56 \pm 24.52$ ) Based on the indicators, the high urinary excretion of angiogenesis regulators in patients with nephrosclerosis due to chronic pyelonephritis can be considered as an integral indicator of renal glomerular damage, and this condition indicates proteinuric/hypoxic disorders of the tubulointerstitium.



a



b

**Figure (a, b). Urinary excretion of markers of angiogenesis according to the presence/absence of nephrosclerosis in patients with chronic pyelonephritis**

#### 4. Conclusions

It should be noted that the level of VEGF as the most important activator of angiogenesis was shown by S.V. Plotnikova (2020). According to the author, the higher

the production of VEGF by renal glomeruli, the higher the density of atherosclerosis, glomerulosclerosis and peritubular capillary network to assess the condition of the kidney microcirculation network.

Secretion of the antiangiogenic factor thrombospondin-1 was high in the presence of reduced kidney function and morphological signs of severe nephrosclerosis.

Based on the obtained results, it can be said that in nephrosclerosis developed on the basis of chronic pyelonephritis, activation and damage of endothelial cells occurs, as a result of which pathological reactions in the form of vasoconstriction, thrombosis, hypercoagulation with intravascular fibrinogen deposition, microrheological disorders appear. A change in the rheological properties of blood with damage and separation of the vascular endothelium contributes to the reduction of adaptation in nephrons, and then to the development of glomerular and tubulointerstitial fibrosis.

The obtained data allow us to consider the increase in the level of VEGF in the urine of patients with renal nephrosclerosis developed on the basis of chronic pyelonephritis as an early sign of kidney hemodynamic disorders, as well as a criterion for the onset of an irreversible nephrosclerotic process.

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