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The role of neutrophil-to-lymphocyte ratio in left ventricular hypertrophy development in patients with comorbid course of hypertension, diabetes mellitus, and obesity

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SOUHRN

Cíl: Současná hypertenze, diabetes mellitus a obezita patří v nynější klinické praxi k nejčastějším přidruženým onemocněním. Zásadní význam má vyšetření rozvoje hypertrofie levé komory (LVH) u výše uvedených komplikovaných komorbidních pacientů. Souvislost poměru neutrofilů a lymfocytů (NLR) s rozvojem LVH není dostatečně prozkoumána. Cílem práce bylo studovat roli NLR při vzniku hypertrofie levé komory u hypertoniků zatížených diabetem 2. typu a obezitou.
Materiál a metoda: Do studie bylo zařazeno 297 hypertoniků s diabetes mellitus 2. typu a obezitou. Byly vytvořeny dvě skupiny: první skupina – LVH, n = 153, s hypertrofií levé komory a druhá skupina, n = 144, bez přítomnosti LVH. Výpočet hmotnosti LK použil modifikovaný Devereuxův vzorec, kde hodnoty přesahující 95 g/m^2 (ženy) a 115 g/m^2 (muži) byly indikativní pro LVH. Analýza dat byla provedena pomocí statistického softwaru MedCalc verze 20.111. K prozkoumání rizikových faktorů pro LVH byla použita logistická regresní analýza.
Výsledky: NLR byl významně zvýšen ve skupině LVH 3,21 ± 1,33 vs 2,65 ± 1,19, p = 0,0002 a trvání esenciální hypertenze bylo také významně delší ve skupině LVH 17,87 ± 7,23 roku vs. 15,35 ± 6,41 roku, p = 0,0017. Procento cirkadiánního rytmu krevního tlaku „non-dipperů" bylo významně vyšší ve skupině LVH 53 (34,64 %) oproti 31 (22,92 %), p = 0,0263. Zvýšené hodnoty NLR byly spojeny s vyšším rizikem LVH s poměrem šancí (OR) 1,570, 95% interval spolehlivosti (CI) = 1,080–2,911, p = 0,019. Multivariační logistická analýza odhalila, že NLR spolu s délkou trvání hypertenze jsou nadále významnými prediktory rozvoje LVH u jedinců s EH, DM a obezitou OR – 1,299; 95% CI: 1,009–2,105; p = 0,037 a OR – 1,089; CI: 1,019–3,539; p = 0,043.
Závěr: Výsledky studie zjistily vliv poměru neutrofilů a lymfocytů na progresi hypertrofie levé komory u jedinců s esenciální hypertenzí spojenou s diabetem a obezitou. Lze navrhnout, že NLR by se mohl objevit jako nový indikátor LVH ve stratifikaci rizika esenciální hypertenze. Identifikace NLR u hypertoniků s diabetem a obezitou by mohla být nápomocná v efektivnější léčbě těchto pacientů.

ABSTRACTS

Objective: The patients with concurrent hypertension, diabetes mellitus (DM), and obesity are among the most common associated conditions in contemporary clinical practice. It is of crucial importance to investigate the development of left ventricular hypertrophy (LVH) in above mentioned complicated comorbid patients. The association of neutrophil-to-lymphocyte ratio (NLR) with the development of LVH is not researched enough. The aim of the work was to study the role of NLR in the development of LVH in hypertensive patients burdened with type 2 diabetes and obesity.
Methods: 297 hypertensive patients with diabetes mellitus type 2 and obesity were enrolled into the study. Two groups were created: the first group – LVH, n = 153, with left ventricular hypertrophy and the second one, n = 144, without the presence of LVH. The calculation of LV mass employed the modified Devereux formula, where values exceeding 95 g/m^2 (females) and 115 g/m^2 (males) were indicative of LVH. Data analysis

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was conducted using MedCalc version 20.111 statistical software. Logistic regression analysis was utilized to explore the risk factors for LVH.

Results: The NLR was significantly elevated in LVH group 3.21±1.33 vs 2.65±1.19, $p = 0.0002$, and duration of essential hypertension (EH) was also significantly longer in LVH group 17.87±7.23 years vs 15.35±6.41 years, $p = 0.0017$. The percentage of "non-dippers" blood pressure circadian rhythm was significantly higher in LVH group 53 (34.64%) vs 31 (22.92%), $p = 0.0263$. The increased NLR levels were associated with higher risk of LVH with odds ratio (OR) 1.570, 95% confidence interval (CI) = 1.080–2.911, $p = 0.019$. The multivariate logistic analysis revealed that NLR together with duration of hypertension continued to be substantial predictors of LVH development in individuals with EH, DM, and obesity OR – 1.299; 95% CI: 1.009–2.105; $p = 0.037$ and OR – 1.089; CI: 1.019–3.539; $p = 0.043$, respectively.

Conclusion: The study findings affirm the impact of the neutrophil-to-lymphocyte ratio on the progression of left ventricular hypertrophy in individuals with essential hypertension associated with diabetes and obesity. It can be suggested that NLR could emerge as a novel indicator for LVH in essential hypertension risk stratification. Identification of NLR in hypertensive patients with diabetes and obesity could be helpful in more effective management of these patients.

Keywords:
Diabetes
Essential hypertension
Left ventricular hypertrophy
Neutrophil-to-lymphocyte ratio
Obesity

Introduction

The patients with concurrent hypertension, diabetes mellitus (DM), and obesity are one of the most common associated conditions in contemporary clinical practice. Current researches show that hypertension and diabetes mellitus often progress together over time and these diseases are among the most common cardiovascular risk factors.[1] Up to date studies prove that major percentage of patients with diabetes mellitus have arterial hypertension.[2–4] And obesity is a common additional comorbidity in diabetic and hypertensive patients.[5,6]

Current studies indicate the valuable pathogenetic role of the neutrophil-to-lymphocyte ratio (NLR) in patients with obesity, hypertension and diabetes mellitus.[7–11]

Thus, it is of crucial importance to investigate the development of target organ damage such as left ventricular hypertrophy (LVH) in above mentioned complicated comorbid patients. It is of high clinical value because the left ventricular hypertrophy functions as a predictive marker associated with increased chances for acute myocardial infarction, mortality, and eventual heart failure. To date, the effect of NLR on the development of LVH has not been examined in the hypertensive patients with the mentioned aggravating risk factors.

Thus, **the purpose of our work** was to study the role of NLR in the development of left ventricular hypertrophy in hypertensive patients burdened with type 2 diabetes and obesity.

Methods

Study population

Two hundred and ninety-seven hypertensive patients were enrolled from the Cardiology Department of the Kharkov Regional Clinical Hospital and the Cardiology Department of City Clinical Hospital of Urgent and Emergency Medical Care. The diagnosis of hypertension was made in accordance with the ESH/ESC guidelines.[12] Patients were categorized into two groups, namely group LVH (n = 153, with present of left ventricular hypertrophy and group non-LVH (n = 144, without the presence of LVH), based on echocardiographic assessment.

Inclusion and exclusion criteria

Inclusion criteria were: essential hypertension, diabetes mellitus type 2, obesity class 1–2. Exclusion criteria encompassed various heart diseases (myocardial infarction and a history of the acute coronary syndrome and/or previous myocardial infarction, ischemic heart failure, congenital heart failure, valvular heart failure, myocarditis, acute or chronic heart failure, secondary hypertension, level of systolic blood pressure over 180 mmHg, ejection fraction [EF] <50%, HbA_{1c} >8%), chronic inflammatory and acute infectious diseases, as well as pulmonary conditions (COPD, asthma, and sleep apnea), kidney disorder with an estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 m^2, obesity over 40 kg/m^2, BMI less 30 kg/m^2, immune diseases, malignancies, thyroid disorders, diabetes mellitus type 1, and anaemia of any type.

Ethical disclosure

This investigation was done in accordance with the provisions of the Declaration of Helsinki. All enrolled patients provided informed consent before participating in any study procedures, and the study received approval from the local Ethics Committee.

Patient management

Demographic information, risk factors, and prior medical history were gathered from patient records, interviews, and clinical examinations, which included measurements of blood pressure, weight, and height. Body mass index (BMI) was determined as weight (kg)/height (m)^2. Further cardiovascular risk assessment followed the guidelines outlined by the European Society of Cardiology on hypertension. Baseline evaluations for all enrolled patients included the collection of blood samples and cardiac echocardiography. Morning blood samples, assessing total, LDL, and HDL cholesterol, triglycerides, glucose, creatinine, serum albumin, uric acid, sodium, and potassium, were obtained after an overnight fast and following a 5–10-minute rest period.

Echocardiography

Echocardiography was conducted utilizing a 2–5 MHz probe on a Medison SonoAceX6 (Korea) ultrasound machine. An experienced echocardiographer, unaware of the patients' medical history, performed the procedure

in adherence with the guidelines of the American Society of Echocardiography and the European Association of Cardiovascular Imaging,[13] with a specific emphasis on assessing cardiac remodelling, as well as systolic and diastolic function. Measurements of the cardiac walls and chambers during systole and diastole were acquired using M mode. The calculation of left ventricular (LV) mass employed the modified Devereux formula, where values exceeding 95 g/m^2 in women and 115 g/m^2 in men were indicative of LVH.[14] LV ejection fraction was estimated using Simpson's biplane method.

Statistical analyses

Data analysis was conducted using MedCalc version 20.111 and statistical software. The normality of the data was assessed using the Kolmogorov–Smirnov test. In cases where the measurement data adhered to a normal distribution, the independent sample t-test was employed to analyse differences between the two groups. Alternatively, the Mann–Whitney U test was used for group comparisons when the data did not exhibit normal distribution. Non-normally distributed data were presented as median (interquartile range, IQR), while other measurement data were expressed as mean ± standard deviation (mean ± SD). Count data were reported as cases/percentage (n/%) and subjected to chi-square (χ^2) testing. Logistic regression analysis was utilized to explore the risk factors for LVH in hypertensive diabetic obese patients. A significance level of $p < 0.05$ was considered statistically significant.

Results

All patients enrolled in this study were hospitalized with a diagnosis of EH and diabetes mellitus. All subjects had increased BMI in the ranges 30.0–39.9 kg/m^2 (I–II classes according to WHO classification). Patients were divided into the LVH group (n = 153) and the non-LVH group (n = 144). The baseline characteristics are presented in **Table 1**. In both groups, gender was distributed evenly and equally; approximately half of the subjects in both groups were men. It should be noted that the levels of systolic and diastolic blood pressure were comparable in both groups with and without LV hypertrophy 153.29±12.55 mmHg vs 151.73±11.91 mmHg, p = 0.2734, 93.79±8.61 mmHg vs 95.55±7.95 mmHg, p = 0.068 7, respectively. All clinical, anthropometric, laboratory and instrumental parameters were also statistically comparable in both groups: BMI 34.38±4.95 kg/m^2 vs 33.41±4.63 kg/m^2, p = 0.0827, smoking status 49 subjects (32.0%) vs 43 subjects (29.9%), p = 0.6962, diabetes duration 9.03±5.09 years vs 8.78±4.53, p = 0.6558, serum glucose 139.35±29.76 mg/dL vs. 133.38 ± 32.54 mg/dL, p = 0.0997, HbA_{1c} 7.73±3.31% vs 7.05±2.88%, p = 0.0606, serum creatinine 0.93±0.29 mg/dL vs 0.89±0.55 mg/dL, p = 0.4299, lipid profile indices as

Table 1 – Baseline characteristics of the participants

Characteristics	LVH (n = 153)	Non-LVH (n = 144)	*p*
Mean age (years)	59.07±8.85	57.89±9.42	0.267
Males, n (%)	89 (58.2%)	86 (59.7%)	0.793
Body mass index (kg/m^2)	34.38±4.95	33.41±4.63	0.083
Hypertension duration (years)	17.87±7.23	15.35±6.41	0.002
Diabetes duration (years)	9.03±5.09	8.78±4.53	0.656
History of smoking, n (%)	49 (32.0%)	43 (29.9%)	0.696
Systolic blood pressure (mmHg)	153.29±2.55	151.73±11.91	0.273
Diastolic blood pressure (mmHg)	93.79±8.61	95.55±7.95	0.069
Non-dipper BP profile (disrupted circadian rhythm), n (%)	53 (34.64%)	31 (22.92%)	0.026
Serum glucose (mg/dL)	139.35±29.76	133.38±32.54	0.0997
HbA_{1c} (%)	7.73±3.31	7.05±2.88	0.061
Serum creatinine (mg/dL)	0.93±0.29	0.89±0.55	0.423
Total cholesterol (mg/dL)	205.31±41.32	199.81±36.51	0.226
Triglyceride (mg/dL)	137.56±26.39	141.03±39.21	0.369
HDL-C (mg/dL)	49.85±8.34	47.91±9.65	0.064
LDL-C (mg/dL)	121.93±39.42	122.01±33.89	0.985
LVMI (g/m^2)	131.09±17.53	95.11±15.22	<0.0001
Ejection fraction (%)	55.31±4.12	56.29±4.93	0.0635
NLR	3.21±1.33	2.65±1.19	0.0002

HDL-C – high-density lipoprotein cholesterol; LDL-C – low-density lipoprotein cholesterol; LVH – left ventricular hypertrophy; LVMI – left ventricular mass index; NLR – neutrophil-to-lymphocyte ratio.

HDL 49.85±8.34 mg/dL vs 47.91±9.65 mg/dL, p = 0.0643, triglycerides 137.56±26.39 mg/dL vs 141.03±39.21 mg/dL, p = 0.3691, total cholesterol 205.31±41.32 mg/dL vs 199.81±36.51 mg/dL, p = 0.2262, ejection fraction were statistically equal 55.31±4.12% vs 56.29±4.93%, p = 0.0635.

In addition to above mentioned results we found that NLR was significantly elevated in LVH group 3.21±1.33 vs 2.65±1.19, p = 0.0002, and duration of essential hypertension was also significantly greater in LVH group 17.87±7.23 years vs 15.35±6.41 years, p = 0.0017, and we detected that percentage of improper 24 hours ambulatory blood pressure monitoring (marked as "non-dippers") was significantly higher in LVH group 53 (34.64%) vs 31 (22.92%), p = 0.0263. We revealed also positive correlation between NLR and the LVMI, r = 0.395, p = 0.041, and duration of EH, r = 0.433, p = 0.028. On the other hand results did not show any correlation of NLR with other investigated parameters.

On the next phase of our study we investigated characteristics by univariate logistic regression to find independent predictors. The greater NLR levels were associated with an increased risk of LVH with odds ratio (OR) 1.570, 95% confidence interval (CI) = 1.080–2.911, p = 0.019. The performed univariate regression analysis found that together with NLR such indices as duration of EH (OR: 2.015, 95% CI: 1.045–4.395, p = 0.038); duration of diabetes mellitus (OR: 1.033, 95% CI: 1.003–2.871, p = 0.041); and 24 AMBP non-dipper BP profile (OR: 3.141 95% CI: 1.459–7.518, p = 0.002) were significantly valuable factors for left ventricle hypertrophy development in obese hypertensive diabetic patients (**Table 2**). It is important to indicate that parameters of glycaemic and lipid balances, body mass index, and BP level did not show significance in such analyses.

The multivariate logistic analysis, incorporating confounding variables with a p-value less than 0.1 from the univariate logistic regression analysis, revealed that NLR and duration of hypertension continued to be substantial predictors of LVH development in individuals with EH, DM, and obesity (OR – 1.299; 95% CI: 1.009 – 2.105; p = 0.037 and OR – 1.089; CI: 1.019-3.539; p = 0.043, respectively), as depicted in **Table 2**.

Discussion

The key findings of our study can be emphasized as follows. Initially, NLR values were found to be significantly elevated in hypertensive, obese, and diabetic patients with LVH compared to those with a normal LV mass. Additionally, NLR emerged as an independent predictor for the onset of left ventricle hypertrophy in individuals with EH, obesity, and DM2T. Notably, our investigation represents the inaugural effort to establish a correlation between NLR and cardiac hypertrophy in hypertensive patients harbouring well-established risk factors such as obesity and DM2T. The results presented herein underscore the significant association between NLR levels and LVH, suggesting its potential utility for more effective management of hypertensive obese diabetic patients and even useful in avoiding LVH development.

It is worth noting that an important result of our study was the identification, in addition to the NLR index, of

Table 2 – Univariate and multivariate logistic analysis of the influence of the studied factors on the left ventricle hypertrophy in patients with EH, DM, and obesity

Indices	Univariate logistic regression		Multivariate logistic regression	
	OR (95% CI)	p	OR (95% CI)	p
NLR	1.570 (1.080–2.911)	**0.019**	**1.299 (1.009–2.105)**	**0.037**
SBP (mmHg)	1.051 (0.967–1.917)	0.537		
DBP (mmHg)	1.039 (0.889–2.165)	0.553		
Disrupted circadian rhythm, n (%)	3.141 (1.459–7.518)	**0.002**	–	–
Gender (M/F)	3.021 (0.538–6.939)	0.771		
Age (years)	0.899 (0.975–1.231)	0.693		
BMI (kg/m^2)	1.787 (0.591–2.845)	0.357		
Smoking	2.956 (0.549-9.571)	0.841		
TC (mg/dL)	0.981 (0.693–2.451)	0.293		
HDL-C (mg/dL)	0.346 (0.126–1.498)	0.057		
LDL-C (mg/dL)	1.754 (0.441–2.4335)	0.135		
Triglyceride (mg/dL)	2.733 (0.909–3.411)	0.597		
Duration of EH (years)	2.015 (1.045–4.395)	**0.038**	**1.089 (1.019–3.539)**	**0.043**
Duration of DM (years)	1.033 (1.003–2.871)	**0.041**	–	–
Serum glucose (mg/dL)	3.874 (0.719–5.548)	0.297		
HbA_{1c} (%)	1.789 (0.981–3.753)	0.061		
Serum creatinine (mg/dL)	3.995 (0.813–11.372)	0.893		
EF (%)	1.055 (0.845–4.395)	0.339		

DBP – diastolic blood pressure; EF – ejection fraction; HDL-C – high-density lipoprotein cholesterol; LDL-C – low-density lipoprotein cholesterol; LVH – left ventricular hypertrophy; LVMI – left ventricular mass index; NLR – neutrophil-to-lymphocyte ratio; SBP – systolic blood pressure; TC – total cholesterol.

the duration of hypertension and the incorrect ABPM profile was valuable in the prediction of left ventricular myocardial hypertrophy.

W. Song et al. discovered a strong association between inflammation, indicated by CRP, and the occurrence of LVH in elderly individuals with hypertension. Moreover, the levels of hs-CRP were identified as a substantial predictor for LVH in elderly patients with EH. Their study revealed a positive correlation between hs-CRP and LVMI.[15]

Similar to our findings, Abdulmecit Afşin's et al. study from Turkey reported elevated NLR in individuals with newly diagnosed increased blood pressure and LVH compared to those without LVH. Notably, their research highlighted NLR as a predictive factor for LVH in hypertensive patients, suggesting a potential role of inflammation in LVH pathogenesis among hypertensive subjects. However, it is important to note that Afşin's study specifically involved subjects with hypertension, excluding those with DM and obesity. In contrast, our focus was on individuals with obesity and DM.[16]

Another study supporting obtained our results is Chinese investigation by Xuefang Yu et al.[17] In this study it was demonstrated that NLR independently correlates with LVH in individuals with hypertension. This finding aligns with the diagnostic effectiveness observed for CRP and BNP, suggesting that NLR could be a straightforward and convenient indicator for LVH assessment. However, it is important to note a distinction from our study, as the subjects in their research predominantly had a normal BMI, with only one third of the participants having DM.[17]

A similar trend to our findings was observed in a small-scale study conducted in a paediatric cohort. M. Hou discovered that NLR is increased in hypertensive children and exhibits a positive correlation with office blood pressure levels. Additionally, their study suggested that NLR could serve as a valuable indicator for evaluating left ventricular diastolic function in children with hypertension.[18]

Xing Liu et al. concluded that heightened NLR levels are strongly associated with an elevated risk of hypertension development.[19] This outcome could contribute to a better understanding of the mechanisms involved in hypertension development. Novel therapeutic strategies targeting inflammation may be considered to manage hypertension and related damage. It is established that low-grade inflammation plays a role in the progression of essential hypertension and hypertensive organ damage. The NLR, as a straightforward and dependable indicator of inflammation, holds potential for predicting hypertension. This was underscored during the approximately six-year follow-up period, during which 1,824 subjects developed hypertension.[19]

Hypertensive patients with concurrent obesity and diabetes constitute a challenging population due to their heightened cardiovascular risk. Recent studies have shed light on the potential of the NLR as a predictive marker of adverse outcomes in this specific cohort. This discussion delves into the multifaceted implications of elevated NLR levels, emphasizing its association with a worse prognosis, the development of cardiovascular events, and a severe hypertension disease profile.

A significant discovery in recent research by Shumilah et al. highlights a robust connection between elevated NLR and the onset of cardiovascular events in hypertensive individuals with obesity and diabetes.[20] Particularly, there is a noteworthy increase in the risk of stroke or myocardial infarction among those with heightened NLR levels. In patients with acute coronary syndrome (ACS), total neutrophil counts were markedly higher, while lymphocyte counts were significantly lower compared to healthy controls (p <0.001). NLR and MLR exhibited substantial elevation in ACS patients compared to healthy controls (p <0.001). Among all the examined markers, NLR emerged as the most potent predictive marker for ACS, boasting an odds ratio of 3.3, p <0.001. A cut-off value of 2.9 for NLR demonstrated 90% sensitivity and 88% specificity in predicting the presence of ACS.[20]

Consistent findings from year-long longitudinal studies consistently reveal a correlation between elevated NLR and an increased incidence of hospitalizations related to cardiovascular events. This finding emphasizes the potential of NLR as a predictive indicator of adverse cardiovascular outcomes, prompting a more detailed examination of its implications in clinical management. Hashemi et al. explore a potential connection between NLR and metabolic syndrome. Functioning as a marker of low-grade inflammation, NLR exhibits a positive correlation with central obesity. Moreover, research indicates that NLR is associated with the occurrence, severity, and management of diabetes. Elevated NLR levels are also observed in individuals with hypertension and hyperlipidaemia. This succinct review assesses the relationship between metabolic syndrome and NLR.[21] The diagnostic accuracy of the NLR suggests a moderate level of utility, positioning it as a promising biomarker of the detection of deep vein thrombosis (DVT). However, conclusive cut-off values and the clinical significance of these indicators require additional evidence, specifically from upcoming prospective studies characterized by well-designed methodologies and larger sample sizes.[22]

Beyond cardiovascular events, heightened NLR levels have emerged as a predictor of the worsening of heart failure, leading to hospitalization. The intricate interplay of hypertension, obesity, and diabetes contributes to the complexities of heart failure in this patient population. The recognition of NLR as a marker for heart failure exacerbations underscores its potential utility in risk stratification and targeted therapeutic interventions. Baguyra et al. demonstrated that NLR values were comparable in the lower visceral adiposity index (VAI) tertiles but exhibited an increase in the 3rd VAI tertile for CACS >100. The association persisted even after adjusting for age, sex, smoking, and history of hypertension, hyperlipidaemia, diabetes mellitus, and high-sensitivity C-reactive protein. These findings emphasize the independent correlation between subclinical, chronic, systemic inflammation, and subclinical coronary disease in individuals with obesity.[23]

Monitoring NLR levels could enable healthcare professionals to identify patients at higher risk of heart failure complications, allowing for timely and proactive management strategies.[24] Vakshoori et al. performed an investigation involving a total of 18,231 participants, were ultimately chosen, reporting on NLR in individuals with heart failure (HF).[25] Among these, deceased patients exhibited higher NLR levels compared to those who sur-

vived, p <0.001. NLR was identified as correlating with an increased risk of mortality, p <0.001. The circadian blood pressure variation, characterized by dipping patterns, provides crucial insights into the overall hypertension disease profile. Elevated NLR levels are associated with deviations from the norm, including non-dipper, over-dipper, and inverse dipper patterns. The normal dipper pattern, where blood pressure decreases by 10% during the night, is disrupted in patients with higher NLR values. Non-dipper patterns, indicative of insufficient nocturnal blood pressure reduction, are associated with an increased risk of cardiovascular events. Over-dipper and inverse dipper patterns, reflecting exaggerated or increased nocturnal blood pressure reduction, also point towards a disrupted circadian rhythm. NLR, when considered alongside circadian blood pressure patterns, offers a comprehensive assessment of the disease profile, aiding in risk stratification and tailored therapeutic approaches.

Cardiovascular disease (CVD), although traditionally viewed as male-dominated, stands as the primary cause of death in women. The role of chronic inflammation in the development of insulin resistance, type 2 diabetes, and CVD is pivotal. Males and females, differing in sex hormones, immune responses, and CVD expression, can influence NLR values across the life course. Menopause, a period marked by significant physiological and hormonal changes in women, coincides with the aging process.[26] Elevated NLR levels are not only predictive of specific adverse outcomes but are also indicative of the overall severity of hypertension disease.[27] The correlation between higher NLR levels and the presence of severe hypertension underscores the potential clinical utility of this marker. The inflammatory milieu captured by NLR may contribute to vascular dysfunction, exacerbating hypertension. Monitoring NLR levels provides clinicians with an additional tool for risk stratification, guiding decisions on the intensity of therapeutic interventions and the frequency of follow-up assessments in this specific patient cohort. The association between NLR and existing chronic conditions is explored as an indicator of systemic inflammation. Beyond foreseeing the risk of impending chronic conditions, NLR might offer understanding into their advancement. The review encapsulates the disruptions in NLR mechanisms at the cellular and molecular levels, along with highlighting the pivotal inflammatory signalling pathways implicated in the progression of chronic diseases.[28]

Neutrophils, integral to chronic inflammation, and lymphocytes, reflecting immune regulation pathways, play a crucial role in the intricate balance of the immune system. Chronic hyperglycaemia in DM contributes to the release of reactive oxygen species from neutrophils, leading to decreased lymphocyte levels. This chronic hyperglycaemia also directly causes diminished lymphocyte proliferation, with implications for the immune response.

The neutrophil-to-lymphocyte ratio serves as a promising and multifaceted biomarker in hypertensive patients with obesity and diabetes. Elevated NLR levels not only indicate a worse prognosis and an increased risk of cardiovascular events but also provide insights into the severity of the hypertension disease profile. As we delve deeper into the mechanistic links between inflammation, immune response, and cardiovascular health, NLR stands out as a valuable tool for risk stratification and personalized management strategies in this complex patient population.

This study is characterized by several limitations. Firstly, the relatively small sample size hinders the ability to draw definitive conclusions. Additionally, the investigation was conducted at only two clinical centres, possibly limiting the representation of the entire population. It is noteworthy that hypertensive patients with commonly associated conditions, such as coronary artery disease or kidney disorders, were not included in the study. Moreover, severe cases involving obesity exceeding 40 kg/m^2, severe diabetes, and others were also absent. There was a prevalence of patients with controlled glycaemic levels, which may introduce some statistical discrepancies. The study focused solely on LVH as an outcome without distinguishing between types of LVH, such as concentric remodelling, eccentric LVH, concentric LVH, and normal geometry. Future studies are needed to delve into the role of NLR and other inflammatory markers in the pathogenesis of LVH and explore effective preventive measures. A promising avenue for further investigation involves examining the relationship between LVH and heart hypertensive damage with inflammatory markers as potential indicators.

Conclusion

In conclusion, our findings affirm the impact of inflammation, as indicated by the neutrophil-to-lymphocyte ratio, in the progression of left ventricular hypertrophy in individuals with essential hypertension associated with diabetes and obesity. Moreover, our study proposes, for the first time, a connection between elevated NLR levels and LVH in mentioned cohort of patients. The NLR levels are notably elevated in diabetic obese individuals with essential hypertension with LVH. This suggests that NLR could emerge as a novel indicator for LVH in essential hypertension risk stratification, assessment of cardiac target organ damage, or potentially as a therapeutic target to intervene in myocardial changes, aiming to reverse left ventricular remodelling. Larger-scale studies focusing on NLR levels and LVH development are necessary to precisely define its potential role in the pathogenesis of complications related to hypertension-mediated organ damage in diabetic obese patients.

Conflict of interest
All authors declare that there was no conflict of interest.

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Ethical statement
The study was approved by the Ethics Committee of Kharkiv National Medical University.

Informed consent
Informed consent was signed by all participants accordingly to GMP ICH procedures, no vulnerable subjects were enrolled.

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