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International Journal of Diabetes in Developing Countries

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International Journal of Diabetes in Developing Countries

COUNTRY

India

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Media Ranking in India

SUBJECT AREA AND CATEGORY

Medicine
Endocrinology, Diabetes and Metabolism
Internal Medicine

PUBLISHER

Springer India

H-INDEX

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PUBLICATION TYPE

Journals

ISSN

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COVERAGE

2001-2002, 2006-2022

INFORMATION

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How to publish in this journal

SCOPE

International Journal of Diabetes in Developing Countries is the official journal of Research Society for the Study of Diabetes in India. This is a peer reviewed journal and targets a readership consisting of clinicians, research workers, paramedical personnel, nutritionists and health care personnel working in the field of diabetes. Original research articles focusing on clinical and patient care issues including newer therapies and technologies as well as basic science issues in this field are considered for publication in the journal. Systematic reviews of interest to the above group of readers are also accepted.

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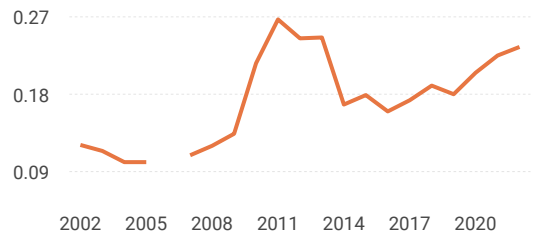

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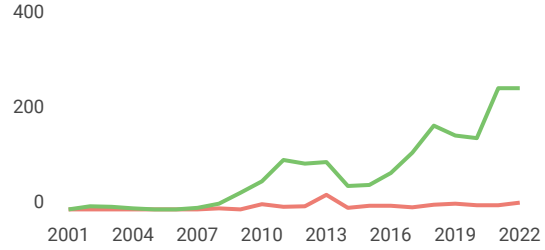

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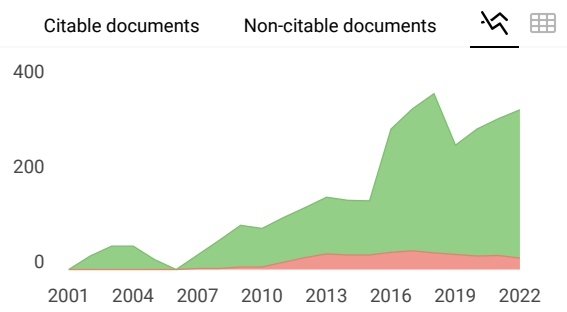

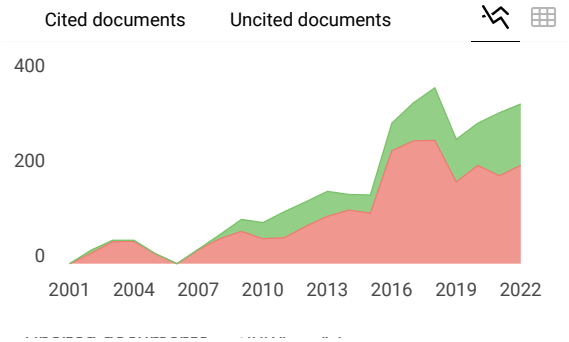

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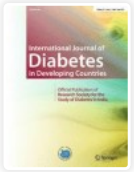

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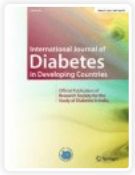

International Journal of Diabetes in Developing Countries

Incorporating Diabetes Bulletin

Volume 42, issue 2, April 2022

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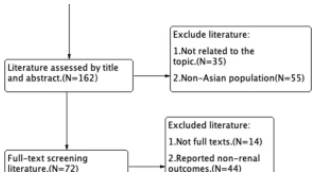

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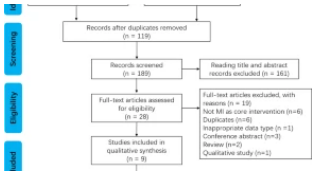

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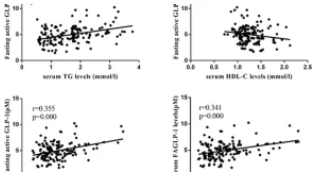

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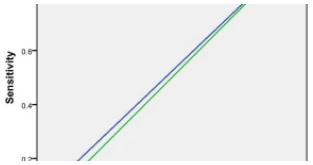

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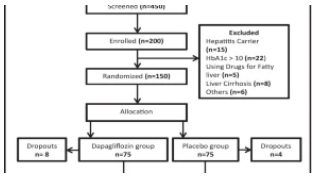

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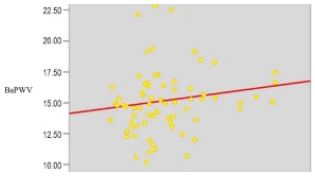

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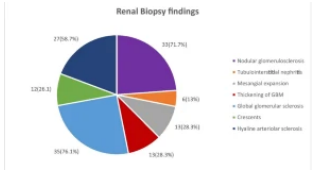

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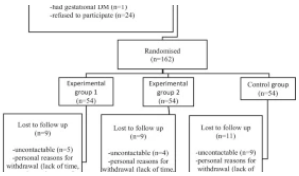

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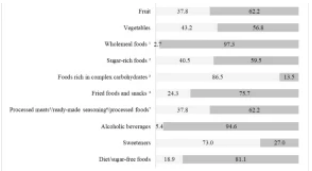

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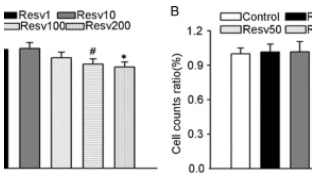

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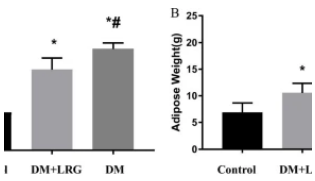

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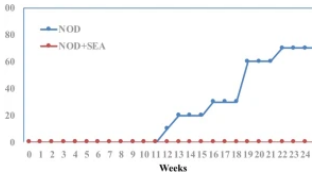

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International Journal of
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Study of Diabetes in India

International Journal of Diabetes in Developing Countries (April–June 2022) 42(2):305–312
https://doi.org/10.1007/s13410-021-00965-1

ORIGINAL ARTICLE

Association between neutrophil–lymphocyte ratio on arterial stiffness in type-2 diabetes mellitus patients: a part of DiORS Study

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Received: 18 March 2020 / Accepted: 9 June 2021 / Published online: 9 July 2021

Abstract

Introduction Type-2 diabetes mellitus (T2DM) enhances the risk of atherosclerosis and cardiovascular diseases, which are the primary cause of death among T2DM patients. Neutrophil–lymphocyte ratio (NLR) is a widely available, easy-to-use, and reproducible inflammatory marker. Brachial-ankle pulse wave velocity (baPWV) serves as the indicator for early atherosclerosis changes. The exact mechanism of association between the high NLR and diabetes complications is still unclear, and the most significant mechanism may be related to inflammation. Since an inflammatory marker in clinical practice is limited, a simple, easy-to-use, and widely available marker is needed. The aim was to analyze the association between NLR and arterial stiffness in T2DM patients.

Method This study is part of the Diabetic Ocular Renal Surabaya Study (DiORS Study). Participants were measured for their NLR count by dividing absolute neutrophil count with absolute lymphocyte count in peripheral blood and measuring of arterial stiffness with baPWV. The statistical analysis in use included independent t-test, Mann–Whitney test, Pearson correlation test, or Spearman correlation test. The results of the statistical analysis were significant if $p < 0.05$.

Result The participants' mean age was 54.33 ± 11.34 years, with the duration of diabetes for 7.34 ± 6.80 years. The mean of BMI was 25.47 ± 4.10 kg/m^2, most patients were overweight and obese. The mean of HbA1c was 8.14 ± 1.59% and only 24% participants with good glycemic control. The mean of NLR was 2.69 ± 1.23, with a range of 0.95–6.24, while 84.7% of participants with a high count of NLR (NLR > 1.65). The mean of baPWV was 15.19 ± 2.72 m/s with a range of 10.20–23.30 m/s, and 75.0% of them saw an increased arterial stiffness (baPWV > 13.5 m/s). Association analysis between NLR count and arterial stiffness shows significant results ($r = 0.235$; $p < 0.047$).

Conclusions There is a significant association between NLR with arterial stiffness and the higher NLR count, the more stiffening of the arteries experienced by the participants.

Keywords Arterial stiffness · Brachial-ankle pulse wave velocity · Neutrophil–lymphocyte ratio · Type-2 diabetes mellitus

Introduction

Type-2 diabetes mellitus (T2DM) is the leading health issue with a growing prevalence around the world. Globally, the figures for diabetes cases on 20–79-year-old people in 2019 were estimated at 463 million cases or 9.3% of the world's population and will increase to 578 million in 2030 (10.2%). Indonesia belongs to the top ten countries with the most estimated diabetes cases, collecting around 10.7 million cases in 2019 and is bound to leap to 13.7 million in 2030, then 16.6 million in 2045 [1]. The prevalence of diabetes complications, as a multinational study indicated, recorded 27.2% of macrovascular complications and 53.5% of microvascular complications. In comparison, renal complications accounted for 27.9%, eye

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disease 26.3%, diabetic foot 5.4%, and neuropathy 38.4% [2].

Diabetic macroangiopathy, atherosclerosis due to diabetes can cause cerebrovascular diseases, ischemic heart diseases, peripheral arterial diseases, and other vascular diseases, which are the significant causes of death in diabetic patients and the reducer the quality of life [3]. The latest studies show that arterial inflammation plays a vital role in the pathogenesis of atherosclerosis. The high level of inflammatory markers such as C-reactive protein (CRP), interleukin-6 (IL-6), IL-18, and tumor necrosis factor-α (TNF-α) are connected to the morbidity and mortality of cardiovascular diseases. These inflammatory markers are related to asymptomatic atherosclerosis but are challenging to conduct in daily clinical practices. Therefore, simple and easy markers are needed. White blood cells (WBC) count is one of the inflammatory biomarkers in clinical practice. Nowaday, WBCs are useful predictors for certain diseases in addition to being an infection marker [4].

Neutrophil–lymphocyte ratio (NLR) is an independent prognostic factor of coronary heart disease and can predict mortality on cardiovascular diseases [5]. Differences are found between NLR counts on diabetes patients with and without complications. An increase in NLR counts is related to a microvascular complication on elderly diabetic patients [6]. NLR is associated with atherosclerosis, which is measured by brachial-ankle pulse wave velocity (baPWV) and coronary calcium score (CCS). Having a high rate of NLR is connected to arterial stiffness and CSS [4].

One of the clinical implication of stiffness in the artery is to predict the increasing risk of cardiovascular disease. Inflammation takes the primary role in stiffness in a large artery, which connects to atherosclerosis, arteriosclerosis, and endothelial dysfunction. The last mentioned can be measured with non-invasive measurement of pulse wave velocity (PWV), which serves as the parameter for arterial stiffness [7]. PWV is a predictor of cardiovascular cases in the general population with hypertension, diabetes mellitus, and end-stage renal disease. Carotid-femoral PWV test is known to be a conventional method. The baPWV tool is currently a more accessible device to use compared to other non-invasive automatic devices. This method can be used to measure PWV in studies with a large volume of samples. BaPWV is related to carotid artery intima-media thickness, which marks the severity of atherosclerosis [8]. The Rotterdam study reported that arterial stiffness is closely related to atherosclerosis in various vascular branches [9]. Pulse wave velocity is the measure of the speed of the pulse wave between two distant places in the arterial system. Since the PWV correlates with distensibility and arterial stiffness, the hardening of the artery walls will cause a high rate of PWV [10]. The latter is then related to cardiovascular diseases and can be considered the marker connecting hyperglycemia and vascular complications [11].

NLR and baPWV increase in T2DM. Early detection of abnormal NLR counts could help find subclinical atherosclerosis in T2DM patients [12]. NLR is a readily available, easy-to-use, and reproducible inflammatory marker. It also can add cardiovascular risk stratification alongside the current risk score [5]. Strong evidence shows that inflammation plays a considerable role in arterial stiffness, and an inflammatory marker can be used as an additional examination to assess cardiovascular risk in clinical practice. The combination of measurement of arterial stiffness and inflammatory marker can complement the non-invasive cardiovascular risk assessment, thus being able to detect high-risk patients and give them preventive care or more regular medical check [13].

The exact mechanism of association between the high NLR and diabetes complications is related to inflammation [14–16]. In Indonesian clinical practice, inflammatory markers such as fibrinogen, CRP, IL-18, and TNF-α were limited. Therefore, more simple and easy markers were needed. This research was conducted to study NLR as a marker of systemic inflammation and its correlation to arterial stiffness, which is a marker of subclinical atherosclerosis in T2DM.

Methods

Participant

Those who participated in this study were T2DM patients who met the inclusion and exclusion criteria. Inclusion criteria include those who had been diagnosed with T2DM and were over 18 years of age. Exclusion criteria include signs of infection (swelling, pain, redness at the site of infection), complaints of fever, abnormal markers of complete blood count tests (WBC count > 12,000/mm^3) or increased erythrocyte sedimentation rate (ESR), active smoker, diagnosed with cancer/malignancy, diagnosed with chronic kidney disease (CKD) stage 5 with hemodialysis, and CKD with kidney transplantation. Participants who are willing to be included in this study were obligated to fill in the consent form.

Design

This study is a cross-sectional design conducted in the Endocrinology and Diabetes outpatient clinic at the Dr. Soetomo General Academic Hospital in Surabaya, Indonesia, from July to December 2019. The total number of study participants was 72 patients who met the inclusion and exclusion criteria. The sampling technique in this study is purposive sampling, based on the sample size formula for the correlation

coefficient of one sample [17], in which the minimum sampling was $n=69$ (r = 0.38) as the equation below [12].

$$n = \left[\frac{Z\alpha+Z\beta}{0.5ln\frac{1+r}{1-r}}\right]^2 + 3$$

$$n = \left[\frac{1.95+1.282}{0.5ln\frac{1+0.38}{1-0.38}}\right]^2 + 3$$

$$n = 69$$

This research was part of the Diabetic Ocular Renal Surabaya Study (DiORS Study). Participants were measured for their characteristics, NLR count, and arterial stiffness. Participants' characteristics include age, sex, body mass index (BMI), duration of diabetes, HbA1c levels, blood pressure, lipid profiles (total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol and triglycerides), glomerular filtration rate estimation (eGFR) (which measured using the MDRD equation formula), and hematological parameters (hemoglobin, WBC, and platelets count). This study applied a procedure in which patients' data was collected through anamnesis and physical examination according to the required characteristic data. Their venous blood was collected around ± 3 mL, then stored in the EDTA tube. The blood was taken to Dr Soetomo General Academic Hospital Laboratory in Surabaya, Indonesia, to be thoroughly tested using the flow cytometry method with Sysmex XN 1000 (Sysmex Corporation, Kobe, Japan). In a Hematology Analyzer Sysmex XN-1000, there are two kinds of reagent for carrying out the quality control, being XN Check and XN Check BF. Besides doing quality control, calibration using XN CAL dan XN CAL PF of the instrument has been done periodically. Arterial stiffness was examined with baPWV by using VeraSera VS-1000 (Fukuda Denshi, Tokyo, Japan).

NLR is the result of neutrophil count divided by lymphocyte count. Neutrophils are the most numerous type of leukocyte cells, which account for about 50–70% among other leukocyte cells. Absolute neutrophil count (ANC) can be calculated from the type count results by adding up the percentage of segments and stems, then multiplying it with the total leukocyte number. Lymphocytes are the second most leukocyte type after neutrophils (20–40% of total leukocytes). Lymphocyte's rate is calculated from multiplying lymphocyte percentage with the total number of leukocytes. NLR is normal if < 1.65 [18].

In this study, arterial stiffness is obtained when the pulse wave delivery is faster than normal, indicating vascular stiffness. Arterial condition is normal if PWV < 13.5 m/s [9].

Statistical analysis

Results of measurement were presented in the distribution of frequency and average value based on the variable. Statistical analysis was carried out using the IBM SPSS Statistics software version 23.0 (IBM Corp., Armonk, NY, USA). The data of measurement results were tested normality using Kolmogorov–Smirnov test, in which the data distribution was not normal. The statistical test used to compare the NLR and baPWV values was the Mann–Whitney test (nonparametric). Meanwhile, the statistical test used for the association between neutrophil–lymphocyte ratio on arterial stiffness is the rank Spearman correlation test (nonparametric). The results of the statistical examination are significant if $p < 0.05$.

Result

Participant characteristics

Characteristics of the participants based on age were 54.33 ± 11.34 (18–76) years old. The mean of BMI was 25.47 ± 4.10 (15.6–36.6) kg/m^2. Based on the Asian BMI category, the results showed a normal BMI (18.5–22.9 kg/m^2) in 18 participants (25.0%), overweight (23.0–24.9 kg/m^2) in 20 participants (27.8%), obesity I (25.0–29.9 kg/m^2) in 23 participants (31.9%), and obesity II (≥ 30.0 kg/m^2) in 11 participants (15.3%; Tables 1 and 2).

Neutrophil–lymphocyte ratio

The mean of NLR participants was 2.69 ± 1.23 (0.95–6.24). Most of them (84.7%) or 61 participants had high NLR count (> 1.65), and the other 11 participants (15.3%) in the normal category (≤ 1.65). Analysis of NLR by sex, HbA1c levels, and systolic and diastolic blood pressure factor resulted in a mean NLR count for male and female which were 2.73 ± 1.03 (1.21–5.62) and 2.66 ± 1.36 (0.95–6.24)

Table 1 Distribution of participants' characteristics frequency

Characteristics ($n=72$)	n (%)
Sex, n (%)	
Male	29 (40.3)
Female	43 (59.7)
Body mass index, n (%)	
Normal	18 (25.0)
Overweight	20 (27.8)
Obesity I	23 (31.9)
Obesity II	11 (15.3)
T2DM, n (%)	
Controlled	17 (24.0)
Uncontrolled	55 (76.0)
Hypertension, n (%)	
Yes	30 (41.7)
No	42 (58.3)

Abbreviations: *T2DM* type-2 diabetes mellitus

Table 2 Average of participants' characteristics

Characteristics ($n=72$)	Mean ± SD
Age, years	54.33 ± 11.34
Body mass index, kg/m^2	25.47 ± 4.10
T2DM	
Duration, years	7.34 ± 6.80
HbA1c, %	8.14 ± 1.59
Hypertension	
Systolic, mmHg	139.29 ± 20.30
Diastolic, mmHg	85.18 ± 14.50
Lipid Profile	
Total cholesterol, mg/dL (normal < 200 mg/dL)	206.86 ± 53.30
LDL, mg/dL (normal < 100 mg/dL)	128.44 ± 44.87
HDL, mg/dL (normal ≥ 40 mg/dL)	54.65 ± 20.75
Triglyceride, mg/dL (normal < 150 mg/dL)	157.36 ± 101.85
eGFR, mL/min/1.73 m^2 (normal ≥ 90 mL/min/1.73 m^2)	69.90 ± 34.65
Hematology	
Hemoglobin, g/dL (normal range 11.5–15 g/dL)	12.86 ± 1.75
Platelets, × 10^9/L (normal range 125–350)	302,277.78 ± 111,421.07
WBC, × 10^9/L (normal range 3.5–9.8)	8.16 ± 1.64

Abbreviations: *T2DM* type-2 diabetes mellitus, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *eGFR* estimated glomerular filtration rate, *WBC* white blood cell

respectively ($p=0.358$). The mean NLR count based on HbA1c value for patients with controlled glycemic (HbA1c < 7%) and uncontrolled glycemic (HbA1c ≥ 7%) was 2.62 ± 0.99 (1.11–5.13) and 2.71 ± 1.30 (0.95–6.24) respectively ($p=0.816$). In accordance with the systolic blood pressure (SBP) level, the participants' mean NLR count in normotensive (SBP < 140 mmHg) and hypertensive (SBP ≥ 140 mmHg) category was 2.48 ± 1.07 (0.95–6.15) and 2.94 ± 1.36 (1.00–6.24) respectively ($p=0.106$). Meanwhile, based on diastolic blood pressure (DBP) level, the participants' mean NLR count in normotensive (DBP < 90 mmHg) and hypertensive (DBP ≥ 90 mmHg) category was 2.64 ± 1.19 (0.95–6.24) and 2.79 ± 1.32 (1.00–6.24) respectively ($p=0.603$; Table 3).

Table 3 Neutrophil–lymphocyte ratio and brachial-ankle pulse wave velocity values

Characteristics ($n=72$)	NLR		baPWV	
	Mean ± SD	*p*	Mean ± SD	*p*
Sex				
Male	2.73 ± 1.03	0.358	15.51 ± 2.96	0.650
Female	2.66 ± 1.36		14.97 ± 2.57	
HbA1c				
Controlled	2.62 ± 0.99	0.819	14.62 ± 1.28	0.181
Uncontrolled	2.71 ± 1.30		15.35 ± 3.03	
Systolic hypertension				
Yes	2.48 ± 1.07	0.106	14.21 ± 2.41	0.000**
No	2.94 ± 1.36		16.35 ± 2.65	
Diastolic hypertension				
Yes	2.64 ± 1.19	0.603	14.50 ± 2.43	0.003*
No	2.79 ± 1.32		16.48 ± 2.83	

Statistical analysis using Mann–Whitney test *significant $p<0.05$; **significant $p<0.001$

Abbreviations: *NLR* neutrophil–lymphocyte ratio, *baPWV* brachial-ankle pulse wave velocity

Arterial stiffness measured with baPWV

The mean values of the participants' baPWV were 15.19 ± 2.72 m/s (10.20–23.30 m/s). Most of them, or 54 participants (75.0%), saw an increase in their baPWV level, which is a marker of arterial stiffness or subclinical atherosclerosis, while the remaining 18 participants (25.0%) showed normal baPWV. According to sex, the mean baPWV value of male and female participants were 15.51 ± 2.96 m/s (11.05–22.85 m/s) and 14.97 ± 2.57 m/s (10.20–23.30 m/s) respectively ($p=0.650$). Based on HbA1c level, it was found that the mean baPWV values of the participants with controlled glycemic and uncontrolled glycemic were 14.66 ± 1.28 m/s (11.60–17.20 m/s) and 15.35 ± 3.03 m/s (10.20–23.30 m/s) respectively ($p=0.362$). In accordance with the SBP, the participants' mean baPWV values in normotensive and hypertensive category were 14.21 ± 2.41 m/s (10.20–22.10 m/s) and 16.35 ± 2.65 m/s (12.00–23.30 m/s) respectively ($p<0.001$). Meanwhile, based on DBP level, the participants' mean baPWV values in normotensive and hypertensive category were 14.50 ± 2.43 m/s (10.20–22.50 m/s) and 16.48 ± 2.83 m/s (10.60–23.30 m/s) respectively ($p=0.003$; Table 3).

Association between neutrophil–lymphocyte ratio and arterial stiffness

Analysis result of the association between participants' NLR count and baPWV level showed $p = 0.047$ with $r = 0.235$. The result showed that there was a significant association between the participants' NLR count and baPWV value. The higher NLR count, the more arterial stiffness were experienced by the participants (Fig. 1).

Discussion

NLR is a biomarker of the inflammatory process involved in atherosclerosis that is effective, simple, and inexpensive to use in diagnosis and as a prognosis of coronary artery disease (CAD) [19]. In this research, it was found that the mean NLR of T2DM patients is 2.69. A study on healthy participants shows a lower mean of NLR at 2.1 [4]. Meanwhile, a study of acute coronary syndrome patients of low baPWV group shows NLR rate of 3.1, lower than that of high baPWV group with a 4.0 rate [20].

A study in the USA, comparing mean NLR in different races, indicated that all races, except non-Hispanic black patients, have mean NLR more than 2 [21]. The Asian population shows lower results of the normal NLR rate compared to those in the western country. The normal value of NLR in the Indonesian population is not available. The normal cutoff point of NLR in this study was referred from a study from South Korea, which has similar races with Indonesia. A study involving 12,160 healthy subjects in South Korea resulted in an average NLR rate of 1.65 (0.107–3.193) [18].

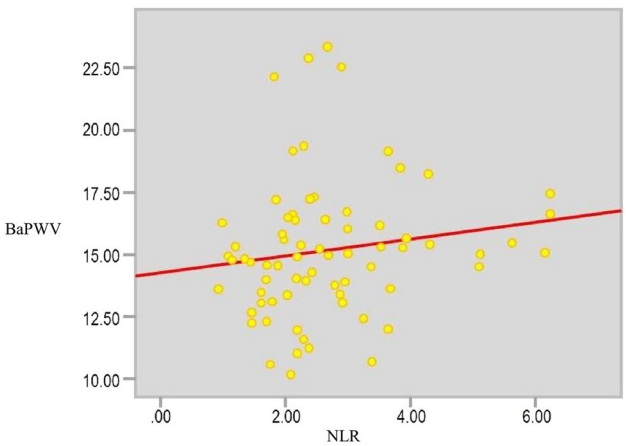

Fig. 1 Our study displays the association between NLR and baPVW in 72 participants. Spearman correlation shows positive significant correlation between NLR count and baPWV value ($p = 0.047$; $r = 0.235$). baPWV was a tool to detect arterial stiffness. This linear association indicates that increased NLR was associated with higher risk of arterial stiffness

A similar result was also shown in a study with adult, non-geriatric, healthy, and non-smoking populations, which showed a mean value of normal NLR of 1.65 (0.78–3.53) [22]. This study, with participants of T2DM patients, showed that most participants have high NLR count. Another study obtained an average NLR of 2.15 in which subjects with diabetes, cardiovascular diseases, and smoking habit have higher NLR than those without [21].

The results of this study do not show a significant difference in the NLR rate between male and female participants. Based on systolic blood pressure value, the average NLR of T2DM patients with normotension does not show a significant gap compared to the average of those with hypertension. Similarly, NLR numbers on controlled glycemic and uncontrolled glycemic show no noticeable differences. Former studies gained NLR count that had a significant correlation with glycemic control, in which the NLR count on HbA1c < 7% was at 2.0 ± 0.5, on HbA1c 7–9% at 2.7 ± 1.0, and on HbA1c > 9% at 4.3 ± 2.8. The elevated NLR number was related to poor glycemic control, which was marked by high HbA1c value on T2DM patients [23].

The Rotterdam study results showed that PWV numbers are normal if < 13.5 m/s [9]. While in this study, results show that the average baPWV value of T2DM patients is high. A study in Brazil recorded an average PWV value on DM patients that was higher than that of non-DM patients, namely 11.6 vs 9.3 m/s. The baPWV numbers of the healthy population in South Korea were found to be lower than those of the DM patients in this study, with 13.985 m/s [4].

This study results show that most participants saw an increased rate of baPWV. A study conducted by TODAY (The Treatment Options for Type 2 Diabetes in Adolescents and Youth) on 453 type-2 DM patients found arterial stiffness on more than 50% of its subjects [23]. In several studies, hyperglycemia and hyperinsulinemia contribute directly or indirectly to stiffness in the arteries, through the accumulation of advanced glycation end-product/AGE, endothelial dysfunction, and changes in the activity of vasoactive substances. Additionally, the increase in plasma glucose results in an increase in oxidative stress and activation of vascular inflammation, which directly causes arterial stiffness [24]. This study shows that HbA1c ≥ 7 group has a higher average rate of baPWV than the HbA1c < 7% group. However, this result is statistically not significant. In addition to glycemic control, other factors that play a role in arterial stiffness are age, race-ethnicity, gender, hypertension, dyslipidemia, and BMI [25]. Of all the factors above, age and hypertension are the most relevant factors [26]. Studies on type 1 diabetes mellitus indicated that PWV is significantly related to age, duration of diabetes, SBP, DBP, and eGFR, but are not related to total cholesterol and BMI [27].

In this study, it is found that baPWV in men is higher than in women, which statistically is not significant. Systolic and

diastolic blood pressure parameters found that the baPWV value is higher in the hypertension group compared to normotension, which is statistically significant. PWV can predict changes in systolic blood pressure and the occurrence of hypertension in the future [28].

NLR is an inflammatory marker that is easy to use and is also used as an indicator of risk for cardiovascular disease. BaPWV is an indicator of early atherosclerosis. Atherosclerosis is a disease triggered by chronic inflammation, which plays a role in its formation. In this study, the association between NLR values and arterial stiffness was measured by baPWV, which in line with other studies where there is an association between NLR values and arterial stiffness measured by baPW ($r=0.403$; $p=0.005$). This study, however, was conducted in a population of CAD patients [20]. Another study in CKD patients with peritoneal dialysis found high NLR values in the high baPWV group. In multiple linear regression analysis, NLR is found to be an independent factor in the increase of baPWV [29].

NLR is a predominant factor in increasing baPWV, which is part of arterial stiffness. Some studies suggest that vascular dysfunction, caused by inflammation, is a pathomechanism of arterial stiffness. Neutrophils attach to vascular endothelium that triggers microvascular and inflammatory dysfunction, vascular endothelial dysfunction, and increased expression of proinflammatory cytokines. These events lead to increased vascular inflammation and proliferation of smooth muscle, which causes vascular stiffness [12]. NLR and baPWV both increase in T2DM patients. There is a significant association between NLR and baPWV in patients with T2DM and diabetic retinopathy patients. In multiple linear regression analysis, NLR is found to be an independent and significant determinant of the increase in baPWV [30].

Advanced glycation end products (AGE) is produced from enzymatic processes of protein glycation, forming irreversible cross-links in stable tissue proteins such as collagen. When cross-links occur, it produces collagen that is rigid and inhibits replacement. AGE also influences endothelial function through cooling nitric oxide and increases reactive organ species (ROS) generation. The current study shows that AGE stimulates stress signals and inflammatory responses such as nuclear factor-ƙβ (NF-Ƙβ), ROS synthesis, cytokines, growth factors, and intercellular adhesion molecule (ICAM). These responses will result in arterial stiffness through matrix metalloproteinases (MMP) activity, endothelial dysfunction, increased smooth muscle tone, disrupting response endothelium against injury, influencing angiogenesis, and encouraging the process of atherosclerosis [31].

The limitations of our study include the limited number of samples and the short follow-up time of the participants; our findings are even better when such comparators (healthy patients or control group) are available and need to include its clinical significance. Our recommendation for further studies is to conduct over a longer period of time in order to acquire larger sample size in order to achieve more accurate correlation.

Conclusion

T2DM enhances the risk of atherosclerosis and cardiovascular diseases, which is the primary cause of death. NLR is an inflammatory marker that is readily available, easy-to-use, and reproducible. BaPWV is an indicator of changes in early atherosclerosis. Early detection of abnormal levels of NLR can help look for subclinical atherosclerosis in T2DM patients. These patient's NLR were mostly in the high category. There was no significant association between NLR with sex, HbA1c, systolic, and diastolic blood pressure. Besides, the measurement of arterial stiffness with baPWV were mostly found in the abnormal category. Arterial stiffness has a significant association with systolic and diastolic blood pressure. In contrast, gender and HbA1c show no significant association. There was a significant association between NLR and arterial stiffness, and the higher the NLR value, the more arterial stiffness experienced by participants.

Acknowledgments We would like to express our gratitude to Prof. Soetojo as a Dean of Universitas Airlangga, and Joni Wahyuhadi, PhD, as their permission has allowed this research to be conducted in Dr Soetomo General Academic Hospital in Surabaya, Indonesia. We also want to thank Prof. Askandar Tjokroprawiro, PhD; Prof Ami Ashariati, PhD; UgrosenoYudhoBintoro, PhD; NoviraWidajanti MD; and Hermina Novida, MD, for their support and inputs for our study. We would also like to thank Fis Citra Ariyanto for helping us in editing and proof our manuscript.

Author contribution All authors contributed toward data analysis, drafted and revised the paper, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

Declarations

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the ethics committee of Dr Soetomo General Academic Hospital, Surabaya, Indonesia (1311/KEPK/V/2019).

Conflict of interest The authors declare no competing interests.

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