URINARY NGAL AS AN EARLY MARKER OF NEPHROPATHY IN PATIENTS WITH LIVER DISEASES AND EXCESSED BODY WEIGHT.

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Abstract. Nephropathy in patients with liver diseases often develops in the early, preclinical stages and remains unrecognized for a long time when traditional kidney function indicators are used. The combination of liver pathology with excess body weight and metabolic disorders significantly increases the risk of early kidney damage, necessitating the search for sensitive markers for timely diagnosis.

Keywords: urinal NGAL, early diagnosis, nephropathy, liver diseases, excess body weight, tubular kidney damage, comorbid diseases.

Introduction. In recent years, chronic non-communicable diseases have become a leading cause of overall morbidity and mortality, with comorbid conditions becoming increasingly important. Liver diseases, including non-alcoholic fatty liver disease and chronic hepatitis of various etiologies, often coexist with excess body weight and metabolic disorders, forming a pathogenetic continuum that also involves the kidneys. Nephropathy in this category of patients often develops gradually and is asymptomatic in the early stages, complicating its timely diagnosis and prevention.

Traditional laboratory parameters of kidney function, such as serum creatinine and estimated glomerular filtration rate, have limited sensitivity in the preclinical stages of kidney injury. Changes in these parameters typically reflect established nephron dysfunction and fail to detect early structural and functional changes, particularly in the tubular apparatus. In the setting of comorbid liver disease and excess body weight, this is particularly important, as metabolic, inflammatory, and hemodynamic factors can initiate kidney injury long before clinical manifestations.

Current understanding of the pathogenesis of nephropathy in liver disease and obesity points to the key role of systemic chronic inflammation, insulin resistance, lipotoxicity, and oxidative stress. These mechanisms contribute to damage to the renal tubulointerstitial tissue, disruption of intrarenal microcirculation, and activation of fibrogenesis. The relationship between liver and kidney dysfunction is mediated through the so-called "hepatorenal axis," whereby even moderate changes in liver function and metabolic status can lead to early kidney damage.

Therefore, there is growing interest in identifying sensitive and specific biomarkers that can detect early stages of renal damage before the development of significant functional impairment. One such marker is neutrophil gelatinase-associated lipocalin (NGAL), which is synthesized by renal tubular epithelial cells in response to ischemic, toxic, and inflammatory conditions. Elevated urinary NGAL levels reflect early tubular damage and precede changes in traditional renal function tests.

Despite the availability of data on the diagnostic value of NGAL in acute and chronic kidney injury, its role in the early diagnosis of nephropathy in patients with liver disease, especially in those with excess body weight, remains poorly understood. The literature contains limited studies evaluating urinary NGAL as an early marker of nephropathy in comorbid conditions, highlighting the relevance and scientific novelty of this research.

In connection with the above, the study of the role of urinary NGAL in the early diagnosis of nephropathy in patients with liver pathology and overweight seems relevant and clinically significant, since it can contribute to the improvement of approaches to the early detection and prevention of chronic kidney disease in this group of patients.

Purpose of the study. To evaluate the role of urinary NGAL in the early diagnosis of nephropathy in patients with liver disease and overweight.

Study design

A single-center, observational, comparative study with a cross-sectional design was conducted.

Characteristics of the examined patients

The study included 120 patients who underwent examination and treatment in specialized gastroenterology departments from January 2024 to September 2025.

Depending on the presence of liver pathology and excess body weight, patients were divided into the following groups:

- The main group (n = 60) included patients with chronic liver diseases and overweight (body mass index ≥ 25 kg/m²).
- The comparison group (n = 40) included patients with chronic liver diseases and normal body weight (BMI 18.5–24.9 kg/m²).
- The control group (n = 20) consisted of practically healthy individuals without signs of liver and kidney disease, with normal body weight.

Diagnoses of liver diseases were established on the basis of clinical data, laboratory parameters and instrumental examination methods in accordance with current clinical guidelines.

Inclusion criteria

- age from 18 to 65 years;
- the presence of chronic liver disease (non-alcoholic fatty liver disease, chronic hepatitis of various etiologies);
- Informed consent of the patient to participate in the study.

Exclusion criteria

- chronic kidney disease stage III and higher (SCF < 60 ml/min/1.73 m²);
- acute inflammatory kidney diseases;
- type 1 diabetes mellitus;
- decompensated cardiovascular diseases;
- oncological diseases;
- taking nephrotoxic drugs within the last 3 months.

Research methods

Physical and clinical anamnestic methods

All patients underwent:

- collection of anamnesis and assessment of complaints;
- measurement of body weight and height with calculation of body mass index (BMI);
- waist circumference measurement;
- blood pressure assessment;
- general clinical examination.

Laboratory methods

Renal function assessment:

- serum creatinine level;
- estimated glomerular filtration rate (eGFR) according to the CKD-EPI formula;
- determination of albuminuria (albumin/creatinine ratio in the morning urine sample);
- **determination of urinary NGAL levels**by enzyme-linked immunosorbent assay (ELISA).

Liver function assessment:

- alanine aminotransferase (ALT);
- aspartate aminotransferase (AST);
- gamma-glutamyl transferase (GGT);
- alkaline phosphatase;
- total bilirubin.

Metabolic profile:

- fasting blood glucose;

- insulin with calculation of the HOMA-IR index;
- total cholesterol, LDL, HDL, triglycerides.

Instrumental methods

- ultrasound examination of abdominal organs;
- assessment of the structural state of the liver (signs of steatosis);
- ultrasound examination of the kidneys with Doppler ultrasonography of the renal vessels (assessment of the resistive index - RI);

Statistical analysis

Statistical data processing was performed using an Excel software package. Quantitative indicators are presented as mean and standard deviation (M ± SD) or median and interquartile range. Parametric and nonparametric methods were used to assess intergroup differences, depending on the nature of the data distribution. Correlation analysis was performed using Spearman's rho coefficient. Differences were considered statistically significant at $p < 0.05$.

Ethical aspects

The study was conducted in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the local ethics committee, and written informed consent was obtained from all participants.

Research results

General characteristics of the surveyed groups

The study included 120 patients divided into three groups. The groups were comparable for age and gender ($p>0.05$). The average patient age was 47.5±8.9 years. Patients in the study and comparison groups were predominantly of working age.

Patients in the study group (liver disease + overweight) had significantly higher body mass index and waist circumference values compared to the comparison and control groups ($p<0.001$). In the control group, anthropometric parameters were within the normal range (Table 1).

Table 1.

Clinical and anthropometric characteristics of the examined patients

Indicator	Main group (n=60)	Comparison group (n=40)	Control group (n=20)	p
Age, years	48.6±9.4	46.9±8.7	45.2±7.9	>0.05
Men/women, n	32/28	21/19	10/10	>0.05
BMI, kg/m²	29.8±3.1	23.4±1.8	22.6±1.9	<0.001
Waist	102.4±9.6	88.1±7.4	84.3±6.9	<0.001

circumference, cm				
Systolic blood pressure, mmHg	134±12	128±10	122±8	<0.05

Note: data are presented as M±SD; p is the significance of intergroup differences.

Liver function and metabolic status parameters

In the study group, a statistically significant increase in liver enzyme activity (ALT, AST, GGT) was observed compared to the control group ($p<0.05$). In the comparison group, these indicators also exceeded control values but were lower than in the study group, indicating the exacerbating effect of excess body weight on the severity of liver dysfunction.

The metabolic profile of patients in the main group was characterized by higher levels of fasting glucose, insulin, and the HOMA-IR index compared to the comparison and control groups ($p < 0.05$), which reflected the presence of insulin resistance.

Table 2.

Laboratory parameters of liver function and metabolic profile

Indicator	Main group	Comparison group	Control	p
ALT, U/L	62.4±18.7	48.6±15.2	29.8±8.4	<0.001
AST, U/L	55.1±16.3	42.9±13.6	27.5±7.9	<0.001
GGT, U/L	78.3±26.5	59.2±21.4	31.6±9.7	<0.001
Glucose, mmol/l	6.1±0.8	5.5±0.6	5.0±0.4	<0.01
HOMA-IR	3.6±1.2	2.4±0.9	1.8±0.6	<0.001

Note: data are presented as M±SD; p is the significance of intergroup differences.

Traditional indicators of kidney function

Analysis of traditional renal function parameters showed that serum creatinine levels and estimated glomerular filtration rate were within reference ranges in most patients examined. No significant differences in creatinine levels or eGFR were found between the study and comparison groups ($p > 0.05$).

Microalbuminuria was detected mainly in patients of the main group, but its frequency and severity were moderate and did not allow the diagnosis of early stages of nephropathy in all cases (Table 3).

Table 3.

Traditional indicators of kidney function

Indicator	Main group	Comparison group	Control	p

Creatinine, μmol/l	86.2±12.4	83.1±11.8	79.6±10.2	>0.05
eGFR (CKD-EPI), ml/min/1.73 m²	92.6±14.8	95.4±13.9	98.7±12.6	>0.05
Albuminuria, mg/g	28.4±10.6	21.7±9.4	12.3±4.8	<0.05

Note: data are presented as M±SD; p is the significance of intergroup differences.

Urinary NGAL level

The key result of the study was the identification of reliable differences in the level of urinary NGAL between the examined groups.

In patients in the study group, urinary NGAL levels were statistically significantly higher compared to those in the comparison and control groups ($p<0.001$). Moreover, in a significant proportion of patients in the study group, elevated NGAL levels were recorded despite maintained serum creatinine levels and normal eGFR, indicating the presence of preclinical tubular renal injury.

In the comparison group, urinary NGAL levels also exceeded those in the control group ($p<0.05$), but were significantly lower than in the main group ($p<0.01$). In the control group, NGAL values were within the reference range.

Thus, the greatest increase in urinary NGAL levels was observed in patients with a combination of liver pathology and excess body weight, which indicates a synergistic effect of these factors on the development of early renal damage.

Table 4.

Urinary NGAL level in examined patients

Group	Urinary NGAL, ng/ml	p
Main group	124.6 ± 34.8	<0.001*
Comparison group	86.9 ± 27.3	<0.05**
Control group	42.5 ± 15.6	—

Note: * compared to the comparison group and control group ** compared to the control group

Correlation analysis

Correlation analysis showed the presence of a significant positive relationship between the level of urinary NGAL and body mass index ($r = 0.489$, $p < 0.05$), waist circumference ($r = 0.517$, $p < 0.05$), and insulin resistance indicators (HOMA-IR) ($r = 0.521$, $p < 0.01$).

No association was found between urinary NGAL levels and serum creatinine or eGFR ($p>0.05$), highlighting the independent diagnostic value of NGAL as an early marker of renal tubular injury.

Discussion

The results of this study demonstrate that urinary NGAL is a highly sensitive marker of early renal damage in patients with liver disease, especially when combined with excess body weight. Despite normal kidney function parameters,

such as serum creatinine and estimated glomerular filtration rate, these patients showed a significant increase in urinary NGAL, indicating preclinical tubular damage.

The obtained data are consistent with current understanding of the pathogenesis of nephropathy in comorbid non-communicable diseases. Several international studies have shown that NGAL is an early indicator of tubular stress and inflammation and increases long before the development of renal dysfunction. However, most studies focus on acute kidney injury or diabetic nephropathy, while data on the role of NGAL in liver disease and obesity remain limited. In this context, the results of this study complement existing knowledge and highlight the importance of NGAL as a marker of early nephropathy in metabolically associated liver diseases.

The significant increase in urinary NGAL levels observed in patients in the study group compared to the comparison group indicates a synergistic effect of liver disease and excess body weight on the development of early renal damage. Obesity is known to be accompanied by chronic low-grade inflammation, activation of the adipokine system, increased insulin resistance, and oxidative stress. These factors contribute to damage to the renal tubular epithelium, which is reflected by increased urinary NGAL levels. Liver dysfunction, in turn, exacerbates systemic metabolic disturbances, creating the so-called "hepatorenal axis," in which the kidneys become one of the target organs.

Of particular interest is the identified correlation between urinary NGAL levels and obesity indicators (body mass index, waist circumference), as well as the HOMA-IR insulin resistance index. These data confirm the pathogenetic role of metabolic disturbances in the development of early renal damage and emphasize that NGAL reflects not only local kidney damage but also systemic processes associated with metabolic stress. Similar correlations have been described in separate international studies, but primarily in patient populations with diabetes mellitus and metabolic syndrome, highlighting the novelty of these findings in the context of liver pathology.

The lack of a significant correlation between urinary NGAL levels and traditional renal function indicators in our study confirms its independent diagnostic value. Unlike creatinine and eGFR, which change with significant nephron loss, NGAL reflects early structural and functional changes in the tubular apparatus, making it a promising tool for preclinical nephropathy screening. This is particularly important for patients with liver disease and overweight, for whom early diagnosis of renal damage can significantly impact management and prevent the progression of chronic kidney disease.

From a clinical perspective, the use of urinary NGAL in practice can facilitate the development of personalized approaches to monitoring patients with liver disease and obesity. Incorporating this marker into early screening algorithms allows for the identification of high-risk groups and the timely implementation of metabolic disorders, lifestyle modifications, and renal protective measures aimed at slowing the progression of kidney damage.

However, this study has several limitations. The single-center design and relatively limited sample size may impact the generalizability of the results. Furthermore, the study did not include dynamic assessment of NGAL levels, limiting the ability to analyze its prognostic significance. Given the identified patterns, multicenter prospective studies that include dynamic observation and assess the impact of therapeutic interventions on NGAL levels and nephropathy progression appear promising.

Thus, the results of the study confirm the diagnostic value of urinary NGAL as an early marker of nephropathy in patients with liver pathology and overweight and justify the feasibility of its further study and implementation in clinical practice.

Conclusions

1. In patients with liver disease and overweight, signs of early renal damage were detected with preserved traditional indicators of renal function (serum creatinine, estimated glomerular filtration rate).
2. The level of urinary neutrophil gelatinase-associated lipocalin (NGAL) in patients with liver disease and excess body weight was significantly higher compared to patients without excess body weight and practically healthy individuals, indicating the presence of preclinical tubular kidney damage.
3. A positive correlation was found between the level of urinary NGAL and obesity indicators (body mass index, waist circumference), as well as the insulin resistance index (HOMA-IR), which confirms the pathogenetic role of metabolic disorders in the development of early nephropathy.
4. The lack of a reliable association between urinary NGAL levels and traditional indicators of renal function highlights its independent and higher diagnostic value for identifying early stages of renal damage.
5. Urinary NGAL can be considered as an informative and promising marker for early screening of nephropathy in patients with liver pathology and overweight and can be recommended for inclusion in algorithms for early diagnosis and prevention of chronic kidney disease in this category of patients.

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