# MANAGEMENT OF ARTERIAL HYPERTENSION IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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**ABSTRACT:**Hypertension (HTA) is a global public health problem, and is considered to be one of the major risk factors for heart disease, stroke and kidney failure. Chronic kidney disease (CKD) is a complication of uncontrolled hypertension. The positive correlation between CKD and HTA is very complex and the impact of HTA on the progression and deterioration of renal function is a multifactorial mechanism increasing the risk of both cardiovascular disease (CVD) and cerebrovascular disease. A large number of different H in patients with chronic renal disease including electrolyte dysregulation (especially sodium), changes in renin-angiotensin-aldosterone system activity, and increased sympathetic nervous system. Standardized measurement of blood pressure is essential in establishing the diagnosis, early detection and management of hypertension in patients with CKD in the early stages (1). Uncontrolled high blood pressure is the second leading cause of renal failure in the general population. Chronic renal disease (CKD) is a clinical condition associated with progressive and irreversible damage to kidney tissue during various diseases of the urinary tract. . Hypertension (HTA) still remains the most common cardiovascular manifestation in patients with CKD. In the pretermal stage of the disease it is known to lead to hyperhydration, respectively to an increase in the volume of extracellular fluid, which results in HTA and edematous syndrome. HTA during CKD is most often of the volume type, despite the fact that sometimes it may be due to other mechanisms such as during hypernatremia, etc. This basically determines the progressive loss of kidney tissue and leads to the progression of CKD.**The purpose of this study**: was to verify the correlation between HTA and CKD as well as the role of HTA in the progression of chronic kidney disease.**Materials and methods**: this prospective cohort study includes a total number of 80 patients with HTA and CKD (of whom 45 were male, with a mean age of 55.60 ± 10.0, and 35 patients were female with age average of 57.50 ± 8.60 years. All patients were followed for a period of 12 months and every three months we measured lipid fractions. proteinuria and measurement of urea, creatinine, uric acid, electrolytes, ECG, some patients even monitor blood pressure for 24 hours and follow the effects of antihypertensive therapy.**Conclusion:** in conclusion we can propose that the correlation between CKD and HTA requires a more serious approach in achieving control of blood pressure, reduction of proteinuria, avoidance of salt in food, hypoproteinemic diet as well as modifications of healthy lifestyle should to always be considered as a vital component of any management of antihypertensive therapy as well as the avoidance of all factors that contribute to the presentation of HTA. Treatment of HTA is of great importance to maintain residual renal function. There are a large number of studies on the high positive effects of ACE inhibitors or ACE inhibitors combined with diuretics on the treatment of HTA in patients with CKD.

**Keywords**: Chronic kideny disease (CKD), Arterial hypertension (ATN)

## ENTRY

Chronic kidney disease (CKD) is defined as persistent kidney damage accompanied by a decrease in glomerular filtration rate (GFR) and the presence of albuminuria. The prevalence of CKD has increased steadily over the past two decades and was reported to affect over 13% of the U.S. population in 2004. In the U.S. nearly 45% of the population suffers from hypertension (HTA). Only about 1 in 4 people with hta (24%) have their blood pressure under control. in the usa about 37 million people, suffer from CKD (2). The increase in the incidence of CKD is attributed to an aging population and an increase in hypertension, diabetes, diabetic nephropathy, and obesity within the U.S. population and the general population. CKD is associated with a number of complications, including electrolyte imbalance, in particular sodium imbalance, mineral and bone disorders, anemia, dyslipidemia, and HTA. It is well known that CKD is a risk factor for cardiovascular disease (CVD) and that a decrease in GFR and manifestations of proteinuria are independently associated with an increase in mortality due to CVD.In 2017, the American College of Cardiology and the American Association of Cardiology published new guidelines for the management of hypertension and defined high hypertension as blood pressure ≥ 130/80 mmHg while stage 2 hypertension is defined as blood pressure at or ≥ 140/90 mmHg. There is documented evidence from a large number of studies on HTA and the high positive correlation with chronic kidney failure and HTA is counted as the second leading cause in the US after diabetic nephropathy. In the US approximately 20-28%) of adults have HTA and chronic kidney disease (3,4,5). CKD is a chronic reduction in glomerular filtration rate, with a progressive increase in creatinine and urea. CKD can also be defined as a summary of common biological and clinical disorders called chronic uremia. This occurs as a result of progressive loss of

function. .In many cases of progression, the rate of impairment of renal function is a silent process and the patient is unaware that a serious disease with irreversible consequences is operating in his kidneys. The progression and progression of CKD are also influenced by other factors such as: underlying disease, age, sex and genetic predisposition, etc. The rate of progression of CKD depends on the underlying disease leading to damage to the renal tissue and nephrons. Patients with glomerulopathy, vascular nephropathy, diabetic nephropathy and renal polycystosis suffer faster kidney damage, compared to patients with hypertensive nephroarteriolosclerosis, systemic diseases, hereditary diseases, undifferentiated nephroptites, etc. The most important and earliest prognostic marker of renal impairment is proteinuria, microalbuminuria, the severity of which is directly correlated with the rate of progression of renal impairment. The etiology of CKD is diverse and multifactorial (renal disease can be congenital / inherited and acquired) which leads to gradual, progressive, total and irreversible loss of renal function. Renal disease is often chronic and mostly progressive. CKD can be a consequence of diseases that damage the renal parenchyma or that create urinary tract obstruction. The frequency of occurrence of chronic kidney disease varies in different regions of the world. Recently, however, diabetes (diabetic nephropathy) and arterial hypertension have been the main causes of IRK, especially in developed countries. IRK expression is also increasingly seen in the elderly. Kidney diseases by their pathological nature (immunological, infectious, degenerative, hormonal) gradually reach the progressive complete anatomofunctional destruction of the kidney tissue. All this situation causes a reduction of the primary glomerular filtration, respectively the reduction of the glomerular filtration (FG) as a very important element of the kidney function and at the same time the kidneys are not able to perform the excretory function first of all. Then follows the gradual disruption of tubular and medulointerstitialfunction of the kidneys and finally the disorder of hormonal secretion which is responsible for extra and intrarenal hemodynamics, erythropoiesis, homeostasis of calcium (Ca), phosphorus (target) phosphorus (target) these hormones had to act. Hypertension (HTA) remains one of the most important and common disease factors worldwide. In recent years, a number of studies have found and verified a positive and high correlation between HTA and CKD progression. End-stage renal disease (ESRD) is a significant global health problempublic, with an estimated prevalence between 15-46%.

## THE PURPOSE OF THIS STUDY

Was to verify the correlation between HTA and CKD as well as the impact of HTA on the progression of chronic kidney disease.



## MATERIALS AND METHODS:

this prospective cohort study includes a total number of 80 patients with HTA and CKD (of which 45 patients were male, with a mean age of 55.60 ± 10.0 and 35 patients were female with age average of 57.50 ± 8.60 years. All patients were followed for a period of 12 months and every three months we measured lipid fractions, we also examined the progress of proteinuria and measurement of urea, creatinine, uric acid, electrolytes, ECG , in some patients also monitoring blood pressure for 24 hours and monitoring the effects of antihypertensive therapy.

**Table no. 1: Patients presentation based on gender, number of patients, average age**

| | Total number of patients No=80) | Average age ±SD |
|---|---|---|
| Male | 45 (60 %) | 55,60 ±10,0 |
| Female | 35 (40%) | 57,50±8,60 |

Table no 2. Presentation of patients according to nationality

| Gender | Albanian ( 70% ) | Macedonian (30%) |
|---|---|---|
| Male | 35 | 10 |
| Female | 25 | 10 |

Of the total number of patients, 20 of them (30%) were of Macedonian origin while 60 (70%) were Albanian. Of the total number of 30% of Macedonian patients, 10% were male and 10% were female. Of the total number of Albanians 70%, the male gender was 35% while the female gender was 25%.

# IV. RESULTS

The results from the average measurements obtained within 12 months (with measurements every three months - a total of four average measurements) are presented in tabular and graphical form.

Table number 3: Presentation of obtained values of patients with HTA, total- (No = 80) for Total Lipids (LT), total cholesterol (ChT), Treglicerides (TG), HDL-ch and LDL-ch

| | Number of patients | Average ± SD |
|---|---|---|
| LT | 80 | 8.50 ± 1,90 |
| TG | 80 | 4.60±1,00 ↑ |
| ChT | 80 | 8.50 ± 1,80 ↑ |
| HDL-ch | 80 | 1,0± 0,60 ↓↓ |
| LDL-ch | 80 | 4.90 ± 1,80 ↑ |



From the table number 3 of the examined patients in the examined parameters is noticed a significant increase of LDL-ch, TG, Tot.Ch with a decrease of the values of HDL-ch. compared to lipid reference values.

Table 4: Presentation of values of progress, remission and regression of proteinuria and glomerular filtration rate (Glomerular Filtration Rate) according to the formula of Coccroft& Gault

| | Progresioni | Remisioni | Regresioni |
|---|---|---|---|
| Proteinuria | >1.4 g/24 h | <1.0 g/24 h | < 0.4 g/24 h |
| Levels of GF | GF lowered | GF stabile | GF stabile |
| Renal damage | GF lowered | GF stabile | GF better |

The obtained results from the measurements are presented in tabular forms:

Table no 5: Presentation of proteinuria values for 80 patients, obtained from patients before and after application of 20 mg ACEi therapy, and values of the control group

| | Proteinuria before application of ACE i therapy (20 mg) | After 12 months of application of ACEi therapy | Total Number of individuals in control group No=60 |
|---|---|---|---|
| Male – 60 | >3.2 g/24 h | 1.06 g/24 h | <0.36 g/24 h |
| Female – 40 | >3.5 g/24 h | 1.15 g/24 h | <0.36 g/24 h |

Table no 6: Presentation of average values for patients (No= 80) for urea, creatinine, and uric acid; before beginning of treatment of HTA

| Measurements | Female No=35 (average ±SD) | Male No=45 (average ±SD) |
|---|---|---|
| Urea | 15,60 ±2.15 | 18,50 ±3.00 |
| Creatinine | 260.00 ±10,00 | 300.00 ±8.00 |
| Uric acid | 460.00 ±14.00 | 490.00 ±15,00 |

**Table no 7: Presentation of average values for patients (No=80), for urea creatinine, and uric acid; after 12 months treatment with ACEi**

| Measurements | Female No=35 (average ±SD) | Male No=45 (average ±SD) |
|---|---|---|
| Urea | 18.00 ±3.00 | 20,00 ±3,50 |
| Creatinine | 290.00 ±7,00 | 345,00 ±8,40 |
| Uric Acid | 310.00 ±10.00 | 340.00 ±9,50 |



# DISCUSSION

Chronic kidney disease (CKD) regardless of etiology has variable course of progress. Contemporary studies have documented that there is a close positive positive correlation between HTA and CKD. HTA with its daily variations significantly affects apolpoprotrinermic disorders by affecting their stratification in the walls of blood vessels which consists of premature manifestations of coronary atherosclerosis with frequent manifestations of acute myocardial infarction, ventricular hypertrophy of May. pectoris, congestive heart failure and cerebrovascular stroke. Current HTA management guidelines for preventing the progression of chronic renal disease are primarily blockade of the renin-angiotensin system and aggressive control of blood pressure. Several studies have found that people of color black or African-American make up about 35% of people with kidney failure in the United States. These figures are troubling and reflect some of the non-medical reasons for the high rates of high blood pressure in the African-American community. High blood pressure and the early stages of CKD (Chronic KidnayDissaese) usually do not cause clinical or physical symptoms, which which is an important reason to make regular blood pressure checks in order to balance HTA in the initial stages which will prevent or slow down renal damage and rapid progression to terminal renal insufficiency as a result of uncontrolled action of high blood pressure when the only method of secretion is chronic intermittent hemodialysis. Following a healthy diet with extremely minimal amounts of salt, hypoproteinemic diet and taking medications against high blood pressure can prevent the worsening of CKD which in turn can prevent other

cardiovascular and cerebral complications. In addition to HTA, uremic dyslipidemia, manifested by nephroangio-sclerosis, also affects the change of renal functions. And gloemrulosclerosis. It is estimated that 10-13% of elderly patients in the US suffer from SKV and HTA regardless of the degree of CKD. HTA in patients with CKD is most often of the hypervolemic type (6,7). Early detection of HTA in patients with CKD and quality treatment that in the initial stages significantly affects the slowing of chronic renal failure and cardiovascular disease (CVD). Based on the etiology, HTA is classified into: Essential HTA with unknown etiology and HTA is present in 80-90% of the population where the following are counted as causes: genetic predisposition, adiposity, sedentary life, age, gender, hyperlipidemia, etc. And HTA as a cure for various kidney diseases (parenchymatous diseases, nephrosclerosis, renal polystyrene, endocrine disorders, Cushing's syndrome), etc. HTA in patients with CKD is still a major problem for nephrologists in the management of HTA because in addition to the aforementioned disorders of this group of patients there are also disorders of the electrolytes and the renin-angiotensin-aldosterone system. .During HTA in patients with CKD there is an inability to maintain the balance of Na + and water .Treatment of arterial HTA slows the progression of CKD especially in patients who have proteinuria> 1 g / 24 hours.In recent years it has been proven that the most effective good in the treatment of HTA in patients with CKD has been achieved using ACE inhibitors (Lisinopril, Captopril Skopryl, Ramipril, etc.). ACE inhibitors also reduce the effect of angiotensin, but by reducing the amount produced by your body, rather than blocking receptors. ACE inhibitors can often cause a dry cough before it is sometimes necessary to replace them with ARB drugs. If this does not go away, patients are often given an ARB. Proper effects are also shown by angiotensin II-ARB receptor blockers (Avapro (irbesartan), Atacand (candesartan), Benicar (olmesartan), Diovan (valsartan), Micardis (telmisartan), Teveten (eprosartan), Cozaar (losartan) etc. (R = 4.5) Angiotensin receptor blockers (ARBs), also known as angiotensin II receptor antagonists, are used to treat high blood pressure. high blood pressure in patients with CKD, heart attack and heart failure.ARBs reduce the action of the hormone angiotensin II.This hormone has a powerful astringent effect on blood vessels, increasing blood pressure.Angiotensin II also stimulates the maintenance of salt and water in the body, which further increases blood pressure. ARBs work by blocking the receptors on which the hormone acts, especially AT1 receptors, which are found in the heart, blood vessels and kidneys. II helps lower blood pressure and prevent heart and kidney damage. Both groups of drugs are drugs of first choice for younger patients with CKD and high blood pressure (8.9). Prevention of CKD progression requires treatment and medication of HTA, keeping it within acceptable limits, at a pressure of 130/80 mmHg. In the management of HTA, the treatment of proteinuria has an important role, which is an independent factor in determining the rate of progression of CKD as well as the effectiveness of action and impact of drugs of the ACE inhibitor group, serving as a parameter for measuring proteinuria. over 24 hours.Many studies suggest that slowing the course of CKD is achieved when protein loss through urine is <0.3 g / 24 hours and there is improvement in glomerular filtration rate (GFR). Hypertension is one of the leading causes of CKD due to the detrimental effects that increased blood pressure has on the kidney vasculature. Uncontrolled long-term high blood pressure leads to high intraglomerular pressure, impairing glomerular filtration. Damage to the glomeruli causes an increase in protein filtration- proteinuria and microalbuminuria (10,11). The onset of proteinuria (protein-creatinine ratio ≥200 mg / g) develops as chronic kidney disease progresses and is associated with a poor prognosis as for kidney disease as well as for the occurrence of cardiovascular diseases (12,13). The increase in blood pressure leads to damage to the blood vessels inside the kidneys as well as throughout the body. This damage impairs the ability of the kidneys to filter fluids and debris from the blood, leading to an increase in the volume of fluid in the blood with an increase in blood pressure. Primary pathological processes in hypertensive conditions result in progressive loss of glomerular capillaries and filtration capacity in patients with CKD. However, the slower progression of vascular damage to benign nephrosclerosis eventually results in glomerular ischemia and nephron loss. In contrast, significant reduction in functional renal mass in CKD is associated with afferent arteriolar vasodilation, impaired autoregulation, and increased systemic blood pressure transmission to glomerular capillaries, resulting in glomerular damage, proteinuria, glomerulosclerosis, and a progression rapid onset of the disease.Hypertension is an important cause and consequence of CKD. In addition, CKD includes a large group of clinical disorders with a history, course, and heterogeneous pathogenesis. The latest national guidelines from the Joint National Commission for the Prevention, Detection, Evaluation and Treatment of High Blood Pressure VII (JNC VII) and the National Kidney Foundation's Kidney Disease Quality Outcomes Initiative (NKF KDOQI) recommend that blood should be intended to be maintained at <130/80 mmHg as the goal of treatment for patients with CKD. Treatment of HTA is of great importance for maintaining residual kidney function and also prevents damage to blood vessels. It is important to note that one of the important symptoms and complications that occurs during CKD is congestive heart failure (CHF). which is the result of added salt intake. The occurrence of renovascular hypertension occurs due to several mechanisms: disorders of water absorption, disorders of electrolytes, disorders of homeostasis concentration of RAAS and Na +, disorders of "autoregulatory" functions of peripheral vasculature, increased consumption of salt, etc. (14,15). Malignant HTA remains the most common complication which occurs due to volume disorders, although it may be with the etiology of high renin concentrations (hyperreninemia) .The diagnosis is based not only on absolute values of blood pressure but also on the basis of accompanying symptoms such as: headache, nausea, vomiting, confusion, acute left ventricular failure, pulmonary edema, etc. Numerous studies have shown that increased peripheral vascular resistance is closely related to RAAS and disorders between concentrations of calcium and parathyroid hormone (HPT), vasodilator disorders (quinine, prostaglandins), and adjustments of the neuromuscular system of the arterioles. There are a large number of studies on the effects and action of antihypertensive drugs in patients with HTA, of the ACEigroup of 10 mg or 20 mg or ACE inhibitors in combination with diuretics Coprenesa 8mg.2.5 mg (Perindopril / Indopamide). Calcium channel blockers (CCBs) are considered second- or third-line therapy in the treatment of HTA in patients with CKD. (15,16) While there may be no difference in the effect on lowering blood

pressure between iodihydropyridine CCBs (ND-CCBs; e.g., diltiazem, verapamil) and dihydropyridine CCBs (e.g., amlodipine, nifedipine), ND-CCBs have been shown to significantly reduce proteinuria either when used alone or in combination with an ACE inhibitor or an ARB. (16,17). Because of their potential to reduce proteinuria, in addition to their antihypertensive effects, ND-CCBs should be considered as second- or third-line therapy in patients with CKD and diabetes or CKD and non-diabetic proteinuria. Dihydropyridine CCBs can be used as second-line agents in patients with non-diabetic CKD without proteinuria. Common side effects include edema and constipation with ND-CCB (especially verapamil) and rash and peripheral edema with dihydropyridine agents. Common side effects include edema and constipation with ND-CCB (however veraqamil), inhibitors remain as one of the most preferred medications during the HTAN crisis and the treatment of patients with CKD and HTA.

# CONCLUSION

In conclusion we can conclude that the high positive correlation between HTA and CKD requires a very serious approach in achieving control of blood pressure, reduction of proteinuria, avoidance of salt in food, use of a hypoproteinemic diet and modification of the style of healthy living, that all these suggestions should always be considered as a vital component of any management of antihypertensive therapy as well as the avoidance of all the factors that contribute to the presentation of HTA. Treatment of HTA is of great importance to maintain residual renal function. There are a large number of studies on the high positive effects of ACE inhibitors or ACE inhibitors combined with diuretics in the treatment of HTA in patients with CKD. Drugs that reduce proteinuria in addition to lowering blood pressure are generally first-line, but patients may often need two, three to four antihypertensive drugs to achieve their goals and minimize their risk of CVD and CKD.

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