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## **КЛИНИЧЕСКИЕ И МОРФОЛОГИЧЕСКИЕ ХАРАКТЕРИСТИКИ ДИАБЕТИЧЕСКОЙ НЕФРОПАТИИ**

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## **CLINICAL AND MORPHOLOGICAL CHARACTERISTICS OF DIABETIC NEPHROPATHY**

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**Резюме.** В исследовании проанализированы клинические проявления и морфологические изменения в биоптатах почки 13 пациентов с диабетической нефропатией согласно классификации Терверта. Класс III (узелки Киммельстила-Уилсона) оказался наиболее частым (69.2%). Проведено сравнение классов II (n=4, 30.8%) и III (n=9, 69.2%) по клиническим и морфологическим параметрам с определением статистической значимости.

**Ключевые слова:** диабетическая нефропатия, классификация Терверта, узелки Киммельстила-Уилсона.

**Resume.** This study analyzed clinical and morphological data of 13 patients with diabetic nephropathy according to class the Tervaert's classification. Class III (Kimmelstiel-Wilson nodules) was the most frequent (69.2%). Classes II (n=4, 30.8%) and III (n=9, 69.2%) were compared using clinical morphological parameters with the determination of statistical significance.

**Keywords:** diabetic nephropathy, Tervaert's classification, Kimmelstiel-Wilson nodules.

**Relevance.** Diabetic nephropathy (DN), also known as diabetic kidney disease, is the most common cause of end stage renal disease, making up a large part of patients requiring dialysis and kidney transplantation. In 2021 there were 107.6 million cases of DN worldwide [1]. DN develops as a complication of diabetes mellitus types 1 and 2. Great importance is attached to the identification of predictive signs in patients with DN. The severity of the disease and prognosis are based on both clinical (proteinuria) and morphological changes in the kidney tissue. The latter are reflected in the Tervaert's classification, also known as renal pathology society classification, which designates 4 classes based on glomerular lesions [2].

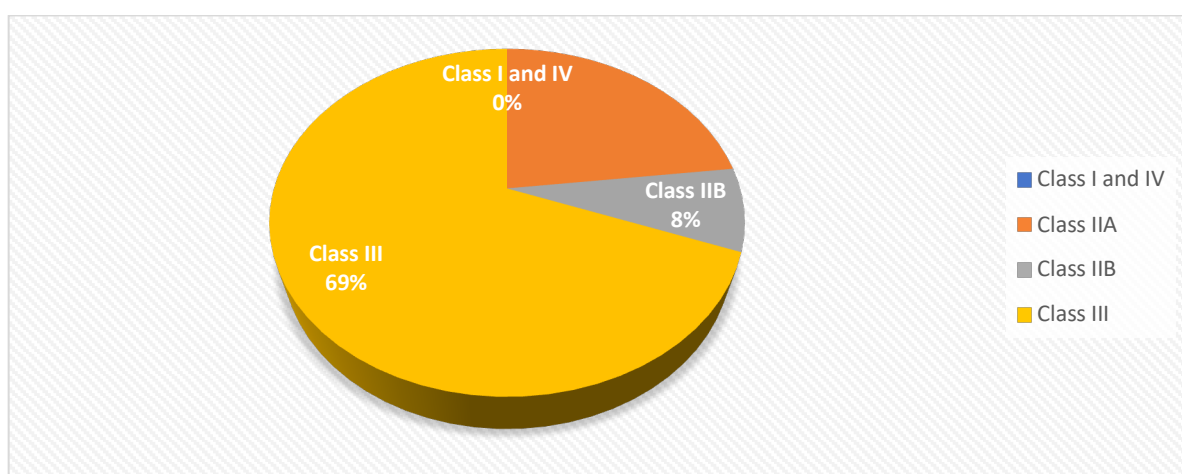
**Aim:** the aim of this study is to characterize morphological changes in the kidneys of DN patients according to the Tervaert's classification.

### **Objectives:**

1. Assign each patient to a DN class (I-IV) based on glomerular lesions.
2. Identify the most frequent DN class and its implications.
3. Compare morphological features across classes II and class III (mesangial expansion, nodular sclerosis, interstitial/vascular changes).
4. Correlate morphological classes with clinical data (proteinuria, hematuria, renal function).

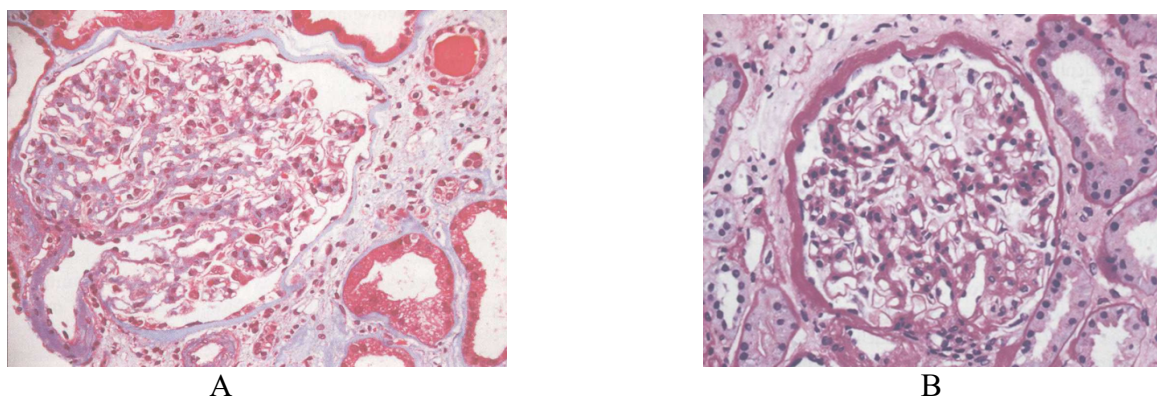
**Materials and methods.** This research is based on 13 kidney biopsy reports of 2 (15.4%) females and 11 (84.6%) males. The morphological study focused on evaluating glomerular parameters such as mesangial proliferation, nodular and global glomerulosclerosis, interstitial fibrosis, and vascular changes. Hematoxylin & Eosin, PAS, Masson trichrome, Congo red, Jones silver stains were used for light microscopy evaluation. Immunohistochemistry (IHC) staining for IgG, IgA, IgM, C3c, C1q, fibrinogen, k, and  $\lambda$  light chains was performed on paraffin sections of all the cases. Each patient was assigned a DN class based on the histopathological changes observed in line with the Tervaert's classification. Laboratory test results, such as general urine test, biochemical and general blood tests, were analyzed from medical records.

**Results and their discussion.** The patient's median age is  $60 \pm 10.5$  years (ranged 33 – 76 years). Among 13 patients, Class I and IV were absent (0%), Class IIa was observed in 3 patients (23.1%), Class IIb in 1 patient (7.7%), Class III in 9 patients (69.2%) (fig.1).



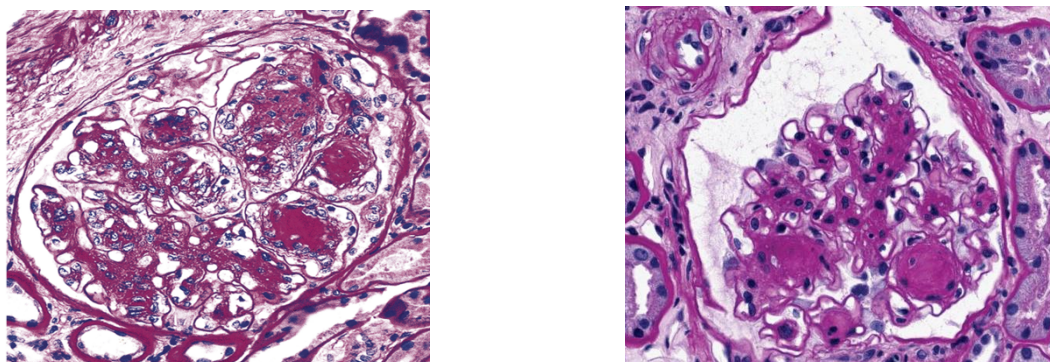
**Fig. 1** – Distribution of Tervaert's classes in the study cohort (n=13)

According to the Tervaert's classification there were no cases of class I which corresponds to cases where no specific widening of the mesangium under light microscopy. Class II is subdivided into two subclasses in relation to percentage of area involving glomerular expansion with the cut-off at 25%: we have 3 (23.1%) patients with class IIa and 1 (7.7%) with class IIb (fig.2) [1].



**Fig. 2** – A - Class IIa: Mild mesangial expansion and B - Class IIb: Severe mesangial expansion (Masson-trichrom, x400)

Class III was assigned in 9 (69.2%) cases when at least one Kimmelstiel-Wilson nodule was observed in glomeruli (fig.3).



**Fig. 3** – Class III: Kimmelstiel-Wilson nodule in glomeruli (PAS, x400)

Kimmelstiel-Wilson syndrome features include the nephrotic syndrome with excessive filtration of protein into the urine, hypertension, and progressively impaired kidney function. The syndrome also characterized by the formation of pathognomonic hyaline nodules in the glomerular mesangium and significant diffuse thickening of the glomerular basement membrane. These changes are accompanied by hyalinosis of both afferent and efferent arterioles. And finally, class IV is assigned when more than half of glomeruli are globally sclerosed (no cases) [3].

For further analysis, Classes IIa and IIb were combined into a single Class II group (n=4, 30.8%) and compared with Class III (n=9, 69.2%).

Patients in Class II were generally older compared to Class III. Hypertension was universal in both groups. Edema was more frequent in Class III, than in Class II. Proteinuria was nearly twice as high in Class III as in Class II. Hematuria was present in all Class II patients but slightly less common in Class III. Anemia affected all Class II patients, whereas it was found in just over half of Class III patients. Glucosuria was more than twice as frequent in Class III compared to Class II. These findings suggest that Class III is associated with more severe proteinuria and edema, while Class II patients paradoxically showed higher rates of hematuria and anemia, possibly due to their older age, longer diabetes duration and certain indications for kidney biopsy (table 1).

**Tbl. 1.** Clinical characteristics comparison of Class II and Class III

| Parameter                  | Class II, n=4 (n/%) | Class III, n=9 (n/%) | p, statistical significance |
|----------------------------|---------------------|----------------------|-----------------------------|
| Mean age, years old        | 69                  | 55.3                 | >0.05                       |
| Hypertension (BP > 140/90) | 4/100               | 9/100                | >0.05                       |
| Edema                      | 2/50                | 6/66.6               | >0.05                       |
| Proteinuria (g/L), mean    | 9.65                | 16.6                 | >0.05                       |
| Hematuria                  | 4/100               | 7/78                 | >0.05                       |
| Anemia (Hb < 120 g/L)      | 4/100               | 5/55.5               | 0.110                       |
| Glucosuria                 | 2/50                | 5/55.5               | >0.05                       |

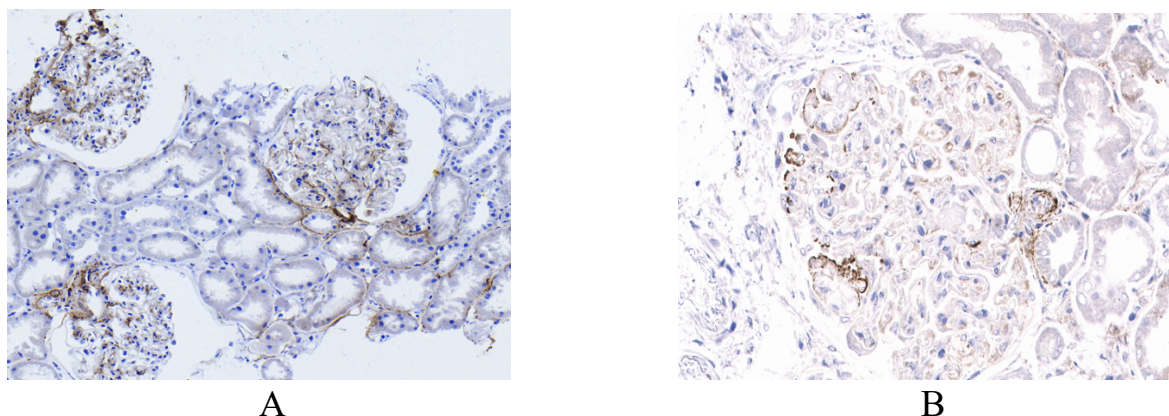
The IFTA (interstitial fibrosis / tubular atrophy) scores reflects the degree of chronic changes in kidney tissue. Among Class II patients, 50% had a score of 1 (<25% fibrosis),

25% had a score of 2 (25–50% fibrosis), and 25% had a score of 3 (>50% fibrosis). In Class III, 33.3% had a score of 1, 55.6% had a score of 2, and 11.1% had a score of 3. Thus, moderate to severe fibrosis (scores 2–3) was more common in Class III (66.7%) than in Class II (50%).

Interstitial inflammation was mild in 50% Class II patients and moderate in 25% with one Class II patient having no inflammation. In Class III, mild inflammation was seen in 33.3% and moderate in 66.7%. Moderate inflammation therefore predominated in Class III.

Vascular lesions were also more advanced in Class III. Moderate arteriolar hyalinosis (grade 2) occurred in 50% of Class II and 77.8% of Class III; mild hyalinosis (grade 1) in 25% of Class II and 11.1% of Class III. Regarding arteriosclerosis, moderate grade was present in 25% of Class II and 33.3% of Class III, while mild grade was seen in 50% of Class II and 44.4% of Class III. Overall, vascular changes were more pronounced in Class III, particularly arteriolar hyalinosis.

IHC staining was performed on paraffin sections of all biopsy samples. Positive granular staining for IgM was observed in the mesangium and along the vessel walls in the majority of cases (fig. 4A). C3c deposition was also detected in the mesangium and vascular walls, showing a similar distribution pattern (fig. 4B). The predominance of IgM and C3 deposits is consistent with the non-immune complex nature of DN, reflecting hemodynamic and metabolic injury rather than true immune-mediated inflammation.



**Fig. 4** – Immunohistochemistry staining in diabetic nephropathy: A – IgM in the mesangium and vessel's wall (x100); B – C3 in the mesangium and vessel's wall (x400)

### Conclusions:

1. Class III was the most frequent DN class (69.2%, 9/13) in kidney biopsies indicating advanced disease, while Class II accounted for 30.8% (4/13). No Class I or IV cases were observed.

2. Compared to Class II, Class III showed more severe morphological changes: universal nodule formation, higher rates of moderate interstitial inflammation and arteriolar hyalinosis, and more advanced IFTA scores but without statistical significance ( $p>0.05$ ).

3. Clinically, Class III patients had higher proteinuria and more frequent edema, while hematuria and anemia were more common (without statistical significance ( $p>0.05$ )) in Class II, possibly due to older age and certain indications for kidney biopsy.

### Literature

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