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Original Article

Association of Plasma Atherogenic Index (PAI) with arterial stiffness in normotensive versus hypertensive Patients

Qurat ul Ain, Muhammad Younas, Muhammad Qaisar Alam Khan, Ayesha Niaz*, Zujaja Hina Haroon, Muhammad Anwar

Department of Chemical Pathology, Armed Forces Institute of Pathology/National University of Medical Sciences (NUMS), Rawalpindi Pakistan,
*Department of Radiology, Armed Forces Institute of Cardiology/National University of Medical Sciences (NUMS), Rawalpindi Pakistan

ABSTRACT

Objective: To find Association of Plasma Atherogenic Index with Arterial stiffness in normotensive and hypertensive patients.
Study Design: Diagnostic Accuracy Study.
Place and Duration of Study: Armed Forces Institute of Cardiology (AFIC) and Department of Chemical Pathology, Armed Forces Institute of Pathology (AFIP), Rawalpindi Pakistan, from Oct 2022 to May 2023.
Methodology: Hypertensive and normotensive patients with age group of 30-50 years were included in this study. Semi-structured Questionnaire was structured to collect the information regarding demographics, any comorbidity and medication history.
Results: Total 140 subjects were included in current research at AFIC. Altogether, 92(65.7%) male and 48(34.3%) female were participated. Plasma Atherogenic Index (PAI) is derived Index used for current study and it is divided into low risk (0.1), Intermediate risk (0.1-0.24) and high risk (>0.24). Out of all patients 13(9.3%) were in low risk, 38(27.1%) were in intermediate risk and 89(63.6%) were in high risk category. For association between PWV and PAI with blood pressure computed results showed significant association with *p*-value <0.001 for both PWV and PAI.
Conclusion: There is strong association between PAI and PWV with hypertension. A calculated index of lipid profile can be used as early predictor for arterial stiffness. PAI can be used as an alternative of PWV as an early screening marker for arterial stiffness in all cardiovascular risk factors.

Keywords: Atherogenic Index, Cardiovascular Disease, Pulse Wave Velocity.

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INTRODUCTION

Atherosclerosis can lead to various health complications, such as cardiovascular disease (CVD), Stroke, and Peripheral artery disease.[1] It is a prevalent condition worldwide and is a leading cause of death in many countries. According to the World Health Organization (WHO), cardiovascular diseases, which include atherosclerosis, are responsible for 31% of all global deaths.[2] Atherogenic dyslipidemia can lead to endothelial dysfunction and oxidative stress, representing possible mechanisms underlying the association between arterial stiffness and cardiovascular disease.[3] Low density lipoprotein (LDL-c) leads to cause intimal thickness by depositing in arterial wall and related to arterial stiffness. From decade it is considered that low density lipoprotein cholesterol (LDL-c) and high density lipoprotein cholesterol (HDL-c) related to cardiac complications.[4]

Atherogenic index of plasma (PAI) which is calculated measure of triglycerides (Tg) and HDL-c (calculated by log of Tg and HDL-c) which is considered as early predictor of arterial stiffness and CVD.[5] A high PAI level is associated with dyslipidemia which is considered as risk factors for atherosclerosis. Pulse wave velocity (PWV) is basically the measurement of pressure wave moving down from a vessel. Pwv is calculated by distance divided by transit time through Bram well hill equation.[6] Increase in PWV has positive correlation with arterial stiffness. PWV at 10 m/s is considered as appropriate and normal.[7]

This study was conducted because there is limited data available at national level and Echocardiography and Carotid Doppler ultrasound facilities are not easily available in peripheries or in every hospital and moreover specific skills & expertise are required to asses early changes through these studies, while PAI is relevant and calculated marker comparative easy to perform, feasible, accessible and cost effective as compared to Carotid Doppler. PWV is a measure of arterial stiffness and is a marker of cardiovascular disease risk.[8] Utilizing both

Correspondence: Dr Qurat ul Ain, Department of Chemical Pathology, Armed Forces Institute of Pathology, Rawalpindi Pakistan
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measurements together might provide more accurate information and identify individuals with a higher risk of developing cardiovascular disease much earlier.[9,10] The present study is aimed to explain the association between PAI and arterial stiffness in hypertensive patients compared to normotensive individuals and to asses and compare level of PAI in normotensive and hypertensive patients.

METHODOLOGY

Current study design was Cross sectional (Diagnostic accuracy) AFIP with collaboration AFIC. Study was conducted after obtaining approval from institutional board committee with IRB reference number 1294. Study conducted within six months duration; from October 2022 to May 2023.

Inclusion Criteria: Hypertensive patients with age group of 30-50 years of age group with diagnosed with hypertension reported in department of endocrinology in AFIP.

Exclusion Criteria: Patients with Endocrine disorders like Hypothyroidism, Nephrotic syndrome, patients with autoimmune disorders. Incomplete lipid profile, repeated hospitalization, infective endocarditis or any cardiac intervention or congenital heart disease and patients on lipid lowering medicines were excluded from study.

Sample size was calculated by keeping confidence level 95%, prevalence of hypertension (HTN) with arterial stiffness in 30-50 years of age group taken as 10.1% through which estimated sample size was 140 by open Epi calculator.[11] Sampling technique was Non Probability Consecutive sampling. Semi structured questionnaire was used for detailed history like any comorbidity and any medication history. Samples were taken after informed consent form study participants in yellow topped tube for lipid profile included TG, LDL-C, HDL, C and Total cholesterol while PWV calculated from Carotid and Femoral pulse wave velocity which is done through carotid Doppler of Toshiba on Aplio 500, linear array transducer with frequency 14L5 in AFIC Rawalpindi by radiologist. PAI is calculated measure of Log of TG and HDL-C analyzed through fully automated routine chemistry analyzer through photometry while serum fasting insulin was analyzed by fully automated immunoassay analyser based on electrochemi-lumiscence principle. Result validation and reliability was ensured through internal quality control for all parameters. Homeostatic model of insulin resistance (HOMA-IR) is calculated by analyzing glucose fasting and serum insulin fasting through formula Glucose fasting* serum insulin fasting/ 22.5.[12] The value of 2.5 is cutoff for HOMA I-R if there is insulin resistance it would be more than 2.5. As per WHO classification body mass index (BMI) is calculated with height in cm and weight in kg, it is normal if it is 18-25, if between 25-29 it is considered as overweight while more than 30 considered as Obese.[13] PAI is divided into low risk (0.1), intermediate risk (0.1-0.24) and high risk (>0.24).

Data was entered and analyzed by statistically package for the social sciences SPSS version 23 and zotero software used for referencing. Test of normality used for data distribution. Descriptive statistics was defined in the form of Mean±SD for quantitave (age, PAI, BP, lipid profile) variables and frequency and percentages for qualitative variables. For inferential statistics association was assessed by chi square. Independent Sample t-test computed to compare means between two groups of blood pressure (hypertensive and normotensive), to see sensitivity and specificity of PAI with PWV computed ROC curve *p*-value <0.001 considered as statistically significant.

RESULTS

A total 140 subjects were enrolled in current research at AFIC. Altogether, 92(65.7%) were male and 48(34.3%) female. Patients were grouped in 2 age categories 30-40 years of age and 41-50 years of age, and that becomes 47(33.5%) and 93(66.5%) respectively. Total of 102(73%) were hypertensive patients and 37(27%) were normotensive patients. BMI grouped in three main categories 18-25 with normal BMI were 48(34.3%), 25-29 over weight were 66(47.1%) and BMI >30 were 26(18.6%) considered as obese. Patients with normal pwv were 29(20.7%) while with pwv more than 10m/sec were 111(79.3%). Out of all patients 13(9.3%) were in low risk, 38(27.1%) were in intermediate risk and 89(63.6%) were in high risk category. Frequency and percentage of pwv and PAI in hypertension and normotensive patients, HOMA-IR, and in BMI shown in Figure-1. Mean±SD of all quantitave variables (age, Tg, HDL-C, BP, pwv, PAI) are shown in Table-I.

Current study findings that whose BMI with 18-25 showed pwv >10m/s in 29(21%), BMI >25-29 showed pwv>10m/s in 58(41.4%) and BMI >30 showed pwv >10m/s in 24(17.1%).

Mean difference of pwv and PAI among normo-tensive and hypertensive, HOMA-IR and BMI showed stastically significant difference (*p*-value= <0.001). Shown in Table-II.

Table-I: Descriptive Statistics of Study Variables with respect to Gender (n=140)

Variables	Male Mean±SD n=92(65.7%)	Female Mean±SD n=48(34.3%)
Age (Years)	41.99±5.3	39.2±4.62
Triglycerides (mmol/L)	3.42±1.13	3.52±1.45
High density cholesterol (HDLC) (mmol/L)	0.59±0.26	0.62±0.20
Plasma atherogenic index (PAI)	0.64±0.36	0.56±0.28
Pulse wave velocity (PWV)	18.6±12.46	20.7±12.40
Systolic Blood pressure (mmhg)	153±16.72	149±18.22
Diastolic Blood pressure (mmhg)	99.5±9.11	101±8.19

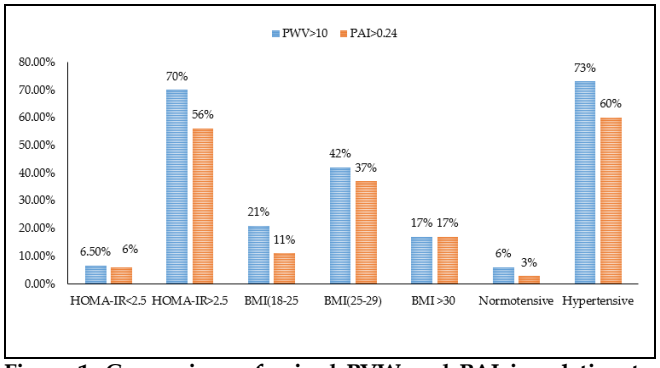

Figure-1: Comparison of raised PVW and PAI in relation to Hypertension, Normotensive patients, HOMA IR and Body Mass Index (n=140)

Table-II: Comparison of Plasma Atherogenic Index and Pulse Wave Velocity among Study Participants (n=140)

Variables		n	Mean±SD	*p*-value (<0.05)
Plasma Atherogenic Index	Hypertension	102	0.7165±0.29	<0.001
	Normotensive	38	0.3358±0.30	
Pulse Wave Velocity	Hypertension	102	22.4804±11.5	<0.001
	Normotensive	38	10.3514±10.15	
Plasma Atherogenic Index	HOMA-IR<2.5	30	0.40±0.35	<0.001
	HOMA-IR>2.5	110	0.66±0.32	
Pulse Wave Velocity	HOMA-IR<2.5	30	14.96±13.64	0.041
	HOMA-IR>2.5	110	20.52±12.05	
Plasma Atherogenic Index	BMI 18-25	48	0.58±0.38	0.678
	BMI 25-29	66	0.616±0.33	
	BMI>30	26	0.664±0.28	
Pulse Wave Velocity	BMI 18-25	48	18.1±13.21	0.670
	BMI 25-29	66	20.2±12.14	
	BMI>30	26	19.1±11.977	

**HOMA-IR= Homeostatic Model Assessment of Insulin Resistance, BMI= Body Mass Index*

To compare sensitivity and specificity of pwv and PAI with hypertension ROC applied taken as pulse wave velocity of carotid, femoral artery as gold standard found significant results shown as in Figure-2.

PAI and pwv increased with highest quartile thatswhy PAI can be considered as independent screening tool for arterial stiffness. PWV and PAI showed significant association with blood pressure with *p*-value <0.001 shown in Table-III.

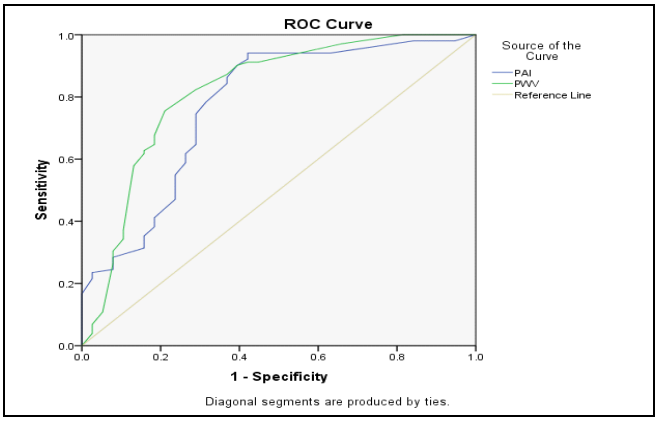

Figure-II: Comparison of PAI and PWV in Hypertension (n=140)

Table-III: Area Under Curve (AUC) ,Sensitivity and Specificity of PAI and PWV in Hypertension keeping gold standard PWV of carotid and femoral

	Area Under Curve	Sensitivity	Specificity	*p*-value
Plasma Atherogenic Index	0.772	97%	79%	<0.001
Pulse Wave Velocity	0.8181	98%	91%	<0.001

DISCUSSION

The aim of current study was to investigate the relationship between the plasma atherogenic index (PAI) and arterial stiffness in hypertensive patients. Arterial stiffness plays a significant role in the development of CVD, which is a major cause of morbidity and mortality worldwide.[14] Additionally, recent studies have reported that atherogenic dyslipidemia, as evidenced by an elevated plasma atherogenic index, is strongly associated with an increased risk of cardiovascular disease. In current study arterial stiffness is calculated from PWV by carotid and femoral velocity through Doppler which is correlated with Zhou *et al.*,[15] while current study contradict findings that brachial and femoral artery pwv calculated but recent study pulse wave velocity calculated of carotid and femoral which is considered as gold standard for arterial stiffness .In recent study PWV cutoff used for assessment of arterial stiffness is 10m/sec if it is more than that it is predictor of arterial stiffness these cutoff is used in another study by Abid *et al.*[16] PAI cutoff is segregated on the basis of cutoff in three categories in recent study which is low risk<0.1, intermediate risk 0.1-0.24 and high risk >0.24 which is same cutoff value used in the study

published in 2018 by Choudary *et al.*[17] In current study cardiovascular variables BMI, hypertension, and HOMA -IR observed for PAI and PWV and these variables also used for association of PAI and PWV for HOMA-IR, BMI and Hypertension by NAM *et al.,* 2022[18] but current study contradict this study because diabetes association was not observed. Current study showed that hypertensive patients had a higher plasma atherogenic index and increased arterial stiffness compared to normotensive individuals as correlated with the findings of Redic *et al.*[19] Furthermore, there was a significant association with *p*-value 0.00 for PAI and *p*-value 0.00 for PWV between hypertension and this finding correlate with the findings of study FAN *et al.*,[20] which also showed positive association of PAI and PWV with hypertension and other cardiovascular risk factors. These findings suggest that arterial stiffness and atherogenic dyslipidemia may be linked and play a crucial role in the pathogenesis of cardiovascular disease in hypertensive patients. As such, monitoring of arterial stiffness and plasma atherogenic index could be essential in identifying hypertensive patients at a higher risk of developing cardiovascular complications. The results of current study may provide new insights into the pathophysiology of cardiovascular disease and guide the development of new strategies to prevent and manage it in hypertensive patients. It is essential to note that our study has some limitations. First, it was conducted as a cross-sectional study design that cannot prove a causal relationship between PAI and arterial stiffness. Second, the sample size was relatively small, and increased data collection in future studies can help to confirm the veracity of our findings. Despite these limitations, this study provides new insights into the possible role of atherogenic dyslipidemia in the development of arterial stiffness in hypertensive patients. Physicians can use our findings to help identify patients at high risk of developing cardiovascular disease and provide intensive interventions to reduce the risk of complications. Future research with a larger sample size and aggressive follow-up can further clarify the potential relationship between plasma atherogenic index and arterial stiffness in hypertensive patients, ultimately contributing to improved patient care.

CONCLUSION

Current study concluded that there is strong association between PAI and PWV with hypertension thatswhy to monitor arterial stiffness PAI can be used as an alternative of PWV as an early predictor in all cardiovascular risk factors.

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Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

QA & MY: Data acquisition, data analysis, critical review, approval of the final version to be published.

QAK & AN: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

ZHH & MA: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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