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# **SCIENCE, THEORY AND PRACTICE**

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# SCIENCE, THEORY AND PRACTICE

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## **PATHOGENETIC FEATURES OF THE COURSE OF HIV-ASSOCIATED NEPHROPATHY**

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The number of newly diagnosed HIV infections in the Odessa region at the end of 2013 was 114.8 people per 100 000 population, with patients with a newly diagnosed AIDS rate of 25.8 per 100 000 population, among them 290 died of AIDS, which corresponds to 12.1 per 100 000 population [1].

As is known, immune system disorders in HIV infection are of a systemic nature and are manifested by imbalance and deep suppression of the T- and B-links of cellular immunity, which leads to changes in both functional lymphocyte and monocyte/macrophage activity and immediate and delayed hypersensitivity reactions, humoral immunity and factors of nonspecific defense of the body. In the dynamics of the disease, the functional insufficiency of CD8 + T-lymphocytes, neutrophils and NK cells is increasing. Also, together with the deficit of CD4 + T-lymphocytes, the level of serum immunoglobulin's and circulating immune complexes, catabolism products of cell receptors and changes in nucleic acids also increase. Clinically, changes in the immune status are manifested by allergic, infectious, autoimmune and lymph proliferative immunodeficiency syndromes that determine the clinical manifestations of HIV infection [2, 3].

It has been established that the tendency to progressive development is attributed to the peculiarities of nephrologist's diseases. According to the latest data on the regularity of chronization of kidney lesions, the end result of a number of renal and external renal diseases is the development of chronic kidney disease (CKD) [4].

The criteria for determining CKD are: damage to the kidneys lasting more than 3 months, manifests itself in the form of structural or functional disorders of the organ, with or without a decrease in the glomerular filtration rate (GFR), the glomerular filtration rate is less than 60 ml per minute per 1.73 m<sup>2</sup>; with or without other signs of damage [5].

It is generally recognized that the pathogenetic basis of CKD development is a progressive decrease in the number of functioning nephrons due to their death. To date, there are two main mechanisms of progression of kidney disease - immune and non-immune [6, 7]. The pathogenetic basis of impaired renal function (including excretory) is the reduction in the number and damage of existing nephrons. In clinical conditions, they are manifested in the development of renal syndromes: urinary, nephritic, azotemia, hypertonic, anemic [8].

In general, progressive renal dysfunction contributes to the development of CKD, which leads to chronic renal failure (CRF). So, the final result for all the above mechanisms of damage is the damage and death of nephrons, a decrease in their number, followed by the formation of CKD, which is transformed into CRF [9,10].

Progressive growth in the number of patients with CKD in the world today is regarded as a pandemic. According to the data of large population registries, the prevalence of CKD in the general population is at least 10%, with an annual growth rate of 5-8%. At the end of 2012, there were 490,234 patients with CKD in Ukraine, with a morbidity rate of 5.8% [11].

It is known that renal dysfunction associated with the development of HIV-associated nephropathy is observed in the majority of AIDS patients. In turn, HIV-associated nephropathy is characterized by rapid progression with outcome in CRF [12,13].

Thus, the goal of the study was to determine the functional state of the kidneys and to identify the pathogenetic features of HIV-associated nephropathy in AIDS patients.

### **Materials and methods**

It was analyzed 2,915 medical records of inpatients who received treatment at the inpatient department of the Odessa Regional Center for AIDS Prevention and Control from 2006 to 2011. Of these, 2,404 patients after treatment were discharged, accounting for 82.47% and 511 deaths (17.53%).

Also, the character of functional changes in the kidneys was studied and analyzed in 129 AIDS patients who were on inpatient treatment at the Odessa Regional AIDS Prevention and Control Center. Morphological studies of the kidneys were carried out on the material obtained from the study of the kidneys from 21 patients admitted to the department of the patanatomy of the 11th City Clinical Hospital in Odessa. The comparison group consisted of materials obtained from 7 patients who did not have AIDS, with concomitant chronic pyelonephritis, and the main group consisted of materials from 15 patients diagnosed with AIDS, IV clinical stage with kidney pathology.

The study of kidney function after water-salt load in 10 patients with AIDS, as well as in 10 patients without AIDS (a comparison group) was performed. For a water-salt load, 0.5% sodium chloride solution was used in a volume of 0.5% of the body weight of the patient, the urine was collected at 1:00.

The study was conducted as follows: at 7 am the day after the study of the day, the study completely releases the bladder, after which he was asked to drink a 0.5% solution of sodium chloride in the calculation of 0.5% of body weight. Further within an hour the patient was at rest in a supine position. An hour later, the urine was

collected, its amount was measured and the concentration of creatinine was determined by a standard procedure. The total volume of the extracted urine was measured, from which a sample was taken to determine the creatinine concentration. Then, creatinine excretion was calculated for water-salt load, urinary flow rate for 1 min., creatinine clearance (CC) filtration.

### Results

Among HIV-infected people diagnosed with chronic pyelonephritis, 1875 patients were found which was 64.3% of the total number of people treated. Of these, men were 984 people (52.48%), women - 891 (47.52%). Among the patients discharged, the number of patients with pyelonephritis was 1,443 (60.0%). Of these, men - 772 (53.5%), women - 671 (46.5%). In patients with a fatal outcome, the diagnosis of pyelonephritis was established in 432 cases (84.5%). Of these, men comprised 296 people (68.52%), women - 136 (31.48%).

Patients with pyelonephritis with III clinical stage of HIV infection among those discharged had 481 patients, which was 33.33%, and with IV clinical stage - 962 (66.67%). All patients with a lethal outcome were diagnosed with IV clinical stage of HIV infection, 1.5 times more than in prescribed patients ( $p < 0.05$ ).

The average age of the group of discharged patients with chronic pyelonephritis was  $(37.5 \pm 1.9)$  years for men and  $(36.3 \pm 1.8)$  years for women, in the group with lethal outcome  $(38.6 \pm 2.3)$  year for men and  $(39.2 \pm 1.7)$  for women.

It is established that signs of a urinary syndrome are defined practically at all sick of a HIV-infection in a stage of AIDS. From 1040 patients without concomitant pyelonephritis in 623 there was a urinary syndrome, was 59.9%. This can be explained by transient proteinuria, which can appear without concomitant kidney pathology with prolonged intoxication, fever and the like. The total number of HIV-infected with urinary syndrome was 2498 people, which is 85.7% of the total number of patients.

The most common manifestation of urinary syndrome was proteinuria, established in 1,371 patients, which in percentage to the total number of patients with pyelonephritis was 73.1% ( $\chi^2 = 9.7$ ,  $p < 0.05$ ), cylindruria was diagnosed in 1123 patients - 59, 9% ( $\chi^2 = 9.2$ ,  $p < 0.05$ ), leukocyturia - in 1037 people (55.3%,  $\chi^2 = 9.1$ ,  $p < 0.05$ ), erythrocyturia in 702 (37.4%;  $\chi^2 = 8.3$ ,  $p < 0.05$ ). In 1,437 individuals, the urinary syndrome was accompanied by bacteriuria (76.6%,  $\chi^2 = 10.1$ ,  $p < 0.01$ ).

Also, the level of urea, the number of erythrocytes and hemoglobin, the total protein and albumin content in the blood in patients with pyelonephritis was analyzed (Table 1).

Table 1. Blood indicators in AIDS patients

Indicators	M±m
1. Urea, mmol / l	12,37±1,26
2. Erythrocytes, $1 \times 10^{12}$ / L	2,363±0,156
3. Hemoglobin, g / l	91,513±4,84
4. Total protein, g / l	78,128±2,52
5. Albumin, g / l	25,62±1,72

When morphological studies of kidney tissue in patients with AIDS with chronic pyelonephritis, noted the absence of lymphocyte infiltration in all cases studied. Periodically, fibrous foci were determined in the tissue of the brain substance, in which the remains of deformed, destroyed tubules with dystrophic epithelium and membrane debris were seen (Fig. 1).

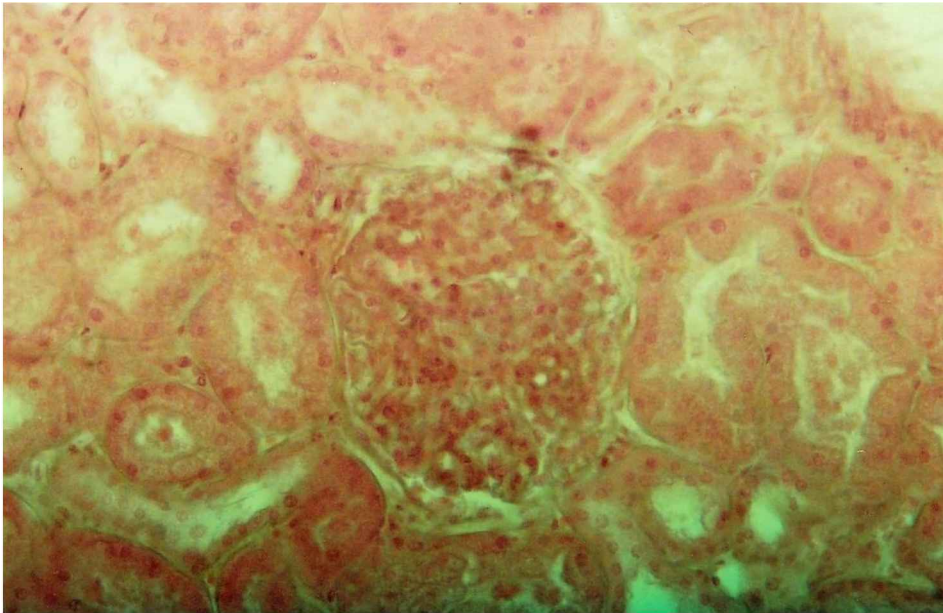


Figure.1 Kidney patient with AIDS, IV clinical stage; concomitant diagnosis - chronic pyelonephritis. Dystrophic changes in tubules. Coloring of hematoxylin-eosin; Sat:  $\times 300$ .

Changes in the distal tubules were very diverse. Along with the tubules of the usual form, in which epithelial cells with a fringe inner margin and a granular cytoplasm with light nuclei are located, strings consisting of dystrophic epithelial cells surrounded by a membrane are determined. There are also tubules, the epithelium in which is partially obliterated, is partially characterized by a pale cytoplasm and a pycnotic nucleus. It should be noted that the basal membrane of all tubules is sharply thickened and consists of coarse fibers.

Based on the morphological changes in the kidneys of AIDS patients, it is not possible to confirm the diagnosis of pyelonephritis, and the presence of a urinary syndrome is evidently due to profound dystrophic changes in kidney tissue.

When performing water-salt load in nephrological healthy individuals, an increase in the glomerular filtration rate (GFR) is increased by an average of 50% due to the inclusion of a functional renal reserve (FRR).

Also, after the salt load and in AIDS patients diagnosed with stage I and II CKD, there is an increase in GFR, which is twofold, which indicates the predominantly functional nature of renal impairment (Table 2). When calculating GFR using the Cockcroft-Gault formula in nephrologically healthy patients, this indicator is  $101.84 \pm 23.20$  ml / min, and in AIDS patients ( $109.5 \pm 12.74$  ml / min) it did not differ from control.

Table 2. Indicators of functional renal reserve in AIDS patients after water-salt load

Indicator	Nephrologically healthy patients	AIDS patients
Rate of glomerular filtration according to the clearance of endogenous creatinine, ml / min	152,2±39,9	223,9±60,52
Functional renal reserve,%	47,61 %	94,97 %
Diuresis, l / 60 min	0,219±0,021	0,155±0,061
Release of water,%	63,75±5,26	46,77±18,89
Concentration of creatinine in urine, $\mu\text{mol} / \text{l}$	3127±287,26	6757,03±1700,93
Creatinine in blood plasma, $\mu\text{mol} / \text{l}$	88,66±5,30	64,4±15,22
The ratio of the creatinine concentration in the urine to the creatinine concentration in the plasma	37,61±4,53	120,14±39,9
Excretion of creatinine, mmol / min	0,0117±0,0011	0,0132±0,0027

Note:  $\leq 0,05$ .

The obtained data show that despite the signs of kidney damage in AIDS patients, the IDF not only did not decrease, but on the contrary grew. This allows us to assert that nephron damage occurs in the initial stages of HIV-nephropathy development, but the number of nephrons does not decrease in both stages I and II of CKD. This is a direct evidence of the possibility of a pathogenetic substantiated effect on the course of CKD and prevention of chronic renal failure.

### Conclusions

It was established that the peculiarity of the course of kidney diseases is their eroded clinical course. At the same time, structural disturbances in the kidneys are dystrophic-atrophic in nature with the primary lesion of the epithelium of the proximal tubules and the absence of lymphocyte infiltration of the cortical substance of the kidney, and glomerular disorders are secondary in nature with a subsequent decrease in the number of functioning nephrons. The frequency and duration of renal dysfunction and azotemia phenomena associated with morphological changes indicate the formation of chronic kidney disease (CKD) in patients, as a consequence of the progression of the pathological process.

In the determination of FRR in nephrological healthy individuals, according to the calculated glomerular filtration rate (GFR) by the Cockcroft-Gault formula, it was  $101.84 \pm 23.20$  ml / min, and after the salt load an increase in GFR was found due to the inclusion of an FRR on average by 50%. In patients with AIDS, diagnosed with stage I and II CKD, the calculated GFR was  $109.5 \pm 12.74$  ml / min, and after the salt load, there was an increase in GFR, twice, which indicates the presence of renal disorders during this period of the disease, mainly of a functional nature.

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