New-onset hypertension is not associated with systemic changes in inflammatory cytokine levels

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Abstract

Introduction: Recent studies have suggested that hypertension development may be associated with an altered immune system. However, there is a paucity of data evaluating the association between blood pressure values and inflammatory markers in patients with new-onset hypertension.
Material and methods: We evaluated 61 subjects, including 24 healthy individuals and 37 newly diagnosed hypertensive patients (aged 45 ±9.6 vs. 43.8 ±11.9 years; SBP_24hours 114 ±7.1 vs. 134.2 ±9.5 mm Hg; DBP_24hours 71.2 ±4.7 vs. 85.8 ±9.3 mm Hg, respectively) without prior antihypertensive treatment. The diagnosis of hypertension was based on 24-hour ambulatory blood pressure monitoring (ABPM). We analysed the association between blood pressure values and levels of individual inflammatory markers (ITAC, GM-CSF, fractalkine, IFN-γ, IL-10, MIP-3α, IL-12, IL-13, IL-17A, IL-1β, IL-2, IL-21, IL-23, IL-5, IL-6, IL-7, IL-8, MIP-1α, MIP-1β, TNF-α, and IL-15) separately, as well as in clusters of inflammatory mediators (factor 1 – proinflammatory: IL-1β, IL2, IL-6, IL-7, IL-12, IL-6, IL-21, TNF-α, IFN-γ; and factor 2 – anti-inflammatory: IL-13, IL-5).
Results: Our study did not show any differences in concentrations of inflammatory markers between patients and controls. Plasma levels of inflammatory markers were not associated with 24-hour ambulatory blood pressure values in patients with new-onset hypertension.
Conclusions: Patients with new-onset hypertension did not differ from healthy subjects regarding the levels of plasma inflammatory markers. Our findings demonstrate the need for larger, more comprehensive studies on this topic to further elucidate the relationship between hypertension and inflammation.

Key words: hypertension, ambulatory blood pressure monitoring, cytokines, inflammatory factors.

Introduction

The regulation of blood pressure involves a complex interplay between the heart, vessels, and kidneys. However, recent studies have suggested that hypertension development may be associated with an altered

immune system [1–3]. Activation of immune cells (cytotoxic T lymphocyte [4], B lymphocyte [5, 6], or T helper lymphocyte [7]) leads to endothelial dysfunction, a process that involves abnormalities in endothelium-derived nitric oxidate production or bioavailability, impaired production of constrictive/relaxant factors, as well as pro-inflammatory and prothrombotic cytokines [8]. Consequently, inflammation increases vascular permeability, formation of neo-intima, and promotes vascular fibrosis [9].

The current scientific literature on the relationship between hypertension and inflammation in humans is limited. However, Siedlinski *et al.* discovered a positive and potentially causal relationship between blood lymphocyte counts and blood pressure [10]. Furthermore, an elevated level of interleukin (IL)-6 or high-sensitivity C-reactive protein (hs-CRP) (but not IL-1β) is associated with an increased risk of developing hypertension [11]. The serum level of IL-17 is also elevated in patients with diabetes, hypertension [7], and pre-eclampsia [12]. The role of tumour necrosis factor α (TNF-α) remains unclear and may depend on the activation of one of the types of TNF-α receptors.

Despite preclinical evidence suggesting elevated levels of IL-1β in mouse models of hypertension are present, administration of canakinumab (a human monoclonal antibody targeted at IL-1β) does not reduce blood pressure or the development of hypertension in patients with cardiovascular disease [13]. In contrast, IL-10 plays a protective role in hypertension development in adults [14] or during pregnancy. Additionally, the serum levels of IL-10 are reduced in pre-eclampsia [15].

Given these limited findings, our study aimed to assess the role of inflammatory cytokines in newly diagnosed hypertensive patients and in healthy controls. We sought to establish the association between inflammatory markers and blood pressure in both groups.

Material and methods

Study population

We investigated a total of 61 adult subjects, comprising 24 healthy individuals and 37 newly diagnosed hypertensive patients without any prior treatment. The participants were recruited form Hypertension Outpatient Clinic and Primary Care Clinic of the University Hospital in Krakow, Poland. The study was conducted in the years 2013–2016. All participants provided informed consent. Patients with heart failure, diabetes, malignant tumour, chronic kidney disease, inflammatory bowel disease, secondary forms of hypertension, or taking statins were excluded from the study. The evaluation included anthropometric measurements (weight, height, body mass index), physical examination, and medical history. The study protocol was approved by the Bioethical Committee of the Jagiellonian University Medical College (no. 151/B/2012).

Ambulatory blood pressure measurement

Ambulatory blood pressure monitoring (ABPM) was conducted using an automatic SpaceLabs-90207 [16] oscillometric device (SpaceLabs Healthcare, Hertford, UK) during the patient's ordinary activity considering both night and day periods. Recordings were taken every 20 min during the day and every 30 min during the night on the nondominant arms, and a minimum of 70% successful readings were required for data validation. A diagnosis of hypertension based on ABPM measurements [17], with patients assigned to the hypertensive group if any value of systolic or diastolic blood pressure (ambulatory blood pressure – daytime mean ≥ 135 mm Hg and/or ≥ 85 mm Hg; night-time mean ≥ 120 mm Hg and/or ≥ 70 mm Hg; 24 h mean ≥ 130 mm Hg and/or ≥ 80 mm Hg 24 h) exceeded the reference range; they were otherwise classified as healthy.

Carotid femoral pulse wave velocity

The evaluation of carotid-femoral pulse wave velocity (cfPWV) was performed using a Complior device (Complior, Colson, Garges-les-Gonesse, France) with 2 pressure-sensitive transducers placed directly on the skin above the femoral and carotid artery track. The distance was calculated as 80% of the direct tape-measured length between those 2 points. The average of 10 consecutive measurements was considered for analysis with the elimination of the 2 extreme values (the minimum and maximum). Measurements were performed according to the expert consensus on cfPWV [18].

Blood analyses

Blood samples were taken after at least 8 hours fasting in the morning (between 7 and 9 a.m.). We assessed the serum levels of glucose, creatinine, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG) using a Hitachi 917 analyser (Roche Diagnostic, Hitachi Ltd., Japan) using standardized laboratory technics. Serum levels of hs-CRP were measured with immunonephelometry (Nephelometer BM II, Siemens Healthcare Diagnostics Inc., USA). The glomerular filtration rate was estimated using the Modification of Diet in Renal Disease (MDRD) equation [19]. Glycated haemoglobin (HbA1c) was assessed in whole blood samples using a Bio Rad D-10 (Bio Rad Laboratories, Inc., USA).

Peripheral blood was collected in tubes containing ethylenediaminetetraacetic acid (EDTA) to

assess circulating biomarkers. Next, the samples were centrifuged at 400 × g for 10 min. The platelet-rich plasma was then collected and centrifuged at 2000 × g for 15 min at 4°C. Plasma samples without pellets were then collected and stored at –80°C until analysis. Samples were analysed for interferon-inducible T-cell alpha chemoattractant (ITAC), granulocyte-macrophage colony-stimulating factor (GM-CSF), fractalkine, interferon-γ (IFN-γ), IL-10, macrophage inflammatory protein (MIP)-3α, IL-12, IL-13, IL-17A, IL-1β, IL-2, IL-21, IL-23, IL-5, IL-6, IL-7, IL-8, MIP-1α, MIP-1β, TNF-α, and IL-15 with Luminex technology using standard kits (MILLIPLEX® Human High Sensitivity T Cell Magnetic Bead Panel, Millipore, Merck and Luminex Performance Human High Sensitivity Cytokine Panel B, R&D, Bio-Techne, respectively) and were read on a Luminex 200 machine (Biorad) in accordance with the manufacturer's instructions.

Statistical analysis

Statistical analysis was performed using Statistica version 13 software (Statistica, StatSoft Poland, Dell Inc.). The normality of distribution was confirmed using the Shapiro-Wilk test. Variables with a Gaussian distribution were presented as mean ± standard deviation (SD) whereas those with a skewed distribution were presented as median and quartile range (upper-lower quartile). Data on frequency were given as numbers and percentages. The comparative analyses were conducted with Student's t-test (normal distribution pattern) or the *U* Mann-Whitney test (skewed distribution) for continuous variables, and the χ^2 test and Fisher exact test for qualitative data. Two-tailed *p* values of less than 0.05 were considered statistically significant. Correlations between variables were assessed with Pearson's or Spearman's tests. Logarithmic transformation was performed with variables with non-Gaussian distribution when necessary. Multivariable regression analyses were performed to assess the independent effects of gender, age, BMI, and appropriate interleukin on the blood pressure value.

Exploratory factor analysis (EFA) with SPSS IBM version 28 (IBM Corporation, Armonk, New York) was used to create pro-inflammatory and anti-inflammatory mediator factors. EFA was performed using principal component analysis and varimax rotation; only factors with an eigenvalue value > 1 were retained. The minimum factor loading criteria was 0.3. The Kaiser-Meyer-Olkin (KMO) value was used to measure sampling adequacy. Factors with double loading or without any were eliminated from the analysis. Finally, based on the literature, we eliminated 2 inflammatory mediators (IL-10 and IL-8 from the pro-inflammatory factor and anti-inflammatory factor, respectively).

Results

We investigated 61 subjects: 24 healthy and 37 with newly diagnosed hypertension without any treatment. The groups differed in terms of BMI and blood pressure values (Table I). We did not find differences in the level of pro-inflammatory and anti-inflammatory factors, such as TNF-α, IFN-γ, IL-1β, IL-2, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, IL-13, IL-15, IL-17A, IL-21, IL-23, hs-CRP, MIP-1α, MIP-1β, MIP-3α, GM-CSF, fractalkine, and ITAC (Table II), nor in arterial stiffness parameters (cfPWV).

There were no differences in lipid levels between patients after Bonferroni corrections.

Table I. Comparison between the 2 groups

Parameters	nHT group *N* = 24	HT group *N* = 37	*P*-value
Age [years]	45 ±9.6	43.8 ±11.9	0.683
Gender – male *n*, (%)	9 (37.5)	20 (54.05)	0.206
BMI [kg/m^2]	24.2 ±3.7	28.2 ±4	0.000
Creatinine level [µmol/l]	72.4 ±10.2	74.3 ±11.8	0.524
HbA1c [%]	5.4 ±0.2	5.38 ±0.37	0.474
SBP_24hours [mm Hg]	114 ±7.1	134.2 ±9.5	0.000
DBP_24hours [mm Hg]	71.2 ±4.7	85.8 ±9.3	0.000
cfPWV [m/s]	8.75 (7.9–10.5)	9.6 (8.6–10.3)	0.167
Cholesterol [mmol/l]	5.2 ±1.1	5.5 ±0.9	0.247
HDL-C [mmol/l]	1.54 (1.2–1.9)	1.4 (1.16–1.72)	0.197
LDL-C [mmol/l]	3.1 ±1	3.3 ±0.8	0.323
TG [mmol/l]	1.0 (0.76–1.63)	1.63 (1.14–1.96)	0.016

Bonferroni correction – p significant < 0.001. Data shown as means (SD), medians (IQR), or numbers (percentages). BMI – body mass index, DBP – diastolic blood pressure, HbA1c – glycated haemoglobin, HDL-C – high-density lipoprotein cholesterol, HT group – group with newly detected hypertension, LDL-C – low-density lipoprotein cholesterol, nHT group – group without hypertension, SBP – systolic blood pressure, TG – triglyceride.

Table II. Comparison of the levels of pro-inflammatory and anti-inflammatory factors in the non-hypertensive and hypertensive groups

Inflammatory factor	nHT group *N* = 24	HT group *N* = 37	*P*-value
IL-1β [pg/ml]	2.53 (1.43–4.59)	1.9 (1.12–3.36)	0.43
IL-2 [pg/ml]	3.53 (6.23–3.29)	2,48 (0.92–4.64)	0.295
IL-5 [pg/ml]	5.19 (2.75–8.31)	5.34 (2.56–8.38)	0.976
IL-6 [pg/ml]	2 ±1.27	1.8 ±1.27	0.551
IL-7 [pg/ml]	0.68 (0.42–4.35)	3.1 (0.42–6.6)	0.144
IL-8 [pg/ml]	4.35 (3.65–5.79)	3.94 (3.06–5.42)	0.301
IL-10 [pg/ml]	9.06 (5.29–27.18)	16.86 (5.92–24.96)	0.600
IL-12 [pg/ml]	7.32 (2.89–10.4)	5.78 (1.78–10.86)	0.38
IL-13 [pg/ml]	4.83 (1.87–9.78)	3.08 (1,46–6.36)	0.220
IL-15 [pg/ml]	1.11 ±0.32	1.04 ±0.37	0.406
IL-17A [pg/ml]	6.13 (3.85–10.08)	5.92 (2.8–13.18)	0.959
IL-21 [pg/ml]	0.45 (0.14–1.68)	0.14 (0.14–1.02)	0.275
IL-23 [pg/ml]	165.33 (34.44–586.88)	85.66 (21.42–430.4)	0.392
TNF-α [pg/ml]	5.46 (3.61–7.82)	5.58 (3.82–7.82)	0.894
IFN-γ [pg/ml]	21.38 ±15.64	25.68 ±17.04	0.324
hs-CRP [mg/l]	0.8 (0.44–1.27)	1.03 (0.66–1.35)	0.159
MIP-1α [pg/ml]	20.67 (17.18–25.43)	21.16 (11.98–26.72)	0.953
MIP-1β [pg/ml]	13.72 (11.36–25.43)	12.7 (8.74–17.4)	0.326
MIP-3α [pg/ml]	0.83 (0.8–2.03)	0.83 (0.83–3.24)	0.808
GM-CSF [pg/ml]	22.65 (2.95–35.58)	14.88 (4.44–42.2)	0.935
Fractalkine [pg/ml]	54.36 (25.88–111.99)	91.38 (23.84–127.82)	0.575
ITAC [pg/ml]	24.68 (15.73–35.66)	29.3 (23.64–38.62)	0.291

Bonferroni correction – p significant < 0.001. Data shown as means (SD) or medians (IQR). GM-CSF – granulocyte-macrophage colony-stimulating, IFN-γ – interferon-γ, IL – interleukin, ITAC –interferon-inducible T-cell alpha chemoattractant, MIP – macrophage inflammatory protein, TNF-α – tumour necrosis factor α.

Correlation between inflammatory factors and the value of blood pressure

We analysed 22 markers of inflammation (TNF-α, IFN-γ, IL-1β, IL-2, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, IL-13, IL-15, IL-17A, IL-21, IL-23, hs-CRP, MIP-1α, MIP-1β, MIP-3α, GM-CSF, fractalkine, and ITAC) and 24-hour blood pressure monitoring of systolic and diastolic blood values during the day and night period (SBP_24hour, DBP_24hour, SBP_DAY, DBP_DAY, SBP_NIGHT, DBP_NIGHT). We found that 4 of these markers (IL-5, IL-8, hs-CRP, and ITAC) were significantly correlated with ambulatory blood pressure values in patients or controls (Table III).

Table III. Correlations (Spearman) between inflammatory indices (hs-CRP, ITAC, IL-5, IL-8) and the value of blood pressure in controls and patients with hypertension

Parameters	nHT group (*N* = 23) hs-CRP		nHT group (*N* = 24) ITAC		HT group (*N* = 37) IL-5		HT group (*N* = 37) IL-8	
	r	*p*-value	*r*	*p*-value	*r*	*p*-value	*r*	*p*-value
SBP_24hours [mm Hg]	0.239	0.272	0.509	0.011	0.079	0.643	0.041	0.808
DBP_24hours [mm Hg]	–0.108	0.624	0.400	0.053	0.361	0.028	0.235	0.162
SBP_DAY [mm Hg]	0.056	0.798	0.423	0.04	0.077	0.652	0.004	0.983
DBP_DAY [mm Hg]	–0.191	0.382	0.411	0.046	0.335	0.043	0.184	0.276
SBP_NIGHT [mm Hg]	0.561	0.005	0.46	0.024	0.232	0.167	0.228	0.175
DBP_NIGHT [mm Hg]	0.23	0.292	0.415	0.044	0.460	0.004	0.436	0.007

nHT group – group without hypertension, HT group – group with newly detected hypertension, r – correlation coefficient, hs-CRP – high-sensitivity C-reactive protein, IL – interleukin, ITAC – interferon-inducible T-cell alpha chemoattractant, DBP – diastolic blood pressure, SBP – systolic blood pressure.

Table IV. A – Multivariable regression analysis in patients and the control group (loghs-CRP, logIL-5, logIL-8)

Parameters	SBP_NIGHT (loghs-CRP)		DBP_24hours (logIL-5)		DBP_DAY (logIL-5)		DBP_NIGHT (logIL-5)		DBP_NIGHT (logIL-8)	
	β (SE)	*p*	β (SE)	*p*	β (SE)	*p*	β (SE)	*p*	β (SE)	*p*
Age	–0.104 (0.13)	0.409	–0.068 (0.13)	0.608	–0.097 (0.13)	0.46	0.026 (0.13)	0.846	0.001 (0.13)	0.996
Gender	1.218 (2.89)	0.676	0.095 (0.14)	0.488	0.129 (0.13)	0.341	–0.014 (0.14)	0.92	–0.491 (2.88)	0.865
BMI	1.226 (0.36)	0.001	0.247 (0.14)	0.075	0.252 (0.13)	0.066	0.21 (0.14)	0.131	0.604 (0.34)	0.086
Inflammatory factor	1.513 (1.68)	0.373	0.136 (0.14)	0.305	0.137 (0.13)	0.296	0.192 (0.13)	0.153	3.284 (3.37)	0.333

hs-CRP – high-sensitivity C-reactive protein; IL – interleukin, ITAC – interferon-inducible T-cell alpha chemoattractant.

Table IV. B – Multivariable regression analysis in patients and control group (logITAC)

Parameters	SBP_24hours		SBP_DAY		DBP_DAY		SBP_NIGHT		DBP_NIGHT	
	β (SE)	*p*	β (SE)	*p*	β (SE)	*p*	β (SE)	*p*	β (SE)	*p*
Age	–0.149 (0.13)	0.269	–0.172 (0.14)	0.223	–0.096 (0.13)	0.449	–0.105 (0.12)	0.399	0.019 (0.13)	0.882
Gender	6.275 (6.28)	0.040	8.28 (3.13)	0.011	2.316 (2.82)	0.416	0.928 (2.78)	0.739	–0.822 (2.88)	0.776
BMI	1.124 (0.37)	0.003	1.152 (0.39)	0.004	0.718 (0.35)	0.044	1.149 (0.34)	0.001	0.612 (0.35)	0.090
logITAC	8.813 (5.63)	0.124	8.899 (5.92)	0.139	–3.316 (5.33)	0.537	6.347 (5.24)	0.231	–2.701 (5.44)	0.622

ITAC – interferon-inducible T-cell alpha chemoattractant.

The remaining inflammatory markers were not correlated with any of the blood pressure values (SBP_24hours, DBP_24hours, SBP_DAY, DBP_DAY, SBP_NIGHT, DBP_NIGHT), either in subgroups or collectively.

Multivariable regression analysis

After adjusting for gender, age, BMI, and the logarithmic value of hs-CRP, IL-5, IL-8, and ITAC levels were not associated with blood pressure values (Tables IV A, B).

Exploratory factor analysis

Initially, we included 22 inflammatory factors in the analysis (KMO value – 0.732; Bartlett's sphericity test was < 0.001). During the analysis only 11 mediators met all the requirements (KMO value – 0.732; Bartlett's sphericity test was < 0.001) and 2 factors were created (Table V) – factor 1 (proinflammatory: IL-1β, IL-2, IL-6, IL-7, IL-12, IL-6, IL-21, TNF-α, IFN-γ) and factor 2 (anti-inflammatory: IL-13, IL-5). The mediators: IL-8, IL-10, IL-15, IL-23, hs-CRP, MIP-1α, MIP-1β, MIP-3α, GM-CSF, fractalkine, and ITAC were eliminated during the analysis.

We did not find any differences in factor 1 (p = 0.825) and factor 2 (p = 0.4) values in the hypertensive or healthy group; nor did we find any correlation between factor 1 or factor 2 and any of the blood pressure values.

Discussion

We did not find any differences in the concentration of multiple inflammatory markers between normotensive and hypertensive patients; nor did we find any correlation between blood pressure

Table V. Inflammatory mediator scores in patients and controls

Parameters	Factor 1	Factor 2
IL-1β	0.807	
IL-2	0.873	
IL-6	0.758	
IL-7	0.629	
IL-12	0.802	
IL-17	0.805	
IL-21	0.552	
INF-γ	0.750	
TNF-α	0.687	
IL-5		0.847
IL-13		0.929
Eigenvalue	5.216	1.712
Cumulative %	47.415	62.976
Alfa Cronbach	0.773	0.800

Factor 1: pro-inflammatory, Factor 2: anti-inflammatory.

values and inflammatory factors. However, the patients included in our study had new-onset hypertension and did not show evidence of increased arterial stiffness (cfPWV 8.75 (7.9–10.5) m/s vs. 9.6 (8.6–10.3) m/s, $p = 0.17$; normotensive versus hypertensive patients, respectively). Our findings do not necessarily exclude a connection between inflammatory factors and hypertension, because this may be due to a low level of inflammatory markers in the plasma at this stage of the disease. Similarly, Vazquez-Oliva *et al.*, found no difference in IL-6 levels between normotensive and newly diagnosed hypertensive patients; however, after irbesartan treatment, IL-6 levels decreased significantly [20]. On the other hand, Jayedi *et al.* performed a meta-analysis [11] and showed that there was a relationship between inflammatory markers (hs-CRP and IL-6) and the risk of developing hypertension in a prospective or nested case-control study. Some studies evaluated PCSK9 as an early biomarker of screening-detected hypertension [21]. Our study was cross-sectional; therefore, it was not possible to assess a causal association between inflammation and hypertension.

Contrary to our results, the study by Stumpf *et al.* showed elevated levels of hs-CRP, IL-6, TNFα, and MCP-1 in 15 patients with newly diagnosed mild hypertension compared to healthy controls [22]. Similarly, prehypertensive patients had higher levels of IL-17, even after adjusting for confounding factors [23]. Furthermore, Madhur *et al.* demonstrated that 94 patients with diabetes and hypertension had elevated IL-17 levels compared to healthy patients [7]. However, most patients in the latter study had comorbidities (diabetes, cardiovascular disease, or obesity) and were on anti-hypertensive treatment, which could have affected the IL-17 levels [24, 25], or they took lipid lowering medication, which may have influenced CRP levels [26]. In our study, both groups differed only in blood pressure and BMI values and had no comorbidities.

Considering the complexity of the interaction between the innate and adaptive immune systems in hypertension, we created 2 clusters of inflammatory mediators: factor 1 – pro-inflammatory (IL-1β, IL-2, IL-6, IL-7, IL-12, IL-17, IL-21, INF-γ, TNF-α) and factor 2 – anti-inflammatory (IL-5, IL-13). We did not find any correlation between blood pressure values and clusters of inflammatory markers. However, a similar analysis revealed a relationship between the inflammatory clusters and changes in blood pressure during a 4.5-year follow-up, but not with the baseline blood pressure [27].

The role of the immune system in the development of hypertension is complex and activates both the innate and the adaptive immune system [1]. The suggested mechanism of activation of the immune system assumes that a primary moderate increase in the blood pressure initiates mechanical and oxidative damage, which results in the formation of danger-associated molecular protein (DAMPS) and hypertension-specific neoantigens [28]. Then DAMPS are recognized by TLRs (toll-like receptors) in macrophages and dendritic cells, which in response produce inflammatory cytokines; neoantigens may be presented to B cells and T cells by dendritic cells, which promotes the differentiation of plasma cells and effector T cells [1]. Some immune cells (Treg) may also play a protective role against the development of hypertension.

In summary, our study did not identify any differences in cytokine levels between normotensive and hypertensive patients, nor any correlation with blood pressure values. However, it should be noted that we included subjects with mild hypertension because the mean circadian blood pressure value in the hypertensive group was relatively low (134.2/85.8 mm Hg) and they did not present arterial stiffness. The inclusion of patients with new-onset hypertension could potentially explain the similar levels of inflammatory markers observed in both groups.

Although our study did not find significant differences in inflammatory factors among patients with early hypertension, this does not rule out the possible role of inflammation in hypertension. First, it is possible that local inflammatory processes in the kidneys and blood vessels are not fully reflected by systemic cytokine levels. Second, inflammation may become more pronounced in the advanced stages of hypertension, whereas the initial stimulus for the development of the disease is related to sympathetic activation and other classical mechanisms of hypertension.

One of the limitations of our study is the relatively small number of patients included; however, it is important to note that numerous studies conducted on even smaller-sized groups have yielded insightful and valid results [29]. Additionally, there are several factors, such as smoking, abdominal obesity [30], lifestyle [31, 32], sodium intake, uric acid level, and hormonal status [33], which may have influenced the levels of the studied inflammatory markers but were not included in our analyses.

However, our study has several strengths that contribute to its unique nature. Firstly, we have successfully recruited treatment-naïve patients in the early stages of the disease, allowing us to explore the disease progression with fresh insights. Additionally, our utilization of ambulatory blood pressure monitoring ensures a comprehensive

evaluation of blood pressure. Furthermore, our study stands out due to its novelty in assessing not only common inflammatory markers but also a wide range of inflammatory interleukins, many of which have not been studied in the context of hypertension. Overall, the combined strengths of our study include the enrolment of treatment-naïve patients, the use of ambulatory blood pressure monitoring, and a comprehensive assessment of inflammatory markers separately and combined in pro- or anti-inflammatory factors.

In conclusion, patients with new-onset hypertension did not differ in the levels of plasma inflammatory markers from healthy subjects. IL-5 and IL-8 positively correlated with blood pressure levels in hypertensive patients, and CRP and ITAC positively correlated with blood pressure levels in the normotensive group, but after adjusting for age, sex, and BMI the associations were no longer statistically significant. We did confirm a significant relationship between blood pressure and BMI, so the main effort should be focused on reducing body weight for the prevention and treatment of hypertension. Further research is necessary to evaluate a possible association between inflammation and blood pressure.

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Conflict of interest

The authors declare no conflict of interest.

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