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Cytokine–Adipokine Profile And Microcirculatory Parameters As Interrelated Determinants Of Subclinical Polyneuropathy

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Abstract: Background. Subclinical peripheral polyneuropathy (PPN) frequently develops in prediabetes and obesity but often remains undetected. The contribution of cytokine–adipokine imbalance and microcirculatory dysfunction to early nerve injury requires clarification. Objective. To assess how cytokine–adipokine markers and microcirculatory parameters relate to subclinical PPN and to determine their independent predictive value. Materials and Methods. A cross-sectional study included 120 adults: 80 with prediabetes and obesity and 40 healthy controls. Subclinical PPN was defined by normal neurological scores combined with ≥2 abnormal tests (QST deviations, reduced IENFD, or decreased sensory conduction velocity). Serum leptin, adiponectin, IL-6, TNF-α, hsCRP, and the leptin-to-adiponectin ratio (L/A-ratio) were measured. Microcirculation was evaluated by laser Doppler flowmetry and nailfold capillaroscopy. Multivariable regression and ROC analysis were applied. Results. Subclinical PPN was found in 41.3% of the main group. Affected individuals had significantly higher L/A-ratio and inflammatory cytokines, along with reduced endothelial oscillations, post-occlusive hyperemia, and capillary density. L/A-ratio, IL-6, and endothelial oscillation amplitude were independently associated with PPN, and their combination showed high accuracy (AUC 0.88). Conclusions. Subclinical PPN in prediabetes with obesity is strongly linked to adipokine imbalance, systemic inflammation, and microvascular dysfunction. Combined biochemical and microcirculatory markers may improve early risk identification and warrant longitudinal validation.

Keywords: Peripheral polyneuropathy, quantitative sensory testing, cytokine–adipokine profile, leptin-to-adiponectin ratio, IL-6.

Introduction: Subclinical peripheral polyneuropathy (PPN) has emerged as a frequent yet largely unrecognized metabolic complication that develops long before the onset of overt type 2 diabetes. Evidence obtained through quantitative sensory testing (QST) and intraepidermal nerve fiber density (IENFD) analysis shows that early small-fiber involvement is detected in approximately 25–30% of individuals with prediabetes and in up to 35–40% of those with obesity, even when they report no neurological complaints. More than 70% of these cases remain unnoticed in routine practice, allowing neurovascular dysfunction to progress silently and predisposing patients to future sensory disturbances and neuropathic pain.

Multiple interrelated mechanisms contribute to this early nerve injury. Individuals with obesity exhibit a marked shift in adipokine balance: circulating leptin levels are typically three- to fivefold higher, whereas adiponectin concentrations are reduced by 40–60%, producing a substantial rise in the leptin-to-adiponectin ratio (L/A ratio). This index reflects both systemic metabolic stress and impaired neurovascular regulation. At the same time, 60–70% of patients with prediabetes demonstrate elevated IL-6 and TNF-α levels, indicating persistent low-grade inflammation that affects endothelial function and compromises the

integrity of peripheral nerve fibers.

Microcirculatory disturbances represent another early marker of metabolic nerve injury. Findings from laser Doppler flowmetry reveal that up to 45–50% of patients with prediabetes show reduced capillary perfusion and diminished endothelial reactivity. These alterations impair vasomotor regulation, limit oxygen delivery, and weaken trophic support to small nerve fibers. When considered together, the adipokine imbalance, inflammatory activation, and microcirculatory dysfunction suggest the presence of a closely interconnected adipokine–cytokine–microvascular pathway that underlies the earliest stages of peripheral nerve damage.

Despite growing interest in early metabolic neuropathy, the combined contribution of these biological systems remains insufficiently understood. In particular, it is unclear which markers exert the strongest influence on the development of subclinical PPN and how tightly they interact within a unified pathophysiological framework. Addressing these gaps is essential for improving early detection and identifying patients at the highest risk.

The aim of this study is to characterize the relationship between cytokine–adipokine profiles and microcirculatory parameters and to determine their independent contribution to the development of subclinical peripheral polyneuropathy in individuals with metabolic disturbances.

METHODS

Study Design. A cross-sectional clinical study was conducted to examine the association between cytokine–adipokine balance, microvascular function, and early neurophysiological abnormalities characteristic of subclinical peripheral polyneuropathy (PPN) in individuals with metabolic disturbances. The study adhered to the ethical principles of the Declaration of Helsinki, and all participants provided written informed consent.

Study Population

Participants and Group Allocation. A total of 120 adults aged 35–60 years were enrolled. Participants were assigned to two groups: Main group (n = 80): individuals with prediabetes and obesity (BMI ≥30 kg/m²); Control group (n = 40): metabolically healthy volunteers with normal body weight (BMI 18.5–24.9 kg/m²) and normal glucose tolerance.

Inclusion Criteria: age 35–60 years; prediabetes defined by fasting glucose 5.6–6.9 mmol/L and/or HbA1c 5.7–6.4%; obesity for inclusion in the main group; absence of clinically evident PPN.

Exclusion Criteria: type 2 diabetes mellitus; alcohol-related, toxic, hereditary, inflammatory, or drug-induced neuropathies; acute or chronic systemic inflammatory conditions; use of medications known to influence microcirculation, cytokine levels, insulin resistance, or nerve conduction (e.g., statins, β-blockers, glucocorticoids, NSAIDs); severe cardiac, renal, or hepatic failure.

Standardization of Examination Conditions. All assessments were carried out in the morning (08:00–11:00). Participants refrained from caffeine, nicotine, and strenuous physical activity for at least 12 hours. Before microcirculatory tests and QST, a 15-minute acclimatization period was provided in a temperature-controlled room (22–24 °C).

Outcome Assessment: Subclinical Peripheral Polyneuropathy. Subclinical PPN served as the primary outcome variable.

1. Clinical Evaluation. Neuropathy was screened using two validated scales: Neuropathy Symptom Score (NSS) ≤3, Neuropathy Disability Score (NDS) ≤2.

Participants with higher scores were excluded to ensure the absence of clinical neuropathy.

2. Nerve Conduction Studies (NCS). NCS were performed using the Nicolet VikingQuest system (USA): sensory conduction studies included the sural and median nerves; conduction velocity (CV) and sensory nerve action potential (SNAP) amplitude were recorded; skin temperature was maintained ≥32 °C using continuous thermal monitoring. A decrease in CV was observed in 20% of participants in the main group.

3. Quantitative Sensory Testing (QST). QST was carried out according to the German Research Network on Neuropathic Pain (DFNS) protocol using the Medoc TSA-II system. The following thresholds were assessed: cold detection (CDT), warm detection (WDT), heat detection threshold (HDT), vibration perception threshold (VPT). Abnormality was defined as a deviation of ≥2 SD from DFNS age-adjusted reference values.

Thermal detection abnormalities were found in 34% of the main group.

4. Skin Biopsy. A 3-mm full-thickness punch biopsy was taken 10 cm above the lateral malleolus. Sections were immunostained with PGP 9.5 (Abcam, UK). Intraepidermal nerve fiber density (IENFD) was quantified using ImageJ by an assessor blinded to participants' clinical data and group allocation. An IENFD value <7 fibers/mm was detected in 39% of participants.

Diagnostic Criteria for Subclinical PPN. Subclinical PPN was diagnosed when the following conditions were met:

1. absence of clinical neuropathy (NSS ≤3 and NDS ≤2);
2. at least two abnormal instrumental findings: deviation ≥2 SD in QST, IENFD <7 fibers/mm, reduced CV on NCS without clinical symptoms.

Overall prevalence of subclinical PPN in the main group was 41%.

Predictor Assessment

1. Cytokine–Adipokine Profile

Blood Collection and Processing. Blood samples were drawn in the morning after an overnight fast. Serum was separated by centrifugation at 3000 rpm for 10 minutes.

Adipokines. Serum concentrations of: leptin (ng/mL) — DRG Diagnostics, adiponectin (µg/mL) — RayBio®, were measured by ELISA.The leptin-to-adiponectin ratio (L/A-ratio) was calculated for each participant.

Cytokines. The following markers were assessed: IL-6, TNF-α (R&D Systems ELISA kits; analytical sensitivity 0.1–0.5 pg/mL), high-sensitivity C-reactive protein (hsCRP) — immunoturbidimetric method. Intra-assay variability (CV) for all assays was below 8%.

2. Microcirculatory Assessment

Laser Doppler Flowmetry (LDF). Microvascular perfusion was examined using the LAKK-M device (LAZMA, Russia):

- sampling frequency: 32 Hz;
- measurement site: dorsum of the foot;
- parameters analyzed: baseline perfusion (M, perfusion units), endothelial vasomotion (0.009–0.021 Hz), neurogenic (0.021–0.052 Hz), myogenic (0.052–0.145 Hz), cardiac and respiratory oscillations.

Post-Occlusive Reactive Hyperemia. A 3-minute pneumatic occlusion test was performed, with subsequent calculation of the reactive hyperemia index (peak-to-baseline perfusion ratio).

Nailfold Capillaroscopy. Capillary morphology and density were evaluated using the MS-Capillar 3.0 videocapillaroscope at ×200 magnification. Parameters included: functional capillary density (capillaries/mm), flow uniformity, presence of microangiopathic features (dilatation, tortuosity, avascular zones). All images were analyzed by a blinded investigator.

Statistical Analysis. Statistical analyses were performed using SPSS Statistics 26.0. Descriptive Analysis: Normality was assessed using the Shapiro–Wilk test. Continuous variables were expressed as mean ± SD or median (IQR). Group Comparisons: Student's t-test or Mann–Whitney U test for continuous variables; χ^2 test for categorical variables. Correlation Analysis: Pearson correlation for normally distributed variables; Spearman correlation otherwise. Multivariable Logistic Regression: A stepwise forward likelihood approach was used to identify independent determinants of subclinical PPN. Covariates tested in the model: age, sex, BMI, HOMA-IR; IL-6, TNF-α, L/A-ratio; LDF parameters (endothelial frequency band, reactivity index); functional capillary density. Multicollinearity was assessed using VIF (<2). Model adequacy and variance homogeneity were verified. ROC Analysis: Diagnostic performance of biomarkers was evaluated by: area under the curve (AUC), 95% confidence intervals, optimal cut-off values (Youden index). Significance Threshold: A two-sided p-value <0.05 was considered statistically significant.

RESULTS

A total of 120 participants were included: 80 individuals with prediabetes and obesity (main group) and 40 metabolically healthy controls. The groups did not differ significantly in age (main: 48.6 ± 6.1 years vs controls: 47.9 ± 6.4 years; p = 0.58) or sex distribution (52.5% vs 50.0% women; p = 0.79).

Compared with controls, the main group exhibited higher BMI (33.8 ± 3.9 vs 22.6 ± 2.4 kg/m²; p < 0.001), fasting glucose (6.1 ± 0.4 vs 4.9 ± 0.3 mmol/L; p < 0.001), fasting insulin (18.7 ± 5.6 vs 8.1 ± 2.4 µIU/mL; p < 0.001) and HOMA-IR (5.1 ± 1.6 vs 1.8 ± 0.5; p < 0.001). Data completeness exceeded 97% for all baseline variables.

Prevalence and Characteristics of Subclinical Peripheral Neuropathy

Subclinical PPN was detected in 33 of 80 participants in the main group (41.3%; 95% CI: 30.8–52.6). No cases were observed among controls (0/40).

Instrumental abnormalities (n = 80).

Reduced sensory conduction velocity (CV) on NCS: 16/80 (20.0%). Mean sural CV in PPN+: 41.2 ± 3.7 m/s vs 45.8 ± 4.2 m/s in PPN− (p < 0.001).

Abnormal QST thresholds (≥2 SD deviation from DFNS norms): 27/80 (33.8%). The most frequent deviations were in CDT and WDT.

Reduced intraepidermal nerve fiber density (IENFD <7 fibers/mm): 31/80 (38.8%). Mean IENFD: PPN+ 5.9 ± 0.8 fibers/mm vs PPN− 8.2 ± 1.1 fibers/mm (p < 0.001).

Among participants with subclinical PPN (n = 33), the most common pattern was combined QST abnormalities + reduced IENFD (21/33; 63.6%).

Cytokine–Adipokine Profile

Adipokines. Participants with PPN showed:

higher leptin (36.2 ± 12.8 vs 28.4 ± 10.5 ng/mL; p = 0.004),

- lower adiponectin (5.4 ± 1.7 vs 7.1 ± 2.0 µg/mL; p < 0.001).

The L/A-ratio was significantly higher:

- PPN+: 4.23 ± 1.01 vs PPN−: 2.79 ± 0.84; p < 0.001.

Cytokines. Participants with PPN demonstrated:

Table 1.

Marker	PPN+ (n=33)	PPN− (n=47)	p-value
IL-6 (pg/mL)	4.2 ± 1.1	3.1 ± 0.9	<0.001
TNF-α (pg/mL)	8.5 ± 2.2	6.9 ± 1.8	0.002
hsCRP (mg/L)	3.9 ± 1.4	2.8 ± 1.2	0.01

Missing cytokine values did not exceed 3% and were excluded pairwise.

Microcirculatory Assessment

Laser Doppler Flowmetry (n = 78). Data were analysable for 78 participants (measurement artifacts: n=2). Participants with PPN (n=32) demonstrated:

- lower baseline perfusion: 6.8 ± 1.9 vs 8.1 ± 2.0 PU; p = 0.002,
- decreased endothelial oscillation amplitude (0.009–0.021 Hz): 0.38 ± 0.12 vs 0.51 ± 0.14; p < 0.001,
- reduced neurogenic (0.021–0.052 Hz): 0.27 ± 0.10 vs 0.33 ± 0.11; p = 0.02,
- reduced myogenic (0.052–0.145 Hz): 0.49 ± 0.15 vs 0.57 ± 0.18; p = 0.03.
- Post-occlusive reactive hyperemia index was also lower: PPN+: 1.72 ± 0.29 vs PPN−: 2.14 ± 0.34; p < 0.001.

Nailfold Capillaroscopy (n = 79). Functional capillary density was reduced:

- PPN+: 6.9 ± 1.1 cap/mm vs PPN−: 8.1 ± 1.3 cap/mm; p < 0.001.

Structural microvascular deviations (dilatation, tortuosity, irregular flow) were present in:

- PPN+: 24/33 (72.7%),
- PPN−: 11/47 (23.4%),

$\chi^2 < 0.001$.

Correlation Analysis

Adipokines and nerve function

- L/A-ratio vs QST z-scores: r = 0.43; p < 0.001.
- L/A-ratio vs IENFD: r = −0.38; p = 0.004.

Cytokines and microcirculation

- IL-6 vs endothelial oscillation amplitude: r = −0.36; p = 0.002.
- TNF-α vs PORH index: r = −0.32; p = 0.006.

Microcirculation and neurophysiology

- Endothelial oscillation amplitude vs IENFD: r = 0.44; p < 0.001.

PORH index vs sural CV: r = 0.31; p = 0.01.

All correlations met assumptions of linearity; heteroscedasticity was absent.

Multivariable Logistic Regression

The final adjusted model identified three independent predictors of subclinical PPN:

Table 2.

Predictor	OR (per 1-unit increase)	95% CI	p-value
L/A-ratio	2.48	1.62–3.81	<0.001
IL-6 (pg/mL)	1.57	1.18–2.16	0.003
Endothelial oscillation amplitude	0.41	0.24–0.70	0.001

Age, sex, BMI, fasting glucose, insulin and HOMA-IR were not significant (p > 0.10). Model calibration (Hosmer–Lemeshow) was adequate (p = 0.47); multicollinearity was low (VIF < 2).

ROC Curve Analysis

Table 3.

Individual biomarkers

Marker	AUC	95% CI	Optimal cut-off	Sensitivity	Specificity

L/A-ratio	0.82	0.74–0.90	> 3.52	78%	74%
IL-6	0.74	0.64–0.84	> 3.55 pg/mL	70%	68%
TNF-α	0.72	0.62–0.82	> 7.38 pg/mL	67%	65%
Endothelial oscillation	0.74	0.65–0.84	< 0.46	72%	70%
PORH index	0.71	0.61–0.81	< 1.88	68%	66%

Combined model. A composite model including L/A-ratio, IL-6 и endothelial oscillation amplitude showed the highest accuracy: AUC: 0.88 (95% CI: 0.82–0.94); Sensitivity: 82%; Specificity: 80%.

DISCUSSION

Principal Findings. This study demonstrates that subclinical peripheral neuropathy is already present in a substantial proportion of individuals with prediabetes and obesity, affecting more than 40% of participants despite normal neurological examination. The pattern of abnormalities—reduced intraepidermal nerve fiber density, impairments in thermal detection thresholds, and modest reductions in sensory conduction velocity—suggests that early injury involves both small- and large-fiber pathways. These data align with the concept highlighted by Carmichael et al. (2021), who reported that small-fiber dysfunction may arise long before clinical manifestation, emphasizing the importance of early diagnostic assessment in metabolic disorders.

A central result of this study is the identification of a distinct inflammatory–metabolic profile in participants with subclinical neuropathy. Higher leptin concentrations, lower adiponectin levels, and an elevated leptin-to-adiponectin ratio were strongly associated with neuropathic abnormalities. These findings support the broader evidence demonstrating that adipokine imbalance accompanies metabolic inflammation (Volkova et al., 2023) and may reflect a shift toward a pro-inflammatory endocrine milieu. Reduced adiponectin is particularly relevant, given its role in activating AMPK and enhancing endothelial nitric oxide production through AdipoR1/R2-mediated pathways.

In addition, individuals with subclinical neuropathy exhibited elevated IL-6, TNF-α, and hsCRP—markers known to impair neural integrity through oxidative stress, mitochondrial dysfunction, and disruption of neurotrophic signaling. Mechanistic work summarized by Dzugkoev & Dzugkoeva (2022) supports this observation, showing that chronic cytokine elevation contributes to early neurovascular damage even before overt hyperglycemia develops. Transcriptional profiling from Golodnikov et al. (2025) further confirmed activation of inflammatory programs within T-cell populations, suggesting that immune priming may amplify vulnerability of peripheral fibers in metabolic states.

Interpretation in the Context of Existing Evidence. The microvascular abnormalities identified in this study—reduced endothelial oscillatory activity, decreased neurogenic and myogenic components of flow regulation, and diminished post-occlusive hyperemia—mirror patterns previously associated with metabolic microvascular dysfunction. Stepanova (2021) reported a close relationship between small-fiber injury and impaired endothelial responsiveness in individuals with early metabolic disturbances. Similarly, Metsker et al. (2020) identified microvascular impairment as a key predictor of neuropathic progression in diabetes, underscoring its importance in prediabetes as well.

Our results extend previous findings by demonstrating that structural capillary abnormalities, including reduced functional density and increased tortuosity, are already evident before clinical neuropathy develops. These changes likely reduce nutritive perfusion of small fibers, which depend on stable oxygen and glucose delivery due to their high metabolic demands. The correlation between endothelial oscillatory amplitude and intraepidermal nerve fiber density observed in this study supports the hypothesis that vascular dysregulation is closely intertwined with early axonal injury.

Proposed Mechanisms. The concurrence of adipokine imbalance, systemic inflammation, microvascular impairment, and neural dysfunction suggests several interacting mechanisms:

1. Inflammation-induced impairment of endothelial nitric oxide signaling. IL-6 and TNF-α suppress endothelial nitric oxide synthase activity and promote oxidative stress, leading to reduced vasodilatory capacity. The observed reduction in endothelial oscillation amplitude and post-occlusive hyperemia is consistent with these effects.
2. Microvascular hypoperfusion affecting small-fiber metabolism. C-fibers are highly sensitive to fluctuations in oxygenation. Diminished capillary

density and oscillatory support may lead to local energy deficits, disrupting axonal transport and resulting in fiber loss.

3. Adipokine-mediated modulation of neural and vascular function. Elevated leptin activates inflammatory pathways via JAK/STAT signaling, while low adiponectin reduces AMPK activation and weakens AdipoR1/R2-dependent cytoprotection. This combination may create a permissive environment for neural injury.
4. Metabolic stress–immune activation synergy. As shown by Golodnikov et al. (2025), metabolic stress primes T-cells toward inflammatory phenotypes, potentially amplifying neurovascular injury even before overt glycemic dysregulation develops.

These mechanisms may collectively explain why neuropathic abnormalities arise early and progress in parallel with inflammatory and vascular changes.

Clinical Implications

The present findings highlight the clinical importance of early screening for neuropathic changes in individuals with prediabetes and obesity. Although traditional nerve conduction studies are often normal at early stages, QST and intraepidermal fiber density measurements proved sensitive for identifying small-fiber involvement. Microvascular assessments using laser Doppler flowmetry and capillaroscopy provided additional insight into microvascular regulation, offering functional markers that correlated strongly with neural integrity.

The strong predictive performance of the combined model—including the leptin-to-adiponectin ratio, IL-6 concentration, and endothelial oscillation amplitude—suggests that integrated biochemical and microvascular markers may help clinicians identify individuals at elevated risk for progression to symptomatic neuropathy. While some methods (e.g., IENFD) may be impractical in routine practice, serum biomarkers, QST, and simple microvascular measurements may form the basis of an accessible screening algorithm.

Strengths of the Study. Major strengths include:

- a multimodal diagnostic approach combining structural, functional, vascular, and biochemical assessments;
- strict inclusion and exclusion criteria, enhancing homogeneity of the cohort;
- the use of validated and standardized methods (DFNS QST protocol, PGP-9.5–based IENFD assessment);
- robust statistical modeling with adjustment for multiple metabolic parameters;
- minimal missing data and high reproducibility of all measurements.

These aspects support the validity of the conclusions and provide a comprehensive understanding of early neuropathic changes.

Limitations

Several limitations should be acknowledged:

1. Cross-sectional design. Causality cannot be established, and temporal relationships remain uncertain.
2. Specialized diagnostic tools. Skin biopsy and advanced capillaroscopy require technical expertise and may not be widely available, limiting general applicability.
3. Potential confounding. Although we adjusted for major metabolic indices, factors such as physical activity, dietary patterns, sleep quality, autonomic variability, and environmental temperature during microvascular testing may influence results.
4. Sample size. While the cohort was sufficient to identify moderate associations, larger datasets are needed to evaluate long-term predictive performance.
5. QST variability. Despite strict standardization, QST is subject to cognitive and attentional influences, which may introduce interindividual variation.

These limitations should be addressed in future research but do not undermine the overall conclusions.

Future Directions

Future work should aim to: conduct longitudinal follow-up to determine which markers predict transformation to clinically established neuropathy; evaluate whether interventions targeting inflammation, adipokine balance, or endothelial function can reverse early abnormalities; develop simplified screening algorithms adaptable for primary care settings; investigate molecular pathways linking adipokines and endothelial dysfunction using experimental models; validate microvascular markers (e.g., endothelial oscillatory activity) as early therapeutic targets.

CONCLUSION

Subclinical peripheral neuropathy was identified in 41.3% of adults with prediabetes and obesity in this cohort, indicating that early nerve involvement is frequent even in the absence of symptoms. Individuals with neuropathy demonstrated significantly lower intraepidermal nerve fiber density, more pronounced microvascular impairment, and a distinct inflammatory–adipokine profile compared with those without neuropathy.

The leptin-to-adiponectin ratio, IL-6 concentration, and endothelial oscillation amplitude were each

independently associated with subclinical neuropathy, and their combination showed high discriminatory ability (AUC 0.88). These findings suggest that integrating biochemical and microvascular markers may help identify individuals at increased risk and justify further longitudinal studies to determine their predictive value.

REFERENCES

1. Volkova L.Yu., Eliashevich S.O., Shepel R.N., Astanina S.Yu., Drapkina O.M. Structured approach to changing the nutritional model in obese adult patients in primary health care. Preventive medicine. 2023;26(2):94-99. https://doi.org/10.17116/profmed20232602194
2. Golodnikov I.I., Podshivalova E.S., Chechekhin V.I., Zubritsky A.V., Matrosova A.A., Dvoryanchikov Ya.V., Samsonova M.D., Markelova E.K., Medvedeva Yu.A., Nikonova T.V., Bondarenko E.V., Popov S.V., Minniakhmetov I.R., Shestakova M.V. Transcriptional features of autoimmune diabetes mellitus: differential gene expression in CD4+ and CD8+ subpopulations of blood T-cells. Diabetes mellitus. 2025;28(2):124-135. https://doi.org/10.14341/DM13316
3. Dzugkoev S.G., Dzugkoeva F.S. Optimization of treatment and prevention of metabolic and functional disorders in diabetic nephropathy. Preventive medicine. 2022;25(3):18-24. https://doi.org/10.17116/profmed20222503118
4. Kurilova O.V., Kiseleva A.V., Meshkov A.N., et al. Scales for assessing the genetic risk of developing type 2 diabetes mellitus. Preventive medicine. 2021;24(12):115-122. https://doi.org/10.17116/profmed202124121115
5. Mehdiyev, T. V., Akhmedova, Z. B., Mamedov, M. N., & Askerov, E. I. (2022). Detection of diabetic neuropathies in patients with diabetes mellitus. Justification for medical rehabilitation. Spa Medicine, (1), 55-61.
6. Stepanova, A. P. (2021). Diabetic peripheral polyneuropathy and vitamin D provision in patients with type 2 diabetes mellitus: clinical and pathogenetic features, possibilities of therapy with cholecalciferol (Dissertation for the degree of Candidate of Medical Sciences). Saint Petersburg. https://www.almazovcentre.ru/wp-content/uploads/Диссертация-Степанова-А.П..pdf
7. Khramilin V.N., Davydov O.S. Pain diabetic polyneuropathy: diagnosis and treatment from the standpoint of evidence-based medicine. Russian Journal of Pain. 2021;19(4):44-59. https://doi.org/10.17116/pain20211904144
8. Carmichael, J., Fadavi, H., Ishibashi, F., Shore, A. C., & Tavakoli, M. (2021). Advances in Screening, Early Diagnosis and Accurate Staging of Diabetic Neuropathy. Frontiers in endocrinology, 12, 671257. https://doi.org/10.3389/fendo.2021.671257
9. Chupryna, G. N., Dubynetska, V. N., Vashenyuk, O. L., & Vashenyuk, N. O. (2021). Features of clinical and paraclinic parameters and comorbidity in patients with diabetic polyneuropathy. Health of Society, 8(5), 174–178. https://doi.org/10.22141/2306-2436.8.5.2019.198386
10. Metsker, O., Magoev, K., Yakovlev, A. et al. Identification of risk factors for patients with diabetes: diabetic polyneuropathy case study. BMC Med Inform Decis Mak 20, 201 (2020). https://doi.org/10.1186/s12911-020-01215-w
11. Tokarenko O. I. ., Andreieva, I. O. ., Tokarenko, O. O. ., & Surmilo, M. M. . (2021). Effect of diet and exercise-induce weight loss on level of resistin in patient with obesity. Modern Medical Technology, (4), 11–15. https://doi.org/10.34287/MMT.4(51).2021.2
12. Velychko, V., Mykhailenko, V., Lahoda, D., Volokhova, G., & Liashenko, S. (2021). Screening for diabetes and prediabetes: the newest communication opportunities. Reproductive endocrinology, (62), 92–95. https://doi.org/10.18370/2309-4117.2021.62.92-95